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Preference-Based Assessments

Development of an EQ-5D Value Set for India Using an Extended Design (DEVINE) Study: The Indian 5-Level Version EQ-5D Value Set

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ABSTRACT

Objectives: This study aimed to develop the Indian 5-level version EQ-5D (EQ-5D-5L) value set, which is a key input in health technology assessment for resource allocation in healthcare.

Methods: A cross-sectional survey using the EuroQol Group's Valuation Technology was undertaken in a representative sample of 3548 adult respondents, selected from 5 different states of India using a multistage stratified random sampling technique. The participants were interviewed using a computer-assisted personal interviewing technique. This study adopted a novel extended EuroQol Group's Valuation Technology design that included 18 blocks of 10 composite time trade-off (c-TTO) tasks, comprising 150 unique health states, and 36 blocks of 7 discrete choice experiment (DCE) tasks, comprising 252 DCE pairs. Different models were explored for their predictive performance. Hybrid modeling approach using both c-TTO and DCE data was used to estimate the value set.

Results: A total of 2409 interviews were included in the analysis. The hybrid heteroscedastic model with censoring at −1 combining c-TTO and DCE data yielded the most consistent results and was used for the generation of the value set. The predicted values for all 3125 health states ranged from −0.923 to 1. The preference values were most affected by the pain/discomfort dimension.

Conclusions: This is the largest EQ-5D-5L valuation study conducted so far in the world. The Indian EQ-5D-5L value set will promote the effective conduct of health technology assessment studies in India, thereby generating credible evidence for efficient resource use in healthcare.

Keywords: EQ-5D, health technology assessment, health-related quality of life, India, population norms, quality of life, utility scores, utility values, utility weights, value set.

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Introduction

In 2017, the Government of India has established *Health Technology Assessment in India (HTAIn)*, the central health technology assessment (HTA) agency of the country, to develop transparent, evidence-informed, and effective health policies.[1,2] The guidelines to conduct HTAs in India were first issued in 2018 and have recommended the quality-adjusted life-year (QALY) as the preferred outcome measure in HTAs and EQ-5D-5L as a preferred instrument to measure health-related quality of life (HRQoL).[3,4] Developed by the EuroQol Group, the EQ-5D is a standardized generic instrument that collects descriptive HRQoL on 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), and EQ-5D-5L is a version having 5 levels of severity associated with every dimension.[5] A QALY is a product of the duration of time spent in a health state and the HRQoL associated with that health state.[6] The HRQoL of a particular health state is measured using EQ-5D-5L descriptive system and then scored and represented by its utility score/weight/value.[6,7] These utility values represent people's preferences and are thus dependent upon the sociocultural settings in which people live.[8,9] This implies that to estimate accurately the value of a QALY, the availability of utility values of a representative local population is essential. This necessitates having an India-specific value set for HRQoL, so that QALYs can be assessed correctly in HTAs.[10] The absence of an India-specific value set is also a hindrance in the conduct of cost-utility analyses, given that between 1980 and 2014 only 9% of the full economic evaluations conducted in India were cost-utility analyses.[11] One of the major reasons for this low uptake was the lack of an Indian value set that is able to generate QALYs from a HRQoL instrument such as EQ-5D.

The absence of an India-specific EQ-5D-5L value set impelled the previous studies to use the value set from Thailand or United Kingdom.[12,13] Apart from HTAs, EQ-5D is increasingly being used

in India in clinical settings also, as more than 500 registrations have been made with the EuroQol Group in the last 5 years for its use (personal communication: Gerben Bakker, EuroQol Research Foundation), but the EQ-5D profile was converted to corresponding utility values using value sets from other countries.[14,15] Hence, the development of an India-specific EQ-5D-5L value set is imperative for a credible and consistent decision-making process in the country.

To address this requirement, the central HTA agency of the Government of India commissioned the development of an EQ-5D value set for India using an extended design (DEVINE) study.[10] This study aimed to determine the HRQoL value set for India by calculating EQ-5D-5L health state values among the Indian population.

Methods

Study Settings

The study was undertaken in 5 regions/states of India. The selection of states was based on 3 criteria: income, health status, and geographical representation. The states selected were Haryana, Uttar Pradesh, Gujarat, Odisha, and Tamil Nadu. The detailed approaches followed in the selection of study settings and samples have been published separately.[10] Due to COVID-19, a slight deviation from the previously published methodology had to be pursued. Initially, the data collection was proposed in 6 Indian states. However, the primary data collection stalled in March 2020 due to the COVID-19 situation. By that time, data collection had been completed in 5 states, but not in Meghalaya. An interim statistical analysis of the data of 5 states suggested that it was possible to generate a good-quality value set using the available data. Hence, the final value set comprised the data from the 5 Indian states/regions, excluding Meghalaya.

Sample Size and Sampling Approach

To have valid regional level estimates, sample sizes were estimated first at the state level. TTO values for all health states were considered as the main variable of interest and the mean of this variable as the target parameter. The estimated SD of this variable (0.53), which was derived from a previous study, was used to calculate the sample size.[16] Assuming absolute precision (d) as 0.05 and a 95% confidence interval, a sample size of 435 was estimated. As the study was conducted in 5 different states, a minimum sample of 2175 comprising all 5 states was considered appropriate for the study.

The respondents were selected using a multistage stratified random sampling technique. The sample selection involved a rigorous process wherein the selection was made at 5 different levels, that is, at the level of states, districts, primary sampling units, households, and the individuals to be interviewed. The detailed sampling approach followed in the study has been published separately.[10]

Study Instruments and Valuation Process

The interviews were conducted using the EuroQol Group's Valuation Technology (EQ-VT). We used the official EQ-5D-5L instrument, which consists of the EQ-5D-5L descriptive system and the EuroQol visual analog scale (EQ VAS).[12,17] The EQ-5D-5L descriptive system covers 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), and each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems/unable to. This descriptive system is followed by self-rating of overall health status by the individual on the EQ VAS ranging from 0 ("worst health you can imagine") to 100 ("best health you can imagine").[17] The EuroQol Group provided English and officially translated versions of EQ-5D-5L in 4 Indian languages (Hindi, Gujarati, Tamil, and Odia).

The participants were interviewed in a face-to-face setting using a computer-assisted personal interviewing technique. The interview comprised the following 10 parts: (1) self-reported health using the EQ-5D-5L descriptive system and EQ VAS, (2) questions on age, gender, and experience of serious illness, (3) instructions to conduct composite time trade-off (c-TTO) valuation and its elaboration with the help of wheelchair example, (4) practice of c-TTO valuation using 3 different EQ-5D-5L health states (mild, severe, and hard to imagine), (5) c-TTO valuation of 10 EQ-5D-5L health states, (6) c-TTO feedback module allowing respondents to identify health states not ranked in the desired order and a c-TTO debriefing (in the feedback module, all the 10 health states presented to the respondent are ranked from mildest to most severe as per respondent's valuation, and the respondent is asked if he/she is satisfied with the shown ranking), (7) instructions regarding discrete choice experiment (DCE) valuation, (8) DCE valuation of 7 pairs of health states which contain 5 attributes of the EQ-5D-5L descriptive system wherein no duration is specified, (9) DCE debriefing, and (10) questions on socioeconomic and demographic characteristics, pre-existing medical history, habits and beliefs, and other attributes of the respondents. During the process of interviews, interviewers also carried along a graphical illustration (Likert scale smileys) explaining the 5 levels of severity. This was done keeping in mind that because it would not be possible for the illiterate respondents to read the description of the health states, they can at least look at the graphical illustration supported by the description provided by the interviewer and make an informed decision. TTO and DCE valuation was undertaken according to the EuroQol protocol using the latest available EQ-VT version 2.1 system.[18–20]

In the standard c-TTO design, there are 10 blocks of health states and each block contains 10 health states.[18] Similarly, there are 28 DCE blocks and each block contains 7 pairs of health states. Thereby, in the standard design, there are 86 c-TTO health states and 196 DCE pairs.[18] In contrast to the standard design, which is optimized for a sample of 1000 respondents, this study used a large sample; hence, an extended design was used. The extended design differs in 3 ways from the original EQ-VT design, that is, an increased number of c-TTO blocks, an increased number of DCE blocks, and an increased number of observations per health state due to a larger sample. The extended design contained 18 c-TTO blocks and 36 DCE blocks. In the extended design, the 8 additional c-TTO blocks consisted of 64 new unique health states and 8 additional DCE blocks comprising 56 new pairs of health states. Hence, the extended design contained 150 unique c-TTO health states and 252 DCE health states pairs.[10] This selection of additional health states was guided by added-value considerations, taking the initial blocks as the points of departure.[10] The additional health states for the c-TTO and pairs for the DCE task were selected using an efficient design procedure, which minimized the D-error. To select 64 additional c-TTO health states, 64 new states were randomly drawn from the 3039 health states and appended on the existing 86 states to form a design. This process was repeated for 5000 times. Candidate designs with poor level balance were discarded. Next, we examined the D-efficiency of the designs and kept the best 100 candidate designs. Then we examined the prediction accuracy of the best 100 designs in the saturated data set and computed the implausible probability of the best 5 candidate designs, and the least implausible candidate design was used. Each respondent was randomly assigned 1 c-TTO

block and 1 DCE block by the EQ-VT software. The order of the health states being valued was also randomized within the c-TTO block. Likewise, in DCE, respondents were randomly assigned to one of the 36 blocks by the EQ-VT. The order in which pairs were valued was randomized, as was the left-right positioning.

Quality Control

To ensure the quality and uniformity of the data collection process, the study followed intensive training and implemented stringent quality control (QC) measures. The recommendations of the latest EQ-VT protocol were followed to standardize the data collection process across different regions of the country.[18,21,22] First, a Training of Trainers on the EQ-VT was organized at EuroQol Head Office. These trainers then organized the hands-on training of interviewers at all the study sites. Given the linguistic diversity among the states, separate sets of interviewers were recruited in every state, and separate training sessions were organized. The interviewers had a postgraduate degree either in public health or medical social work. After the hands-on training, the interviewers were put through a process of pilot interviewing until the point at which protocol compliance had been achieved and interviewer effects had disappeared. A Microsoft Excel–based QC tool developed by the EuroQol Group was used to evaluate interviewers' performance.[23] This QC check was conducted in a cyclical manner throughout the study, once each interviewer had performed a predetermined number of interviews. The details of the QC indicators used in the study to assess the performance of the interviewers have been published separately.[10] The interviewers could start the substantive data collection only after achieving a stable performance on the QC protocol. This QC check and personalized feedback process was continuously followed throughout the study duration.

Statistical Analysis

Descriptive statistics were generated to present the characteristics of the final sample and to summarize self-reported health. Pilot interview data were dropped, and only valid interviews were used for the analysis.

Given that only 150 EQ-5D-5L health states were valued directly, the utility values of all the possible 3125 health states were estimated using statistical modeling. The following models were evaluated for their predictive performance: (1) a main-effects tobit model using only c-TTO data, (2) a generalized least square (GLS) tobit model using only c-TTO data, (3) a tobit model adjusted for heteroscedasticity using only c-TTO data, (4) a conditional logit model using only DCE data, (5) a conditional logit model using only DCE data but rescaled using the multiplicative constant from the hybrid model, (6) a hybrid model with censoring at −1 combining both c-TTO and DCE data, (7) a hybrid model adjusted for heteroscedasticity combining both c-TTO and DCE data, and (8) a hybrid model with censoring at −1 and adjusted for heteroscedasticity combining both c-TTO and DCE data. The predictive performance of the models was evaluated by: (1) logical consistency where the absolute value of parameters associated with logically worse dimension levels must be higher than those associated with logically better levels, (2) goodness of fit for comparable model types using the Akaike and the Bayesian information criteria, and (3) mean absolute error between observed and predicted values for the empirically most commonly observed health states.[24,25]

We used a 20-parameter model where the explanatory variables are incremental dummies for the 5 dimensions of the EQ-5D-5L, with level 1 considered as the reference. Incremental dummies allow to interpret the coefficients as being the variation in the disutility of health when moving from one level to the next. The basic equation for the main-effects GLS regression with random intercept was as follows:

$$\begin{aligned} Y_{it} = {} & \beta_{M1}MO2_{it} + \beta_{M2}MO3_{it} + \beta_{M3}MO4_{it} + \beta_{M4}MO5_{it} \\ & + \beta_{S1}SC2_{it} + \beta_{S2}SC3_{it} + \beta_{S3}SC4_{it} + \beta_{S4}SC5_{it} + \beta_{U1}UA2_{it} \\ & + \beta_{U2}UA3_{it} + \beta_{U3}UA4_{it} + \beta_{U4}UA5_{it} + \beta_{P1}PD2_{it} \\ & + \beta_{P2}PD3_{it} + \beta_{P3}PD4_{it} + \beta_{P4}PD5_{it} + \beta_{A1}AD2_{it} \\ & + \beta_{A2}AD3_{it} + \beta_{A3}AD4_{it} + \beta_{A4}AD5_{it} + \varepsilon_{it} + \mu_{0i}, \end{aligned} \quad (1)$$

where Y_{it} TTO values dependent variable

μ_{0i} respondent specific error component
ε_{it} response-related error term
i respondent
t data set panel structure (since there were 10 c-TTO questions per respondent)
MO, SC, UA, PD, and AD are dummy-coded regressors for mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, representing the 5 levels of EQ-5D-5L.

The constant reflected the utility decrement associated with any deviation from full health. The tobit model assumed a latent variable Y_{it}^{*} underlying the observed Y_{it} c-TTO values. This matched with the censored c-TTO data, which by the nature of the applied c-TTO task was censored at −1. The tobit model accounted for this censored nature of the data by estimating the latent variable Y_{it}^{*}, which could take on predicted preference values extrapolated beyond the range of the observed values. A likelihood function was used to adjust the parameter estimates for the probability of Y_{it} being above the censoring value. Hence, in the tobit model, the observed value Y_{it} had the following properties when the censoring value was −1:

$$Y_{it} = \begin{cases} Y_{it}^{*} \text{ if } Y_{it}^{*} < -1 \\ -1 \text{ if } Y_{it}^{*} \leq -1 \end{cases}$$

The equation for Y_{it}^{*} was linear. The DCE data were modeled under random utility using the conditional logit model. The model included the same 5 parameters as the c-TTO model, reflecting utility decrements associated with levels 2, 3, 4, and 5 for each of the 5 domains: MO, SC, UA, PD, and AD. This model had the same structure as equation 1 regarding the parameters for the level-attribute combinations, so it also had a 20-parameter model. The regression equation is given below.

$$U_{js} = \beta_1 MO_{js} + \beta_2 SC_{js} + \beta_3 UA_{js} + \beta_4 PD_{js} + \beta_5 AD_{js} + \varepsilon_{js}, \quad (2)$$

where js is the choice alternative in the choice sets.

Given that both TTO and DCE data provide information about the values of health states, we also implemented a hybrid modeling approach that made use of both c-TTO and DCE data sets to estimate the potential value set.[21,25–33] The hybrid model combined the likelihood functions of a linear model for the c-TTO data and the conditional logit model for the DCE data. Given that the coefficients were estimated from a conditional logit model and expressed on a latent arbitrary utility scale, we used a rescaling parameter θ, which assumed that the c-TTO model coefficients were proportional to the DCE model coefficients. This method combined the utility values elicited in the c-TTO for the 150 health states with utility values elicited in the DCE experiment for 252 pairs of states. We used cluster estimation to acknowledge that for

each participant included in the models, 10 c-TTO and 7 DCE responses were available.

Ethical Considerations

The ethical approval to conduct the study was obtained from the Institutional Ethics Committee of Postgraduate Institute of Medical Education and Research, Chandigarh, India, vide letter number PGI/IEC/2018/001629.

Results

Sample Characteristics

The interviews were conducted between June 2019 and March 2020. A total of 27 interviewers were involved in the study, and none were dropped due to poor performance. A total of 3548 interviews were conducted, of which 788 were pilot interviews and therefore not included in the final analysis. Such a large pilot was planned to ensure protocol compliance and minimize the interviewers' effect, considering the limited literacy rate of the Indian population and cognitively demanding nature of the valuation interviews, and to standardize the data collection process across all the centers and interviewers. Therefore, every interviewer conducted approximately 30 pilot interviews before starting the real interviews, which were not included in the final analyses as they were preparatory in nature. Of the remaining 2760 interviews, 301 interviews were discarded at the respondents' requests due to their lack of involvement/understanding. This was told to the interviewer in the last part of the interview, where the interviewer asked the respondents about their experience and comments. Moreover, 50 interviews were dropped by the interviewers due to the respondents' lack of understanding, which was assessed by the interviewer where they observed the lack of involvement, limited cognition, hesitation, shyness to interact with technology, and hastening to finish the interview, because it may hamper the appropriateness of the responses. Hence, the data from 2409 interviews were considered in the final analysis. The sample characteristics of the respondents along with utility values and EQ VAS scores for the respective categories are summarized in Table 1. Analysis of variance was used to assess the statistical significance between the mean utility values and EQ VAS scores among patients of different age, education, marital status, and religion, whereas the independent samples *t* test was used to see the difference in mean quality of life scores among patients of different gender and residence. The self-reported health status of respondents on the EQ-5D-5L descriptive system and EQ VAS is presented in Table 2.

Predictive Performance of the Models

All the models prepared to predict the utility value of 3125 health states were consistent and generated statistically significant coefficients, except for the conditional logit models and tobit model adjusted for heteroscedasticity. When modeling was conducted using c-TTO data alone, the GLS tobit model was preferred over the main-effects tobit model, because the data were unable to fulfill the model's underlying assumptions of independence, homoscedasticity, and normality of the error term. The coefficients generated by the GLS tobit model were logically consistent and statistically significant. Furthermore, all 3 hybrid models generated logically consistent and statistically significant coefficients. Among all the models prepared to predict the utility value of 3125 health states, the mean absolute error between observed and predicted values for the empirically most commonly observed health states was lowest for the hybrid model with censoring at −1 and adjusted for heteroscedasticity. Moreover, because it combines the observations of both c-TTO and DCE valuations and is increasingly being used currently to generate country-specific value sets, the hybrid modeling approach was taken forward.[21,25–33] Based on these criteria, the hybrid model with censoring at −1 and adjusted for heteroscedasticity outperformed the other 2 alternatives and hence was used in the generation of the value set.

Modeling Results and Value Set

There were 780 c-TTO observations (3.3%) censored at −1: when respondents gave the highest possible value (2) for a health state in the c-TTO task. The GLS tobit c-TTO model results were logically consistent. Conditional logistic regression was used to model the DCE responses that were inconsistent (using the rescaled DCE coefficients). c-TTO and rescaled DCE predicted values for 3125 health states were correlated, as Appendix Figure 1a in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.11.1370 shows (r = 0.986, $P<.0001$). Table 3 shows that both sets of coefficients were in relative agreement; that is, the most important dimension was pain/discomfort and the least important was anxiety/depression. The hybrid model, which used both c-TTO and DCE data, was also in relative agreement with both c-TTO and DCE models. Appendix Figure 1b and c in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.11.1370 shows a high correlation of hybrid predicted utility with models predicted from c-TTO (r = 0.997, $P<.0001$) and rescaled DCE (r = 0.995, $P<.0001$). The hybrid model with main effects was logically consistent (Table 3). Using this as the final model to obtain 3125 EQ-5D-5L health states, the maximum value was 1.000 for full health (health state "11111") followed by the health state "11112" with value 0.984. The minimum value was −0.923 for the "55555" state. Of the 3125 health states, 874 (27.97%) had negative values using the hybrid model. The coefficients from the hybrid model were also in agreement with the previous 2 models regarding pain/discomfort appearing as the most important dimension and anxiety/depression as the least important. To obtain utility value for an EQ-5D-5L health state, for example, "12345," the following calculation based on the hybrid model (final value set) is needed: utility value ("12345") = 1 – no problems in MO (0) – no problems to slight problems in SC (0.0513) – no problems to slight problems in UA (0.0455) – slight problems to moderate problems in UA (0.0431) – no problems to slight problems in PD (0.0514) – slight problems to moderate problems in PD (0.0741) – moderate problems to severe problems in PD (0.2643) – no problems to slight problems in AD (0.0163) – slight problems to moderate problems in AD (0.0464) – moderate problems to severe problems in AD (0.1009) – severe problems to extreme problems in AD (0.0835) = 0.2232. The pain/discomfort dimension was assigned the most value by the respondents. Predicted utilities of all 3125 health states and comparison of observed and predicted utilities of 150 health states are presented in Figure 1. The full EQ-5D-5L value set for India containing the utility values of all the possible 3125 health states is presented as Appendix Material 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.11.1370. The details of all the models considered in the study are provided in Appendix Material 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.11.1370. Appendix Figure 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.11.1370 shows all the observed c-TTO value distribution for all health states.

Table 1. Sociodemographic characteristics and corresponding health-related quality of life of the respondents in the DEVINE study

Characteristics	N	% (study population)	% (Indian population)	Utility score		*P* value	EQ VAS score		*P* value
				Mean	SD		Mean	SD	
Age group (in years)									
17-19	101	4.2*	3.1	.933	.126	<.001	84.85	13.25	<.001
20-29	651	27.0	26.9	.919	.132		82.68	13.20	
30-39	540	22.4	24.1	.877	.164		78.35	13.23	
40-49	487	20.2	19.0	.841	.201		73.82	14.64	
50-59	340	14.1	14.3	.801	.205		67.93	15.10	
60-69	196	8.1*	9.8	.740	.245		63.23	17.38	
70+	94	3.9*	2.8	.542	.455		52.53	19.96	
Sex									
Male	1179	48.9	48.1	.862	.195	.007	76.04	15.84	.025
Female	1230	51.1	51.9	.840	.209		74.52	16.52	
Educational status									
Illiterate	261	10.8*	24.2	.708	.301	<.001	62.62	18.25	<.001
Primary	308	12.8*	33.4	.816	.233		70.39	16.42	
Middle	412	17.1*	15.1	.835	.201		73.33	15.61	
Matric	457	19.0*	11.2	.854	.199		75.66	15.75	
Senior secondary	422	17.5*	8.3	.897	.141		78.78	13.82	
Graduate and above	549	22.8*	7.8	.902	.177		82.03	13.85	
Marital status									
Married	1700	70.6*	45.6	.848	.188	<.001	74.22	15.47	<.001
Never married	519	21.5*	49.8	.917	.150		83.38	13.42	
Widow/divorced	190	7.9*	3.6	.665	.383		61.27	20.06	
Residence									
Urban	755	31.3*	34.5	.844	.244	.564	75.74	17.14	.276
Rural	1654	68.7*	65.5	.850	.196		74.92	16.07	
Religion									
Hindu	2133	88.5*	79.8	.854	.197	<.001	75.35	16.08	.001
Muslim	124	5.1*	14.2	.834	.205		77.14	15.63	
Christian	120	5.0*	2.3	.811	.238		72.95	16.87	
Other	32	1.3*	3.7	.661	.632		64.48	30.45	
Total	2409	100	100	.849	.212		75.18	16.416	

Note. A general z test was used to investigate whether the proportions in the sample were similar to, or different from, the general population. Proportions in sample were similar to the Indian population for gender (male, female) and age group (20-29, 30-39, 40-49, 50-59 years).
EQ VAS indicates EuroQol visual analog scale.
*Significant difference at a = 0.05 from z test.

Discussion

This is the largest EQ-5D-5L valuation study conducted so far worldwide and the first preference-based valuation study to determine the value set for HRQoL in South Asia.[10,34] The value set generated as a part of this study will be useful for clinicians undertaking studies to measure clinical effectiveness of interventions, epidemiologists to measure the burden of disease,

Table 2. Self- reported health status of the respondents in the DEVINE study

EQ-5D-5L descriptive system					
	Mobility (%)	Self-care (%)	Usual activities (%)	Pain/discomfort (%)	Anxiety/depression (%)
No problems	67.29	85.46	70.01	45.22	45.31
Slight problems	20.51	11.29	19.77	31.16	26.61
Moderate problems	9.17	2.21	7.83	19.43	19.43
Severe problems	2.42	0.78	2.16	4.15	7.53
Extreme problems	0.61	0.26	0.22	0.35	1.13
EQ VAS score					
	Mean	SD	25th percentile	Median	75th percentile
EQ VAS score	75.18	16.416	65.0	80.0	90.0

EQ VAS indicates EuroQol visual analog scale.

Table 3. Modeling results for GLS tobit model, rescaled conditional logit model, and hybrid model with censoring at −1 and adjusted for heteroscedasticity.

	GLS tobit model			Rescaled conditional logit model			Hybrid model with censoring at −1 and adjusted for heteroscedasticity		
	Coefficient	SE	*P* value	Coefficient	SE	*P* value	Coefficient	SE	*P* value
Mobility									
MO2	0.0462	0.006	<.01	0.061	0.008	<.01	0.0497	0.006	<.01
MO3	0.0366	0.007	<.01	0.0478	0.010	<.01	0.0492	0.006	<.01
MO4	0.1729	0.008	<.01	0.1482	0.010	<.01	0.1553	0.007	<.01
MO5	0.1054	0.008	<.01	0.1697	0.010	<.01	0.1333	0.006	<.01
Self-care									
SC2	0.0381	0.007	<.01	0.0639	0.009	<.01	0.0513	0.006	<.01
SC3	0.0907	0.008	<.01	0.0498	0.009	<.01	0.0793	0.006	<.01
SC4	0.1756	0.008	<.01	0.163	0.010	<.01	0.1709	0.007	<.01
SC5	0.0553	0.007	<.01	0.13273	0.010	<.01	0.0784	0.006	<.01
Usual activity									
UA2	0.0418	0.007	<.01	0.0462	0.009	<.01	0.0455	0.006	<.01
UA3	0.0376	0.007	<.01	0.0449	0.009	<.01	0.0431	0.006	<.01
UA4	0.1702	0.008	<.01	0.1331	0.010	<.01	0.1529	0.007	<.01
UA5	0.0372	0.007	<.01	0.1369	0.010	<.01	0.0824	0.006	<.01
Pain/discomfort									
PD2	0.0528	0.006	<.01	0.0535	0.009	<.01	0.0514	0.006	<.01
PD3	0.0677	0.008	<.01	0.0791	0.009	<.01	0.0741	0.006	<.01
PD4	0.2946	0.008	<.01	0.2281	0.010	<0.01	0.2643	0.007	<0.01
PD5	0.1841	0.008	<.01	0.2398	0.011	<0.01	0.1945	0.007	<0.01
Anxiety/depression									
AD2	0.0366	0.007	<.01	-0.0113	0.009	.21	0.0163	0.006	<.01
AD3	0.041	0.008	<.01	0.0457	0.010	<.01	0.0464	0.007	<.01
AD4	0.1126	0.008	<.01	0.1008	0.010	<.01	0.1009	0.007	<.01
AD5	0.0879	0.007	<.01	0.0891	0.010	<.01	0.0835	0.006	<.01
lntheta constant							1.476	0.018	0.00
AIC	16436.84			16798.852			41149.52		
BIC	16614.56			16967.373			41502.68		
MAE (most commonly observed health states)	0.05602			0.05760			0.05464		
U (12121)	0.9091			0.8826			0.8973		
U (31111)	0.9172			0.8912			0.9011		
U (41111)	0.7443			0.743			0.7458		
U (51111)	0.6389			0.5733			0.6125		
U (12345)	0.1893			0.260			0.2232		
U (34521)	0.2732			0.1999			0.2243		
U (55555)	-0.8849			−1.022			-0.9227		

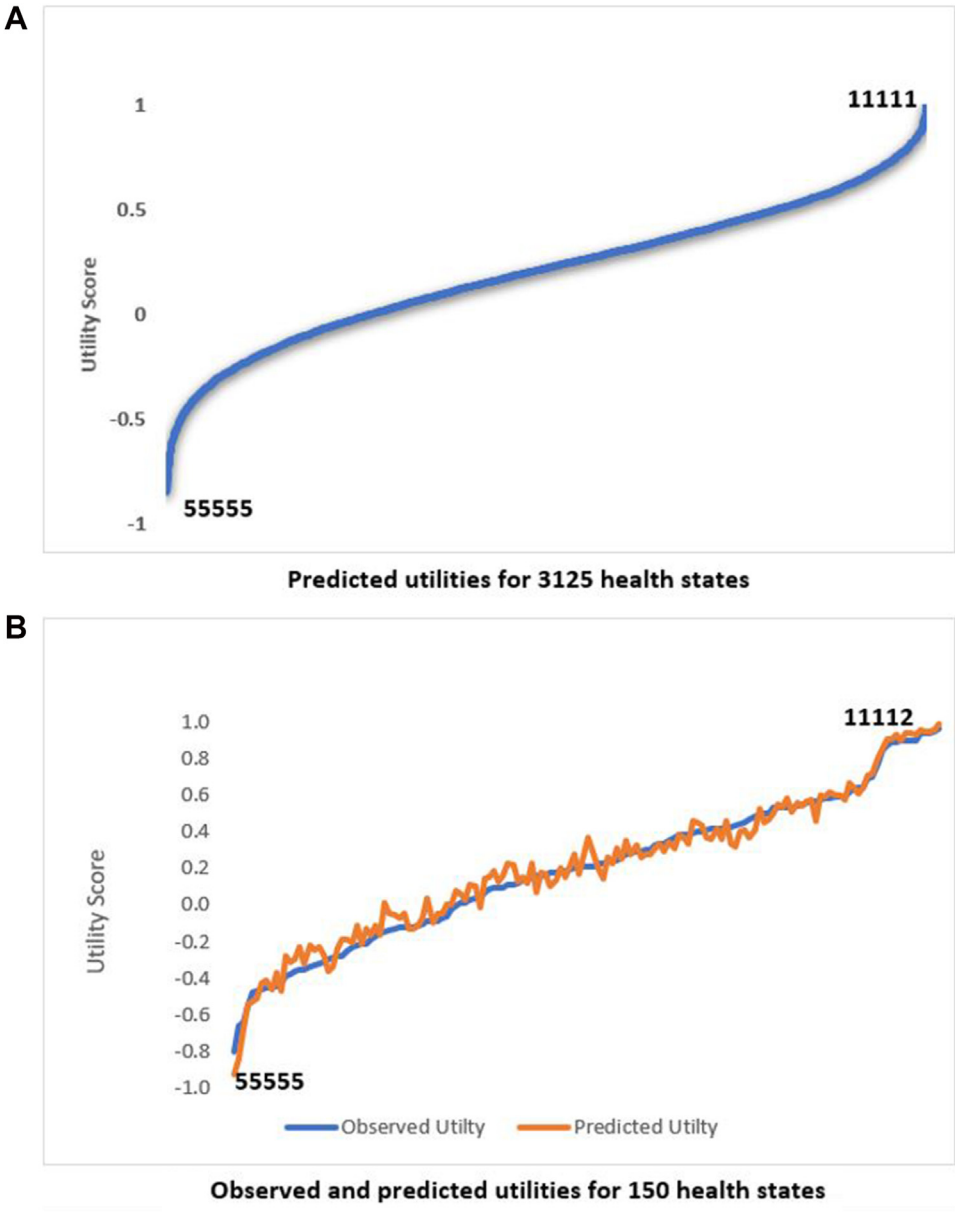
AIC indicates Akaike information criteria; BIC, Bayesian information criteria; GLS, generalized least square; MAE, mean absolute error; SE, standard error; U, utility value.

and health economists to undertake economic evaluations. The absence of an India-specific EQ-5D-5L value set impelled the previous studies to use the value set from Thailand and United Kingdom.[12,13] Hence, the development of an India-specific EQ-5D-5L value set was imperative for a more transparent and consistent decision-making process.

It has been illustrated that the process of data collection has a significant bearing on the validity of health state valuations.[23] Accordingly, this study used a multistage stratified random sampling technique. This is in contrast with most of the previous studies aimed at generating country-level EQ-5D-5L value sets, which pursued purposive or quota sampling.[26,35–38] Using such a rigorous sampling approach has averted the potential issues related to purposive or quota sampling, such as (1) the chances of missing out respondents who clearly do not fall into any of the quota groups and (2) the nonrandom selection of respondents. Moreover, an iterative QC approach was used to obtain high-quality data.

Given that the previous studies conducted to generate EQ-5D-5L value sets used either c-TTO or hybrid models, we analyzed the predictive performance of all these models.[25,26,36,39–41] All the models in our study demonstrated logical consistency and significant regression coefficients (except for conditional logit models and tobit model adjusted for heteroscedasticity, where one of the 20 coefficients was not statistically significant). This points to the high quality of the data set, assured by the rigorous quality check process followed throughout the study. Finally, we used the hybrid model that combined the responses and allowed

Figure 1. Predicted utilities of all 3125 health states and comparison of observed and predicted utilities of 150 health states.



us to maximize information extraction from both c-TTO and DCE data sets. All 3 hybrid models generated logically consistent and statistically significant coefficients. Moreover, because it resulted in the lowest mean absolute error between observed and predicted values for the empirically most commonly observed health states among all the models, combines the observations of both c-TTO and DCE valuations, and is increasingly being used currently to generate country-specific value sets, the hybrid modeling approach was taken forward.[21,25–33]

It is worthwhile highlighting that, compared with the developed countries, the Indian results demonstrated a greater number of worse than dead (negative) values and a lower value for the worst health state (55555).[25,40–42] This observation can possibly be explained by the rigorous QC measures followed in the study, which provided better understanding and the skills to administer the complex worse than dead trade-off scenarios. Because both the administration and response to the lead-time TTO questions are relatively difficult, if enough attention is not paid on the standardized process of asking the lead-time questions, it may develop confusion for interviewer and respondent. If it happens, the interviewer/respondent may become hesitant to enter the lead-time TTO and end up finishing the TTO exercise in the better than dead part (conventional TTO) only. This would result in a lesser number of worse than dead values in the data. However, our study used an extensive pilot phase, which might have led to a more thorough administration of the c-TTO tasks, especially the worse than dead trade-offs, which could have led to a higher proportion of worse than dead values.

Our study has demonstrated that the Indian population has reported the highest number of problems in the dimension of pain/discomfort, followed by anxiety/depression among all 5 dimensions of the EQ-5D-5L instrument. This is in line with the

other studies reporting HRQoL among Indian population.[12] Furthermore, it was found that pain/discomfort had the most significant bearing on the utility value for the Indian population, which was similar to the EQ-5D-5L value sets for England and the Netherlands.[40,42] In the Indian context, these findings imply that clinical interventions should focus on the control of pain and the relief of anxiety to achieve better patient-centered outcomes.

Our study has a number of limitations. Initially, it was proposed that the study be conducted in 6 Indian states.[10] However, the primary data collection stalled in March 2020 due to the COVID-19 situation. By that time, data collection had been completed in 5 states, but not in Meghalaya. Nevertheless, an interim statistical analysis by our team along with EuroQol scientists suggested that it was possible to generate a good-quality value set using the available data. Moreover, it did not have any adverse impact on the power of the study, given that the sample size was calculated at the state level. Hence, the final value set comprised the data from the 5 Indian states/regions, all of which had been collected before the emergence of COVID-19 pandemic in India.

Although we used the hybrid model that combined the responses and allowed us to maximize information extraction from both c-TTO and DCE data sets, its use has been argued as it assumes linear associations between DCE and TTO utilities.[43,44]

As the demand for value sets rapidly increases due to the increased use of HTA in decision-making across the globe, there has been a felt need for more efficient ways to obtain value sets. This presents 2 pertinent questions which require further research: (1) How many health states are required to be directly valued (through interviewing respondents) to predict correctly valid utility values for all 3125 health states in the EQ-5D-5L descriptive system? (2) How many observations per health state are required to obtain sufficiently stable (reliable) states? Previous research using a smaller subset of health states found that although the design with 25 states performed closely to the standard EQ-VT with 86 states,[45] there were large mispredictions in case of mild health states. Therefore, the current study aimed to use an increased number of health states and increased number of observations per health state using extended design. As a prospective research area, it would be interesting to assess the performance of different variations of these extended designs.

Conclusion

This is the first study in the South Asian region to present utility values for all the possible EQ-5D-5L health states based on preferences representative of the adult Indian population. This value set will be used to compute QALYs for Indian HTAs and economic evaluations. The value set will facilitate effective conduct of HTAs in India, thereby generating transparent and robust evidence for efficient resource use in healthcare. The study is a stepping stone for further development of a more transparent and consistent decision-making process in healthcare in India. It will also provide a measure of the health status of the general population in India, which could feed into better public health interventions and policies for different patient groups.

Supplemental Materials

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2021.11.1370.

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