# Effect of Feasibility and Religion on Health Utility Questionnaire Responses of Elderly Ophthalmic Patients: A Pilot Study

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**Objective**: To study the effect of religion on the imagination of death/shortening of life in time tradeoff questions and to explore the feasibility of open-question time tradeoff methods (TTO1), modified EQ-VT time tradeoff (TTO2), EQ-visual analog scale (VAS), EQ5D-5L, and HUI3 patient-reported outcomes in elderly ophthalmic eye patients in Thailand.

Materials and Methods: Face-to-face interview, cross-sectional study.

**Results**: Among 40 ophthalmic patients, there were 16 diabetic retinopathy cases, 15 cataract cases, and 8 wet-age related macular degeneration cases with a mean age of 63, 58, and 72 years, respectively. The mean utility scores obtained from the TTO1, TTO2, EQ-5D-5L, and HUI3 were 0.5, 0.49, 0.80, and 0.61, respectively. The HUI3 required the longest mean interview time at 5.5 minutes, whereas the NEI-VFQ-25 required the shortest mean interview time at 1.08 minutes. Of the patients, 87.5%, 10%, and 2.5% reported a mild, moderate, and marked effect of their religion on their decisions made during TTO answering. The utility scores from the EQ-VAS, EQ-5D-5L, and HUI3 showed a significant positive correlation with the NEI-VFQ-25 quality of life score. The utility scores from the EQ-5D-5L and HUI3 were significantly associated with the severity of visual impairment. Four participants were not willing to trade in TTO1. TTO2 methods were less complicated to answer as compared with TTO1.

**Conclusion**: The HUI3 utility score was correlated with change in visual impairment and vision-specific quality of life, and its use is recommended in the utility assessment in eye disease. TTO1 is more complicated compared with TTO2. In clinical ophthalmic practice, the use of indirect utility assessment methods is preferred over direct methods.

Keywords: Tradeoff method; Religion; Quality of life; TTO

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Visual impairment (VI) and blindness are global concerns that affect 293 million and 43 million people worldwide, respectively. The prevalence of these two conditions has been doubling in the past 10 years<sup>(1)</sup>. 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 based on Snellen visual

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Pongsachareonnont PF, Sakthong P, Kulvichit K. Effect of Feasibility and Religion on Health Utility Questionnaire Responses of Elderly Ophthalmic Patients: A Pilot Study. J Med Assoc Thai 2022;105:457-65. **DOI:** 10.35755/jmedassocthai.2022.05.13307 acuity (VA) worse than 6/40 to 6/70, moderate based on VA worse than 20/70 to 20/200, severe based on VA worse than 20/200 to 20/400, and blindness based on VA worse than  $20/400^{(2)}$ . Among retina diseases, age-related macular degeneration (AMD) and diabetic retinopathy (DR) are top major causes of VI<sup>(3)</sup>.

Quality-adjusted life-years (QALYs), which represent a combination of life duration and quality, are used in economic evaluations. The quality of life (QoL) weighted in QALYs is described as a health state utility value ranging from 0 (death) to 1 (full health)<sup>(4)</sup>. The closer the health utility (HU) score is to 1.0, the better the QoL, whereas a lower HU reflects poor QoL.

The utilities can be measured by various methods. Direct evaluations such as time tradeoff (TTO), standard gamble (SG), and visual analog scale (VAS) have been used. The use of the TTO concept has been proposed for ophthalmic utility assessment as compared with standard gamble<sup>(5-8)</sup>.

TTO tasks have a varied methodology but the same underlying concept<sup>(9)</sup>. With this variability of technique, a questionnaire-based or patient-reported outcome (PRO) utility measurement can be used as an indirect method for utility measurement. PROs have been widely used in ophthalmic clinical studies such as in cataract, diabetic eye disease, AMD, and glaucoma<sup>(10,11)</sup>. 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<sup>(10)</sup>. The EQ-5D-5L, developed by the EuroQoL group<sup>(12)</sup>, is a generic questionnaire widely used to evaluate general health status and has been translated into more than 100 official languages. It is composed of five domains, mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The questionnaire has been validated in the Thai population<sup>(13,14)</sup>. The Health Utilities Index (HUI; HUInc, Hamilton, ON, Canada) was developed 40 years ago. The original HUI version (HUI2) was composed of six domains and has been used to assess the outcome of low-birthweight infants. The HUI3 questionnaire subsequently expanded the sensation domain. The HUI3 consists of eight domains, vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain. The main problem of general PROs is the lack of sensitivity of the impact on eye treatment. Instruments with a vision-related preference have been shown to be more sensitive to visual function(10). The NEI-VFQ-25 is a vision-related QoL questionnaire that has been widely used in retinal disease, glaucoma, cataract, and others(15-18).

Health state preferences are a combination of results from demographic factors such as gender, age, personality, religion, occupation, and individual illness<sup>(19)</sup>. Religions are known to affect the perception of death<sup>(20-22)</sup>. Spiritual well-being and religion can reduce the anxiety related to death and mediate the death perception<sup>(22)</sup>. 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<sup>(23)</sup>. No previous studies have demonstrated the association between religious belief and death-related health preference questions.

In the current study, the authors sought to evaluate the impact of religion on individuals' answers to TTO questions as well as the feasibility of using open-ended variation in TTO questions<sup>(24)</sup>, a modified TTO from the EuroQoL protocol, and generic preference-based measures of the EQ-5D-5L and HUI3 questionnaires among elderly ophthalmic patients in Thailand.

# **Materials and Methods**

The present study was a cross-sectional study that interviewed patients from an ophthalmic outpatient clinic at King Chulalongkorn Memorial Hospital between October and December 2019. The authors recruited consecutive patients attending the retina clinic and general eye clinic. Before the interview process, all patients were informed about the study and provided consents to be interviewed and for their clinical data record to be used. The present study was approved by the local Institutional Review Board Committee (IRB No. 340/62) and registered in the Thai Clinical Trial Registry before began data collection (TCTR20190831002). The inclusion criteria were patients who diagnosed of cataract, wetage-related macular degeneration (WAMD) or DR. Patients who had mental impairment or non-native Thai speaker were excluded from the present study.

### **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 one year conducted the face-to-face interviews. All interviews consisted of the same sequences of questionnaires. The licensed questionnaires were authorized before data collection started. After completion of the QoL questionnaires, respondents and interviewers were asked their opinions about the feasibility of the interview and their responses recorded at the end of the interview.

TTO1 is a conventional TTO, as described by Sharma et al<sup>(25)</sup>. It was calculated as utility value = (Number of years expected life – Number of years tradeoff) / Number of years expected life<sup>(25)</sup>. The TTO1 question started with, "What is your expected age that you will die?" followed by the tradeoff question, "If you can trade your life to gain full health state for your vision, how many years are you willing to shorten your life to trade this condition?". The TTO2 questionnaire was a composite TTO modified from the EQ-VT protocol for TTO evaluation in the EuroQoL protocol<sup>(26)</sup>. The visual aid TTO board was used instead of a digital presentation. The full health state was defined as perfect vision in each eye. The Thai version of the EQ-VT questionnaire was used in assessing the EQ-5D-5L properties in the Thai population<sup>(14)</sup>. The TTO2 question started with an explanation of the interview process and introduced the visual aid for comparison, then started with one sample question, followed by a series of questions with alternative choices to determine how much time the patient was willing to tradeoff for their healthy vision. Patients were asked to choose between x years with healthy eyes then followed by death, and 10 years in their current eye health state followed by death. The x started with 0 and titrated upward every 1 year until an indifference or reversal occurred.

A hybrid model value set was used to calculate the HU<sup>(27)</sup>. The EQ-5D-5L interview started with the EQ-VAS and was followed by five domain questions, as in the EuroQoL protocol. The authors used the translated and validated Thai version of the HUI3 in the present study<sup>(28)</sup>. The interview and HU calculation were followed by instruction from HUI® (HUInc)<sup>(29,30)</sup>. The utility scores of the TTO1, TTO2, EQ-VAS, EQ-5D-5L, and HUI3 were reported. The Thai version of the NEI-VFQ25<sup>(11,31)</sup>, which comprises one general health item and 24 visual-related items, was used to evaluate the visual-related QoL. The QoL from the NEI-VFQ-25 was scored from 0 to 100. 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 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% to 25% of the questions, "1" means that the respondent understood 26% to 50% of the questions, "2" means the respondent understood 51% to 75% of the questions, "3" means the respondent understood 76% to 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 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 TTO1, TTO2, 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. Snellen VA and clinical examination data were collected from the patient's chart of that visit.

#### 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.

### Statistical analysis

A prespecified sample size of 40 subjects was designated for the present 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. The authors used Pearson correlation or Spearman correlation coefficients to explore the correlation between the HU and NEI-VFQ-25 QoL score. Analyses of covariance (ANOVA) were used to compare the mean HU among types of eye disease from all questionnaire instruments. Multivariable linear regression analysis was used to explore the association between VI and HU. Stata/IC 15.1 (StataCorp LLC, College Station, TX, USA) was used for statistical analysis. A p-value of less than 0.05 indicated statistical significance. Complete case analyses were used.

# Results

Forty respondents participated in the present survey but there was one missing demographic data. Table 1 shows the respondents' demographics. All respondents were Buddhist, except for one 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 recruited.

Table 2 shows the mean utility score of the TTO1 and TTO2, EQ-5D-5L, and HUI3 instruments. There was no statistically significant difference in all HU score among DR, WAMD, and Cataract. Four of 40 respondents denied trading their life in TTO1 because of the following reasons, satisfaction with vision status and personal beliefs. Off the four non-traders for TTO1, two respondents had a visual acuity in a best-seeing eye (VABSE) of 20/20 to 20/40, with one

Table 1. Demographics of 39 respondents among diabetic retinopathy (DR), cataract and wet-age-related macular degeneration
(WAMD) patients

Factors	DR (n=16)	Cataract (n=15)	WAMD (n=8)	p-value
Age (year); mean [SD]	63.19 [9.63]	58.47 [7.70]	72.00 [8.40]	>0.001
Sex: male; n (%)	6 (38)	10 (67)	2 (25)	0.12
Location; n (%)				0.65
Bangkok	9 (60)	8 (53)	3 (38)	
Others	6 (40)	7 (47)	5 (62)	
Employment status; n (%)				0.88
Unemployed or housewife	5 (31)	4 (27)	2 (25)	
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 (%)				0.22
Single	3 (18.8)	2 (13)	2 (25)	
Married	7 (43.8)	12 (80)	5 (62.5)	
Others/widow/divorce	6 (37.4)	1 (7)	1 (12.5)	
Education; n (%)				0.19
Lower than grade 3 or none	4 (25)	3 (20)	1 (12.5)	
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 (%)				0.64
No direct income	5 (31.3)	3 (20)	1 (12.5)	
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)	
Freatment coverage; n (%)				0.55
No coverage/others	5 (31.3)	2 (13.3)	2 (25)	
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 (%)				0.83
None	4 (25)	5 (33)	2 (25)	
Family	11 (69)	10 (67)	5 (62.5)	
Others	1 (6)	0 (0)	1 (12.5)	
History of alcohol drinking; n (%)	(-)	<->	,	0.65
No	9 (56)	6 (40)	4 (50)	
Yes	7 (44)	9 (60)	4 (50)	
History of smoking; n (%)		<u><u> </u></u>	<u> </u>	1.00
No	12 (75)	11 (73)	6 (75)	
Yes	4 (25)	4 (27)	2 (25)	
Visual acuity in BSE**; n (%)	. (23)	. (27)	2 (20)	0.99
20/20 to 20/40	6 (38)	7 (50)	3 (37.5)	0.77
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 (%)	1 (0)	± (7)	1 (14.3)	0.74
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	2 (12.5) 9 (56.2)	4 (29)	3 (37.5)	
Less than 20/200	9 (56.2) 4 (25)	4 (29) 5 (36)	2 (25)	

SD=standard deviation; BSE=better-seeing eye; WSE=worse-seeing eye

Categorical p-value calculated by Fisher's exact test

Table 2. Utility score and quality of life score

Instruments	n	Mean	SD	Min	Max			
TTO1	36	0.50	0.50	-1.50	0.94			
TTO2	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								

SD=standard deviation; Min=minimum; Max=maximum

68 years old subject diagnosed as DR and one 73 years old with WAMD, one 65 years old respondent had VA 20/50 to 20/70 with a diagnosis of DR, and finally, one 57 years old respondent had VA 20/80 to 20/200 with a DR diagnosis. All respondents were Buddhist with a high school education level or lower. Among these non-traders for TTO1, three respondents had difficulty understanding the life-trading concept, and they all chose to answer the TTO2 with the reason of easier to understand in concept. Meanwhile, one non-trader in the TTO1 understood the concept of trading life but had an idea of acceptance in life and fatalism that caused a denial to trade for TTO1. All TTO1 traders were able to respond to the TTO2 instruments. Two patients with negative TTO1 were willing to trade more years than their life span with one patient who was diagnosed with cataract with a VABSE in the range of 20/80 to 20/200, and the other who was diagnosed with WAMD with a VABSE less than 20/200. The mean interview duration of the TTO1, TTO2, EQ5D-5L, HUI3, and VFQ-25 were 2.89 minutes (SD 1.68, min-max: 0.3 to 7), 3.92 minutes (SD 2.43, min-max: 1 to 15.16), 3.07 minutes (SD 1.85, min-max: 1 to 12), 5.50 minutes (SD 2.10, min-max: 2 to 13), and 8.20 minutes (SD 2.87, min-max: 3 to 17), respectively. The answers of one respondent received a rating of low confidence accuracy from the interviewer on the TTO1 and TTO2. Two respondents on the TTO1 questionnaire and one respondent on the TTO2 questionnaire had



Figure 1. Correlation between the utility score and the NEI-VFQ-25 score.

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 non-understanding 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.

Figure 1 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 were statistically significant correlated with the VFQ-25 score. For the association of HU and VI status, a univariable analysis is shown in Appendix 1. 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 3.

#### Discussion

The TTO framework concept is related to a shortened life expectancy, which is shown to have

Table 3. Association between health utility (HU) and visual impairment status (VI)

VI	HUI3			EQ-5D-5L			EQ-VAS		TT01			TT02			
	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	Reference				Reference			Reference			Reference		Reference		
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

CI=confidence interval

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

an impact on religious beliefs. These beliefs, in turn, can affect the perception of life and is correlated with utility value in Christian<sup>(32)</sup>, Buddhist<sup>(33)</sup>, and Islamic<sup>(34)</sup>, respondents. Studies in Europe also showed that religious beliefs influence euthanasia and are prone to assigning a value worse than death for HU measurement by TTO<sup>(35)</sup>. 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 the study conducted in an Islamic population, Elbarazi et al reported that 81% of health states in TTO were influenced by respondents' religious beliefs and spirituality<sup>(34)</sup>. However, surveys have shown nonsignificant effects related to the decision of utility measurement<sup>(36)</sup>.

Value-based medicine reflects the QoL perceived by an individual. This PRO is used in an outcome parameter of an evidence-based trial and decision making in an economic evaluation. The standard methods in the direct utility analysis used commonly were the TTO technique and standard gamble technique; the former has been used more frequently because it is easier to understand by older individuals and can be modified to evaluate ocular utility values<sup>(7,37,38)</sup>. In general medicine, a perfect health state in TTO utility analysis is defined as full health status without any systemic disease, whereas in ocular utility analysis, perfect health is defined as normal vision and perfect eye status. The impact of ocular utility can diminish the general utility analysis with the value of  $\pm 0.3^{(37)}$ . VA is a factor with high impact on ocular HU. TTO reflects the impact from a patient perspective. TTO has been more widely used in utility measurement in ophthalmology as compared with the standard gamble technique. It has shown good validity in VI with long-term reproducibility and has a high correlation with vision in the better-seeing eye<sup>(25,39,40)</sup>. Lloyd et al conducted a comparison of HU in DR, diabetic neuropathy, and diabetic nephropathy. They found no significant difference in HU value, but the vision level had a more important effect on the change in HU. Poor VA had a higher effect on the change in HU than did normal vision<sup>(8)</sup>. Knauer et al described an ophthalmic patient with 20/20 to 20/25 vision who was willing to pay only 11% to 15% of their remaining lifetime for perfect vision, whereas a patient with a VA of 20/200 to 20/400 was willing to exchange 39% to 48% of their remaining life, and blind patient wanted to trade 60% of their life to regain their vision. Patients with AMD and low vision would

exchange even more of their lifetime<sup>(41)</sup>. TTO values are decreasing in visually impaired persons<sup>(37,41)</sup>. On average, the mean TTO utility in eye diseases with a 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 the present study, four of the 40 participants were not willing to trade their life in the TTO1 open questions. The main factors associated with a willingness to trade were individual subjective life expectancy and vision status<sup>(38,42)</sup>. The TTO1 was an open-ended questionnaire in which patients were asked to imagine their subjective life expectancy, which can result from multiple factors, including physical, mental, emotional, and perception of life. With these unstable questions, the 10-year lead time of the TTO2 might be more appropriate, and easy to understand for respondents and could eliminate the variability in the life expectancy factor of each individual to 10 years. However, when compared with the TTO concept in TTO1, the 10-year TTO concept might influence losing the expected life-years and amount of tradeoff time<sup>(42)</sup>. For the interview time, the TTO1 was composed of a brief list of questions that require a short interview duration of 2.89 minutes. Thus, this method might be suitable for a clinician to evaluate their patient's QoL during a clinic visit<sup>(24,37)</sup>. However, with the development of multiattribute preference function tools, the HUI3 has been shown to have high sensitivity to the change in visual function and a standardized methodology. Factors associated with a significant decrease in utility in eye problems are decreasing VA and contrast sensitivity in the better-seeing eye<sup>(24,37)</sup>. A shorter duration of AMD diagnosis had a lower utility value compared with a diagnosis of more than one year, with a mean difference of  $0.17^{(24)}$ .

Heintz et al conducted a study in DR and compared the health state valuation among the HUI3, EQ-5D-5L, EQ-VAS, and TTO. They found that the HUI3 was highly correlated with the NEI-VFQ-25, with a correlation coefficient of 0.54, as compared with the TTO and EQ-5D-5L, according to VI status. They also demonstrated that the HUI3 had a greater utility value as compared with the other instruments in all VA categories except for blindness level. Only the HUI3 and EQ-VAS HU were significantly different in terms of staging in the worse eye. The EQ-5D-5L also could not identify a difference in DR staging classified by the VABSE<sup>(38)</sup>. VA and asymptomatic eye diseases have been shown to be related to the

inconsistent ordering of the HU, and, if no adjustment is made, the HU value is thus affected by systemic disease<sup>(8,38)</sup>. Bozzani et al compared the EQ-5D and TTO utility in open-angle glaucoma and showed that TTO was more sensitive to the progression of glaucoma and correlated with a decreased VFQ-25 score. A willingness to trade time was found among patients with severe glaucoma with poor central VA. Moreover, the EQ-5D-5L did not show a strong association with glaucoma severity<sup>(43)</sup>. Espallargues et al conducted a cross-sectional survey in AMD patients using the EQ-5D, HUI3, and TTO. The HUI3 had a higher correlation with VA and contrast sensitivity, followed by TTO and then EQ-5D-5L and SF-6D (QualityMetric Inc.). Contrast sensitivity also showed a slightly better relationship to the health state when compared with VA. The authors reported that more than 50% of eligible patients in the clinic denied participating in an interview or did not reply to the questions(44). In cataract cases, a study in Singapore showed that the HUI3 and SF-6D were more responsive to changes in VA than the EQ-5D-5L; however, for the Singapore data set, the EQ-5D-5L showed a better response to clinical changes than the older version did, the EQ-5D-3L<sup>(45)</sup>. Unlike the EQ-5D-5L, the HUI3 includes a vision dimension that benefits from demonstrating the effect of visual function. A high correlation between HUI3 and VA changes was also observed in WAMD populations followed by the TTO<sup>(6)</sup>. In the present study, as compared with the EQ-5D-5L, the HUI3 required more response time because of the high number of questions and required usage fees for the instrument. The EQ-5D-5L, with only five dimensions and a lower response time, has been more widely used in general.

In the present study, the authors found that in elderly ophthalmic patients, the TTO2 was easier to follow when compared with the TTO1 but required a longer interview time. The longer interview time can be explained by the higher number of questions on the TTO2. Questions with values "worse than death" were associated with reliability problems of the respondent's answer. The TTO1, HUI3, EQ-VAS, and EQ-5D-5L were significantly correlated with changes in VI and NEI-VFQ-25 QoL score. Although the HUI3 was highly correlated with vision-specific QoL and sensitive to the change in VI stages, because it had the highest number of questions, it required the longest interview time.

The main limitation of the present study is the small sample size, which resulted in low statistical power to detect an association and correlation between HU and NEI-VFQ-25 and associated factors. Even though the HU is highly associated with the visual function and vision-specific quality of life, the disease condition, for instance, cataract, is curable, while WAMD may leave permanent damage. These might affect the patient's perception of their health-related quality of life. Therefore, a more extensive survey might need to compare the difference of HU among disease types. Administration of a face-to-face interview might be associated with higher positive outcomes and lower responsiveness, and data obtained directly from patients might be different from data from the general population, which is widely recommended in cost-effectiveness analysis<sup>(46)</sup>. In terms of the effect of religion, most of the Thai population are Buddhist, and the present study cannot explain the effect comparing to different religions. Moreover, the authors did not evaluate the individuals' active status in religion, which might be one of the factors related to religious beliefs. There are no clear standardized methods to measure an ocular utility from all instruments. However, the present study emphasizes the feasibility of utility measurement instruments in special populations consisting of older individuals with eye disease. The results of the present study will help to select the best instrument to obtain the patient's perspective of ocular HU, which is different from general HU.

# Conclusion

In conclusion, religion seems to influence questions related to death in TTO. The TTO1, TTO2, EQ-5D-5L, HUI3, and NEI-VFQ-25 can be feasible to use in Thai ophthalmic elderly patients. However, worse than dead stage-related questions are not preferred. With prespecified questions and multiplechoice answers, indirect HU methods cause less confusion to respondents.

# What is already known on this topic?

HU is related to quality of life in ophthalmic disease, which could be obtained by different methods as direct evaluation method and indirect or questionnaire instruments. Time trade off techniques has been widely used to evaluate the HU, along with EQ-5D-5L and HUI3. However, there were no report on the feasibility in Thai ophthalmic population and the use of EQ-5D-5L is still debated for its accuracy in eye disease patient.

# What this study adds?

The result of this study shows that question

related to the imaginary stage of death might not be best suited for the elderly ophthalmic population. Along with this, the Buddhist religion are related to the decision of answer and attitude of patient about their disease, which is reflected in the HU. EQ-5D-5L and HUI3 are feasible to use in elderly ophthalmic patient.

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# Ethics approval and consent to participate

The present study was approved by the Institutional Review Board of the Faculty of Medicine; Chulalongkorn University, IRB number 340/62. All participants were informed and signed a written consent before enrolling in the study.

# Availability of data and material

Data sets generated or analyzed during the present study are not publicly available but are available from the corresponding author on reasonable request.

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# **Conflicts of interest**

The authors declare that they have no competing interests.

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