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Health-Related Quality of Life and Willingness to Pay per Quality-Adjusted Life-Year Threshold—A Study in Patients with Epilepsy in China

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ABSTRACT

Objectives: To assess the health-related quality of life (HRQOL) and willingness to pay (WTP) per quality-adjusted life-year (QALY) amount of patients with epilepsy in China. **Methods:** Adults with epilepsy and a healthy control were recruited in two tertiary hospitals in China. Participants completed two indirect utility elicitation instruments (Quality of Well-being Scale-self administered version and EuroQol five-dimensional questionnaire) and a WTP questionnaire. Correlations between sociodemographic or epilepsy-specific variables (age of epilepsy onset, duration of epilepsy, seizure types, types of antiepileptic drug treatment, etc.) and HRQOL or WTP/QALY were assessed to identify the candidate predictor. Multiple linear regression models were adopted to investigate the predictive performances of identified candidate predictors. Data analyses were performed on SPSS 20.0 (SPSS, Inc., Chicago, IL). **Results:** For utilities of both the Quality of Well-being Scale-self administered version and the EuroQol five-dimensional questionnaire, patients with epilepsy had statistically lower values than did the control group ($P < 0.0001$). In terms of the WTP/month, the percentage of WTP accounting for the monthly income and the WTP/QALY values from the epilepsy group were substantially higher than those from the control group ($P < 0.0001$).

$$\text{WTP/QALY} = \frac{12 \times \frac{\text{WTP}}{\text{Month}}}{1 - \text{Utility (Current Health)}}$$

The multiple linear regression model identified working status ($P = 0.05$), seizure types ($P = 0.022$), income ($P = 0.006$), and self-rating health state ($P < 0.05$) as predictors of HRQOL while income ($P = 0.000$) and self-rating health state ($P < 0.05$) statistically contributed to the variations in WTP/QALY value for the epilepsy group. **Conclusions:** Patients with epilepsy had substantially lower HRQOL than did the healthy population.

Keywords: China, cost-effectiveness analysis, epilepsy, health-related quality of life, willingness to pay.

Introduction

Epilepsy, as a chronic disorder, has considerable negative impact on people's day-to-day functioning [1], including impact on cognitive function, self-esteem, and excessive psychological burden (e.g., depression and anxiety) [2–4]. Meanwhile, epilepsy is also well recognized to pose a heavy economic burden on the society and the individual, as indicated in many cost-of-illness studies [5–10]. Although the health-related quality of life (HRQOL) of patients with epilepsy, however, has been investigated in a series of studies, most of these studies were performed in developed countries. Within the developing countries, the relatively few studies that unanimously adopted epilepsy-specific or generic non–preference-based instruments (e.g., Quality of Life in Epilepsy Inventory-89 (QOLIE-89, QOLIE-31, short-form 36 health survey, and WHO Quality of Life-BREF (WHOQOL-BREF) to assess the HRQOL [11–15], from those measures, consequently, cannot be integrated into cost-effectiveness analysis.

In contrast, the Quality of Well-being Scale-self-administered version (QWB-SA) and the EuroQol five-dimensional questionnaire (EQ-5D) are generic preference-based instruments that could estimate the quality-adjusted life-years (QALYs). QALY provides a common currency to assess the extent of benefits gained from various interventions, thus allowing comparison of the effectiveness of health technologies for different diseases.

Furthermore, to make any health resource allocation nowadays, it is necessary to go beyond assessing just the effectiveness of the new drug or the health technology and perform a cost-effectiveness

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or cost-utility analysis. A cost-effectiveness or cost-utility analysis estimates the incremental cost-effectiveness ratio (ICER) by comparisons between two interventions. Common decision rules indicate that an intervention is "good value for money" if the ICER falls below a certain cost-effectiveness threshold. The chosen threshold reflects the acceptable value of a health gain within a specific decision-making context. In practice, many economic evaluations adopted 1 to 3 times of the specific country's gross domestic product per capita as the willingness-to-pay (WTP) per QALY threshold according to the recommendation by the World Health Organization (WHO) [16].

Another popular approach used to define the cost-effectiveness threshold is through the use of contingent valuation. Despite its popularity, there are issues with the obtained WTP estimates. First, the estimates obtained can vary substantially by the elicitation method used (e.g., ex post and ex ante perspectives can create different WTP values). Second, it is important that the WTP estimates obtained are relevant to the decision-making context. Nevertheless, in spite of these issues, WTP studies could provide valuable information to policymakers on the magnitude of individuals' preferences and may better reflect societal value [17].

Moreover, rather than using decision rules such as league tables or the ICER threshold value recommended by the WHO, it may be more reasonable to allocate health care resources on the basis of the societal WTP for health care benefits [18]. This is particularly important for developing countries, including China, because the threshold value recommended by the WHO may be overestimating the WTP values. So, we believe that it might overestimate the true WTP value in China. Adopting these recommendations would therefore likely lead to inappropriate decision making. Hence, investigations on the societal WTP threshold for health care benefits should be a "research priority" [19].

Unfortunately, there is a paucity of this type of studies, particularly in developing countries. Nevertheless, a WTP/QALY threshold study was conducted recently in China by Zhao et al. [20] on patients with chronic prostatitis by measuring the utility (measured by the EQ-5D and the six-dimensional health state short form [derived from SF-36]) and the WTP simultaneously. In that study, based on the indirect preference elicitation method (using the EQ-5D and the six-dimensional health state short form [derived from SF-36]), the WTP/QALY value was successfully elicited for both chronic prostatitis and general populations, with a higher WTP/QALY value in the chronic prostatitis group. In addition, the reported values were close to the lower bound of the WHO-recommended WTP/QALY threshold, but the authors suggested that the type of disease may have an impact on the threshold value.

When it comes to the management of epilepsy, in view of extreme limited access to advanced antiepileptic treatments, due to constraints in health care resources, patients with epilepsy in China (and in this case also other developing countries) might experience more problems than do their Western counterparts. There is a strong rationale for assessing their HRQOL to evaluate the impact of their antiepileptic treatment.

At the same time, we attempted to value the QALY by using the WTP approach in patients with epilepsy and compare their HRQOL and WTP/QALY values with those of the general population. To our knowledge, the empirical WTP/QALY threshold estimations are available only in two Asian countries (one was for the general population only and the other was for both chronic prostatitis and general populations) [20,21] and there is only one study that investigated the WTP value for patients with epilepsy from Norway [22]. Because the WTP/QALY threshold plays a significant role in health care resource allocation, our study would contribute to the resolution of some of the controversies in the determination of an ICER threshold value, especially in countries/regions with less developed economic status.

Methods

Subjects

The cross-sectional study recruited participants between July and October 2012 from two tertiary hospitals in China with specific Institutional Ethics Review Board approval: Renmin Hospital of Wuhan University and the Fifth Hospital of Wuhan (Wuhan, Hubei, China). After informed consent was received from each adult participant, a convenient sample of inpatients or outpatients with diagnosis of epilepsy and a control group (without manifestation of cognitive problems) were recruited. Healthy controls were primarily from the relatives of the patients with epilepsy, medical students, interns, and hospital general staff and were blind to the study design. We do not think that it will bias the result. Each subject was interviewed by a trained interviewer using standardized questionnaires containing the QWB-SA, the EQ-5D/visual analogue scale (VAS), and the WTP questionnaire.

Instruments

QWB-SA

The QWB-SA assesses the presence/absence of symptoms or problems, persons' mobility, physical activity, and social activity. Each participant recalls the answers to particular QWB-SA question within the last 3 days. The preference weights were derived from a community sample [23]. The scoring algorithm and preference weights were provided by the University of California, San Diego Health Services Research Center. The use of the QWB-SA in our study was authorized by the QWB-SA copyright owner, and the validity of Chinese-language QWB-SA was reported by our study group previously [24].

EQ-5D/VAS

The EQ-5D comprises five dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The utility scoring algorithm adopted in our study was developed using time trade-off (TTO)-based preference scores [25] from a UK general population [26]. The EQ-VAS is a 20-cm vertical VAS ranging from 100 (best imaginable health state) to 0 (worst imaginable health state) to represent the overall health of the day.

The WTP questionnaire

The contingent valuation method was adopted to elicit the WTP value. A respondent would be provided with an initial bid and asked whether he or she would like to pay this amount of money on a monthly basis to move from his or her current health state to a perfect health state. If subjects answered positively (negatively), the amount was increased (decreased) by the specified amount. The maximum bidding amount offered would be dependent on respondent's monthly income (maximum price permitted for the close-ended iterative bidding was 10 times the subject's own monthly income) [18]. If the respondent was willing to pay less than the minimum offered bid or higher than the maximum offered bid, his or her WTP amount was determined using open-ended questions. Besides, each respondent would be reminded that the payment cannot be covered by the health care insurance and would reduce the amount of money that could be used in other ways before he or she responds to the bidding game question. To minimize the starting bid bias, five initial bids of US $139, US $224, US $300, US $399, and US $689, representing low, low to middle, middle, middle to high, and high average monthly income in China, were randomly assigned to respondents (National Bureau of Statistics of China, 2012, exchange rate US

$1 = 6.2353 CNY, December 2012) (see Appendix-WTP questionnaire in Supplemental Materials found at http://dx.doi.org/10.1016/j.vhri.2015.03.019) [27].

Data Analyses

HRQOL

Continuous variables were presented by mean, SD/standard error, median, interquartile range, and range where applicable, whereas categorical variables were presented by the number and proportion of the entire sample in the corresponding group. Differences between epilepsy and control groups were assessed by using independent-sample analysis of variance (if the distribution was normal) or the Manny-Whitney *U* test (if the distribution was skewed) n case of continuous variables and the chi-square test in case of categorical variables. Correlations between sociodemographic or epilepsy-specific variables and HRQOL utility scores were assessed via Spearman's correlation coefficient with *P*-value less than 0.1 to identify candidate predictors.

Multiple linear regression (MLR) analysis was performed to investigate the associations between sociodemographic or epilepsy-specific variables (that were significantly correlated with HRQOL as identified by Spearman's correlation tests) and HRQOL utility scores.

WTP/QALY

Analyses were based on subjects who fully completed the questionnaire. Continuous variables were compared using the Mann-Whitney *U* test, and chi-square tests were used to compare the categorical variables. The WTP/QALY ratio for each participant was computed through the following formula:

$$\text{WTP/QALY} = \frac{12 \times \frac{\text{WTP}}{\text{Month}}}{1 - \text{Utility (Current Health)}}$$

Because only 1-year payment was captured, life expectancy and discount rate were not considered. Because of the arithmetic attribute (denominator is zero) of the formula, subjects with perfect health states (defined as utility of 1) were excluded from the WTP/QALY computation regardless of the groups they belonged to. Differences in WTP/QALY values between epilepsy and control groups were compared by using the Mann-Whitney *U* test.

Correlations between sociodemographic or epilepsy-specific variables and WTP/QALY value were assessed via Spearman's correlation coefficient with *P*-value less than 0.1 to identify candidate predictors. In addition, MLR analysis was undertaken to assess associations between sociodemographic or epilepsy-specific variables (that were significantly correlated with the WTP/QALY value according to the Spearman's correlation coefficients) and the WTP/QALY value. To allow for better interpretation, the monthly income was grouped into four categories, US $224 or less (low), US $225 to 300 (lower-middle), US $301 to 689 (upper-middle), and US $ 700 or more (high) [27].

The following variables were considered potential factors: sociodemographic: sex, marital status, age, and working status; epilepsy-specific: age of epilepsy onset, duration of epilepsy, seizure types (partial seizures and generalized seizures), seizure frequency, current antiepileptic drugs (monotherapy vs. polytherapy), refractory epilepsy, epileptic discharges (electroencephalogram), positive lesions on brain computed tomography/magnetic resonance imaging, brain trauma/disease, and brain surgery history. All significant categorical variables (e.g., marital status and diagnosis) were grouped by dummy variables if they were selected in the MLR analysis.

All data analyses were performed using SPSS 20.0 (SPSS, Inc., Chicago, IL).

Results

Participants

Overall, 144 patients with epilepsy and 312 healthy controls completed the QWB-SA and the EQ-5D. Among these, 41 participants in the control group failed to complete the WTP questionnaire, 25 subjects in the control group reported perfect health state on the QWB-SA, and 59 patients with epilepsy and 164 controls reported full utility on the EQ-5D; thus, they were excluded from corresponding analyses.

Demographic Variables

There were statistically significant differences between epilepsy and control groups in terms of age ($P = 0.033$), sex ($P < 0.0001$), working status ($P = 0.029$) (employed vs. unemployed), education ($P < 0.0001$), and monthly income ($P < 0.0001$) (Table 1).

Description Statistics of the QWB-SA and the EQ-5D

Utility scores for both the QWB-SA and the EQ-5D were significantly different between epilepsy and healthy control groups ($P < 0.0001$), whereas the EQ-VAS did not show a difference between the two groups ($P = 0.052$). Two of the four sections of the QWB-SA, namely, CPX ($P < 0.0001$) and SAC ($P < 0.0001$), were significantly different between epilepsy and control groups, with patients with epilepsy tending to experience more problems in these two sections (Table 1).

Description Statistics of WTP/Month, and WTP/QALY

Among subjects with completed WTP questionnaire, patients with epilepsy reported lower utility scores on both the QWB-SA and the EQ-5D than did the control group ($P < 0.0001$). In terms of the WTP/month and WTP as percentage of the monthly income, values from the epilepsy group were substantially higher than those from the control group (both with $P < 0.0001$). Likewise, the WTP/QALY value showed the same trend. The epilepsy group provided a $\text{WTP/QALY}_{\text{QWB-SA}}$ value (median [interquartile range]) of US $ 8799 (10,570), whereas the control group generated a value of US $1740 (4524) ($P < 0.0001$). In addition, when the EQ-5D was adopted as the utility measure, the same tendency was shown accompanied by an even higher $\text{WTP/QALY}_{\text{EQ-5D}}$ value in the two groups (US $ 9446 [12, 843] vs. 2917 [5700]; $P < 0.0001$) (Table 2).

The starting bid might introduce a bias to the final result, and to address this, the Kruskal-Wallis *H* test was undertaken to assess differences in the WTP value for the five starting bids. The results indicated that there was no significant influence on the final WTP value from the different initial bids.

Relationships between Sociodemographic or Epilepsy-Specific Variables and HRQOL

For the epilepsy group, age (−0.260, $P = 0.002$), marital status (0.188, $P = 0.024$), working status (0.213, $P = 0.010$), seizure types (−0.138, $P = 0.098$), age of epilepsy onset (−0.190, $P = 0.023$), refractory epilepsy (−0.220, $P = 0.008$), seizure frequency (−0.178, $P = -0.033$), monthly income (0.296, $P < 0.001$), QWB-SA self-rating health state (−0.525, $P < 0.001$), and the EQ-VAS (0.475, $P < 0.001$) were found to be positively or negatively correlated with utility scores of the QWB-SA according to Spearman's correlation coefficients, whereas age (−0.254, $P = 0.002$), marital status (0.174, $P = 0.037$), working status (0.282, $P = 0.001$), seizure types (−0.165, $P = 0.048$), age of epilepsy onset (−0.175, $P = 0.036$), brain trauma/disease (−0.137, $P = 0.101$), brain surgery history (−0.152, $P = 0.070$), QWB-SA self-rating health state (−0.441, $P < 0.001$), and

Table 1 – Characteristics and HRQOL results of patients with epilepsy and the control population.

Characteristic	Epilepsy (n = 144)	Simple partial (n = 7)	Complex partial (n = 83)	Secondary generalized (n = 50)	Tonic-clonic generalized (n = 4)	Control (n = 312)
Age (y), mean ± SD	33.11 ± 13.044	27.43 ± 12.040	33.95 ± 12.930	31.66 ± 12.847	43.75 ± 16.540	34.52 ± 15.662
16–29	68 (47.2)	5 (71.4)	36 (43.4)	26 (52.0)	1 (25)	144 (46.2)
30–39	31 (21.5)	0	20 (24.1)	10 (20.0)	1 (25)	36 (11.5)
40–49	28 (19.4)	2 (28.6)	16 (19.3)	10 (20.0)	0 (0)	54 (17.3)
50–59	11 (7.6)	0	9 (10.8)	1 (2.0)	1 (25)	47 (15.1)
≥60	6 (4.2)	0	2 (2.4)	3 (6.0)	1 (25)	31 (9.9)
Sex: male (%)	52.1	0	57.8	48.0	75.0	38.8
Han ethnicity	142 (98.6)	7 (100.0)	82 (98.8)	49 (98.0)	4 (100.0)	308 (98.7)
Education (y), mean ± SD	10.56 ± 2.961	10.00 ± 3.162	10.41 ± 2.745	11.02 ± 3.298	9.00 ± 2.449	13.16 ± 2.871
≤6	16 (11.1)	1 (14.3)	7 (8.4)	7 (14.0)	1 (25.0)	16 (5.1)
7–12	106 (73.6)	5 (71.4)	66 (79.5)	32 (64.0)	3 (75.0)	139 (44.6)
>12	22 (15.3)	1 (14.3)	10 (12.0)	11 (22.0)	0	157 (50.3)
Marital status						
Unmarried	71 (49.3)	4 (57.1)	42 (50.6)	24 (48.0)	1 (25.0)	123 (39.4)
Married	70 (48.6)	2 (28.6)	40 (48.2)	25 (50.0)	3 (75.0)	184 (59.0)
Divorced	2 (1.4)	1 (14.3)	1 (1.2)	0	0	2 (0.6)
Widow/widower	1 (0.7)	0	0	1 (2.0)	0	3 (1.0)
Working status						
Employed	65 (45.1)	4 (57.1)	37 (44.6)	22 (44.0)	2 (50.0)	175 (56.1)
Unemployed	69 (54.9)	3 (42.9)	46 (55.4)	28 (56.0)	2 (50.0)	137 (43.9)
Age of onset (y), mean ± SD	23.22 ± 14.726	19.43 ± 11.688	24.90 ± 14.396	20.12 ± 14.553	33.50 ± 22.927	–
Duration (y), mean ± SD	9.64 ± 9.142	8.86 ± 11.393	8.80 ± 7.852	11.11 ± 10.710	10.25 ± 10.404	–
Brain trauma/disease (%)	31.94 (n = 46)	42.86 (n = 3)	30.12 (n = 25)	32.00 (n = 16)	50.00 (n = 2)	–
Brain surgery (%)	15.28 (n = 22)	14.29 (n = 1)	16.87 (n = 14)	12.00 (n = 6)	25.00 (n = 1)	–
Head CT/MRI (%)	30.56 (n = 44)	14.29 (n = 1)	33.73 (n = 28)	26.00 (n = 13)	50.00 (n = 2)	–
EEG (%)	43.06 (n = 62)	71.43 (n = 5)	39.76 (n = 33)	42.00 (n = 21)	75.00 (n = 3)	–
Refractory epilepsy (%)	25.69 (n = 37)	14.29 (n = 1)	25.30 (n = 21)	28.00 (n = 14)	25.00 (n = 1)	–
Seizure frequency (%)						
Daily	3.47 (n = 5)	0 (n = 0)	3.61 (n = 3)	4.00 (n = 2)	0 (n = 0)	–
Weekly	11.81 (n = 17)	0 (n = 0)	8.43 (n = 7)	20.00 (n = 10)	0 (n = 0)	–
Monthly	29.17 (n = 42)	42.86 (n = 3)	22.89 (n = 19)	36.00 (n = 18)	50.00 (n = 2)	–
Bimonthly	10.42 (n = 15)	0 (n = 0)	9.64 (n = 8)	12.00 (n = 6)	25.00 (n = 1)	–
Quarterly	21.53 (n = 31)	0 (n = 0)	31.33 (n = 26)	10.00 (n = 5)	0 (n = 0)	–
Half-yearly	9.03 (n = 13)	28.57 (n = 2)	10.84 (n = 9)	4.00 (n = 4)	0 (n = 0)	–
Yearly	10.42 (n = 15)	28.57 (n = 2)	10.84 (n = 9)	6.00 (n = 3)	25.00 (n = 1)	–
More than yearly	4.17 (n = 6)	0 (n = 0)	2.41 (n = 2)	8.00 (n = 4)	0 (n = 0)	–
QWB-SA						
Mean ± SD	0.657 ± 0.135	0.681 ± 0.146	0.636 ± 0.135	0.687 ± 0.127	0.671 ± 0.174	0.802 ± 0.155
Median ± IQR	0.673 ± 0.172	0.744 ± 0.216	0.673 ± 0.134	0.676 ± 0.133	0.707 ± 0.321	1.000 ± 0.152

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QWB-SA self-rating health status						
Excellent	2 (1.4)	0	1 (1.2)	1 (2.0)	0	37 (11.5)
Very good	26 (18.1)	0	14 (16.9)	12 (24.0)	0	86 (26.6)
Good	53 (36.8)	5 (71.4)	28 (33.7)	17 (34.0)	3 (75.0)	94 (29.1)
Fair	56 (38.9)	2 (28.6)	36 (43.4)	17 (34.0)	1 (25.0)	98 (30.3)
Poor	7 (4.9)	0	4 (4.8)	3 (6.0)	0	8 (2.5)
EQ-5D						
Mean ± SD	0.828 ± 0.206	0.890 ± 0.148	0.798 ± 0.211	0.867 ± 0.203	0.854 ± 0.170	0.923 ± 0.132
Median ± IQR	0.848 ± 0.275	1.000 ± 0.275	0.848 ± 0.275	1.000 ± 0.204	0.863 ± 0.302	1.000 ± 0.152
EQ-VAS						
Mean ± SD	79.57 ± 16.419	74.43 ± 20.239	79.63 ± 16.835	79.80 ± 15.935	84.50 ± 6.403	82.64 ± 13.939
Median ± IQR	80.00 ± 20.00	69.00 ± 38.00	80.00 ± 20.00	80.00 ± 20.00	85.00 ± 11.50	85.00 ± 11.00
Income						
≤1500 (US $241)	9 (6.3)	0	4 (4.8)	4 (8.0)	1 (25.0)	0
1501–2000 (US $241–321)	25 (17.4)	2 (28.6)	17 (20.5)	5 (10.0)	1 (25.0)	4 (1.6)
2001–3000 (US $321–482)	43 (29.9)	1 (14.3)	24 (28.9)	17 (34.0)	1 (25.0)	83 (33.7)
3001–4000 (US $482–643)	44 (30.6)	3 (42.9)	24 (28.9)	16 (32.0)	1 (25.0)	113 (45.9)
4001–5000 (US $643–803)	12 (8.3)	1 (14.3)	8 (9.6)	3 (6.0)	0	43 (17.5)
≥5000 (US $803)	11 (7.6)	0	6 (7.2)	5 (10.0)	0	3 (1.2)

CT, computed tomography; EEG, electroencephalogram; EQ-5D, EuroQol five-dimensional questionnaire; HRQOL, health-related quality of life; IQR, interquartile range; MRI, magnetic resonance imaging; QWB-SA, Quality of Well-being Scale-self administered version; VAS, visual analogue scale.

Table 2 – Utilities, WTP/mo, and WTP/QALY values (Median [IQR]).

Variable	Utility and WTP			N	WTP/QALY			
	Epilepsy	Control	P-value		Epilepsy	N	Control	P-value
Total	N = 144	N = 271						
QWB-SA	0.673 (0.172)	0.775 (0.258)	<0.0001	144	8,799.265(10,570.02)	246	1740.388(4523.505)	<0.0001
EQ-5D	0.848 (0.275)	1.000 (0.152)	<0.0001	85	9,446.073(12,843.369)	107	2916.54(5700.217)	<0.0001
WTP/mo	241.014 (184.777)	48.203 (160.676)	<0.0001	/	/	/	/	/
Percentage	0.465 (0.267)	0.100 (0.267)	<0.0001	/	/	/	/	/

Note. Money was presented as US $; US $1 = 6.2237 CNY (January 2013). Percentage calculated via WTP/mo divided by monthly income.
EQ-5D, EuroQol five-dimensional questionnaire; IQR, interquartile range; QALY, quality-adjusted life-years; QWB-SA, Quality of Well-being Scale-self administered version; WTP, willingness to pay.

the EQ-VAS (0.538, $P < 0.001$) were shown to be associated with utility scores of the EQ-5D (see Appendix Table 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.vhri.2015.03.019).

For the control group, utility scores of both the QWB-SA and the EQ-5D were significantly correlated with age, marital status, education, QWB-SA self-rating health state, and the EQ-VAS. Monthly income, however, was not shown to be associated with HRQOL of the healthy population (see Appendix Table 2 in Supplemental Materials found at http://dx.doi.org/10.1016/j.vhri.2015.03.019).

Relationships between Sociodemographic Variables or Epilepsy-Specific Variables and WTP/QALY

For QWB-SA utility score–based WTP/QALY calculations by epilepsy group, working status (0.141, $P = 0.091$), duration of epilepsy (−0.149, $P = 0.074$), refractory epilepsy (−0.242, $P = 0.003$), QWB-SA self-rating health state (−0.332, $P = 0.000$), the EQ-VAS (0.235, $P = 0.005$), and monthly income (0.752, $P = 0.000$) were significantly associated with $WTP/QALY_{QWB\text{-}SA}$ values. When the WTP/QALY value was derived from the EQ-5D utility score, it was statistically correlated only with working status (0.220, $P = 0.043$), QWB-SA self-rating health state (−0.333, $P = 0.002$), and monthly income (0.296, $P = 0.000$) (see Appendix Table 3 in Supplemental Materials found at http://dx.doi.org/10.1016/j.vhri.2015.03.019).

Spearman's correlation coefficients between sociodemographic variables and WTP/QALY for the control group are presented in Appendix Table 4 in Supplemental Materials found at http://dx.doi.org/10.1016/j.vhri.2015.03.019.

MLR Analyses for HRQOL

Epilepsy group

Two models were used to investigate the relationships between sociodemographic or epilepsy-specific variables and utility scores of the two instruments, with statistically significant factors (identified by Spearman's correlation) as independent variables. In the first model, 22.6% of the variation in utility scores of the QWB-SA was accounted for by the model while only seizure types (standardized coefficient $\beta = -0.179$; $P = 0.022$) and monthly income ($\beta = 0.217$; $P = 0.006$) statistically contributed to the model. In terms of model 2, the QWB-SA health state ($\beta = -0.296$; $P = 0.000$), the EQ-VAS ($\beta = 0.279$; $P = 0.000$), and monthly income ($\beta = 0.172$; $P = 0.013$) significantly contributed to the model, with 42.1% of the variation in utility scores being accounted for by the model. For utility scores derived from the EQ-5D, the two models accounted for 14.9% and 37.0% of the variations in utilities, respectively. Particularly, working status ($\beta = 0.166$; $P = 0.050$) in model 1 and the QWB-SA health state ($\beta = -0.251$; $P = 0.002$) and

Table 3 – Multiple linear regression analyses for HRQOL scores of patients with epilepsy.

	QWB-SA				EQ-5D		
Model 1 enter	**R^2**	**Standardized coefficient β**	**Significance**	**Model 1 enter**	**R^2**	**Standardized coefficient β**	**Significance**
	0.226				0.149		
Age		0.149	0.290	Age		0.197	0.179
Marital status		0.102	0.289	Marital status		−0.056	0.579
Working status		0.143	0.078	**Working status**		**0.166**	**0.050**
Diagnosis		**−0.179**	**0.022**	Diagnosis		−0.109	0.173
Age of onset		0.092	0.462	Age of onset		0.058	0.653
Seizure frequency		0.165	0.172	Brain injury/ disease		−0.045	0.661
Refractory epilepsy		−0.060	0.535	Brain surgery history		0.176	0.091
Income		**0.217**	**0.006**	Income		0.144	0.077
Model 2 enter	**R^2**	**Standardized coefficient β**	**Significance**	**Model 2 enter**	**R^2**	**Standardized coefficient β**	**Significance**
	0.421				0.370		
Age		0.068	0.584	Age		0.081	0.534
Marital status		0.151	0.076	Marital status		−0.009	0.920
Working status		0.095	0.196	Working status		0.091	0.235
Diagnosis		−0.121	0.078	Diagnosis		−0.064	0.361
Age of onset		0.031	0.283	Age of onset		0.059	0.600
Refractory		0.018	0.833	Brain injury/ disease		−0.065	0.471
Seizure frequency		0.110	0.212	Brain surgery history		0.118	0.195
QWB-SA health state		**−0.296**	**0.000**	**QWB-SA health state**		**−0.251**	**0.002**
EQ-VAS		**0.279**	**0.000**	**EQ-VAS**		**0.345**	**0.000**
Income		**0.172**	**0.013**	Income		0.085	0.235

EQ-5D, EuroQol five-dimensional questionnaire; HRQOL, health-related quality of life; QWB-SA, Quality of Well-being Scale-self administered version; VAS, visual analogue scale. Bold terms and values are statistically significant.

Table 4 – Multiple linear regression analyses for WTP/QALY of patients with epilepsy.

QWB-SA				EQ-5D			
Model 2 enter	R^2	Standardized coefficient β	Significance	Model enter	R^2	Standardized coefficient β	Significance
	0.510				0.497		
Working status		−0.051	0.415	Working status		−0.103	0.209
Duration		0.121	0.055	**QWB-SA health state**		**−0.248**	**0.003**
Refractory epilepsy		0.036	0.573	**Monthly income**		**0.629**	**0.000**
QWB-SA health state		**−0.134**	**0.049**	/		/	/
EQ-VAS		**−0.156**	**0.022**	/		/	/
Monthly income		**0.640**	**0.000**	/		/	/

EQ-5D, EuroQol five-dimensional questionnaire; QALY, quality-adjusted life-year; QWB-SA, Quality of Well-being Scale-self administered version; VAS, visual analogue scale; WTP, willingness to pay. Bold terms and values are statistically significant.

the EQ-VAS ($\beta = 0.345$; $P = 0.000$) in model 2 were shown to positively contribute to the variation (Table 3).

Control group

Both age ($\beta = -0.226$, $P = 0.002$, and $\beta = -0.173$, $P = 0.014$) and the EQ-VAS ($\beta = 0.240$, $P = 0.000$, and $\beta = 0.356$, $P = 0.000$) statistically contributed to the model in predicting utility scores for the QWB-SA or the EQ-5D. In addition, QWB-SA utility scores could be predicted by the QWB-SA health state ($\beta = -0.142$; $P = 0.027$) (see Appendix Table 5 in Supplemental Materials found at http://dx.doi.org/10.1016/j.vhri.2015.03.019).

MLR Analyses for WTP/QALY

Epilepsy group

For either $WTP/QALY_{QWB\text{-}SA}$ or $WTP/QALY_{EQ\text{-}5D}$, the QWB-SA health state ($\beta = -0.134$, $P = 0.049$, and $\beta = -0.248$, $P = 0.003$) and monthly income ($\beta = 0.640$, $P < 0.001$, and $\beta = 0.629$, $P < 0.001$) could be regarded as predictors of the WTP/QALY value, with around 50% of the variation in the WTP/QALY value predicted in the two models. Besides, the EQ-VAS contributed to the variations in the values of $WTP/QALY_{QWB\text{-}SA}$ ($\beta = 0.640$; $P < 0.001$) (Table 4).

Control group

Because the residual distribution of $WTP/QALY_{QWB\text{-}SA}$ values in the control group was skewed, logarithm transformation was applied to this value. Neither the $WTP/QALY_{QWB\text{-}SA}$ value nor the $WTP/QALY_{EQ\text{-}5D}$ value, however, was satisfactorily predicted by the models ($R^2 = 0.099$ and 0.104, respectively). When the WTP/QALY value was calculated on the basis of the QWB-SA utility, age ($\beta = 0.175$; $P = 0.009$) and the QWB-SA health state ($\beta = -0.199$; $P = 0.012$) were predictors of the $WTP/QALY_{QWB\text{-}SA}$ value, whereas the $WTP/QALY_{EQ\text{-}5D}$ value was predicted only by monthly income ($\beta = 0.239$; $P = 0.018$) (Table 5).

Discussion

The burden of epilepsy on a sufferer not only encompasses the unpredictability of seizures but also includes the social exclusion as a result of negative attitudes toward patients with epilepsy. For instance, the stigma may even preclude adult patients from marrying or being denied employment opportunities. Hence, primary treatment goals should not just be to reduce the seizure frequency and seizure severity but also to promote the quality of life of those being affected. As such, factors that impact the quality of life could become potential targets of antiepileptic management. Furthermore, WTP/QALY, which theoretically incorporates the cost of pain, suffering, anxiety, or fatigue because of a disease, would measure the intangible. Hence, quantifying WTP/QALY and the associated factors for patients with epilepsy would provide a more accurate picture of the global burden of this disease. To our knowledge, there was only one study that adopted the WTP method to measure how much patients with epilepsy

Table 5 – Multiple linear regression analyses for WTP/QALY of the control population.

QWB-SA*				EQ-5D			
Enter	R^2	Standardized coefficient β	Significance	Enter	R^2	Standardized coefficient β	Significance
	0.099				0.104		
Age		**0.175**	**0.009**	Age		0.098	0.441
Monthly income		0.128	0.723	Marital status		0.066	0.572
QWB-SA health state		**−0.199**	**0.012**	QWB-SA health state		0.170	0.091
EQ-VAS		−0.007	0.930	**Monthly income**		**0.239**	**0.018**

EQ-5D, EuroQol five-dimensional questionnaire; QALY, quality-adjusted life-year; QWB-SA, Quality of Well-being Scale-self administered version; VAS, visual analogue scale; WTP, willingness to pay. Bold terms and values are statistically significant.

* Log-transformed WTP/QALY was applied.

were willing to pay for a hypothetic "imaginary" new technology that would cure epilepsy permanently [22]. Although the high response rate indicated great acceptability, the associations between WTP and other preference measures were low (Spearman's correlation coefficients ranged from −0.09 to −0.12 for WTP and standard gamble [SG] or TTO). In addition, only 59 subjects completed the study without a control group [22]. Nevertheless, the median WTP amount was US $20,000 (which could inflate to US $30,984 in 2012), accounting for 47% of the annual household income in this aforementioned study. In terms of the proportion of WTP-constituted income, our result (46.5%) was comparable to this one.

With cost-effectiveness/cost-utility analysis increasingly being adopted by various jurisdictions, quantifying the threshold of cost-effectiveness analysis would offer a benchmark for interpreting economic evaluation. Using the stated preference data to quantify the WTP/QALY has been explored previously by our study group, and this elicitation method for WTP/QALY ratio was found to be acceptable and feasible, as well as produce meaningful answers among Chinese subjects [20].

From our study, two interesting findings are worth noting: first, more predictors were identified for $WTP/QALY_{QWB\text{-}SA}$ than for $WTP/QALY_{EQ\text{-}5D}$, which might indicate better sensitivity of the QWB-SA as a utility elicitation instrument. In addition, age was capable of predicting $WTP/QALY_{QWB\text{-}SA}$ values for the healthy population only, with more advanced age associated with greater WTP per QALY value. Because the negative association between $HRQoL_{QWB\text{-}SA}$ and age was shown in the normative data for the QWB-SA (QWB-SA User Manual) as well as in our data set, it might mean that the proportional increase in the WTP of the healthy respondents with increasing age would exceed the magnitude of the decrease in the utility as measured by the QWB-SA. This was supported by the WTP/QALY value increasing with increasing age in our study. In other words, this finding suggested that the WTP value disproportionally increases with age. Nonetheless, this finding was not consistent because one study based on a community sample observed that there was a negative association between age and WTP/QALY [28]. Another review study, however, reported that relative to the baseline assumption of 40 years, the WTP/QALY value would decrease by 7% for those aged 35 years and increase by 9% for those aged 45 years, which was similar to our finding [29]. Although different elicitation methods and targeted populations were used in the studies, this inconsistency still warrants future investigations.

The median of $WTP/QALY_{QWB\text{-}SA}$ value or $WTP/QALY_{EQ\text{-}5D}$ value for the epilepsy group was nearly 2 times the gross domestic product per capita in China (International Monetary Fund, 2012, US $5417 for China), but fell within the range of WHO's recommendation (1–3 times the gross domestic product per capita) [30]. On comparing with the result from a previous WTP study, we see that patients with epilepsy afforded greater amount of WTP and WTP/QALY values than did Chinese patients with chronic prostatitis based on the same indirect utility elicitation method (EQ-5D), and this might reflect the different impacts on patients with these two chronic diseases.

In our study, $WTP/QALY_{QWB\text{-}SA}$ and $WTP/QALY_{EQ\text{-}5D}$ values from the epilepsy group were a great deal higher than those from the control group, suggesting that the WTP/QALY value is context specific. In theory, perceptions of the WTP question for patients with epilepsy and healthy subjects are essentially different. For patients, the scenario provided is probably perceived as a curative treatment, whereas for healthy respondents, the scenario offered is more like considering prevention because they are not experiencing health problems at the moment of the study. Because the WTP amount for prevention is remarkably less than the quantity for treatment, an obvious difference in the WTP value estimated from treatment and prevention situations was previously reported [21,31], According to a prospect theory, the preference of an individual is related to a reference point [32]. In our study, patients with epilepsy were in declined health states compared with healthy subjects; thus, reference points for epilepsy and healthy control cohorts were essentially distinctive. This would offer another explanation for the huge gap in the WTP amount between the two groups other than the inherent difference in the intangible cost for two distinct cohorts. Taken together, these results also imply that one ceiling threshold should not be applied to all the interventions when deciding resource allocation.

Our present results showed that working status, seizure types, monthly income, and self-rating health state might be predictors of HRQOL of patients with epilepsy, which is in line with a previous study [33], whereas epilepsy-specific parameters such as age of epilepsy onset, duration of epilepsy, epileptic discharge (electroencephalogram), seizure frequency, and antiepileptic drugs did not statistically contribute to the variation in HRQOL. A literature review, however, indicated that except for seizure frequency, severity, and psychological factors, other disease variables had affected HRQOL only in limited studies. Furthermore, the proportion of HRQOL variance explained by the MLR model was low in our study, ranging from 14.9% to 42.1% corresponding to different models and utility measures. This might be due to the insensitivity of the generic preference-based HRQOL instrument to capture characteristics inherent to a specific disease. In addition, depression and anxiety have been demonstrated to exert a high impact on HRQOL, but were not independently assessed in our study (though there are items in the EQ-5D and the QWB-SA to assess the psychological problems) and thus not included in the MLR model [34,35].

Our study was subject to some limitations as well. First, a direct utility elicitation method such as SG or TTO would be superior to the indirect method as used in the present study. Both SG and TTO, however, are hard to understand and respond for participants; thus, indirect methods might serve as a substitute to direct methods. This is supported by the higher convergent validity between $WTP/QALY_{QWB\text{-}SA}$ and $WTP/QALY_{EQ\text{-}5D}$ in the present study than in studies adopting SG and TTO. Second, because epilepsy, generally, is not a life-threatening disease, as reported by previous literature, a QALY gained by improving the quality of life or extending a life is worth less than a QALY gained by saving a life, so the WTP/QALY estimation derived from this cohort might not be comprehensive enough to reflect the societal perspective [36–39]. Last, epilepsy and control groups were heterogeneous in terms of several sociodemographic characteristics, which would introduce a confounding factor into the final result.

Conclusions

Patients with epilepsy had substantially lower HRQOL than did the healthy population. Seizure types, working status, monthly income, and self-rating health state could be considered as predictors of HRQOL of this cohort. In spite of controversies over underlying theoretical and methodological issues, our study demonstrated the feasibility and acceptability to quantify monetary value per QALY with the WTP approach. Particularly, WTP/month and the WTP/QALY value of patients with epilepsy were considerably greater than those of the general population, which also revealed increased intangible cost for the sufferers. Nevertheless, it is questionable to apply one WTP/QALY threshold to all the situations. Finally, the methods to elicit QALY and WTP should also be taken into consideration.

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Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at http://dx.doi.org/10.1016/j.vhri.2015.03.019 or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

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