VALUE IN HEALTH REGIONAL ISSUES 18 (2019) 170–175

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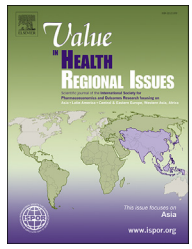

Economic Evaluation

Valuation of Quality Weights for EuroQol 5-Dimensional Health States With the Time Trade-Off Method in the Capital of Iran

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ABSTRACT

Background: The EuroQol 5-dimension (EQ-5D) is a standard instrument that is widely used for measuring health-related quality of life and quality-adjusted life years in economic evaluation of healthcare interventions. **Objective:** To estimate a preference valuation set for EQ-5D 3-level (3L) health states from the perspective of the general population in the capital of Iran. **Methods:** Eight hundred seventy adults aged ≥18 years were interviewed in Tehran (Iran's capital) from July to November 2013. The participants were selected by a stratified random sampling method and were interviewed face-to-face at their usual residence. Forty-two health states were selected and valued from the 243 states derived from the EQ-5D-3L instrument. Each respondent valued 11 health states using the time trade-off method. Generalized least squares regression with random effect was used to predict values for health states. **Results:** The analysis was performed for 846 respondents. The final model yielded the best fit for the time trade-off value at the individual level with an overall R^2 of 0.45 and a mean absolute error of 0.214. The mean values for the 42 health states ranged from 0.934 for state 11121 to -0.142 for state 33333. **Conclusions:** This study provided for the first time a value set for calculating quality-adjusted life years from the EQ-5D instrument in Iran. The Iranian EQ-5D-3L value set slightly differs from the value sets of the UK and the United States.

Keywords: EQ-5D-3L, general population, preference-based measures, time trade-off, value set

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Introduction

Cost–utility analysis is a standard economic evaluation technique routinely used for assessment of healthcare interventions. This technique is particularly helpful for allocation of healthcare resources and in the process of evidence-based policy making.[1] This method has been used for a long time in developed countries[2]; however, the method has not been well developed and used in developing countries.

A cost–utility analysis is normally used when the health-related quality of life (HRQL) and the quality-adjusted life year (QALY) are considered important outcomes of the healthcare interventions.[1] The EQ-5D is a standard and one of the most frequently used instruments for measuring HRQL and QALY in economic evaluations. The EQ-5D-3L questionnaire has 5 dimensions, including mobility, self-care, usual activity, pain or discomfort, and anxiety or depression, and each dimension has 3 levels of no, moderate, and severe problems.[3] A new version of EQ-5D named EQ-5D-5L has 5 levels in each dimension, which is not the subject of this study. Therefore, using the EQ-5D-3L questionnaire, people might have 243 health states (3^5), and each health state can be associated to a defined level of quality of life ranging from 0 to 1. Many countries, including the UK,[4] The Netherlands,[5] the United States,[6] Japan,[7] Denmark,[8] South Korea,[9] New Zealand,[10] Sweden,[11] and Sri Lanka,[12] have used their own local weights and value sets for translating various health states

Conflict of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

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https://doi.org/10.1016/j.vhri.2019.01.007

into a quality-of-life score. These weights are calculated usually based on the preferences of general or specific groups of the population in each country; therefore, the weights might fluctuate among countries. There might be even more variations between developed and developing countries owing to differences in their culture, socioeconomic status, and level of uncertainties.[13]

This study aims to develop a customized value set for EQ-5D-3L health states in the capital of Iran and compare the preferences of the Iranian general population with the weights and value sets of the UK and United States.

Methods

The EuroQol Instrument

We used the standard TTO approach to estimate the EQ-5D-3L value sets from a sample of the Iranian population. In this technique, the respondents are asked to choose between 2 specified alternatives. The first alternative is a person with a health state of "better than death, lower than full health" who lives for a defined period of time (eg, 10 years) and then dies. The second alternative is the same person with "full health" who lives for a defined period of time that is shorter than 10 years (t < 10 years) and then dies. During the interview the amount of t is changed until the respondent becomes indifferent in selecting between the first and the second alternative.[14]

The EQ-5D-3L instrument, whose license has been acquired from EuroQol, explores 5 dimensions of health, and each dimension has 3 levels: no problem (score 1), some or moderate problems (score 2), and severe problem (score 3); therefore, a total of 243 (3^5) possible health conditions can be obtained.[15] These scores would abbreviate the health condition of the study population. The abbreviation 11111, for instance, represents "full health" with HRQL of 1 (100%), and the abbreviation 12132 represents a health state with no problem in mobility, some problems with self-care, no problem in usual activities, extreme pain or discomfort, and moderate anxiety or depression.

The EQ-5D instrument also contains a question designed to directly translate the health states into HRQL by a 20-cm vertical visual analog scale (VAS of EQ-5D), with the endpoints labeled "best imaginable health state" at the top and "worst imaginable health state" at the bottom, which has numeric values of 100 and 0, respectively.[13]

Study Setting and Sampling

Forty-two of 243 health states plus unconscious were selected for interview as recommended by the previous studies (Table 1).[3,4] Because a respondent cannot value 43 health states in an interview session, 40 of these states were divided into 5 groups, and the remaining 3 states (including unconscious) were added into all groups, making 11 states to be evaluated by each interview group. Assuming 170 respondents were required to evaluate each group of health states[16] and adding 20 persons for the pilot study, 870 people were selected for interview.

Eight hundred seventy adults aged ≥18 and over were interviewed in Tehran (Iran's capital) from July to November 2013. The Iran Statistics Center approach was used to select 87 blocks from 22 Tehran districts. About 15% of the Iran population lives in Tehran, so the Tehran population includes the complete variety of Iran ethnic groups and races that can be considered representative for Iran. Then in each block, 10 houses (870 households) were randomly selected for interview. The number of blocks selected in each district was proportionate to the population of that district. Participants were interviewed face-to-face at their usual residence by trained interviewers. Households unwilling to participate in the study were replaced by new households.

Interview Procedure and TTO Protocol

Participants completed a questionnaire that contained information about their age, sex, marital status, educational status, living conditions, working status, and smoking status in addition to self-reported EQ-5D questions to collect data about the 5 domains of their health state and a VAS question to directly report their HRQL.[3,13] Then the TTO exercise was conducted for a set of selected health states (Table 1). During the process of the interview, each respondent valued a set of 11 health states; finally, a total of 43 health states were valued.

For valuing the health states that were considered better than death, the TTO method was conducted to identify the respondent equivalent value (t ≤ 10 years) for "10 years of life in a certain health state followed by death" compared with "living t ≤10 years in the full health state followed by death" (11111). For valuing the health states that were considered worse than death, the TTO method was conducted to identify the respondent preferences about "10-t years of life in a certain health state followed by t < 10 years in the full health state, followed by death," compared with death. The TTO method was continued (the amount of t was changed) until the indifference point was identified for each selected health state.[3]

The TTO responses were obtained in 6-month intervals, allowing a range from 1 to -19. For consistency across measures, the responses to the TTO exercise were then linearly transformed by Dolan's transformation approach to obtain values between 1 and -1. For states "better than death," the TTO value (U[Hi]) was

Table 1 – Sets of health states valued by the respondents

Category	Set 1	Set 2	Set 3	Set 4	Set 5
Common	22222	22222	22222	22222	22222
	33333	33333	33333	33333	33333
	Unconscious	Unconscious	Unconscious	Unconscious	Unconscious
Very mild	11112	11121	11211	12111	21111
Mild	11122	11131	11113	11312	21222
	21312	12211	11133	21133	12121
				22121	22112
Moderate	13212	32331	13311	22122	12222
	21323	32211	12223	22331	21232
			32313		
Severe	33232	23232	23321	13332	22233
	22323	32223	32232	33321	33323
	23313	33212			

assessed with the following formula: $U(H_i) = t/10$, where t is the number of years in state 11111.

For states "worse than death," we used the following monotonic transformation:

$$V = \frac{-t}{10-t} \quad => U(H_i) = \frac{V}{1-V}$$

with t being the number of years in full health.[14]

Data Management and Statistical Analyses

Eight interviewers were trained to conduct the face-to-face interviews at the respondents' homes. The interviewers were affiliated with the Iranian Students Polling Agency and had at least a bachelor's degree. Two training workshops were conducted before the interviews. The workshops included a detailed review of the study protocol, a brief introduction to TTO method, TTO theoretical background, a rationale, and the EQ-5D–specific interviewer guide. Simulated interviews were conducted to acquaint interviewers with an interview session, reduce errors during interviews, and evaluate the interviewer's skills.

To assure the inter-rater reliability, 15% of the interviews were cross-examined by a second interviewer. Therefore, 140 respondents were reinterviewed by telephone to confirm the interview and to double-check the demographic characteristics, for example, age, household dimension, and occupational status. The interrater reliability score obtained was 85%. No monetary or non-monetary incentives were given to the respondents before or after the interview. Statistical analyses were conducted using STATA SE 11.0.

The study was approved by the ethics committees in the Tehran University of Medical Sciences. Participants signed a consent form before filling in the questionnaire.

Modeling

A total of 43 selected health states were valued during the interviews. Then appropriate modeling and analyses were used to identify HRQOL for 243 health states, from the values respondents gave to the 43 selected health states. The analyses were conducted at the individual level. The respondent score for each health state was checked against the estimated model to ensure the quality of each interview. Differences in personal preferences were explored by Breusch-Pagan test for heteroscedasticity.[17] A series of preliminary analyses were carried out to compare the simple generalized least-squares regressions with random (RE) or fixed-effects (FE) models. The generalized least-squares regression and RE models were used at the individual level based on the result of Hausman's test.

The dependent variable was computed as "1 minus observed TTO value" and ranged from 0 to 2, where a lower value corresponds to a higher utility. We explored the results of several models with a different set of independent variables that have been used previously[2-4,9,15,18,19] to find a regression model that best fitted our data. The models were tested and compared with each other according to the number of incoherent coefficients, statistical significance of coefficients, predictive ability of the goodness-of-fit such as overall R^2, and the mean absolute error (MAE). Various tests including MAE and Akaike information criterion were conducted to examine the assumptions made in the models.[20,21]

We reported the results of the model that satisfied all the criteria specified below, then compared the main results of this model, with the UK model[4] and the US model.[6] Subsequently, some variables were adopted to account for interactions between different dimensions in the Iranian model (hereafter called the final model).

Table 2 – Study sample characteristics in comparison with general population aged 18 or more

	Total sample (n = 869)	Iranian general population aged 18 or more*
Sex, n (%)		
Male	480 (55.24)	42 407 049 (50.48)
Female	389 (44.76)	41 585 166 (49.52)
Age, n (%)		
18-24	176 (20.25)	11 275 668 (20.94)
25-34	246 (28.31)	15 644 578 (29.05)
35-44	166 (19.10)	10 477 767 (19.46)
45-54	147 (16.92)	7 557 889 (14.03)
55-64	87 (10.01)	4 543 026 (8.43)
65+	47 (5.41)	4 343 091 (7.98)
Mean (SD)	38.16 (14.73)	29.86 (NA)
Number of years of education, n (%)		NA
Low (<10)	186 (21.45)	
Middle (10-13)	317 (36.56)	
High (14+)	364 (41.98)	
Average household size, n (%)		
1-2 elements	148 (17.03)	5 402 339 (25.5)
3-4 elements	544 (62.60)	11 313 136 (53.4)
5 or more elements	177 (20.37)	4 470 172 (21.1)
Mean (SD)	3.71 (1.31)	3.55 (NA)
EQ-5D questionnaire any problems, n (%)		NA
Mobility (MO)	94 (10.82)	
Self-care (SC)	11 (1.27)	
Usual activities (UA)	35 (4.03)	
Pain/discomfort (PD)	299 (34.41)	
Anxiety/depression (AD)	290 (33.37)	
EQ-VAS own health		
Mean (SD)	79.49 (16.01)	

EQ indicates EuroQol; NA, not available; SD, standard deviation; VAS, visual analog scale.
* Source: National Statistical Center, The Islamic Republic of Iran, 2012.

The regression equation for modeling was as follows:

$$y = \alpha + \sum_{d}\sum_{l}\beta_{dl}X_{dl} + e$$

where y is 1 minus value; X_{dl} represents the 10 dummy variables, which indicate the presence of either a level 2 or 3 in a given dimension; and *d* stands for the dimensions and l for either level 2 or 3. The dependent variable (y) in the regression analysis is computed as 1 minus the transformed TTO value. It represents the measure of disutility by subtracting the value of a given health state from the value of full health. As a result, the predicted value for state 11111 is equal to 1.[9]

The model included the following variables:

- two dummy variables for level 2 and level 3 in each dimension
- a dummy N2, for any dimension that is either at level 2 or level 3 (any move away from full health)
- a dummy N3 for the presence of 1 or more dimensions on level 3
- an ordinal variable D1 that represented number of movements away from full health beyond the first (ie, it took on values ranging from 0 to 4)
- an ordinal variable I3 that represents number of dimensions at level 3 beyond the first

- the square of the I3 term to allow for nonlinearity in its association with the dependent variable
- the square of I2, an ordinal variable that represents number of dimensions at level 2 beyond the first[4,6,9,22]

Exclusion Criteria

Respondents were excluded from the dataset when they satisfied the following criteria:

- completely missing TTO data
- less than 4 health states valued
- all states given the same value
- all states valued as "worse than death"
- more than 1 logical inconsistency[4,6,7,19,23,24]

The logical consistency approach was applied to examine the quality of data. The logical consistency is defined as: "for a given pair of health states, if state A of a pair is better than the state B in at least 1 dimension and not worse in any other, then the valuation for the former state (TTO_A) must be at least as good as the valuation for the latter state (TTO_B)."[3,13] In a situation where this rule is breached, the logical inconsistency occurs. For instance, if state 11122 is valued higher than state 11121, this is logically inconsistent.

Results

A total of 869 interviews were completed. Twenty-three interviews were excluded because they had logical inconsistencies (9 interviews), gave the same value for all states (9 interviews), and valued less than 4 health states (5 interviews). Finally, 846 respondents were included in the analysis. The interviews lasted 25 minutes on average. Demographic characteristics of the study sample are presented in Table 2.

Pain or discomfort was the most common type of health problem (34.41%) followed by anxiety or depression (33.37%), mobility (10.82%), usual activities (4.03%), and self-care (1.27%). The mean value for the VAS of EQ-5D was 79.58 (standard error = 0.54).

After the transformation to the lower bound of -1, the mean values for the 42 valued health states ranged from 0.934 for state 11121 to -0.142 for state 33333. The mean value for the "unconscious" states was 0.156 (SD = 0.36).

The final model presented in Table 3 is suggested as the best fitted Iranian societal tariff for the EQ-5D-3L. All parameters in this model were statistically significant. In addition, based on the Hausman test, the fixed-effects specifications were not presented as the estimates of the RE models that were consistent with the study sample.

Because the Breusch and Pagan Lagrangian multiplier test was significant (Prob = 0.0001), the null hypothesis was rejected and the RE could be safely estimated. The goodness-of-fit statistics were satisfactory and quite similar to the 4 models. The MAE was around 0.214 for the final model, which was less than the first Measurement and Valuation of Health study in the UK (0.245).[4] The R2 was estimated equal to 0.45 in this study, which is not unusual in cross-sectional studies. Because it is specified in the base studies, this parameter was equal to 0.38 in the US (page 74), 0.46 in UK (page 71), 0.40 in Japan, (Page 64), and 0.38 in Netherlands (page 66) studies.[13]

The results obtained from goodness-of-fit statistics of the main effect model were approximately similar compared to the results of N3, D1, and final models. All main coefficients of the final model were statistically significant and logically in order with I3 terms positive.

The mathematical representation of the final model for the utility value of each health state (H_i) is:

$$U(Hi) = 1 - 0.081 - 0.093\,MO2 - 0.220\,MO3 - 0.103\,SC2 - 0.235\,SC3 - 0.085\,UA2 - 0.127\,UA3 - 0.075\,PD2 - 0.149\,PD3 - 0.098\,AD2 - 0.205\,AD3 - 0.024\,I3$$

For example, we calculated the predicted values of state 13232 as follows:

Predicted values = full health − disutility

Full health = 1.000

$$\text{Disutility for 13232 state} = 0.081 + 0.235\,(SC3) + 0.085\,(UA2) + 0.149\,(PD3) + 0.098\,(AD2) + 0.024\,(I3) = 0.672.$$

Predicted values = 1 − 0.672 = 0.328

With the same transformation method for a state "worse than death" and model specification, estimates for dummies representing the differences between level 1 and level 2 (MO2, SC2, UA2, PD2, AD2) were lower than the difference between level 1 and level 3. The respondents gave the greatest importance to the self-care and mobility dimensions. The disutility of being in level 3 in 1 of these 2 dimensions was greater than the disutility of being in any level of the other dimensions.

Comparison of the valuation from different utility of selected EQ-5D-3L health states across TTO-based surveys is presented in Figure 1. In comparison with other studies, the value set obtained from our final model was highly correlated with the official value sets in the UK ($r = 0.924$, $P < 0.0001$), the United States ($r = 0.989$, $P < .0001$), Japan ($r = 0.969$, $P < .0001$), and Portugal ($r = 0.924$, $P < .0001$), respectively.[4,6,7,16] We selected these countries because the value sets that we used as a benchmark for comparison were similar to value sets of these countries.

Discussion

This was the first study to provide a population-based value set for health states in the Eastern Mediterranean region. For identifying the value sets, we relied on a sample of the Iranian urban population.[25] This sample might not be fully representative of the entire Iranian adult population; but because around 15% of the total population from a wide range of races, ethnic groups, and socioeconomic status live in Tehran, the sample is assumed to be highly representative.

Considering the caution for comparing the value sets among countries,[26] our TTO value set showed a general trend toward higher values compared with the UK, US, and Portugal TTO value sets.[4,6,16] This has been shown by statistically significant coefficients derived from the Wald test. At level 3, the dimension receiving the highest coefficient was self-care, indicating the largest contribution in worsening the health state. This dimension is followed by mobility, anxiety or depression, pain or discomfort, and usual activity. The order of these coefficients also differed from the UK, the United States, and Japan,[4,6,7] although the overall value set showed a trend similar to these countries.

In the TTO method, the personal surveillance dimension had the highest weight between EQ-5D-3L dimensions, whereas a study in Iran using the VAS method indicated that the highest weight was related to anxiety.[27]

Self-care had the highest weight in this study, whereas in most reports from other countries, mobility had the highest weight.[6,8,9,12,15,16,18,26,28-32] Nevertheless, in our study the self-care

Table 3 – Parameter estimates and fit statistics of individual's level models using GLS regression and random effects models

	GLS/Random Effect							
	Main effects model		UK model (N3)		US model (D1)		Final model	
	β	SE	β	SE	β	SE	β	SE
MO2	0.093	0.006	0.093	0.006	0.092	0.008	0.093	0.006
MO3	0.242	0.008	0.244	0.008	0.280	0.013	0.220	0.012
SC2	0.107	0.007	0.103	0.007	0.106	0.008	0.103	0.007
SC3	0.259	0.008	0.259	0.008	0.299	0.013	0.235	0.012
UA2	0.078	0.008	0.085	0.008	0.065	0.009	0.085	0.008
UA3	0.140	0.008	0.151	0.009	0.172	0.010	0.127	0.009
PD2	0.079	0.006	0.075	0.006	0.071	0.008	0.075	0.006
PD3	0.168	0.007	0.173	0.007	0.201	0.011	0.149	0.010
AD2	0.099	0.007	0.098	0.007	0.076	0.009	0.098	0.007
AD3	0.222	0.007	0.229	0.008	0.239	0.010	0.205	0.010
Constant (N2)	0.073	0.009	0.081	0.010	0.080	0.011	0.081	0.010
N3			−0.024	0.009				
D1					Omitted			
I3					−0.101	0.015	0.024	0.009
I2square					0.004	0.001		
I3square					0.018	0.002		
Goodness-of-fit statistics								
R^2	0.450		0.452		0.453		0.452	
MAE	0.213		0.214		0.215		0.214	
AIC	0.541		0.539		0.518		0.539	

Note. The intercept is a measure of any shift away from perfect health (11111). The dummy independent variables are MO2 (1 if mobility level = 2, 0 otherwise); MO3 (1 if mobility level = 3, 0 otherwise); SC2 (1 if self-care level = 2, 0 otherwise); SC3 (1 if self-care level = 3, 0 otherwise); UA2 (1 if usual activities level = 2, 0 otherwise); UA3 (1 if usual activities level = 3, 0 otherwise); PD2 (1 if pain/discomfort level = 2, 0 otherwise); PD3 (1 if pain/discomfort level = 3, 0 otherwise); AD2 (1 if anxiety/depression level = 2, 0 otherwise); AD3 (1 if anxiety/depression level = 3, 0 otherwise); N2 = 1 if any dimension is at either level 2 or level 3, N3 (1 if any dimension is at level 3; 0 otherwise). The ordinal independent variables are D1 (number of dimensions at level 2 or level 3 beyond the first, ranging from 0 to 4); I3 (number of dimensions at level 3 beyond the first, ranging from 0 to 4), I3sq (square of I3), and I2sq (square of the number of dimensions at level 2 beyond the first).
All parameters statistically significant (P <.05).
AIC indicates Akaike information criterion; GLS, generalized least-squares; MAE, mean absolute error; SE, standard error; TTO, time trade-off.

value was also close to the value of mobility. Usual activities had the lowest weight in the social valuation of EQ-5D-3L health state. Evidence reported by Xie et al also shows that in most countries, usual activities has the lowest weight.[33]

This EQ-5D-3L valuation study differed in several aspects from the original UK Measurement and Valuation of Health protocol, which can be partly due to the cultural norms and religious beliefs. For example, a proportion of the study population might believe that health problems are a means to absorb God or are

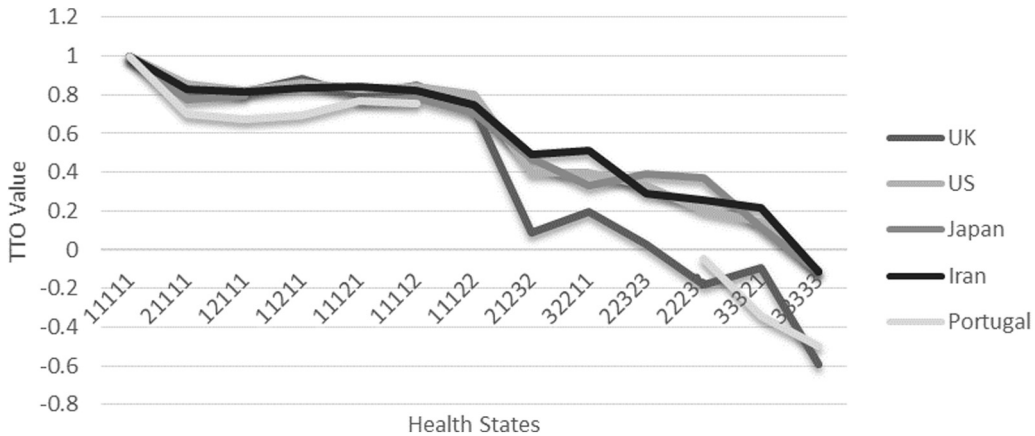

Fig. 1 – Comparison of the valuation from different utility of selected EuroQol 5-dimesion (EQ-5D) health states across TTO-based surveys.

even God's justice and therefore a means to overcome sins. Therefore, they might give lighter value to health problems compared with the nonreligious or unspiritual population. In Iran, the death scenario owing to religious beliefs might be more valuable than some severe or moderate scenarios.

Our sample size was larger than the sample size of studies in Japan,[7] Portugal,[16] Australia,[15] Italy,[34] France,[26] and The Netherlands.[35] The sample size seems sufficient to obtain statistically significant coefficients with 95% confidence intervals. The representativeness of the sample was controlled with respect to 2 characteristics—age and sex—through quotas.[25] Our study sample was, therefore, representative for age, sex, and geographical distribution, but we are not able to judge the representativeness of the sample for other characteristics.

We found that age had a statistically significant negative effect on the TTO values. The TTO values were higher in people with higher education and were lower in smokers, whereas the coefficients for sex, hospitalization, marital status, and other socioeconomic parameters did not reveal any statistically significant differences.

Conclusion

This study determined for the first time the weights for EQ-5D-3L health states using a standard TTO method in the general population of the Iran capital. The final values derived by this study differed from the value sets observed in the United States and UK, but the model fit was very similar. Therefore, economic evaluations using the EQ-5D-3L values from other countries may provide inaccurate estimates in Iran. The final model suggested by this study is culturally and socioeconomically adapted for the Iranian population; therefore, it provides a more accurate base for the economic evaluation of healthcare interventions in Iran. Researchers are encouraged to apply these local values when using the EQ-5D-3L questionnaire to calculate QALYs based on Iranian preferences.

Acknowledgments

Source of financial support: This study was funded by Knowledge Utilization Research Center (KURC) of Tehran University of Medical Sciences (grant number 117591).

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