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Mapping Catquest Scores onto EQ-5D Utility Values in Patients With Cataract Disease

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Abstract

Background: Mapping from non-performance-based measures onto generic performance-based measures provides an appropriate solution to derive utilities to be used in economic evaluations.

Objectives: This study aimed to create a model through which EQ-5D utilities for cataracts can be obtained from scores on the disease-specific Catquest measure.

Patients and Methods: One hundred ninety-nine observations from 103 patients who self-administered the EQ-5D, the Catquest and questions on demographic and clinical characteristics were included in the analysis. Data was divided into estimation and validation datasets. To predict EQ-5D utilities, multiple regression analysis, using the Ordinary Least Square (OLS) and the censored least absolute deviation (CLAD), was performed. Catquest scores, age, gender, and performing surgery were included as explanatory variables. An estimation dataset was used to derive the coefficients, and these coefficients were then validated using a validation dataset. Based on the explanatory power, the consistency, the simplicity, the mean absolute error (MAE) and the correlations between observed and fitted utilities, the most appropriate model was selected.

Results: The mean EQ-5D and Catquest scores of the total sample were 0.631 and 15.8, respectively. Age and surgery showed no significant effect for either method. Removing age and surgery, model II was built and given an R^2 of 0.697, an MAE of 0.1176 for the OLS and an R^2 of 0.614, and an MAE of 0.1153 for the CLAD method. In the validation stage, the CLAD revealed better prediction ability, with an MAE of 0.198 versus an MAE of 0.209 for the OLS. ICC and Bland-Altman analysis put the CLAD as a preferred method with the following equation: Utilities (EQ-5D) = 0.988 - 0.0281 × Catquest (PD) + 0.102 × gender (male = 1).

Conclusions: Based on these results, a mapping function was obtained which appears to be valuable in predicting EQ-5D utilities from Catquest scores. This function gives an appropriate solution to estimate utilities when primary EQ-5D data is not available. Although the model represents good consistency and predictive ability, further examination of obtained function is required with large samples.

Keywords: QALYs, Mapping, Regression Analysis, Quality of Life, Cataracts, EQ-5D, Disease-Specific Instrument

1. Background

The existence of market failure in health care has meant that economic evaluation has become inevitable. Cost-utility analysis, using quality-adjusted life-years (QALYs) as a single measure of outcomes, is one of the most common forms of economic evaluation (1). QALYs integrate both quantitative and qualitative aspects of life in a single measure of health outcomes. In this context, the quality of life is measured in terms of health-related quality of life (HRQL) according to a preference-based utility scale anchored at 0 (death) and 1 (full health), although a negative value (states worse than death) is possible. QALYs are calculated by incorporating these values to length of time in each health state (2). There are several generic, preference-based, quality of life measures, and these generic instruments are featured in eliciting a population's preferences regarding the different health states. The EQ-5D (EuroQol 5D index) is one of the most frequently-used, generic, preference-based measures, so that population tariffs for this measure have been elicited in a number of countries (3). Despite the significant benefits of generic instruments in providing a unique solution for the comparison of health outcomes across interventions, these instruments, in comparison with disease-specific instruments, suffer from a responsiveness to small changes (4, 5). Therefore, when the interest is in clinically important differences, because of the high sensitivity, disease-specific instruments are preferred (4). On the other hand, eliciting a population's preferences for each economic evaluation may require the allocation of a lot of resources, and there also may be previous studies or data collections that only included disease-specific measures and not a generic measure (5, 6). Because disease-specific instruments cannot be used to calculate QALYs, one way to deal with this limitation is to map disease-specific scored measures to indexed values obtained through the preference-based instruments. Addressing these issues, mapping would provide us with the estimation of QALYs where the preference-based instruments were not included.

Cataracts are the leading cause of blindness throughout the world (7). They are also the most common cause of eye operations. The number of cataract operations that will be performed throughout the world is projected to be 32 million by 2020 (8). For diseases like cataracts that are chronic with long morbidity and a documented impact on HRQL (9, 10), integrating HRQL data in the evaluation of treatment is essential. HRQL can be measured based on health utilities (HU) for use in economic evaluations to inform healthcare decision-making. The Catquest is a widely used, disease-specific instrument that contains questions useful for evaluating health-related quality of life pertaining to cataract surgery. In addition, it is not a preference-based measure (11).

2. Objectives

This study aimed to create a model to allow EQ-5D utilities for cataracts to be obtained from scores on the disease-specific Catquest measure.

3. Patients and Methods

3.1. Design and Recruitment

This is a longitudinal study with two points of measurement that was approved by the ethics committee of Kerman University of Medical Sciences in July 2013 (with code number "134.29"). The study was conducted in Kashani hospital, a large, tertiary referral, government and educational hospital with 15 departments and 1000 beds. The hospital is affiliated with Shahrekord University of Medical Sciences in Iran. Initially, 106 patients who were scheduled for cataract surgery agreed to participate in the study. The sample size was estimated using the rule of thumb proposed by Green (12) for determining the minimum sample size for regression analysis. Accordingly, the size should be greater than 104 + K, where K represents the number of independent variables. Patients were included if they met the inclusion criteria as having confirmed cataract disease by an ophthalmologist, and if they had given written informed consent. All participants were reassured about confidentiality, and that participating in the study did not influence the treatment they received in any way. Three out of 106 patients did not consent to participate and were excluded from the study. The 103 patients that met the inclusion criteria were consecutively recruited between July 2013 and January 2014. Patients were asked to self-administer the questionnaire package at two points in time. The package included the EQ-5D, Catquest, and questions on demographic characteristics. The first administration was done while they were in the hospital, and before they entered the hospital operating room. At the end of the first administration, patients were informed about the second administration, which would occur after six months, and that the same questionnaire package with a postage-paid return envelope enclosed would be sent to their addresses. Keeping in mind the time it would take the post to reach them, we had telephone contact with patients to make sure that the packages were delivered. Ninety-six out of 103 first-administered patients responded at second administration; that is, we had a total of 199 observations.

3.2. Disease-Specific Instrument

The Catquest is a disease-specific questionnaire that has been developed to assess visual disability through patients' self-reported visual function. It consists of questions encompassing four dimensions of daily life: frequency of doing activities (six questions), perceived disability (seven questions), cataract symptoms (two questions), and satisfaction with vision (two questions). For perceived disability and cataract symptoms, there are four response options as follows: 1 = no difficulty; 2 = some difficulty; 3 = much difficulty; 4 = extreme difficulty. Within this range, higher scores correspond to worse visual disability. Response options in the area of satisfaction vary from 1 (very satisfied) to 4 (very dissatisfied), with intermediate options for 2 and 3 corresponding to rather satisfied and rather dissatisfied, respectively. The four response options for the frequency of doing activities are as follows: 1 =

does the activity frequently; 2 = does the activity more frequently; 3 = does the activity rarely; 4 = does not perform the activity (11, 13, 14). The Catquest has demonstrated good reliability and validity in cataract surgery (15). Based on the previous studies, perceived disability domain is one of the most important areas, and the correlation of this area with utility is well documented (9). Therefore, the score sum of the perceived disability (PD) domain was used for the main analysis. By summing each score for each question, the total score sum for this domain is obtained. Thus, this score is ranked between 7 (indicating the best score) and 28 (indicating the worst score) (9).

3.3. Utilities

Utility values for this study were derived using the EQ-5D instrument. The EQ-5D (3, 5) is a generic, standard, preference-based instrument that is used to indirectly drive utility values. It consists of five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each of which has three response levels (no problems, some problems, and extreme problems). It gives a total of 243 health states. These health states are assigned scores, using a tariff based on the time trade-off method from a sample of 3,395 respondents from the UK general population. Scoring ranges from -0.59 to 1.00, with 0 indicating dead, 1 representing a state of full health, and negative scores representing health states that are perceived to be worse than death. The reliability and validity of the EQ-5D have been well documented in different settings (3, 16-18). Because there was no Iranian population tariff for the EQ-5D when the study was conducted, the U.K. scoring algorithm was used to drive utilities.

3.4. Analysis

In order to estimate EQ-5D index scores from Catquest scores, multiple regression analysis was performed. The utility index obtained from the EQ-5D was taken as the dependent variable, and the summary score of perceived disability domain of the Catquest as the independent variable, controlled for surgery, gender and age. Surgery and gender were included as dummy variables and defined with 0 (female) and 1 (male) for gender, and for surgery by 0 (before) and 1 (after). Other studies have revealed that there is a ceiling effect in EQ-5D index scores (19-21); therefore, ordinary least squares (OLS) produce inaccurate estimates. The Tobit and the censored Least absolute deviation (CLAD) methods are appropriate for right censoring data (19, 20, 22). However, because the Tobit model is performed under the assumptions of normality and homoscedasticity, where these assumptions are violated, this model also produces biased estimates (22). In contrast, because the CLAD method does not require normality and homoscedasticity assumptions, it produces consistent estimates (23). The CLAD is a reasonable alternative, even in the presence of heteroscedasticity, non-normality, and censoring. As is common with other studies (24) and for the purpose of comparison, we used two OLS and CLAD methods to estimate a mapping algorithm. We examined the goodness of fit by adjusted R^2 and mean absolute error (MAE). The total dataset was divided into two datasets, estimation (60 percent) and validation (40 percent). The estimation dataset was used to derive regression coefficients, and the validation dataset was used to validate derived mapping functions of both the OLS and CLAD methods. The performance of the models in the validation stage was assessed in terms of mean absolute deviation between observed and fitted utilities, correlation between predicted and observed values and Bland-Altman analysis. All statistical analyses were performed using STATA 12.0 and MedCal 13.0.6 software.

4. Results

4.1. Descriptive Summary

One hundred ninety-nine observations of the patients with cataracts who self-administered the questionnaires were included in the analysis. Of these, 119 (60 percent) of the observations were in the estimation dataset, and 80 (40 percent) were in the validation dataset. Table 1 provides the demographic and clinical characteristics of the total sample. The mean age at the time of the operation was 59.2, most of the patients were females (56 percent), and 52 percent of the patients were in pre-operative and 48 percent in post-operative states. Table 2 shows the mean EQ-5D and Catquest (PD) scores in the pre-operative patients, post-operative patients and in the total samples. The mean index scores of the EQ-5D were 0.608, 0.778 and 0.631 in the pre-operative patients, post-operative patients and in the total sample, respectively. The mean Catquest (PD) scores for the aforementioned samples were 21.8, 8.6 and 15.8, respectively.

4.2. Regression Analysis

Table 3 presents the mapping models that were built, using two OLS and CLAD methods, based on the estimation dataset. Model I, using the OLS method (indicated on the left side of Table 3), included the Catquest (PD), age, gender and surgery as explanatory variables. These variables explained about 0.693 (adjusted R^2) of the variations and gave an MAE of 0.1186. Age and surgery showed no statistically significant effects. In addition, the coefficient for

Table 1. Demographic and Clinical Characteristics of Patients Having Cataracts[a]

Characteristics	Values
Mean age at operation in years	59.2 (5.5)
Female	112 (56)
Male	87 (44)
Pre-operative	103 (52)
Post-operative	96 (48)

[a]Data are presented as No. (%), except for age, which is represented by mean (SD).

age showed no expected sign that did not make sense. Removing age and surgery from the regression equation, we constructed model II, which adjusted R^2 (0.697), and MAE (0.1176) were consequently both improved. These two models (I, II) (Table 3, right-hand side) were then applied for the CLAD method and given an R^2 of 0.596, and an MAE of 0.1184 for model I; and an R^2 of 0.614, and MAE of 0.1153 for model II.

4.3. External Validation

Based on the explanatory power, consistency of the estimated coefficients, simplicity and mean absolute error criteria, model II, for both the OLS and CLAD methods, was adapted to be validated externally. Table 4 describes the performance of the models in terms of the mean fitted EQ-5D, the difference of the observed and fitted mean, and confidence intervals for the fitted EQ-5D. The mean observed EQ-5D for the validation dataset was 0.671. The fitted means of the OLS and CLAD methods were 0.683 and 0.656, respectively. As is obvious in terms of mean differences, the CLAD method overestimated the mean EQ-5D, with 0.012 differences, and the OLS method underestimated the mean utility value, with 0.015 differences. The differences for both methods were below the minimal important differences (MID) (0.074) for the EQ-5D (25).

The ICCs for fitted and observed utilities using the OLS and CLAD methods were 0.498 and 0.506, respectively. Figure 1 and 2 show the Bland-Altman plot of the differences between the observed and predicted utilities versus the mean observed and fitted utilities for the OLS and CLAD methods in the validation dataset, respectively. In general, two plots showed reasonable agreement, and revealed that a substantial proportion of the observations fell within the area of zero $\pm$ 1.96 $\times$ (standard deviation) of the differences. In both methods, the differences between observed and predicted values exceeded the MID.

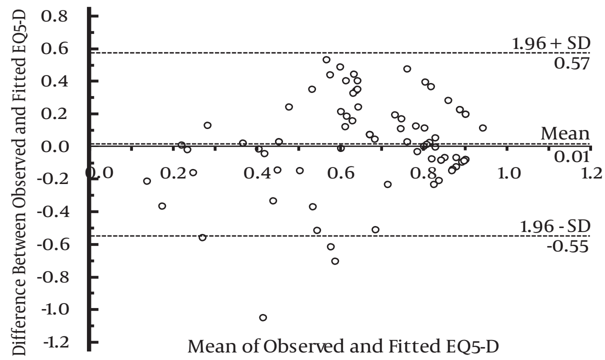

Figure 1. Bland-Altman Plots of Agreement Between Fitted and Observed Utilities Using the OLS Method from Model II in the Validation Dataset

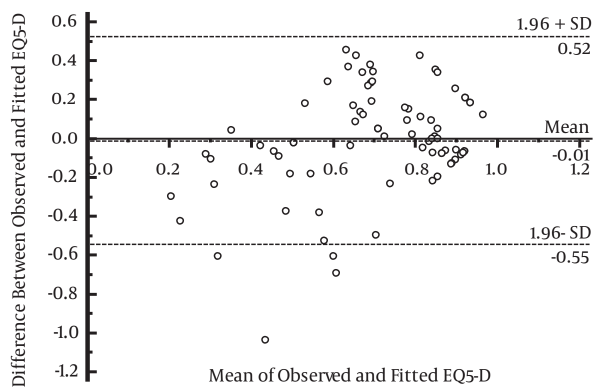

Figure 2. Bland-Altman Plots of Agreement Between Fitted and Observed Utilities Using the CLAD Method from Model II in the Validation Dataset

5. Discussion

The EQ-5D, as a generic measure, is frequently used to derive utilities. On the other hand, the Catquest, as a disease-specific measure, is used to assess the visual disability of patients with cataracts. Taking the benefits and limitations of two generic and disease-specific measures into account, mapping provides a useful way to derive utilities for different health states. Several studies, using different measures, have attempted to develop mapping equations in different areas of disease (24). In the present study, the EQ-5D utilities regressed on Catquest scores, controlling for age, gender and surgery (Model I). In both the OLS and CLAD methods, age and surgery gave no statistically significant coefficients. This is most likely because of the high correlation (> 0.80) between these variables, with Catquest scores as another independent variable. Further-

Table 2. Distribution of EQ-5D and Catquest (PD) Scores in Pre- and Post-operative Patients[a]

	OLS		CLAD	
	Model I	**Model II**	**Model I**	**Model II**
Catquest (PD)	-0.0233 (0.0038) [a]	-0.0278 (0.001) [a]	-0.0246 (0.004) [a]	-0.0281 (0.0021) [a]
Age	0.0001 (0.0826)	-	-0.0007 (0.0825)	-
Gender	0.142 (0.0304) [a]	0.139 (0.0299)[a]	0.093 (0.0309) [a]	0.102 (0.025) [a]
Surgery	0.0840 (0.0639)	-	0.0674 (0.0918)	-
R^2	0.693 [b]	0.697 [b]	0.596 [c]	0.614 [c]
MAE [d]	0.1186	0.1176	0.1184	0.1153
Constant	0.871 (0.188)	0.980 (0.034) [a]	0.982 (0.185)	0.988 (0.031) [a]

[a]Data are presented as mean (SD).

Table 3. Regression of the EQ-5D Utility Index Upon Catquest (PD) by the Ordinary Least Square (OLS) and Censored Least Absolute Deviation (CLAD) Methods

	OLS		CLAD	
	Model I	**Model II**	**Model I**	**Model II**
Catquest (PD)	-0.0233 (0.0038) [a]	-0.0278 (0.001) [a]	-0.0246 (0.004) [a]	-0.0281 (0.0021) [a]
Age	0.0001 (0.0826)	-	-0.0007 (0.0825)	-
Gender	0.142 (0.0304) [a]	0.139 (0.0299)[a]	0.093 (0.0309) [a]	0.102 (0.025) [a]
Surgery	0.0840 (0.0639)	-	0.0674 (0.0918)	-
R^2	0.693 [b]	0.697 [b]	0.596 [c]	0.614 [c]
MAE [d]	0.1186	0.1176	0.1184	0.1153
Constant	0.871 (0.188)	0.980 (0.034) [a]	0.982 (0.185)	0.988 (0.031) [a]

[a]Significant ($P < 0.05$).
[b]Adjusted R
[c]Pseudo R
[d]Mean absolute error.

Table 4. Performance of Model II Using a Validation Dataset for two OLS and CLAD Methods

	Mean Fitted EQ-5D	Difference of Means (Observed-Fitted)	Confidence Interval of Fitted EQ-5D	MAE [a]
CLAD [b]	0.683	-0.012	(0.640 - 0.725)	0.198
OLS [c]	0.656	0.015	(0.608 - 0.707)	0.209

[a]Mean absolute error.
[b]Censored least absolute deviation.
[c]Ordinary least square.

more, other studies obtained similar results for age (9). Dropping two non-significant variables, we built model II. The explanatory power, in terms of R^2 and MAE, improved either for the OLS and CLAD methods. The coefficient of the Catquest was significant and consistent for both methods. Even though the amount of the coefficient was small, considering the fact that the Catquest measures just that aspect of quality of life that pertains to visual function, and the EQ-5D measures aspects other than visual function, this seems to be reasonable. This is consistent with results that were obtained by other authors (9). In terms of explanatory power, two methods showed somewhat similar results. Even though R^2 for the OLS was higher than that for the CLAD, the MAE was also higher. Because the CLAD offers pseudo R^2, directly comparing this with adjusted R^2 obtained from the OLS method is not methodologically without limitations (26, 27). In comparison with results obtained by others (9), these amounts appeared to be reasonable for both methods.

To give further assurance in determining the most appropriate method, we used a separate dataset for validation of both methods. The CLAD revealed lower values for the MAE and the difference between the mean of observed and fitted utilities. In addition, the ICC between observed and fitted utilities presented better agreement for the CLAD method than the OLS. Furthermore, the Bland-Altman plots showed similar patterns for two methods. Both methods underestimated the utilities for higher values, and overestimated at lower values. Similar patterns have been seen in the published mapping studies (28). While most of the observations were within the area of 1.96 SD, the limits for the CLAD method were narrower (CI; 0.640 - 0.725) than those for the OLS (CI; 0.608 - 0.707).

Based on the baseline regression analysis and the validation dataset, this study suggests the CLAD method as being the preferred method, and the following equation as a mapping function to derive utilities from Catquest (PD) scores:

$$Utilities\,(EQ-5D) = 0.988 - 0.0281 \times Catquest\,(PD) + 0.102 \times gender\,(male = 1) \quad (1)$$

Some other studies have suggested the CLAD as being the preferred choice in mapping literature (19). This study provides an easy way for clinicians and other researchers to derive utilities from a disease-specific measure when primary EQ-5D data is not available in patients with cataracts. In addition, this study investigates the performance of two different methods and chooses the most appropriate method. Despite these advantages, there are two limitations of this study. First, the sample size used in the present study was small. Second, participants were not assigned randomly, although they were recruited consecutively and controlled for some variables. The results of this study should be used cautiously, particularly when other directly-obtained, social preference-based values are available.

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Footnote

Authors' Contribution: Mahmood Yousefi participated in developing the study design, doing the statistical analysis and drafting the manuscript. Yousef Behzadi Sheikhrobat participated in data acquisition. Safa Najafi provided technical support. Shahram Ghaffari revised the manuscript for important intellectual content. Hossein Ghaderi contributed to statistical analysis and interpretation of data and helped draft the manuscript. Mohsen Barouni participated in data analysis.

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