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Valuing health-related quality of life among the Indian population: a protocol for the Development of an EQ-5D Value set for India using an Extended design (DEVINE) Study

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ABSTRACT

Introduction Quality-adjusted life year (QALY) has been recommended by the government as preferred outcome measure for Health Technology Assessment (HTA) in India. As country-specific health-related quality of life tariff values are essential for accurate measurement of QALYs, the government of India has commissioned the present study. The aim of this paper is to describe the methods for the Development of an EQ-5D Value set for India using an Extended design (DEVINE) Study. Additionally, this study aspires to establish if the design of 10-time trade-off (TTO) blocks is enough to generate valid value sets.

Methods and analysis A cross-sectional survey using the EuroQol Group's Valuation Technology (EQ-VT) will be undertaken in a sample of 2700 respondents selected from six different states of India using a multistage stratified random sampling technique. The participants will be interviewed using computer-assisted personal interviewing technique. The TTO valuation will be done using 10 composite TTO (c-TTO) tasks and 7 discrete choice experiment (DCE) tasks. Hybrid modelling approach using both c-TTO and DCE data to estimate the potential value set will be applied. Values of all 3125 health states will be predicted using both the conventional EQ-VT design of 10 blocks of 10 TTO tasks, and an extended design of 18 blocks of 10 TTO tasks. The potential added value of the eight additional blocks in overall validity will be tested. The study will deliver value set for India and assess the adequacy of existing 10-blocks design to be able to correctly predict the values of all 3125 health states.

Ethics and dissemination The ethical approval has been obtained from Institutional Ethics Committee of PGIMER, Chandigarh, India. The anonymised EQ-5D-5L value set will be available for general use and in the HTAs commissioned by India's central HTA Agency.

Strengths and limitations of this study

- This is the largest EQ-5D-5L valuation study of the world, and the first preference-based valuation study in the South Asia.
- Generation of the value set will facilitate effective conduct of health technology assessments in India, thereby generating transparent and robust evidence for efficient resource use in healthcare.
- The study will present a useful insight on testing the sensitivity of the current design of the EuroQol Valuation Technology and will present an empirically tested design to generate valid country-specific value sets.
- Due to the exhaustive and lengthy process of interviewing, the respondent fatigue may set in, which may adversely impact the valuation of health states during the latter part of the interview.
- The study aspires to capture health state preferences of the Indian population on the original five dimensions included in the EQ-5D-5L, which was developed in European context, hence there are chances of certain aspects of health being missed, which are important in Indian culture but missing in EQ-5D tool.

INTRODUCTION

Judicious allocation of monetary resources in healthcare is imperative for low/middle-income countries, as they face the problem of large disease burdens and resource scarcity at the same time.[1 2] Health Technology Assessment (HTA) provides valuable evidence for rational allocation of resources for maximising health and enhancing equity.[3–5] HTA refers to the systematic evaluation of properties, effects and/or impacts of healthcare interventions.[6] Economic evaluation is the tool used in HTA to support decision-making in health, where the costs and the consequences of competing interventions are compared.[7] Among the different methods for economic evaluation, cost-utility analysis is preferred to aid in a comparative assessment of several interventions. For such

assessments, the consequences need to be measured in terms of a utility-based index, mostly quality-adjusted life years (QALYs). The quality adjustment in the QALY framework is based on a set of weights called utilities, one for each possible health state. These utilities, which represent people's preferences, are likely to be influenced by several social and cultural factors—necessitating individual country-level assessments.[8–11] However, there are no Indian population-specific value sets available, which limit effective conduct of HTA studies in India.

Meanwhile, India has taken a big leap towards evidence-based policy making by establishing the Health Technology Assessment in India (HTAIn)—an institutional structure created in the Department of Health Research (DHR), Government of India to support credible evidence for supporting policy decisions.[3 4 12] The guideline document for the conduct of HTAs in India has recommended QALY as the preferred outcome measure in HTAs, and EQ-5D-5L as a preferred instrument to measure health-related quality of life (HRQoL) in HTA studies in the country.[13] This necessitates having an India-specific value set for HRQoL, so that QALYs can be assessed correctly in HTAs.[14] Absence of India-specific value set is also a hindrance in undertaking cost-utility studies in the country, as between 1980 and 2014, only 9% of the 104 full economic evaluations were cost-utility analysis.[15] One of the major reasons cited for its low uptake was data limitations including lack of an Indian HRQoL tariff value sets.

In spite of the fact that in absence of a country-specific HRQoL value set, a value set from another country may be used, various socio-demographic and cultural differences between the countries limit the appropriateness and transferability of tariff to Indian population.[16] Comparisons of different national value sets have underlined the existence of differences across countries and the importance of assessing utilities that are country specific.[16] This suggests that choice of tariff has an important impact on economic evaluation studies and funding decisions. Therefore, development of India-specific EQ-5D-5L value set is imperative for a more transparent and consistent decision-making process.

In order to address this requirement, the central HTA agency of the government of India has commissioned the Development of an EQ-5D Value set for India using an Extended design (DEVINE) Study. The proposed study aims to determine the value set for HRQoL for EQ-5D-5L health states among Indian population. Second, the study aims to assess the methodological robustness of the currently used design for generation of value sets, which uses 10-time trade-off (TTO) blocks. In the descriptive system of the EQ-5D-5L, there are 3125 health states. The direct valuation of all the health states by interviewing members of the population is not possible, as it will require a very large sample. Therefore, in the current design, only 86 health states are valued directly using a 10-blocks design, and the values of other 3039 health states are predicted using statistical modelling.[17] However, it has not been established if the currently used number of health states (86) is enough to generate valid value sets. Using the extended design with a richer number of health states (150), this study will not only give an idea about the methodological robustness of current health state valuation studies, but also propose a sound and empirically tested methodology for undertaking health state valuations in HTAs.

METHODS AND ANALYSIS

Study settings

The study will be undertaken in six states of India (figure 1). The selection of states is based on three criteria, that is, income, health status and geographical location of the state. States thus selected are—Haryana, Uttar Pradesh, Gujarat, Odisha, Tamil Nadu and Meghalaya.

Sample size

Sample sizes were estimated first at the level of state, in order to have valid regional level estimations. In order to estimate the sample size, 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 that variable (S=0.53) was used.[18] Assuming absolute precision (d) as 0.05% and 95% CI and applying the formulae of the stratified sampling with allocation based on population proportional to size (PPS), a sample size of 353 was estimated. Assuming a non-response rate of 15%, a sample size of 450 is considered appropriate. Since the data will be collected from six states, the total sample size will be 2700.

Sampling approach

The primary consideration while designing the sampling approach is that the selected sample should be representative of the population composition of the country as much as possible. As a first step in the sampling approach, selection of states (a political unit representing a province) has been made on the basis of a composite criteria, which comprised of indicators related to economic status and income as well as health status of the population. In order to do it, the 29 Indian states were grouped into six categories based on the gross state domestic product[19] and infant mortality rate.[20] One state from each of the six groups has been selected to provide a good mix in terms of their geographical location. A comparison of these states with the country-level estimates on the indicators of income, health and education has been presented in table 1.

In the second stage, two districts will be selected from each state using stratified random sampling approach. The stratification of the districts will be done on the basis of Multi-Dimensional Poverty Index (MDPI),[21] which comprises of three indicators—education, health and living standards. All the districts will be divided into two strata—high MDPI and low MDPI districts. One district

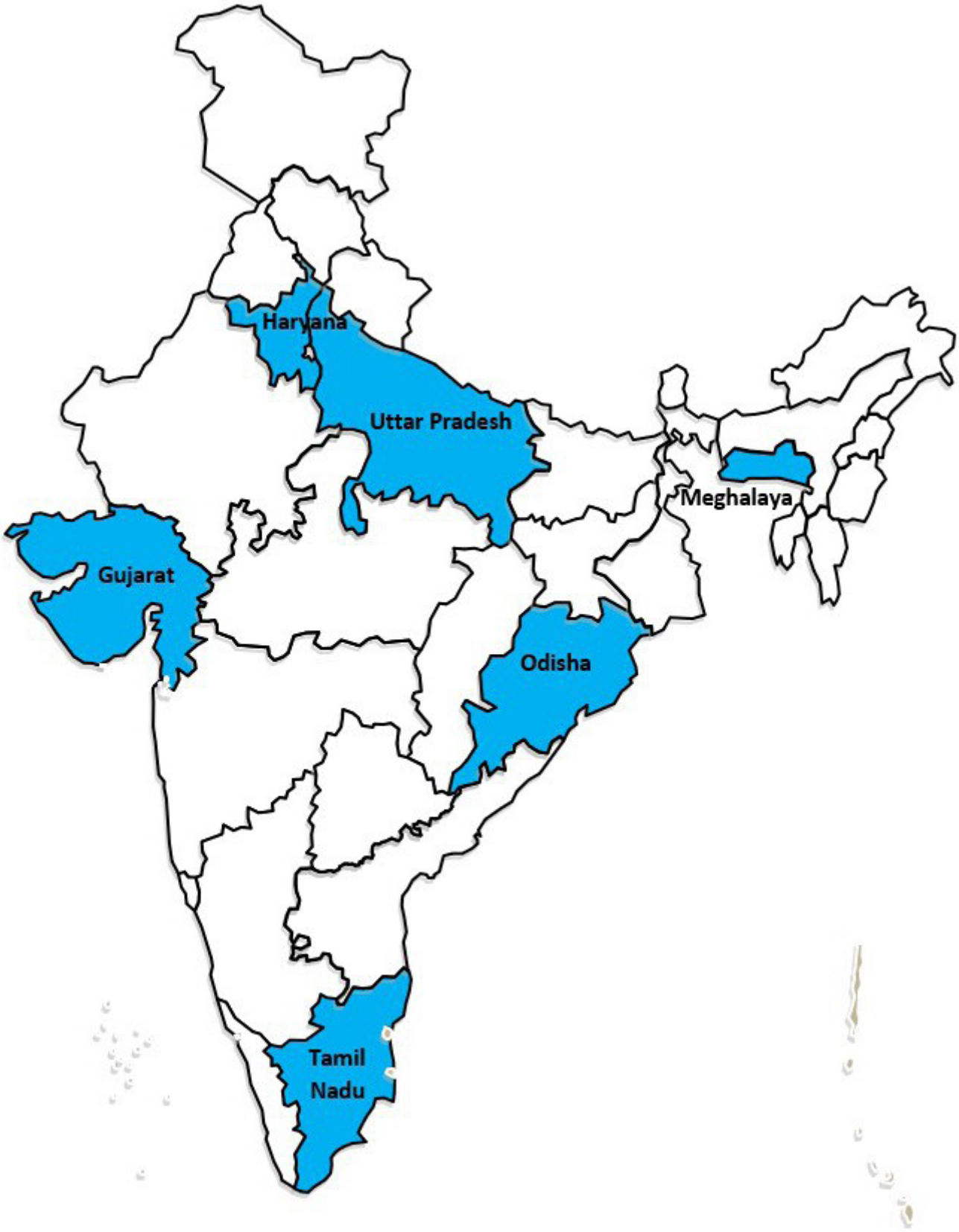

Figure 1 Sites of data collection for development of EQ-5D-5L value set for India.

Table 1 A comparison of the states included in the DEVINE Study with the country-level estimates on the indicators of income, health and education (2018–2019)

	Per capita state domestic product (in INR)[39]	Infant mortality rate[40]	Literacy rate[41]
Uttar Pradesh	66512	41	73
Meghalaya	89024	39	75.5
Odisha	95164	41	77.3
India	126406	33	77.7
Tamil Nadu	193750	16	82.9
Gujarat	197447	30	82.4
Haryana	236147	30	80.4

DEVINE, Development of an EQ-5D Value set for India using an Extended design; INR, Indian rupees.

will be selected randomly from each stratum using simple random sampling approach.

The third stage of the sample selection is to select primary sampling units (PSUs) in each of the selected districts. Villages and Census Enumeration Blocks (CEBs) will be taken as PSUs in rural and urban areas, respectively. The study will employ the '30-cluster sampling approach' which has been recommended by the WHO.[22] Originally used to measure immunisation coverage, it is now used as a standard approach for various public health studies and government surveys. One of the advantages is that this approach uses PPS method for selection of the sampling unit. Within a district, the 30 clusters to be selected would be distributed between rural and urban areas in accordance with the proportion of rural and urban population in the composition of the district.

The next step of sample selection will be to select households within the PSU (village/CEB). For this, first the sample size will be fixed for each PSU, which comes around eight. Thereafter, households within the PSU will be selected using systematic random sampling. As the people belonging to different castes and socioeconomic groups are usually aggregated in the clusters in every village, systematic random sampling after selecting the first household randomly, would allow to select a sample which has representation from each of these communities.

The last step in the process of sampling is selection of respondent from each household. An adult (more than 18 years of age) household member having birthdate most proximal to the day of interview will be selected for interview. Block randomisation on the basis of gender will be done to select the respondent from the household.

Valuation methods

The participants will be interviewed in a face-to-face setting using computer-assisted personal interviewing technique. We will be using EuroQol Group's Valuation Technology (EQ-VT) software generated by the EuroQol Group. Each respondent will be asked to complete sociodemographic details and self-reported health questionnaire using EQ-5D-5L and the EuroQol Visual Analogue Scale (EQ-VAS). TTO valuation will be done using 10 composite TTO (c-TTO) tasks and 7 discrete choice experiment (DCE) tasks.

In the standard design of c-TTO, there will be 10 blocks of health states. Each block will contain 10 health states which include one anchor state (55555). The blocks used for interview will be randomly selected by the EQ-VT software. In TTO valuation, the respondent is asked to indicate the amount of time he/she is willing to give up to attain perfect health. The respondent will be asked to imagine two alternative health states (life A and life B) described on screen and express the preference using TTO. The respondents will be asked whether they prefer to live for 10 years in perfect health (life A) or 10 years in some inferior health state (life B). It will also be explained to the respondents that at the end of the stated time, there will be an immediate painless death in both the lives. If the respondent prefers life A, he or she will be presented with the next question, in which he or she will have to choose between dying immediately or living for 10 years in life B. If the respondent prefers living in an inferior health state (as described in life B) over the immediate death (life A), he or she will be presented with the next question, where 5 years in full health will be provided in life A, and 10 years in some inferior health state will be provided in life B. Hence, the time available in life B will be kept constant at 10 years, while the time available in life A will be changed sequentially, and the respondent will be asked to select the better alternative between life A and life B. Thereby, the respondent will be asked to state its preference between 'living for 10 years in an inferior health state', or 'living for less than 10 years in perfect health'. This exercise will be done until the point of indifference is achieved (when the respondent feels that both life A and life B are of equal value). At this point of indifference, the traded-off time in life A will be recorded, which reflects the time in perfect health the respondent is willing to give up in order to avoid living in the inferior health state (life B). The severe the health state, the more is the time the respondent wants to give up to avoid it. This exercise is known as conventional TTO.

Nevertheless, there are certain health states, for which the respondent may prefer to die immediately rather than living in that health state. These health states are known as worse than dead (WTD). We will use lead time TTO (L-TTO) for health states that respondents consider WTD. The c-TTO approach is a combination of the conventional TTO (which is used for better than dead health states) and L-TTO (which is used for states WTD). The c-TTO approach will begin with the conventional TTO for all health states, followed by an L-TTO in the scenario where the participants' response will indicate the health state to be WTD. The L-TTO involves adding healthy life years ('lead time') before both the alternatives (life A and life B) being compared. This will allow the respondent to trade off these additional years when

he or she considers the health state in life B to be WTD. As per the EuroQol group's recommendations, a lead time of 10 years will be used.[17] The value of health will be calculated as x/t for better than dead health states and (x−10)/t for WTD health states, where 'x' is the time remaining in life A at the point of indifference, and 't' is the time offered in life B, that is, 10 years.[23] This being a cognitively demanding exercise, first a small training exercise using an example of 'being in a wheelchair' as life B will be performed with the respondent to make sure the respondent understands the concept of TTO.[23] The concept trading off the time in both 'better than dead' and 'WTD' health states will be explained in this exercise. This will be followed by three practice tasks in which the respondent will be asked to value three health states of varying severity (mild, severe and difficult to imagine). Once the wheelchair example and practice exercises get over, the respondents will be assigned a block of 10 health states, on which the valuation will be done.

In the DCE task, the respondents will be presented with two different health states in which the levels, but not the order of the attributes, will be differed and the respondents will be asked to choose one among the two. The 196 pairs of DCE health states will be distributed over 28 blocks thus resulting in seven pairs per respondent.[24] These DCE task blocks will be balanced in terms of their severity, which will be calculated as the sum of the level scores on all dimensions.

Modelling

Modelling will be undertaken using the Stata statistical package. TTO data will be modelled using the response values as dependent and the health states as explanatory variables. A main effects model will be employed that will include a constant and five main effects derived from the EQ-5D-5L descriptive system, using generalised least squares (GLS) and tobit models. The constant will reflect the utility decrement associated with any deviation from full health. Random effects will be included to account for the panel structure in the data. The basic equation for the random-effects GLS regression with random intercept will be as follows:

$$Y_{it} = \beta_{0i} + \beta_{MO}MO_{it} + \beta_{SC}SC_{it} + \beta_{UA}UA_{it} + \beta_{PD}PD_{it} + \beta_{AD}AD_{it} + \varepsilon_{it} + \mu_{0i}, \quad (1)$$

where Y_{it} refers to the TTO values dependent variable, μ_{0i} will be the respondent specific error component and ε_{it} refers to the response-related error term, i indicating the respondent and t accounting for the panel structure of the dataset (because there are 10 c-TTO questions per respondent). The terms MO, SC, UA, PD and AD refer to five dummy-coded regressors for mobility, self-care, usual activities, pain/discomfort and anxiety/depression, each representing the five levels of the EQ-5D-5L. So in the equation 1, each dimension has four coefficient with first level as baseline is:

$$\beta_{MO}MO_{it} = \beta_{M1}MO2_{it} + \beta_{M2}MO3_{it} + \beta_{M3}MO4_{it} + \beta_{M4}MO5_{it},$$

which is similar for SC, UA, PD and AD, leading to a total of 20 regressors plus the constant. The tobit model will assume a latent variable Y_{it}^{*} underlying the observed Y_{it} c-TTO values. This will match with the censored c-TTO data, which by nature of the applied c-TTO task will be left-censored at −1. The tobit model will account for this censored nature of the data by estimating the latent variable Y_{it}^{*}, which can take on predicted preference values extrapolated beyond the range of the observed values. A likelihood function will be 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} will have the following properties when the censoring value is −1:

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

The equation for Y_{it}^{*} will be linear. The DCE data will be modelled under random utility using the conditional logit model. The model will include the same five parameters as the c-TTO model, reflecting utility decrements associated with levels 1, 2, 3, 4 and 5 for each of the five domains: MO, SC, UA, PD and AD. This model will have same structure as equation 1 regarding the parameters for the level-attribute combinations, so it will be a 20-parameter model as well. 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 will be the choice alternative in the choice sets.

As both TTO and DCE data provide information about the values of health states, we will also implement a hybrid modelling approach that will make use of both c-TTO and DCE datasets to estimate the potential value sets. This approach has been used in several national EQ-5D-5L valuation studies.[25–33] The hybrid model will combine the likelihood functions of a linear model for the c-TTO data and a logit model for the DCE data. As the coefficients will be estimated from a conditional logit and expressed on a latent arbitrary utility scale, we will use a rescaled parameter θ, which will assume that the c-TTO model coefficients are proportional to DCE model coefficients. This method will combine the utility values elicited in the c-TTO for the 150 health states with utility values elicited in the DCE experiment for 196 pairs of states. We will use cluster estimation to acknowledge that for each participant included in the models, 10 c-TTO and 7 DCE responses are available. We will also estimate adjusted hybrid model which adjusts the social demographical variables like age, sex and so on.

Sensitivity analysis

A sensitivity analysis will be conducted to explore the mechanism through which presence of severely inconsistent responses impacts the modelling of c-TTO results. All c-TTO responses will be removed for respondents who will value state 55555 higher than any other state.

A pair of c-TTO responses will be considered logically inconsistent if the observed values of two states, state A and state B, will contradict the logical ordering of health states. That is if state A is better on at least one dimension and no worse on other dimensions compared with state B, then state A should logically receive a higher value. If state B receives a lower value instead, the response will then be considered as logically inconsistent. Considering, however, that many inconsistencies may occur as a result of random error, the 'seriousness' of the inconsistencies will be evaluated by the size of utility difference between two states. Random error will always occur and is typically not considered a sufficient reason for exclusion. For this reason, the sensitivity analysis will exclude only a subset of inconsistent responses.

DCE responses will be considered to be problematic if the responses of the respondent follow a particular pattern (eg, AAAAAA, BBBBBB, ABABABAB and so on) Regression will be reperformed in order to assess the impact of removing DCE data that follows a particular pattern.

EQ-5D-5L reference values

Reference values for the Indian population will be calculated by multiplying the EQ-5D scores of the respondent selected for the model (N=2700) with the coefficients of the preferred regression model. The sample will be stratified on age, sex and education and it is for this stratification that the sample is representative.

Quality control

In order to ensure standardisation of the data collection process, stringent quality control (QC) process will be followed throughout the study. As the difference among relative severity of the EQ-5D health states is subtle, it is important that the differences observed in the health state valuation of the different health states is because of the difference in the population preferences and not because of the difference in the process of conducting the interview. Therefore, the recommendations of the latest EQ-VT protocol will be followed to standardise the data collection process across different regions of the country.[17 23 34] First, a training of trainers on EQ-VT was organised at EuroQol Head Office. These trainers will organise hands-on training of interviewers at all the sites using a uniform training agenda. Given the linguistic diversity among the states, every state will be assigned its own set of interviewers and separate training sessions will be organised for all the states. For the purpose of data collection, EQ-VT and EQ-5D-5L have been translated into five different Indian languages (Hindi, Gujarati, Tamil, Odia and Assamese). After the hands-on training, the interviewers will be put through a process of pilot interviewing. Every interviewer will be conducting pilot interviews until the point the protocol compliance has been achieved and the interviewers' effects have disappeared. The EuroQol Foundation has developed an MS Excel-based QC tool, which will be used to evaluate interviewers' performance.[35] This tool determines protocol compliance, interviewers' effects and mean values by health state severity.[36] This QC check will be run once each interviewer will have performed a round of 10 interviews. Observations of the QC check will be used by the EuroQol experts and local team of investigators to provide personalised feedback via phone calls to all the interviewers. Interviews are flagged as non-compliant if the explanations for the two wheelchair example exercises last for less than 3 min, if the WTD element is not shown in the examples, if the duration of the 10 real c-TTO tasks is less than 5 min, or if the value given to the worst health state (health state '55555', which is always the worst state presented to every respondent) is not the lowest and at least 0.5 higher than that of the state with the lowest value.[35–37]As a part of quality control, interviewers' effect will also be assessed in addition to the protocol compliance. The presence of interviewers' effect in the data will be assessed by indicators like distribution of TTO responses with respect to different health states for each interviewer, presence of clustering the TTO responses, health states given a value of '0' in the TTO tasks, health states given value of 'less than 0' in the TTO tasks and proportion of non-traders (individuals who refuse to give up any amount of time in the TTO, thus giving all health states the value of 1) in the respondents. The distribution of TTO responses will be interpreted by comparing the data of a specific interviewer with the pooled data from all interviewers. Any interviewer reflecting interviewers' effect will be assisted by local team of investigators via phone and video calls during the conduct of next round of pilot interviews. During this process, we will investigate whether the interviewer's behaviour is influencing the responses of the respondent, whether the interviewer explains the task well, and the interviewer is not shortcutting the tasks. Personalised feedback will be provided to interviewers to overcome any such difficulty. Poor performing interviewers will be retrained and removed from the team if no improvement is seen after retraining. The interviewers will be allowed to start the real data collection once they will have achieved a stable performance on the QC protocol. This QC check and personalised feedback process will constantly be followed throughout the process of real data collection.

Testing the extended EQ-VT design

Over the last several years, a lot of formal studies tried to create methodological convergence in the valuation work.[17 25 34 36] It has been done with the aim to assign a valid utility value to every health state. However, as the number and requirement of the value sets rapidly increase due to the increased use of HTA in the decision-making across the globe, there has been a felt need for more efficient ways to obtain a value set, than in the past. The pertinent questions are: first, how many health states are required to be directly valued (through interviewing respondents) to correctly predict the valid utility score of all 3125 health states in the EQ-5D-5L descriptive system,

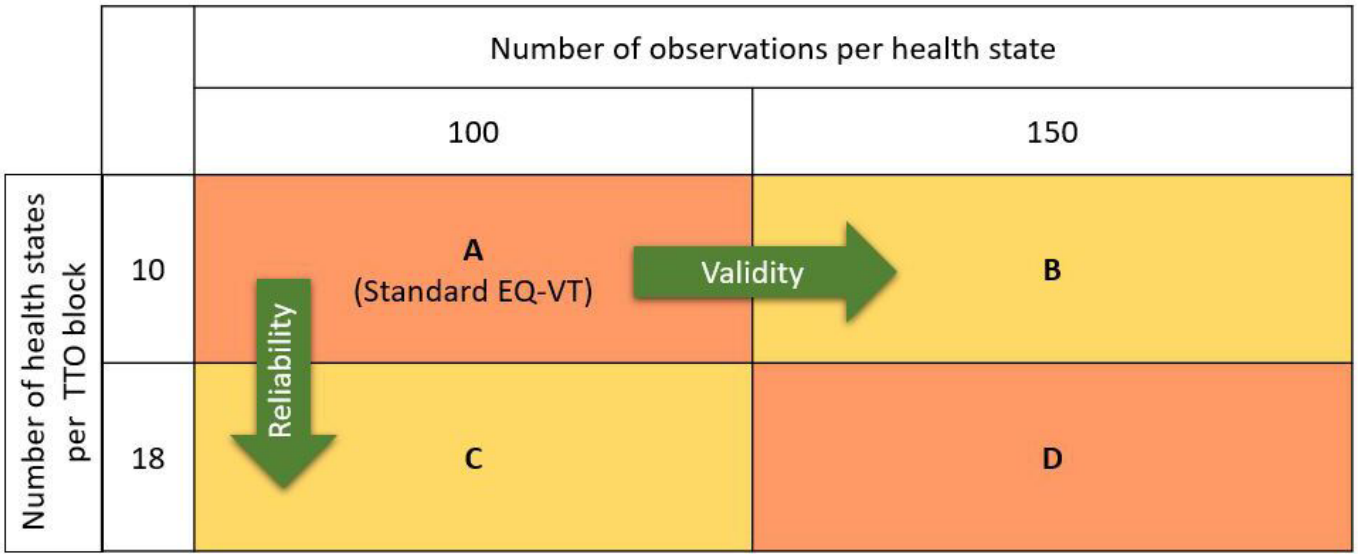

Figure 2 Analytical strategy to assess the validity and reliability of the extended EQ-VT design. EQ-VT, EuroQol Group's Valuation Technology; TTO, time trade-off.

and second, how many observations per health state are required to obtain sufficiently stable (reliable) states (figure 2).

In contrast to the conventional EQ-VT protocol, which is optimised for a sample size of around 1000, the current study aims to collect data from 2700 respondents. This offers an opportunity to add more health states and assess the additional value of using a richer number of health states in predicting the utility value of all 3125 health states. In the conventional EQ-VT design, for the method TTO, 10 blocks of health states are used, which account for 86 different health states. These health states are selected using DCE technique, combining orthogonality with priors. Each block includes one most severe health state (55555) as anchor state, and one of the five very mild health states (which demonstrates slight problem in any one of the five dimensions, that is, 11112, 11121, 11211, 12111 and 21111). The remaining eight unique health states in each block (in total 80 health states in 10 blocks) are selected using Monte Carlo simulations to predict the prior values obtained from the multinational pilot study.[17] This set of 80 states is selected on the mean squared error (MSE) between the prior parameters and estimated parameters from a main effects model, and level balance, but without making orthogonality an explicit criterion.[24 38] A dedicated direct EQ-VAS valuation study employing saturated VAS dataset compared the prediction performance of the 86 health states subset with alternative smaller subset of health states.[38] The study found that the orthogonal design with 25 states performed closely to the standard EQ-VT with 86 states. However, a caveat to the use of the small orthogonal design lies in the large mispredictions in case of mild health states. Therefore, the current study aims to assess the added value of increased number of health states and increased number of observations per health state using extended design. In the extended design for the current study, 8 additional blocks have been added, consisting of 64 new health states. This selection was guided by added-value considerations, taking the initial 10 blocks as point of departure. Hence, we have a conventional 10 blocks design, and an extended 10+8 blocks design. The potential added value of eight blocks is not in more precision (reliability) but in more overall validity.

In order to assess the increased value of the eight added blocks, we will compare the value set (coefficients, error, MSE) derived from the predefined 10 blocks with 1000 sample size (from 25 random drawings of 10 out of the 18 blocks), and from 18 blocks with 2700 sample size. If going from 10 to 18 blocks does not add precision nor induce systematic value changes, then we may safely state the earlier design of 10 blocks was enough for correct prediction of utility values for all the health states of the EQ-5D-5L descriptive system. If the standard 10-block design will not perform essentially different from 10 randomly drawn blocks, it would reflect that all sophistication in design does not pay off. The result per health state will be compared for different n=10 block selections. It will be assessed whether the current 10 standard blocks are systematically closer to the assumed best estimate obtained by any other n=10 block selection. We will also analyse results of different n=10 block drawings by assigning some imbalance of domain/level indicator.

As defined in figure 2, we have four models (A, B, C and D) with different configuration of blocks and number of observations (sample size). We will make pairwise comparison for these models to check the reliability of the models as follows:

To investigate reliability effects (from A to B), we will carry out standard TTO analysis with the 10-block (100 observations per health state) dataset, essentially all regions combined. We will explore possibility to conduct the same analysis within each region as well. The 18-block (150 observation per health state) dataset permits an

analysis of stability, where the most interesting seems the precision of the mean (hence size of SEM) of health states with 'known' higher random error, such as with large stress. We will compare results obtained with standard 100–150 (A vs B).

We will compare observed values of additional 64 health states and predicted values of traditional method with 10 blocks and 1000 sample after controlling the sociodemographic variables like age, gender and so on by using scatter plot with calculated R square value (correlation coefficient) or Wilcoxon match pair signed rank test (non-parametric test).

The value set generated as a part of this study will be useful for clinicians to measure clinical effectiveness of interventions, epidemiologists to measure the burden of disease and health economists to undertake 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. Using the extended design, the results of the study will also suggest the optimum number of health states required to be directly valued in order to correctly predict the values of all 3125 health states of the EQ-5D-5L. Thus, the present study would be a stepping stone for further development of a more transparent and consistent decision-making in healthcare. 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.

Patient and public involvement

No patient or public involvement was there in the designing of this research protocol. Public involvement during the conduct and dissemination of the study will strictly be as per the established standards of ethics in research.

ETHICS AND DISSEMINATION

All interviews will be conducted with care and sensitivity and with respect for participants' ethnicity, religion, language, sexual orientation or literacy level. Participants will be presented the study's participant information sheets, sign the informed consent forms and be interviewed, all within one visit. All participants will be given enough time to read or be read the participant information sheet and to ask questions and discuss concerns regarding potential participation in the study. The ethical approval to conduct the study has been obtained from Institutional Ethics Committee of Postgraduate Institute of Medical Education and Research, Chandigarh, India vide letter no. PGI/IEC/2018/001629.

The dissemination plan for this project includes deliverables for the scientific community in the form of scientific articles and conference presentations. Publication guidelines will be followed as per the international guidelines for authorship as per specific contribution according to International Committee of Medical Journal Editors. The anonymised EQ-5D-5L value set will be available for general use via website hosted by School of Public Health, Postgraduate Institute of Medical Education and Research, and HTAIn, DHR, Ministry of Health and Family Welfare, Government of India.

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