Journal of the Formosan Medical Association (2013) 112, 699–706

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ORIGINAL ARTICLE

Estimating quality weights for EQ-5D (EuroQol-5 dimensions) health states with the time trade-off method in Taiwan

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Received 31 March 2011; received in revised form 8 December 2012; accepted 26 December 2012

KEYWORDS
EQ-5D (EuroQol-5 dimensions);
health state utility;
quality of life;
Taiwan;
time trade-off (TTO)

Background/Purpose: EQ-5D (EuroQol-5 dimensions) is a preference-based measure of health, which is widely used in cost–utility analyses. It has been suggested that each country should develop its own value set. We therefore sought to develop the quality weights of the EQ-5D health states with the time trade-off (TTO) method in Taiwan.
Methods: A total of 745 respondents consisting of employees and volunteers in 17 different hospitals were recruited and interviewed. Each of them valued 13 of 73 EQ-5D health states using the TTO method. Based on the three exclusion criteria for valuation data, only 456 (61.21%) respondents were considered eligible for data analysis. The quality weights for all EQ-5D health states were modeled by generalized estimating equations (GEEs).
Results: Over half of the responses were given negative values, and the medical personnel seemed to have a significantly higher TTO value (+0.1) than others after controlling for other

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http://dx.doi.org/10.1016/j.jfma.2012.12.015

predictors. The N3 model (level 3 occurred within at least 1 dimension) yielded an acceptable fit for the observed OTT data [mean absolute error (MAE) = 0.056, R^2 = 0.35]. The magnitude of mean absolute differences (MADs) between Taiwan data and those from the UK, Japan, and South Korea ranged from 0.146 to 0.592, but the rank correlation coefficients were all above 0.811.

Conclusion: This study reaffirms the differences in health-related preference values across countries. The high proportion of negative values might indicate that we have also partially measured the intensity of fear in addition to the utility of different health states.

Introduction

The EQ-5D (EuroQol-5 dimensions) questionnaire is a preference-based, generic, and self-reported instrument that provides a utility value based upon the five-dimensional health state classifications.[1] The five domains include mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. There are three levels of severity: no problems, some/moderate problems, and severe/extreme problems. The time trade-off (TTO) method is one of the most widely accepted preference elicitation techniques to estimate values or preference weights for EQ-5D health states in many countries.[2–6] The obtained data can be further analyzed using the regression model to derive a value set needed for the calculation of utility for each possible health state. These utilities reflect the relative desirability of the health state, and can be used as quality adjustments in the measurement of quality-adjusted life-years in cost–utility analysis.[7]

It has been suggested that each country should develop its own social value set because previous studies have found that there are differences between different countries in the observed quality weights for some EQ-5D health states.[8–10] The Taiwanese version of the EQ-5D was developed and validated in a study by Chang et al.[11] We decided to develop a Taiwanese valuation set for EQ-5D health states using the TTO method and a statistical model based on quality weights. As the decision making made during the TTO valuation protocol is usually based on hypothetical health states, we assumed that it would be easier for health service workers to imagine different health problem conditions more than the general population. Therefore, we conducted this study using hospital worker subpopulations throughout Taiwan, instead of directly sampling from the general population.

Materials and methods

Study population

We invited 17 hospitals (medical centers, district and regional hospitals) covering all the different geographical areas of Taiwan. There were four hospitals in the northern region, six in the center, four in the southern region, and three in the eastern region, approximately reflecting the population sizes in these four regions. Those answering the questionnaires consisted of medical personnel, administrators, and volunteers. The survey was conducted during face-to-face interviews by seven mutually standardized interviewers from September 2007 to November 2007. Prior to commencement, all the interviewers received training based on the TTO valuation protocol established by the EurolQol Group. The study was approved by the Institutional Review Board of the participating hospitals prior to commencement, and every interviewed patient provided written informed consent.

Quality weights measurements

The valuating processes were modified from the protocol used in the Measurement and Valuation of Health study (MVH) in the UK.[2] From 243 possible EQ-5D health states, a subset of 73 states (72 states plus the worst state scenario, the "33333" state) was selected for direct measurement in this study and divided into six subsets. Each subset was comprised of 12 different health states with a mixture of severity levels (5 very mild, 23 mild, 21 moderate, and 23 severe states), as well as a common state (33333), the worst scenario (Appendix 1). For each individual, the interview included the following components: (1) the standard EQ-5D questionnaire consisting of self-reported health in the five-dimension descriptive system and self-reported health on a visual analogue scale (VAS); (2) a ranking exercise of 13 hypothetical health states expressed in EQ-5D (12 states plus 33333); (3) TTO evaluations of 13 assigned health states; and (4) a demographic characteristics background questionnaire.

During the actual TTO exercise, respondents were asked to select a length of time t in the perfect health state (11111) that they regard as equivalent to 10 years in the target state. The quality weight for states that were regarded as better than death was calculated as $t/10$. In case a respondent preferred death over the target state, the choice was between immediate death and living in the target health state for t years followed by $(10 - t)$ years in state 11111. The more time that is required to be in state 11111 to compensate for a shorter time in the target state, the worse the target state is. The quality weight for "worse than death" was then calculated using the formula $t/10 - 1$. Therefore, all values lie between 1 and −1. Following the MVH study,[2] we excluded the data of respondents that (1) had given negative TTO values to all health states, (2) had given the same TTO value to all health states, or (3) had four or more logical inconsistencies. When compared to another state, the logical inconsistency was defined as the state with a less severe problem in a particular dimension and problems on the other dimensions that are no more severe, to be scored lower by

the respondent. For instance, if state "33333" was valued higher than state "11211" it would be considered a logical inconsistency. These exclusion criteria took into account responses with incomplete or unreliable data. The criterion of the number of inconsistency was based on Ohinmaa and Sintonen's study,[12] where it was found that including valuation data with more than three inconsistencies would significantly affect the estimation of quality weights.

Statistical analysis

Each respondent provided 13 observations, therefore we used the generalizing estimating equations (GEEs) to incorporate the within-person correlation into the analysis. Dummy variables were created for categorical data with levels 2 and 3 in each EQ-5D dimension, so that the models used 10 main effects variables. Some optional variables considered as independent variables for model development were N3, D1, I2, I3, I2-squared, and I3-squared[2,4] described as follows: N3, whether there is any dimension on level 3; D1, the number of movements away from perfect health; I2, the number of dimensions at level 2 beyond the first; I3, the number of dimensions at level 3 beyond the first; I2-squared and I3-squared, the square of "I2" and "I3", respectively.

The demographic variables including age, gender, job identity, and educational level were also put into the model to examine whether these characteristics of the respondents influenced the preference values for EQ-5D health states.

For determining the final model, we compared those models using the mean absolute error (MAE, the average for 73 states of absolute difference per state between the mean observed value and the predicted value), the coefficient of determination (R^2), and the number of prediction errors greater than 0.05 or 0.01 in absolute magnitude. MAE was considered a critical indicator because the aim of this modeling was to predict the quality weights of EQ-5D health states. Therefore, if there were conditions with similar MAE values, the simplest model was selected due to parsimony.

To compare the estimated quality weights for EQ-5D health states among different studies, the rank correlation coefficients and mean absolute differences (MADs) between estimated quality weights of 243 health states from the final model and those estimated in the UK,[2] Japan,[5] and South Korea[6] were calculated. In addition, the differences of characteristics between eligible and excluded respondents were tested with the independent *t* test and Chi-square test. We used version 9.2 of SAS software (SAS Institute, Cary, N.C., USA).

Results

Among the 745 interviewed subjects, we excluded 289 (38.79%) respondents who met at least one of the three exclusion criteria for valuation data. The numbers of excluded respondents included 23 individuals giving negative TTO values to all health states, five individuals giving the same TTO value to all health states given, and 261 individuals having four or more logical inconsistencies. There were some differences between the eligible respondents and excluded ones (Table 1). The excluded respondents appeared to be older, less educated, composed of more volunteers, and on average they took a longer period of time to complete the interview than those included in the eligible sample. However, they did not differ with respect to self-reported rating of overall health measured by EQ-5D VAS ($p = 0.46$) as well as past experience of serious illness among themselves or family.

Table 1 Descriptive statistics for eligible and excluded respondents.

Characteristic	Eligible respondents ($n = 456$)	Excluded respondents ($n = 289$)	p (two-sided)
Age, mean (SD)	42.55 (13.02)	45.89 (14.04)	0.001
Male sex, % (n)	31.14 (142)	23.78 (68)	0.03
Years of education, % (n)			
≤ 6	5.26 (24)	7.61 (22)	<0.001
7—12	22.81 (104)	36.33 (105)	
≥ 13	71.93 (328)	56.06 (162)	
Job title, % (n)			
Medical personnel	41.67 (190)	37.37 (108)	<0.005
Volunteer	37.94 (173)	49.83 (144)	
Administrator	20.39 (93)	12.8 (37)	
Have experienced serious illness in themselves, % (n)	23.18 (105)	29.02 (83)	0.08
Have experienced serious illness in the family, % (n)	71.93 (328)	67.37 (192)	0.19
EQ-5D VAS, mean (SD)	82.68 (11.49)	82.05 (11.28)	0.46
Mean time taken for TTO valuation, mean (SD)	20.2 (11.3)	22.9 (12.7)	0.003

SD = standard deviation; TTO = time trade-off; VAS = visual analogue scale.

Table 2 Parameter estimates of the final alternative models and quality weight calculation from the final model.

Model	5D		5D + N3[a]		5D + Job		5D + N3 + Job	
	β	*p*	β	*p*	β	*p*	β	*p*
Constant	0.242	<0.001	0.185	<0.001	0.289	<0.0001	0.231	<0.0001
Mobility at level 2	0.117	<0.001	0.123	<0.001	0.117	<0.001	0.123	<0.001
Mobility at level 3	0.270	<0.001	0.272	<0.001	0.270	<0.001	0.273	<0.001
Self-care at level 2	0.165	<0.001	0.167	<0.001	0.164	<0.001	0.167	<0.001
Self-care at level 3	0.294	<0.001	0.276	<0.001	0.294	<0.001	0.275	<0.001
Usual activities level 2	0.128	<0.001	0.085	<0.001	0.128	<0.001	0.085	<0.001
Usual activities level 3	0.281	<0.001	0.208	<0.001	0.281	<0.001	0.208	<0.001
Pain/discomfort level 2	0.105	<0.001	0.121	<0.001	0.106	<0.001	0.121	<0.001
Pain/discomfort level 3	0.297	<0.001	0.261	<0.001	0.297	<0.001	0.261	<0.001
Anxiety/depression level 2	0.175	<0.001	0.154	<0.001	0.175	<0.001	0.154	<0.001
Anxiety/depression level 3	0.350	<0.001	0.282	<0.001	0.350	<0.001	0.283	<0.001
N3			0.190	<0.001			0.190	<0.001
Job (medical personnel)					0.113	0.002	0.112	0.002
Adjusted R^2	0.342		0.350		0.350		0.358	
MAE	0.071		0.056		0.071		0.057	
Number (of 73) >0.05	43		35		46		33	
Number (of 73) >0.10	18		14		19		13	

Full health = 1.000, constant term: 0.185.
Mobility: level 1 − 0; self-care: level 2 − 0.167; usual activity: level 1 − 0.
Pain/discomfort: level 2 − 0.121; anxiety/depression: level 3 − 0.282.
N3 (level 3 occurs within at least one dimension): −0.19.
The estimated value for 12123 = 1 − 0.185 − 0.167 − 0.121 − 0.282 − 0.19 = 0.055. If subject is medical personnel, then the estimated value would be adjusted to 0.167 (=0.055 + 0.112).
MAE = mean absolute error.
[a] Example of quality weight calculation from the 5D + N3 model (state 12123).

Table 2 shows the coefficients generated by the GEE model, which functioned better in terms of goodness of fit. The estimates for D1, I2, and I3 were nonsignificant, and the square of these terms only showed a minor impact on variance and the prediction accuracy. All the above terms were excluded in the final model. The best model was the one that incorporated a constant term representing any move away from perfect health, the five dimension variables, and the N3 term, which had the lowest MAE scores (0.056). It was noted that the estimate of one dummy variable of job identity "whether the respondent was a medical personnel member" was significantly positive (0.112), indicating a tendency for higher values given by practitioners than nonpractitioners for the same health states. However, the inclusion of this variable seems to slightly improve the overall predictive performance (namely, the R^2 changed from 0.342 to 0.358), whereas the MAE did not show any change.

The means of observed and predicted TTO values based on the N3 model of the 73 EQ-5D health states are described in Table 3. Over 50% of the states were given a negative value, which is meant to be considered as "worse than death" for the sampled respondents. It was found that the medical personnel had a lower proportion of negative values (48.95%), followed by volunteers (58.96%), and administrators (60.22%). When compared with the estimated quality weights in the UK and Japan, the observed values of this study seem to be consistently lower than the other value sets (Fig. 1). The magnitude of MAD was smaller in comparison with UK weights (namely, 0.146), but those based on comparison with Japan and South Korea were quite substantial, i.e., 0.422 and 0.592, respectively. Nonetheless, the rank correlation coefficient of estimated values between this study and the UK was 0.924, whereas those of Japan and South Korea were 0.879 and 0.811 respectively, indicating a strong positive correlation.

Discussion

The purpose of the present study was to develop a Taiwanese EQ-5D value set. We used TTO values for 73 health states elicited from 456 respondents. Our results suggest that the N3 model is the best prediction model, demonstrating the smallest MAE of 0.056. Moreover, the high rank correlation coefficients of estimated values with several countries also indicates that this study is in good agreement with them on the ranking of the 243 health states, even though fairly large MADs were present between the predicted TTO values based on the value set of this study in comparison with those from Japan and South Korea.

Noticeably, over half (50.7%) of the health states were considered as worse than death for Taiwanese respondents, which is much higher than the proportions reported in other studies.[4–6,10] Such a difference might be due to several

Table 3 Observed and predicted TTO values based on the N3 model of 73 EQ-5D health states.[a]

EQ-5D	*N*	Mean observed value	SE	Mean predicted value	EQ-5D	*N*	Mean observed value	SE	Mean predicted value
12111	83	0.766	0.034	0.648	23222	78	−0.070	0.066	−0.133
21111	74	0.751	0.028	0.693	32212	78	−0.072	0.066	−0.053
11211	86	0.710	0.031	0.730	21323	86	−0.104	0.058	−0.109
11112	65	0.662	0.047	0.661	23321	86	−0.105	0.057	−0.102
11121	69	0.629	0.037	0.694	11333	65	−0.114	0.076	−0.126
12211	65	0.555	0.057	0.563	21233	86	−0.131	0.062	−0.126
22211	78	0.531	0.047	0.441	22331	78	−0.162	0.058	−0.134
21112	78	0.529	0.046	0.539	22132	69	−0.186	0.070	−0.080
12121	86	0.472	0.050	0.527	21313	69	−0.186	0.065	0.012
11122	69	0.459	0.049	0.540	13213	69	−0.190	0.069	−0.018
22121	78	0.444	0.050	0.405	21332	83	−0.190	0.057	−0.120
11312	65	0.418	0.063	0.263	22233	74	−0.224	0.061	−0.293
22112	83	0.364	0.048	0.372	12233	83	−0.229	0.057	−0.171
21222	74	0.358	0.050	0.333	22323	65	−0.250	0.074	−0.276
11131	64	0.322	0.078	0.364	23232	84	−0.251	0.054	−0.273
11113	74	0.312	0.055	0.343	33321	84	−0.261	0.055	−0.252
12222	86	0.278	0.056	0.288	32232	74	−0.271	0.058	−0.315
12131	78	0.240	0.058	0.197	22232	69	−0.284	0.064	−0.165
22122	83	0.234	0.052	0.251	12333	65	−0.287	0.071	−0.293
13212	84	0.211	0.053	0.111	13332	86	−0.297	0.056	−0.273
21312	82	0.196	0.051	0.141	13323	86	−0.301	0.051	−0.262
11322	86	0.194	0.062	0.142	23313	65	−0.313	0.068	−0.263
22222	74	0.192	0.058	0.166	33212	69	−0.343	0.057	−0.162
22113	74	0.179	0.058	0.053	23332	74	−0.356	0.054	−0.396
32211	83	0.175	0.057	0.100	32313	86	−0.370	0.049	−0.305
13311	65	0.123	0.076	0.142	22333	78	−0.384	0.057	−0.416
12113	78	0.114	0.063	0.176	33232	83	−0.399	0.051	−0.423
21232	74	0.114	0.062	0.002	32331	65	−0.402	0.063	−0.284
11133	65	0.089	0.075	0.081	23223	69	−0.413	0.058	−0.262
12313	74	0.082	0.060	−0.032	33322	78	−0.417	0.059	−0.406
11313	86	0.082	0.060	0.135	32332	78	−0.425	0.054	−0.437
21213	69	0.072	0.066	0.135	33323	74	−0.490	0.051	−0.534
22312	65	0.069	0.077	−0.026	23323	69	−0.508	0.052	−0.384
21223	86	0.058	0.059	0.014	32233	69	−0.518	0.050	−0.443
12123	69	0.038	0.070	0.055	33332	78	−0.551	0.053	−0.546
21133	74	0.026	0.063	−0.041	33333	456	−0.623	0.018	−0.674
12223	83	−0.011	0.065	−0.031					

TTO = time trade-off.
[a] Data are rank-ordered by observed mean TTO values.

factors. Firstly, the translation of the EQ-5D descriptive instrument and/or TTO valuation procedure could have introduced some noises such as inappropriate cultural adaption or insufficient cognitive interviews resulting in misunderstandings or deliberately wrong choices. Secondly, unlike other studies,[2,5,6] our respondents were recruited from a subpopulation that work or serve in hospitals, in anticipation that they might be more likely to have a chance to visualize the hypothetical scenarios of different health states during the TTO valuation. As these people have been regularly taking care of various types of patients, they tended to cherish quality of life more than others, and appeared to be more willing to live a shorter but healthier life in exchange for living longer with certain illnesses. In addition, our respondents were 69% females, which can cause lower rating values, as was also noticed by Dolan and Roberts among women in the UK.[13] It has been reported that the employment status where respondents have worked in a job that involves looking after ill people did not affect the TTO values.[13] However, in some studies, healthcare professionals tend to provide lower utility scores than do patients and their parents.[14] In this study, we found that medical personnel appeared less pessimistic (on average 0.1 more) in comparison with the healthy volunteers after controlling for other determinants. The results seem to corroborate the comment made by Kahneman that we might just measure the fear of different health states instead of their utility,[15] because healthcare professionals are more accustomed to dealing with different types and combinations of disabilities or suffering and generally show less fear of them. The higher

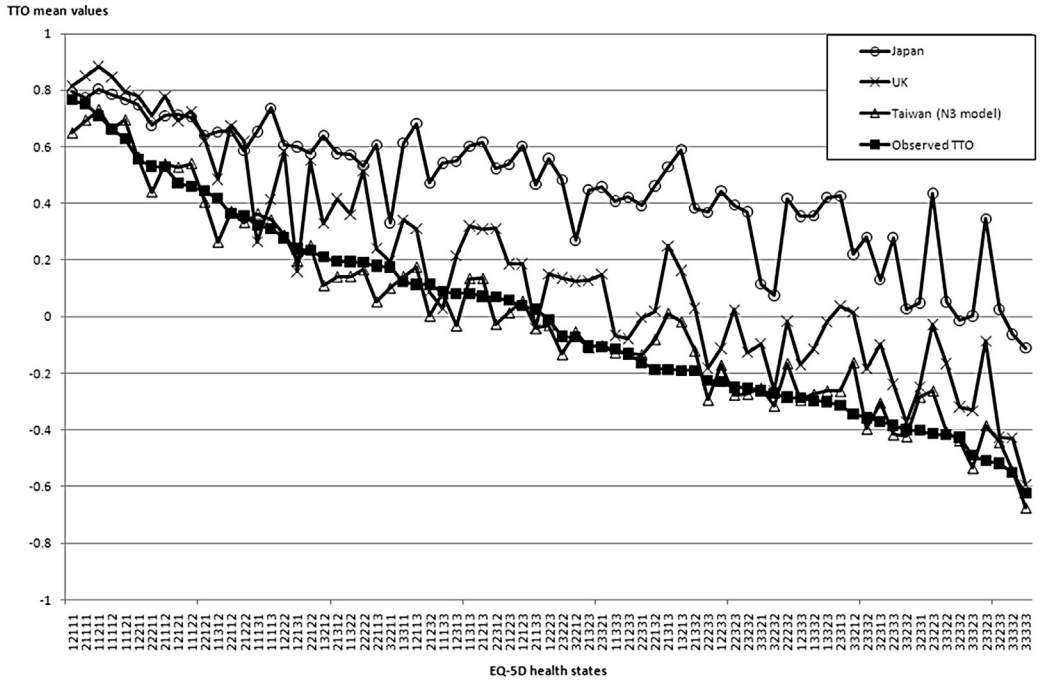

Figure 1 Mean time trade-off (TTO) values for 73 EQ-5D (EuroQol-5 dimensions) health states (from the bottom up): observed TTO values of the Taiwan survey, predicted values using the N3 model, predicted values using UK value sets, and predicted values using Japan value sets.

proportion of negative values expressed by volunteers (58.96%) and administrators (60.22%) also appears to support the above conjecture.

Another possible explanation is the cultural differences in health-related preferences, because it has been demonstrated that the TTO values of the coefficients in their final models differ from country to country even though similar study designs were adopted.[8,10,16] For instance, it is noted that Taiwanese respondents put more weight on the anxiety/depression domain than the other four dimensions because it has the highest regression coefficient among the five dimensions at level 3 followed by "self-care", "mobility", "pain/discomfort", and "usual activity" (Table 2). A similar tendency was also reported in the Dutch study.[9] By contrast, having severe problems in the functional dimensions of mobility and self-care were considered to be of more importance for the respondents from Japan[5] and South Korea,[6] and pain/discomfort for UK respondants[2] (Appendix 2). However, when we had one more level 3 dimension in the health state, the regression coefficient of anxiety/depression was reduced (Table 2). A similar trend was also found for the change of regression coefficient on usual activity level 2/3, when we had an N3 condition (namely, one more dimension level 3). In other words, the independent effect of level 3 for dimensions of mobility, self-care, or pain/discomfort would influence the value in a more stable manner. Such variations should be taken into account when comparing valuations based on the scores obtained in different national settings, although the sequence of ranking may still be similar.

Originally, we assumed that it might be easier for the employees and volunteers of the hospitals to imagine the conditions with different health problems than the general population. However, it raises the issue of the representativeness and generalization of the sample to the whole population of Taiwan. Future investigators are encouraged to conduct a sensitivity analysis by adopting the weights of different health states from other countries, such as the UK and the US. In spite of the above limitation, our data still provide a basis of quality weight of EQ-5D in Taiwan, which could be used for the valuation of quality-adjusted life years (QALYs) in cost—utility analysis. This information can then be used, for instance, to guide policy decisions of national healthcare resources allocation.

Acknowledgments

Financial support for this study was provided by grants from the National Science Council, Taiwan (NSC 99-2811-B-006-051, NSC 99-2628-B-002-077-MY3, and NSC 99-2628-B-006-036-MY3) and the National Health Research Institutes (NHRI-EX96-9204P). We are grateful for the support of the participating hospitals of this study, including Taipei Veterans General Hospital, Chang Gung Memorial Hospital Linkou Branch, National Taiwan University Hospital, Hsin Chu General Hospital, Chung Shan Medical University Hospital, China Medical University Hospital, Changhua Christian Hospital, Puli Christian Hospital, Buddhist Tzu Chi General Hospital, Taitung Christian Hospital, Lotung Poh-Ai Hospital, St. Martin De Porres Hospital, Chia-Yi Christian Hospital, National Cheng Kung University Hospital, Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung Veterans General Hospital, and Pingtung Christian Hospital.

Appendix 1

Health states of the six subtests.[a]

Subset 1	Subset 2	Subset 3	Subset 4	Subset 5	Subset 6
11211 (very mild)	11112 (very mild)	12111 (very mild)	21111 (very mild)	11121 (very mild)	21112 (mild)
12121 (mild)	12211 (mild)	22112 (mild)	21222 (mild)	11122 (mild)	22211 (mild)
21223 (mild)	11312 (mild)	22122 (mild)	22222 (mild)	21213 (mild)	22121 (mild)
12222 (mild)	22312 (mild)	21312 (mild)	11113 (mild)	23121 (mild)	12113 (mild)
11322 (mild)	11131 (mild)	13212 (mild)	22113 (mild)	21313 (moderate)	12131 (moderate)
11313 (moderate)	13311 (moderate)	12223 (moderate)	12313 (moderate)	22132 (moderate)	23222 (moderate)
21323 (moderate)	22323 (moderate)	32211 (moderate)	21232 (moderate)	13213 (moderate)	32212 (moderate)
23321 (moderate)	11133 (moderate)	21332 (moderate)	21133 (moderate)	22232 (moderate)	22331 (moderate)
13132 (moderate)	23313 (severe)	12233 (severe)	23332 (severe)	23223 (severe)	22333 (severe)
21233 (severe)	11333 (severe)	23232 (severe)	22233 (severe)	23323 (severe)	33322 (severe)
13332 (severe)	12333 (severe)	33321 (severe)	32232 (severe)	33212 (severe)	32332 (severe)
32313 (severe)	32331 (severe)	33232 (severe)	33323 (severe)	32233 (severe)	33332 (severe)

[a] The five dimensions assessed by the EQ-5D (EuroQol-5 dimensions) according to their orders in the questionnaire are mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each with three levels of severity (no problems, some/moderate problems, and severe/extreme problems). For instance, 11211 = no problems with mobility, no problems with self-care, some/moderate problems with usual activities, no problems with pain/discomfort, and no problems with anxiety/depression.

Appendix 2

Comparison of the coefficients of TTO values among EQ-5D (EuroQol-5 dimensions) in their final model with results from different countries.

	UK[2]		Japan[5]		South Korea[6]		Taiwan	
	β	*p*	β	*p*	β	*p*	β	*p*
Constant	0.081	<0.001	0.148	<0.001	−2.68	<0.001	0.185	<0.001
Mobility at level 2	0.069	0.389	0.078	<0.001	0.267	<0.001	0.123	<0.001
Mobility at level 3	0.314	<0.001	0.418	<0.001	0.554	<0.001	0.272	<0.001
Self-care at level 2	0.104	<0.001	0.053	<0.001	0.471	<0.001	0.167	<0.001
Self-care at level 3	0.214	<0.001	0.101	<0.001	0.819	<0.001	0.276	<0.001
Usual activities level 2	0.036	0.677	0.040	<0.001	0.374	<0.001	0.085	<0.001
Usual activities level 3	0.094	0.029	0.128	<0.001	0.662	<0.001	0.208	<0.001
Pain/discomfort level 2	0.123	<0.001	0.083	<0.001	0.318	<0.001	0.121	<0.001
Pain/discomfort level 3	0.386	<0.001	0.189	<0.001	0.488	<0.001	0.261	<0.001
Anxiety/depression level 2	0.071	0.305	0.062	<0.001	0.313	<0.001	0.154	<0.001
Anxiety/depression level 3	0.236	<0.001	0.108	<0.001	0.603	<0.001	0.282	<0.001
N3	0.269	<0.001	0.014	0.284	—	—	0.190	<0.001

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