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The Indian EQ-5D-5L Value Set

Development of Health Related Quality of Life Value-set (EQ-5D-5L) for India

Health Technology Assessment in India

Department of Health Research, MoHFW

New Delhi (India)

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Department of Community Medicine & School of Public Health

Postgraduate Institute of Medical Education & Research

Chandigarh (India)

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The Indian EQ-5D-5L Value Set

Health Technology Assessment in India (HTAIn)
Department of Health Research,
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List of Abbreviations

BTD	**:** Better than dead
c-TTO	**:** composite- Time trade off
DCE	**:** Discrete Choice Experiment
DHR	**:** Department of Health Research
EQ	**:** The EuroQol Research Foundation
EQ-5D-5L	**:** EuroQol 5 Dimensions 5 Levels instrument
EQ-VAS	**:** EuroQol Visual Analogue Scale
EQ-VT	**:** EuroQol Valuation Technology
HRQoL	**:** Health related quality of life
HTA	**:** Health Technology Assessment
HTAIn	**:** Health Technology Assessment in India
QALY	**:** Quality adjusted life year
QC	**:** Quality Check
TTO	**:** Time trade off
WTD	**:** Worse than dead

Executive Summary

Health Technology Assessment (HTA) is a tool for prudent resource allocation and evidence informed decision making in health. However, unavailability of country specific health state tariff- values limits effective conduct of HTA in India. DHR HTA guidelines document recommends the use of quality adjusted life years (QALYs) as the preferred outcome measure and EQ-5D as preferred tool for its health state valuation. Therefore, this study has been commissioned to develop EuroQol five-dimensional (EQ-5D-5L) health states value set for Indian population. In this study, a nation- wide cross-sectional survey using the EuroQol Group's Valuation Technology (EQ-VT) software is being undertaken in nationally representative sample. The aim of the study was to generate the Indian tariff values of all the 3125 possible EQ-5D-5L health states, so that the health profiles of the patients can be converted to the corresponding quality of life scores, and outcome valuation in the HTA studies can be done effectively.

The interviews for the study were being administered by qualified interviewers, which were fluent in English as well as local language. Keeping in mind the linguistic diversity of the partner institutes, separate team of interviewers were recruited at all the partner institutes. These interviewers were extensively trained on the EQ-VT software by the PGIMER team. These training sessions were held at every partner institute. It was followed by an intensive pilot- testing, so that the protocol compliance can be ensured and the interviewer effect in the data can be ruled out. Once certified by the EuroQol and PGIMER experts, the interviewers were sent to field to conduct real interviews. To ensure continuous protocol compliance throughout the data collection, daily monitoring of the data collection was

undertaken at PGIMER with the help of Quality Check (QC) software and group calls, and individual telephonic feedback is provided to interviewers. The study was proposed to be conducted in 6 different states of India (Haryana, Uttar Pradesh, Meghalaya, Odisha, Gujarat and Tamil Nadu). Whereas PGIMER Chandigarh served as the nodal centre to carry-out the study activities, the recruitment, training and data-collection at the respective states were undertaken by the partner institutes in these states. JIPMER Pondicherry served as the coordinating institute for Tamil Nadu, IIPH Gandhinagar for Gujarat, AMS Lucknow for Uttar Pradesh, AIIMS Bhubaneshwar for Odisha, and NEIGRIHMS Shillong served as the coordinating institute for Meghalaya. The data collection in Haryana was undertaken by PGIMER Chandigarh itself. The states are so selected that these are representative of geographical location, economic status and health status. The participants, which are selected using multistage stratified random sampling technique, were interviewed in a face to face setting using CAPI (computer assisted personal interviewing) technique.

To estimate the value set, hybrid modeling approach using both composite time trade off (cTTO) and discrete choice experiment (DCE) has been applied. The value set generated as a part of this study will be be useful for clinicians undertaking studies to measure clinical effectiveness of interventions, epidemiologists to measure the burden of disease, and health economists to undertake HTAs. In addition to enabling effective conduct of HTA in India, this value set will also be helpful in clinical practice/research for better monitoring of health-related quality of life. The scores can be used as an important input that better reflect Indian population's preference for health technology assessment research. In addition, the results can be used for international comparison to understand similarities and differences of health preference across populations.

The COVID pandemic has impacted the progress of the study. Prior to the beginning of the pandemic and imposition of nation-wide lockdown, the data collection was completed in the states of Haryana, Uttar Pradesh, Odisha, Gujarat and Tamil Nadu. However, the data-collection in the state of Meghalaya was yet to start. As in interim solution to the problem, the data from the five states was analysed, and the current version of the EQ-5D-5L value-set contains data from these five states (Haryana, Uttar Pradesh, Odisha, Gujarat and Tamil Nadu), barring Meghalaya. The representation from the Meghalaya will be incorporated as soon as it would become feasible to resume the data collection.

In addition to the generation of the Indian EQ-5D-5L value-set, the vast and diverse data collected as a part of this study will be used to improve the methodological rigour of the national valuation studies. This analysis will be incorporated in the final outcome report of the study, which will have the data from all the six states of India.

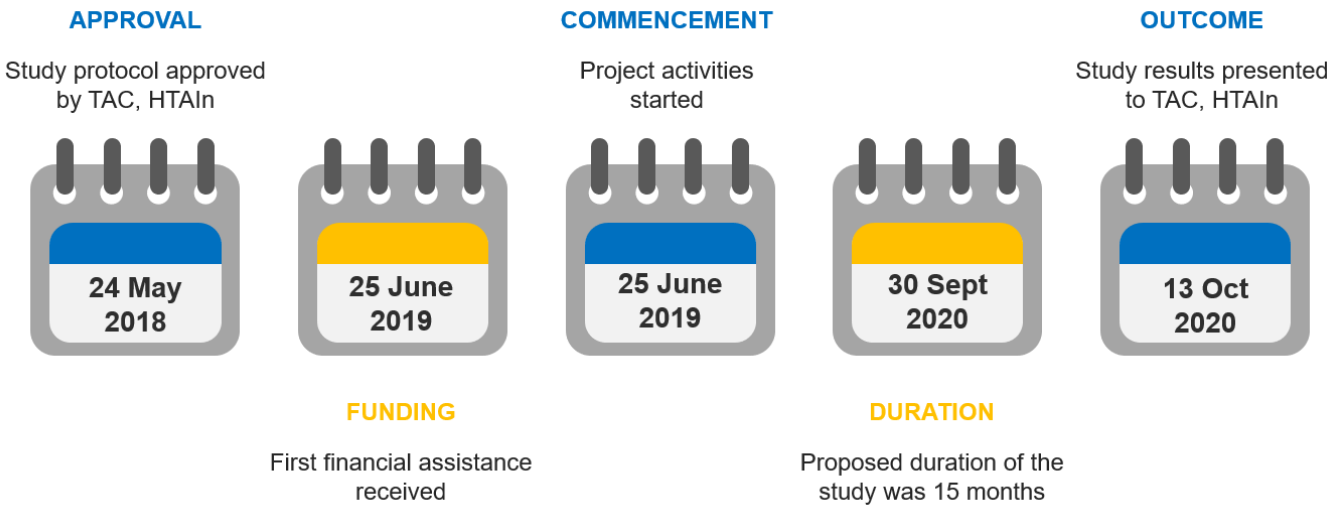
October 2020

Chandigarh

Study Highlights

- This is the largest EQ-5D-5L valuation study of the world, and the first preference-based valuation study in the South- Asia.
- The EQ-5D-5L value set was derived from a highly representative sample of the Indian general population. Data were collected using a rigorous quality control procedure, which led to logical and significant models.
- This value- set will facilitate effective conduct of health technology assessments in India, thereby generating transparent and robust evidence for efficient resource use in healthcare.
- In the Indian EQ-5D-5L value set, the maximum utility value is 1.000 for the full health (health state '11111'). It is followed by the health state '11112', which has the utility value of 0.984.
- The minimum utility value is -0.923 for the '55555' health state, which is the worst possible health state.
- Maximum problems have been reported in the dimension of 'pain/ discomfort'. 55% of the respondents had some kind of pain/ discomfort on the day of interview.
- Minimum problems have been reported in the dimension of 'self-care'. Only 15% of the respondents had some problem in doing self-care activities (washing/ dressing themselves) on the day of interview.
- The mean EQ-VAS score of the Indian population is 75.18

- 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.
- The study aspires to capture health state preferences of the Indian population on the original five dimensions included in the EQ-5D, 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.
- The study was funded by the Department of Health Research, Ministry of Health and Family Welfare, Government of India vide grant number F.NO.T.11011/02/2017-HR/3176774.
- Administrative timelines: The research protocol of the study was approved by the Technical Appraisal Committee (TAC) of HTAIn in its meeting held on 24th May, 2018. The first annual instalment of the financial assistance was received on 25th June 2019. The project started on 25th June 2019, and the total duration of the project is 15 months.



- Details of the valid interviews* conducted in different states for the generation of the value set (as on 9th October 2020):

Sr. No.	Name of the State	Coordinating Institute	Interviewer Training	Pilot Phase- 1, 2 and 3	Proposed number of real interviews	Completed number of interviews as on 9th October 2020	Final Status
1	**Haryana**	PGIMER, Chandigarh	Completed	Completed	435	480	Completed
2	**Tamil Nadu**	JIPMER, Puducherry	Completed	Completed	435	480	Completed
3	**Gujarat**	IIPH, Gandhinagar	Completed	Completed	435	450	Completed
4	**Uttar Pradesh**	AMS, Lucknow	Completed	Completed	435	519	Completed
5	**Odisha**	AIIMS, Bhubaneshwar	Completed	Completed	435	480	Completed
Total	**All sites**	PGIMER, Chandigarh	Completed	Completed	2175	2409	Completed (Meghalaya dropped due to COVID-19)

*This table summarizes the details of valid interviews only, which have been used in the development of the national value set. It omits interviews conducted in pilot phases, blacklisted interviews, and interviews containing invalid observations. The actual number of interviews conducted is 3548, out of which 2409 are valid interviews.

- Verbal consent of study participants was taken prior to clicking their photographs for the purpose of inclusion in the reports/ publications.

Need for the Indian EQ-5D-5L Value- set

Judicious allocation of monetary resources in healthcare is imperative for Low- and Middle-Income Countries (LMICs), 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 maximizing 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, wherein 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 limits 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 hinderance 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 value sets. India does not have an EQ-5D value set, either for the 3-level or for the new 5-level version. Previous HTA/ HRQoL studies conducted in India measured health preferences using the Thailand value set. It is worthwhile to mention here that there are only 26 such value sets are available across the globe, and none from the South Asia. Table-1 summarizes the details of all the EQ-5D-5L value sets developed so far.

Table 1: List of available EQ-5D-5L value-sets (as of September 2020)

Sr. No.	Country	Year	Sample Size
AFRICA			
1	Ethiopia	2018	1050
ASIA			
2	China	2012	1271
3	Hong Kong	2014	1033
4	Indonesia	2015	1054
5	Japan	2013	1026
6	Malaysia	2016	1137
7	Philippines	2017	-
8	Singapore	2014-15	-
9	South Korea	2013	-
10	Taiwan	2017	1000
11	Thailand	2014	1207
12	Vietnam	-	-
EUROPE			
13	England	2012	996
14	France	2018	-
15	Germany	2015	1158
16	Hungary	2018	-
17	Ireland	2015-16	1160
18	Netherlands	2012	1003
19	Poland	2016	1252
20	Portugal	2015-16	1451
21	Spain	2012	1000
NORTH AND SOUTH AMERICA			
22	Canada	2012	1073
23	Peru	2018	1000

24	Uruguay	2013	794
25	USA	2017	1062
OCEANIA			
26	Australia	2017	300

*Value sets for some countries have not been published yet, so exact sample size has not been reported.

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.

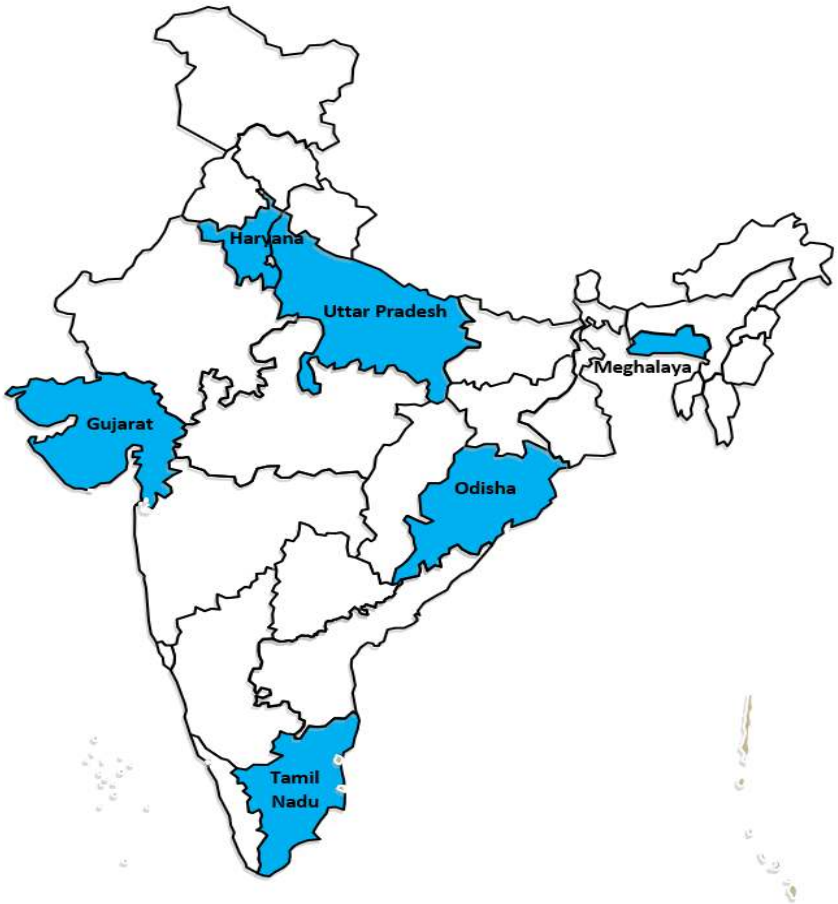
In order to address this requirement, HTAIn (Health Technology Assessment in India), the central HTA agency of Government of India, has commissioned this study. The proposed study aims to determine the value- set for HRQoL for EQ-5D-5L health states among Indian population. Secondly, the study also aims to assess the methodological robustness of the currently used design for generation of value- sets, which uses 10 time trade off (TTO) blocks. Hence, 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 health technology assessments.

Study Execution and Field Work

Study settings

The study was undertaken in 6 states of India (Figure-1). The selection of states is based on three criteria, i.e., income, health status and geographic location of the state. States thus selected are – Haryana, Uttar Pradesh, Gujarat, Odisha, Tamil Nadu and Meghalaya.

Figure 1: Sites of data collection for development of EQ5D5L value set for India



*Representative map, not to scale.

Whereas PGIMER Chandigarh served as the nodal centre to carry-out the study activities, the recruitment, training and data-collection at the respective states were undertaken by the partner institutes in these states. JIPMER Pondicherry served as the coordinating institute for Tamil Nadu, IIPH Gandhinagar served for Gujarat, AMS Lucknow served for Uttar Pradesh, AIIMS Bhubaneshwar served for Odisha, and NEIGRIHMS Shillong served as the coordinating institute for Meghalaya. The data collection in Haryana was undertaken by PGIMER Chandigarh itself.

As a response to the COVID-19 pandemic, the field activities in the state of Meghalaya had to be stopped on 22nd March 2020. At the time of enforcement of the nation-wide lockdown, the interviewer training and three pilot phases of the interviews had been conducted successfully, but real interviews were yet to be started. Thereby, out of the proposed six sites of the data collection, five sites have successfully completed the data collection, however, the data collection in Meghalaya has not been started yet. Overall, out of total interviews proposed in the research protocol of the project, 2409 interviews have been conducted, and 450 interviews are pending. As the data collection had to be stopped, the interim analysis of the data obtained from 2409 interviews had been done to prepare the value set for India. The details of the respective interviews conducted at the respective sites has been mentioned in the Table-2. This table summarizes the details of valid interviews only, which have been used in the development of the national value set. It omits interviews conducted in pilot phases, blacklisted interviews, and interviews containing incomplete and invalid observations. The actual number of interviews conducted is 3186, out of which 2409 are valid interviews. Out of these, 2311 complete interviews were used for generation of the value set.

Table 2: Details of the valid interviews conducted in different states for the generation of the value set (as on 9th October 2020)

Sr. No.	Name of the State	Coordinating Institute	Interviewer Training	Pilot Phase- 1, 2 and 3	Proposed number of real interviews	Completed number of interviews as on 15th September 2020	Final Status
1	**Haryana**	PGIMER, Chandigarh	Completed	Completed	435	480	Completed
2	**Tamil Nadu**	JIPMER, Puducherry	Completed	Completed	435	480	Completed
3	**Gujarat**	IIPH, Gandhinagar	Completed	Completed	435	450	Completed
4	**Uttar Pradesh**	AMS, Lucknow	Completed	Completed	435	519	Completed
5	**Odisha**	AIIMS, Bhubaneshwar	Completed	Completed	435	480	Completed
6	**Meghalaya**	NEIGRIHMS, Shillong	Completed	Completed	435	Dropped due to COVID-19	Dropped due to COVID-19
Total	**All sites**	PGIMER, Chandigarh	Completed	Completed	2175	2409	Completed (Meghalaya dropped due to COVID-19)

Samples 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 was

considered as the main variable of interest and the mean of this variable as the target parameter. The estimated standard deviation of that variable (S = 0.53) was used.[17] Assuming absolute precision (d) as 0.05 and 95% confidence interval and applying the formulae of the stratified sampling with allocation based on population proportional to size (PPS), a sample size of 435 was considered appropriate. Since the data was proposed to be collected from 6 states, the total sample size is 2610. Since the data collection in Meghalaya had to be stopped due to COVID-19, the cumulative sample for five states was estimated as 2175.

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 health status of the population. In order to do it, all Indian states were grouped into six categories based on the Gross State Domestic Product (GSDP) [18] and Infant Mortality Rate (IMR).[19] One state from each of the six groups has been selected to provide a good mix in terms of their geographic location. A comparison of these states with the country level estimates on the indicators of income, health and education has been presented in the Table-3.

Table 3: A comparison of the states included in the study with the country level estimates on the indicators of income, health, and education (2018-19)

	Per Capita State Domestic Product (in INR)[20]	Infant Mortality Rate[21]	Literacy Rate (percentage)[22]
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

In the second stage, two districts have been selected from each state using stratified random sampling approach. The stratification of the districts was done on the basis of Multi-Dimensional Poverty Index (MDPI),[23] which comprises of three indicators - education, health and living standards. All the districts were divided into two strata- high MDPI and low MDPI districts. One district was selected randomly from each stratum using simple random sampling approach.

The third stage of the sample selection was to select primary sampling units (PSUs) in each of the selected districts. Villages and Census Enumeration Blocks (CEBs) were taken as PSUs

in rural and urban areas, respectively. The study employed the '30-cluster sampling approach' which has been recommended by the World Health Organization (WHO).[24] Originally used to measure immunization 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 Probability Proportional to Size (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 was to select households within the PSU (village/ CEB). For this, first the sample size was be fixed for each PSU, which comes around 8. Thereafter, households within the PSU were selected using systematic random sampling. As the people belonging to different castes and socio-economic groups are usually aggregated in the clusters in every village, systematic random sampling after selecting the 1st household randomly allowed us to select a sample which has representation from each of these communities.

The last step in the process of sampling was 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 was selected for interview. Block randomization on the basis of gender was done to select the respondent from the household.

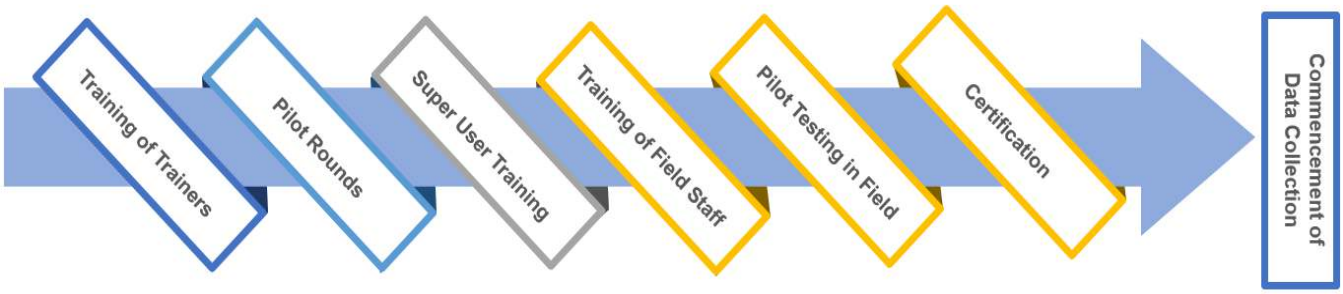
Training of the study team and pilot testing

As the data collection for the study was proposed to be done using EuroQol Valuation Technology (EQ-VT) software, the study team was extensively trained on the use of this software. First, a Training of Trainers on EQ-VT was organized at EuroQol Head Office at Amsterdam, The Netherlands. All the sites were represented in this training of trainers. This was done keeping in mind the linguistic variation among the different study sites. All the participants of this training were made well versed with the operationalization of the EQ-VT software and analysis of its output. The output analysis was explained extensively as it plays a vital role on tracking the performance of the local interviewers using the quality check (QC) indicators. Therefore, the generation and analysis of the individual and group QC reports was explained in this training.

Figure 2: Training of trainers organized at the EuroQol Head Office for the Indian study team

After the training of trainers, all the trainers performed pilot testing of conducting interviews using the EQ-VT. There were three such rounds of pilot testing by the trainers, in which they conducted 10 interviews per round. After every round of the pilot test, the performance of the interviewers was evaluated using the quality check (QC) software designed by the EuroQol group. These pilot phases were conducted ensure standardization of the interview process across all sites, to minimize the interview effect, and to ensure protocol compliance among the trainers. After three rounds of evaluation by the EuroQol experts, the trainers were certified to conducted trainings at their respective sites.

Figure 3: Intensive training of the study team to prepare it for data collection



This training of trainers was followed by an online 'Super user training' for the two members from the Indian study team, who were proposed to serve as the 'super users' for the study. A super user is one having detailed knowledge of troubleshooting for EQ-VT software, and serve as a primary point of contact if any interviewer from the country faces any problem with regard to the use of the software during the conduct of the study. 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). These translations were done by the

certified international translation agencies under stringent quality control measures, as described by the EuroQol group.

After these trainings, recruitment of the field staff was undertaken as respective sites of data collection. Conduct of interviews in the field was the primary responsibility of the field staff. Given the linguistic diversity among the states, every state recruited its own set of interviewers. Separate training sessions were organized for all the states. In order to ensure the uniformity among the training process, these trainings were organized using a uniform set of trainers and uniform agenda. In order to explain the concepts in the regional language, the co-investigators from the respective sites co-facilitated all the training sessions. The primary objectives of these training sessions were as follows:

1. To understand the rationale of the study.

2. To develop the conceptual understanding of EQ5D instrument, health states and health related quality of life.

3. To enable the interviewer to conduct standardized interviews using EQVT.

4. To make the interviewer understand its core tasks, responsibilities, dos, and don'ts during the conduct of the interview.

5. Reduce interviewers' effects and ensure protocol compliance.

6. Achieving high data quality in the interviews.

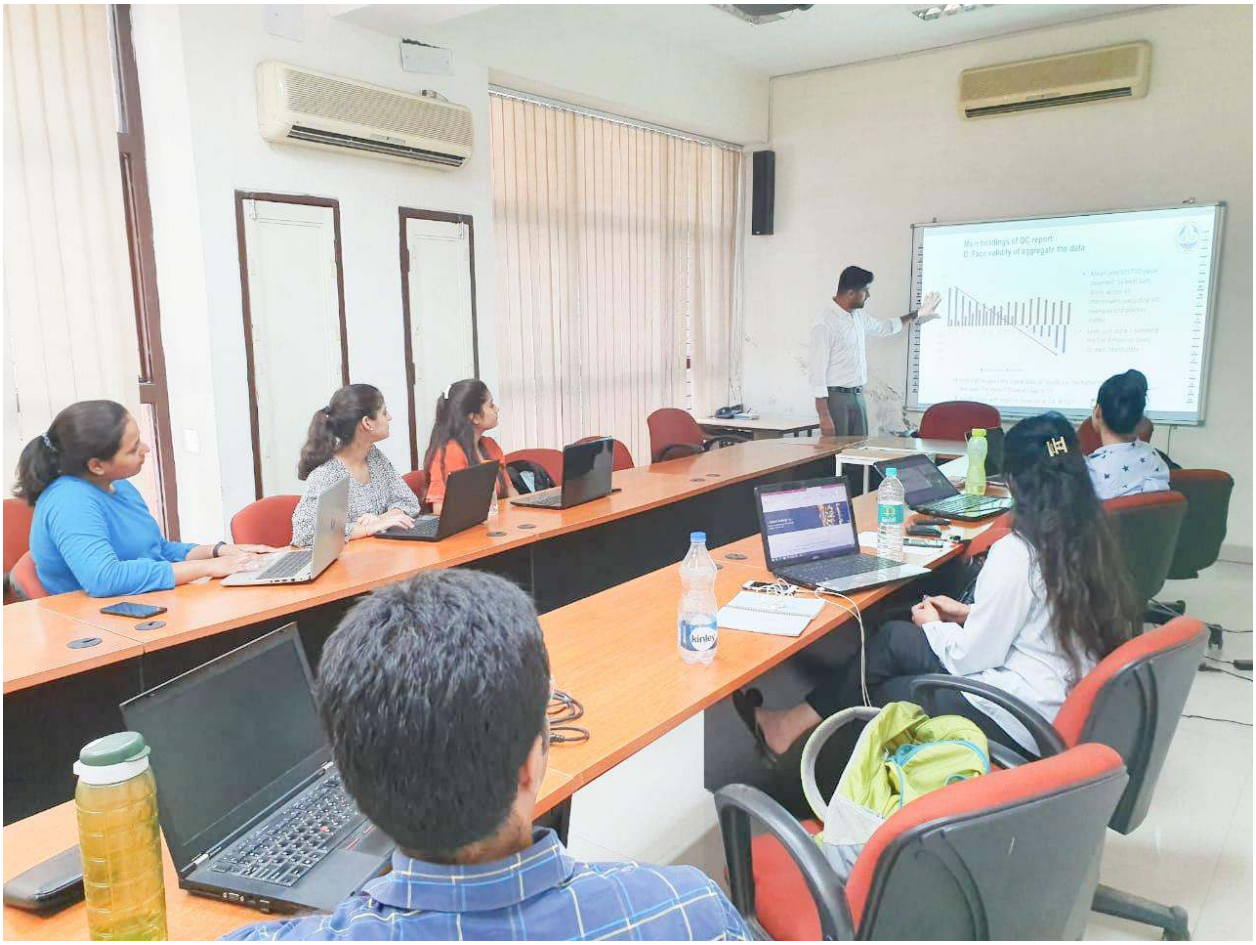
7. Enabling supervisors and site coordinators to design effective intervention if any interviewer is producing strange data.

8. Monitoring of protocol compliance with help of QC graphs.

9. Enabling supervisors to monitor EQVT data on daily basis.

10. Discussing the potential logistic issues during the conduct of the data collection.

Figure 4: Organization of hands on training on EQVT software at all the sites

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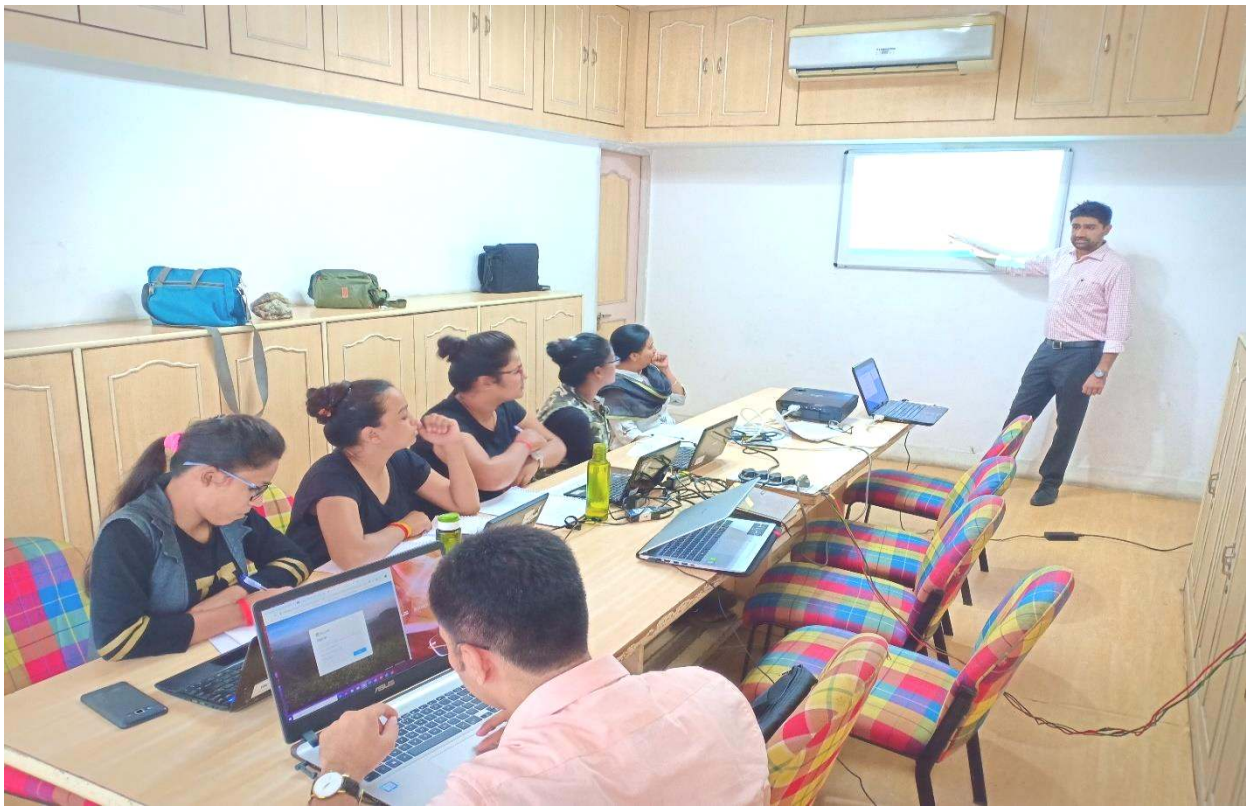
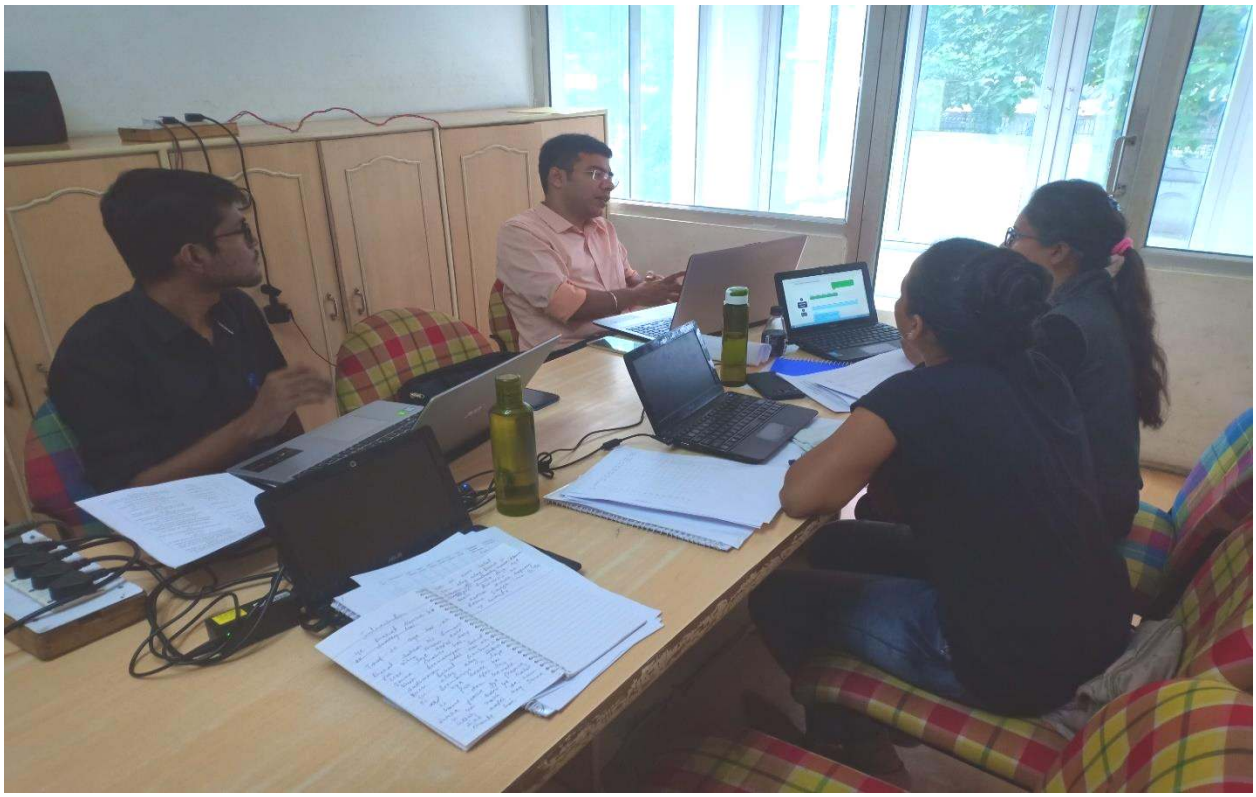




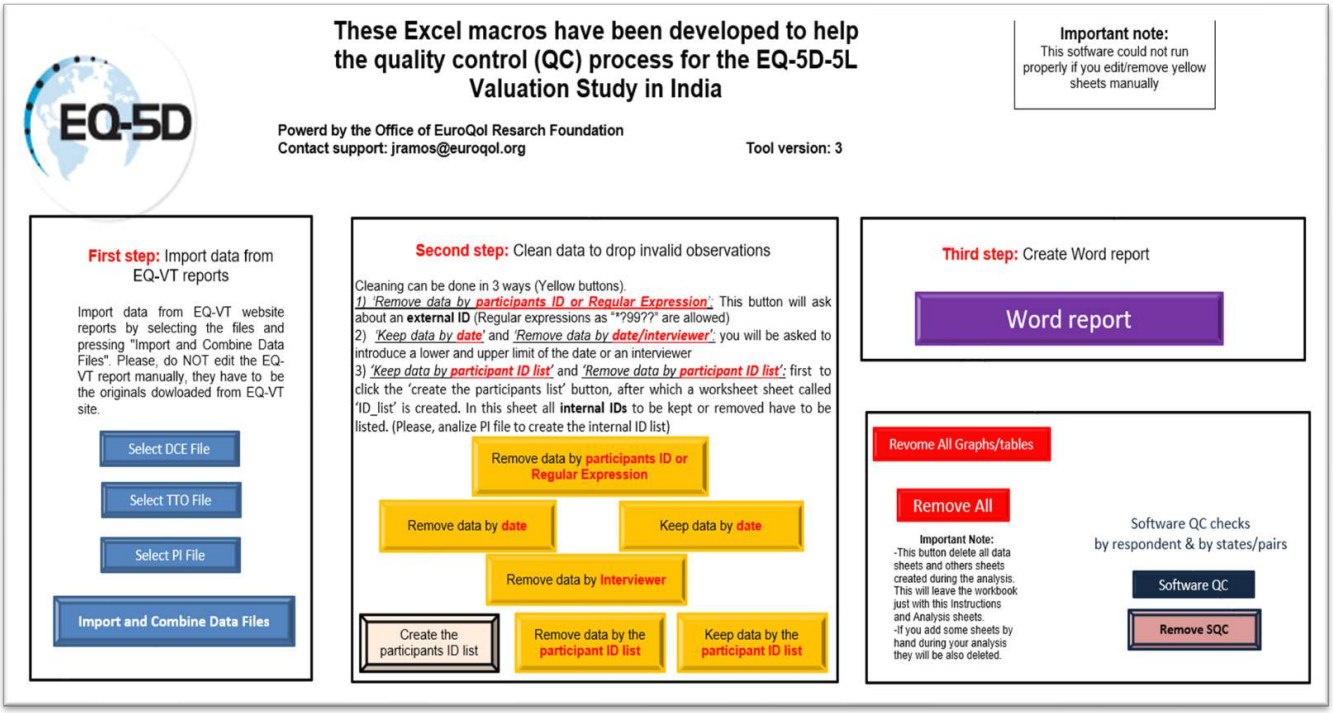
After the hands- on training, the interviewers were put through a process of pilot-interviewing. Every interviewer conducted pilot interviews till the point the protocol compliance had been achieved, and the interviewers' effects have disappeared. The EuroQol Foundation has developed an MS-Excel based QC tool, which will be used to evaluate interviewers' performance.[25] This tool determines protocol compliance, interviewers' effects and mean values by health state severity.[26] This QC check was run once each interviewer had performed a round of 10 interviews. Observations of the QC check were used by the EuroQol experts and local team of investigators to provide personalized feedback via phone calls to all the interviewers.

Figure 4: Interviewers undertaking pilot testing of the EQ-VT software

Quality control during the process of data collection

In order to ensure the standardization of the data collection process, stringent quality control (QC) process was 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 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 were followed to standardize the data collection process across different regions of the country.[27-29] The EuroQol Foundation has developed an MS-Excel based QC tool, which was used to evaluate interviewers' performance through-out the data collection of the study (Figure-5).[25]

Figure 5: The QC Tool (The EuroQol Research Foundation) used in the study to assess the performance of the interviewers



This tool determines protocol compliance, interviewers' effects and mean values by health state severity.[26] This QC check was run at frequent intervals, either when each interviewer had performed a round of defined interviews, or after every week. Observations of the QC check were used by the EuroQol experts and local team of investigators to provide personalized feedback via phone calls to all the interviewers. Interviews were flagged as non-compliant (blacklisted) if the explanations for the first two c-TTO exercises last for less than 3 min, if the worse than dead element is not shown in the examples, if the duration of c-TTO tasks is less than 5 min, or if the value given to the worse health state is not the lowest and at least 0.5 higher than that of the state with the lowest value (Table-4).[25, 26, 30]

Table-4: Assessment of Flagged Interviews with the help of QC Tool after every round of interviews

Interviewer	N	N flagged	% flagged	WC LT	% WC LT	Incon size	% Incon size	WC time	% WC time	TTO time	% TTO time
CHANDIGARH1	164	0	0%	0	0%	0	0%	0	0%	0	0%
CHANDIGARH2	164	3	2%	0	0%	0	0%	2	1%	1	1%
CHANDIGARH5	160	4	3%	0	0%	0	0%	0	0%	4	3%
GUJARAT2	187	0	0%	0	0%	0	0%	0	0%	0	0%
GUJARAT3	180	0	0%	0	0%	0	0%	0	0%	0	0%
GUJARAT5	68	8	12%	8	12%	0	0%	0	0%	0	0%
ODISHA2	132	2	2%	1	1%	0	0%	1	1%	0	0%
ODISHA4	127	2	2%	1	1%	0	0%	1	1%	1	1%
ODISHA5	133	4	3%	4	3%	0	0%	4	3%	4	3%
TAMILNADU2	112	1	1%	0	0%	0	0%	1	1%	0	0%
TAMILNADU3	116	0	0%	0	0%	0	0%	0	0%	0	0%
TAMILNADU4	115	0	0%	0	0%	0	0%	0	0%	0	0%
TAMILNADU5	117	3	3%	3	3%	0	0%	0	0%	0	0%
UTTAPRADESH2	134	0	0%	0	0%	0	0%	0	0%	0	0%
UTTAPRADESH3	138	0	0%	0	0%	0	0%	0	0%	0	0%
UTTAPRADESH4	122	0	0%	0	0%	0	0%	0	0%	0	0%
UTTAPRADESH5	122	5	4%	1	1%	0	0%	1	1%	3	2%
ODISHA3	118	4	3%	3	3%	0	0%	1	1%	1	1%

As a part of assessment of the protocol compliance, first it was observed that how many times each interviewer's TTO data had been flagged for data quality reasons. The total number of

flagged interviews has been shown in column 2, and the proportion of flagged interviews has been shown in column 3. Following was criteria was used to define flagged interviews:

1) WC LT - Interview is flagged if the interviewer does not enter the worse-than-dead element of one of the wheelchair examples.

2) Incon size - Interview is flagged if the respondent has a clear inconsistency in their TTO ratings (the value for 55555 is not the lowest and is at least 0.5 higher than that of the state with the lowest value).

3) WC time - Interview is flagged if the interviewer does not spend at least 180 seconds (3 minutes) on the wheelchair example.

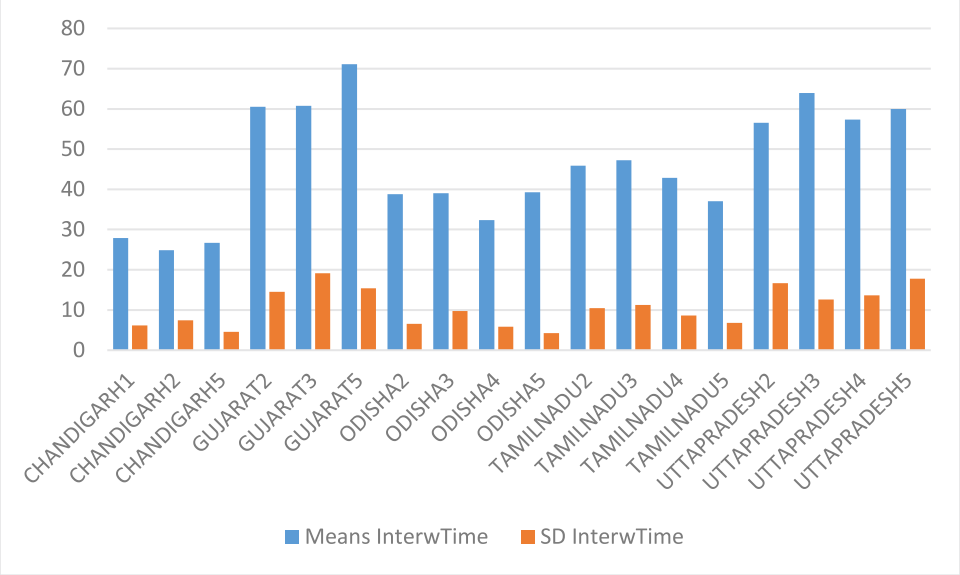
4) TTO time - Interview is flagged if the respondent does not spend at least 5 minutes on the 10 TTO tasks.

After assessment of the flagged interviews, detailed telephonic discussions were held with the interviewers producing flagged data. During these discussions, the reasons for the flagged interviews were assessed and suitable solutions were discussed, so that the same problem would not be reproduced by the interviewers.

Further, the time spent by the interviewers on each step of the interview was also studied to assess whether any interviewer was rushing through the defined tasks. Moreover, number of moves used to complete each step of the interview was also studied to assess if any interviewer is shortcutting any defined task. To assess the performance of the interviewer, these indicators for each of the interviewer were compared against the pooled data from all

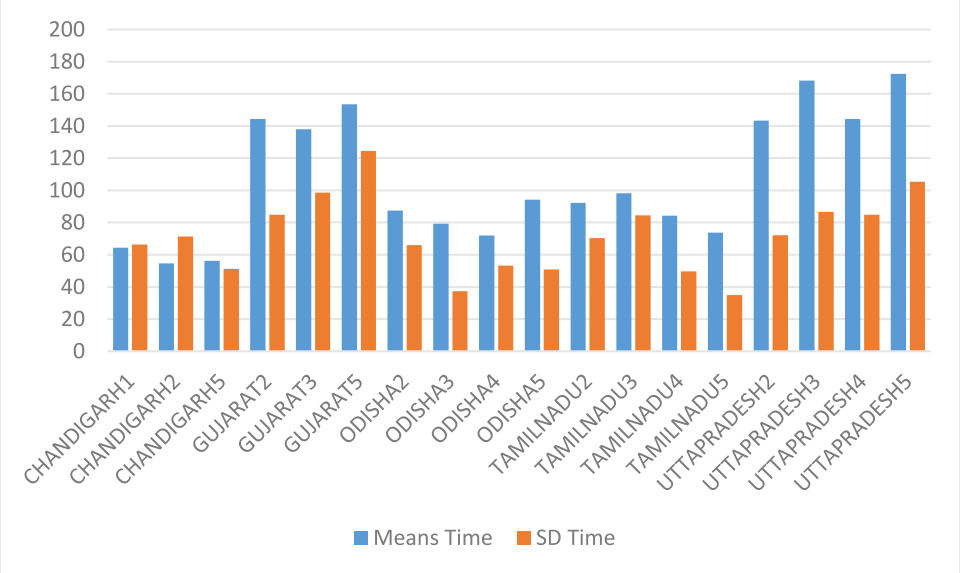
the interviews (Figure 6-14). The interpretation of these graphs has been provided below each figure.

Figure 6: Duration of interviews, by interviewer



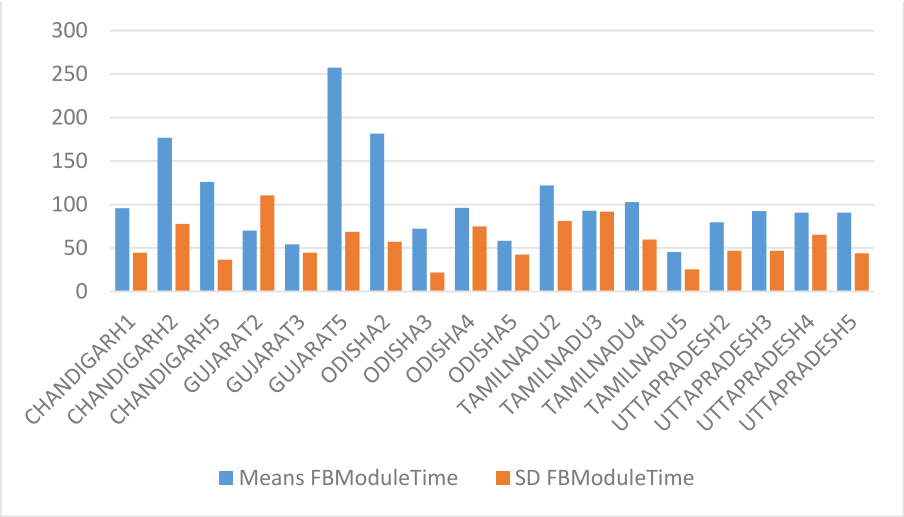
This figure shows the mean (and standard deviation) amount of time taken (in minutes) to complete the valuation questionnaire, by interviewer. This excludes any time taken to complete additional questionnaires such as the country-specific background questionnaire.

Figure 7: Time taken to complete a single TTO task, by interviewer



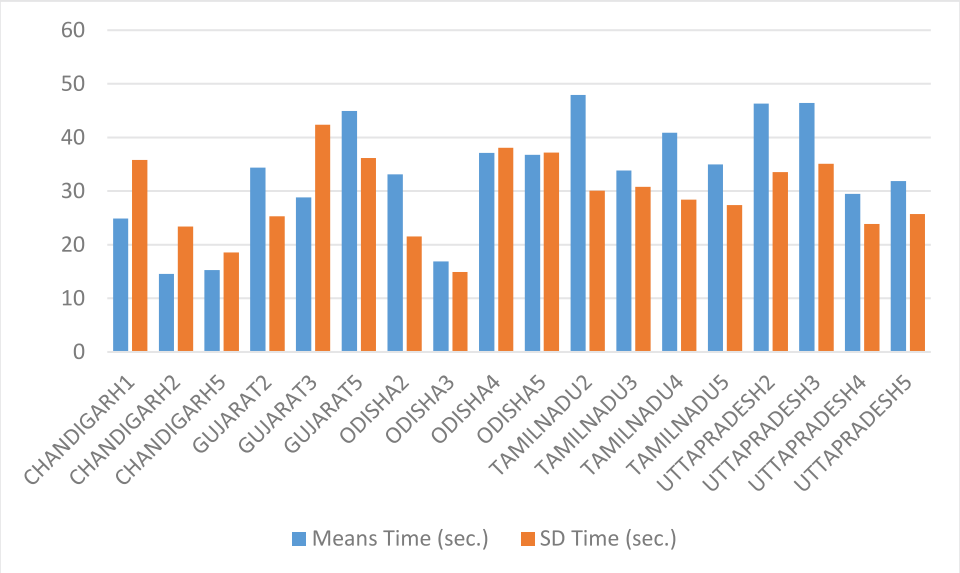
This figure shows the mean (and standard deviation) amount of time taken (in seconds) to complete each TTO task, by interviewer. This excludes the wheelchair example and practice TTO tasks.

Figure 8: Time spent on feedback module, by interviewer



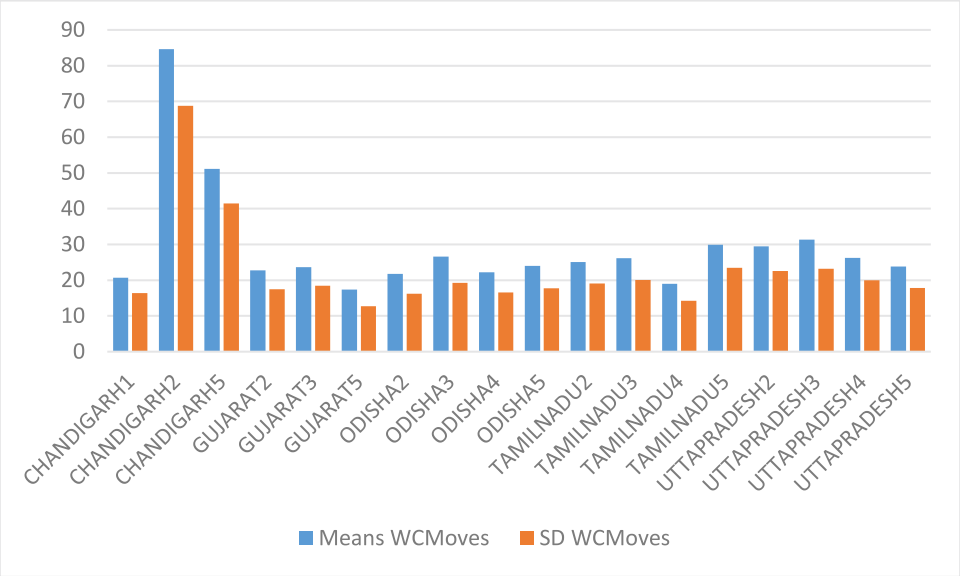
This figure shows the mean (and standard deviation) amount of time taken (in seconds) to complete the feedback module, by interviewer.

Figure 9: Time taken to complete a single DC task, by interviewer



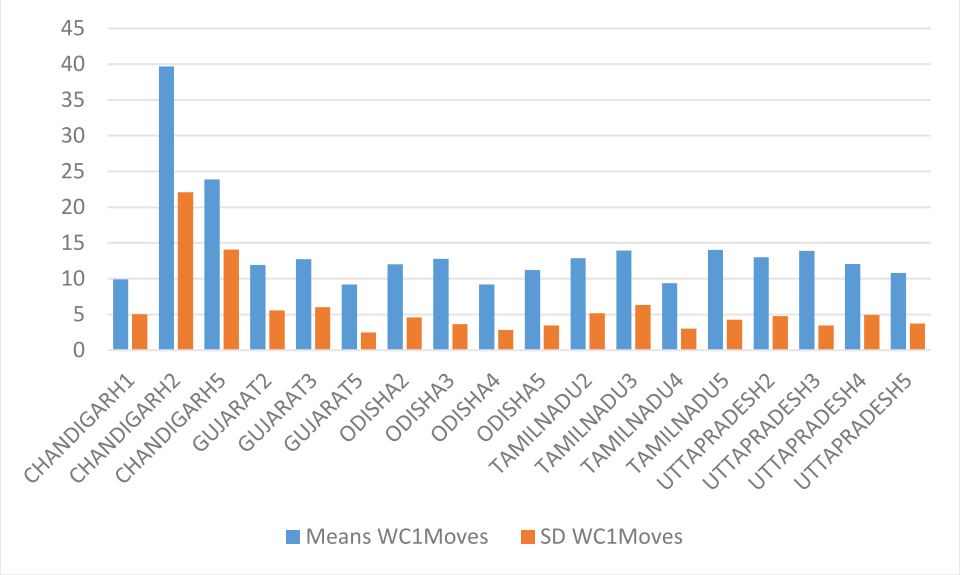
This figure shows the mean (and standard deviation) amount of time taken (in seconds) to complete each DC task, by interviewer.

Figure 10: Number of moves used to complete both TTO wheelchair examples, by interviewer



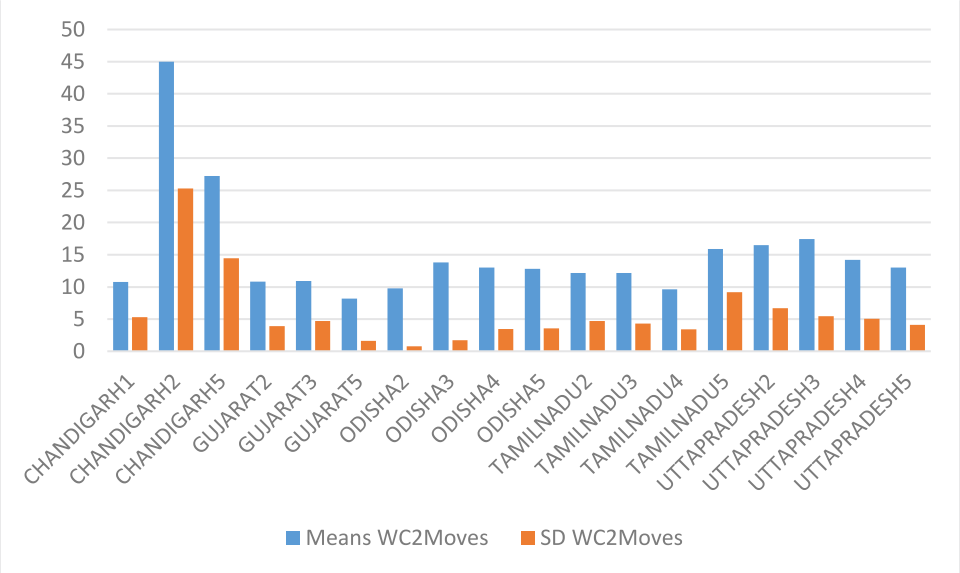
This figure shows the mean (and standard deviation) number of iterative steps used in both wheelchair examples, by interviewer.

Figure 11: Number of moves used to complete TTO wheelchair example 1, by interviewer



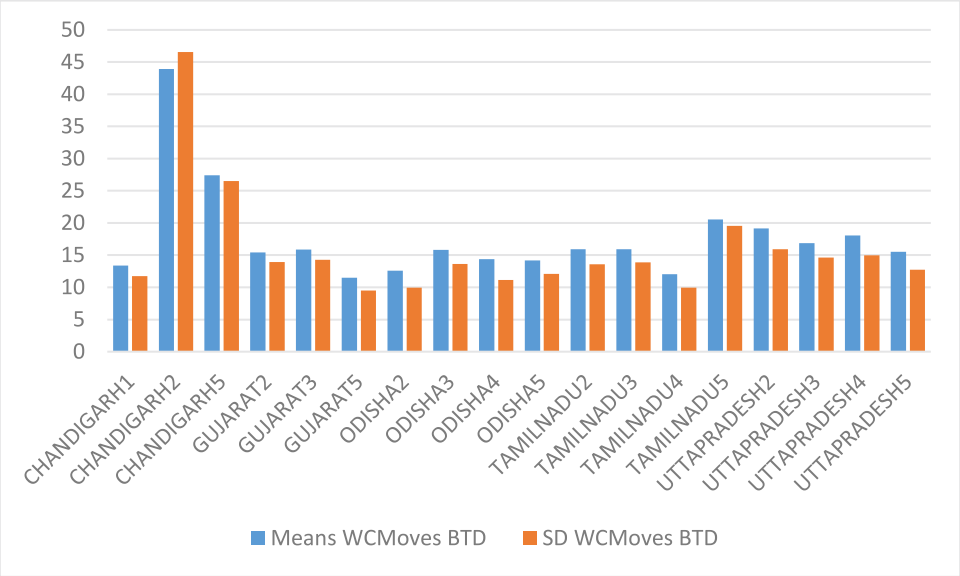
This figure shows the mean (and standard deviation) number of iterative steps used in the wheelchair example 1, by interviewer.

Figure 12: Number of moves used to complete TTO wheelchair example 2, by interviewer



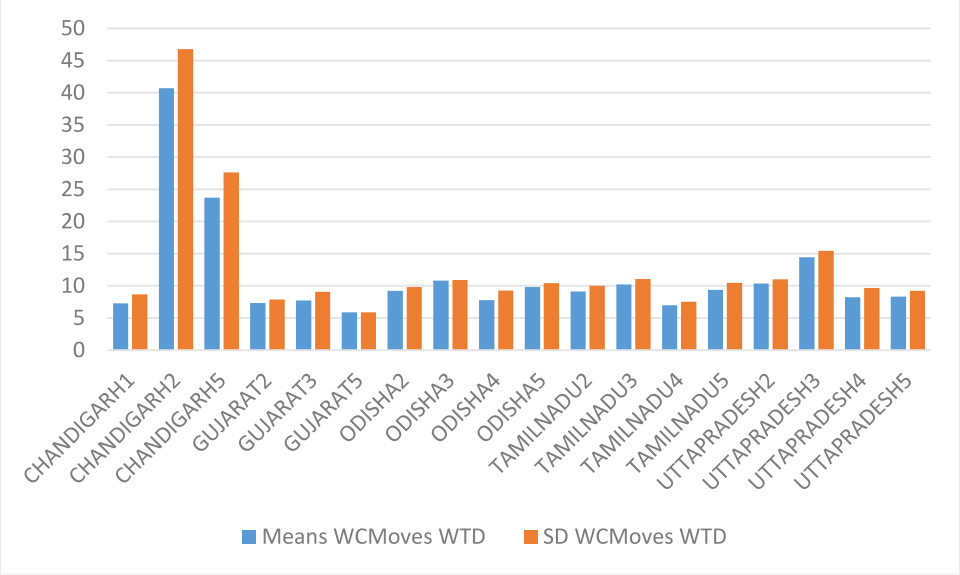
This figure shows the mean (and standard deviation) number of iterative steps used in the wheelchair example 2, by interviewer.

Figure 13: Number of moves used in BTD element of both TTO wheelchair examples, by interviewer



This figure shows the mean (and standard deviation) number of iterative steps used in the better-than-dead element of both wheelchair examples, by interviewer.

Figure 14: Number of moves used in WTD element of both TTO wheelchair example, by interviewer



This figure shows the mean (and standard deviation) number of iterative steps used in the worse-than-dead element of both wheelchair examples, by interviewer.

In order to assess the protocol compliance for the DCE Tasks, interviews producing unusual sets of choices across all seven DCE tasks were identified after every round of interviews (Table 5).

Table 5. Assessment of DCE unusual responses using QC Tool

Interviewer	N	Time (min.)	IF AAAAAAA	IF BBBBBBB	IF ABABABA	IF BABABAB
CHANDIGARH1	164	2.92	0	0	1	0
CHANDIGARH2	164	2.18	0	1	0	1
CHANDIGARH5	160	2.02	0	0	2	3
GUJARAT2	187	3.41	1	0	1	0
GUJARAT3	180	3.57	0	0	1	0
GUJARAT5	68	4.62	2	2	0	1
ODISHA2	132	9.78	0	0	0	1
ODISHA4	127	7.13	0	0	3	2
ODISHA5	133	8.65	2	2	1	2
TAMILNADU2	112	5.27	1	1	0	0
TAMILNADU3	116	3.82	0	2	0	0
TAMILNADU4	115	4.13	0	0	0	0
TAMILNADU5	117	4.66	0	0	1	0
UTTAPRADESH2	134	8.63	0	0	0	1
UTTAPRADESH3	138	9.24	0	0	1	0
UTTAPRADESH4	122	7.05	0	0	1	0
UTTAPRADESH5	122	7.53	1	0	0	2
ODISHA3	118	5.38	0	1	0	1

This table shows, by interviewer: the number of interviews completed (column 2); the mean amount of time taken (in minutes) to complete the 3 DC tasks (column 3); and the number of respondents who gave unusual sets of choices across all seven DCE tasks (columns 4-7). For example, if the respondent chose state A in all seven tasks, this is flagged in column 4.

As a part of quality control, interviewers' effect was assessed in addition to the protocol compliance. Therefore, apart from assessing the issue of flagged interviews, clustering in the TTO data of all the interviewers was also studied to ascertain the presence of interviewer's effect in the collected data (Table- 6).

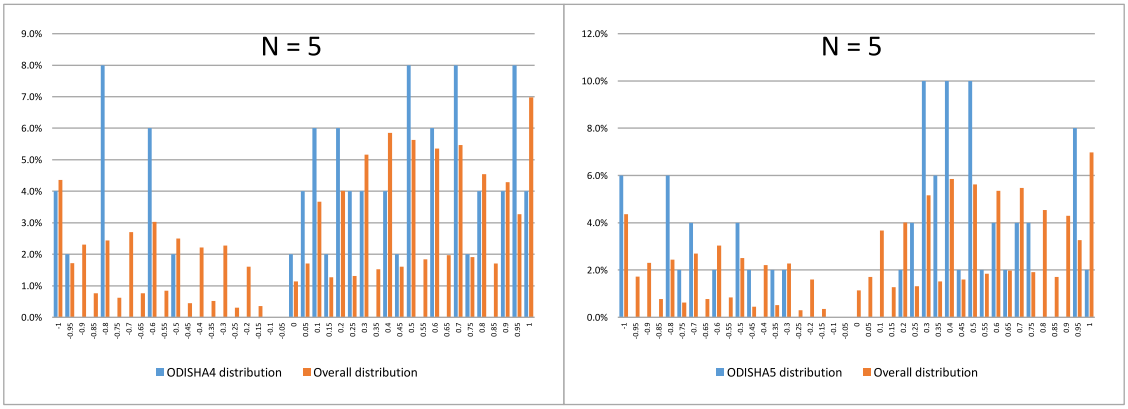
Table 6: Clustering table as generated after every round of interviews to assess the interviewer's effect

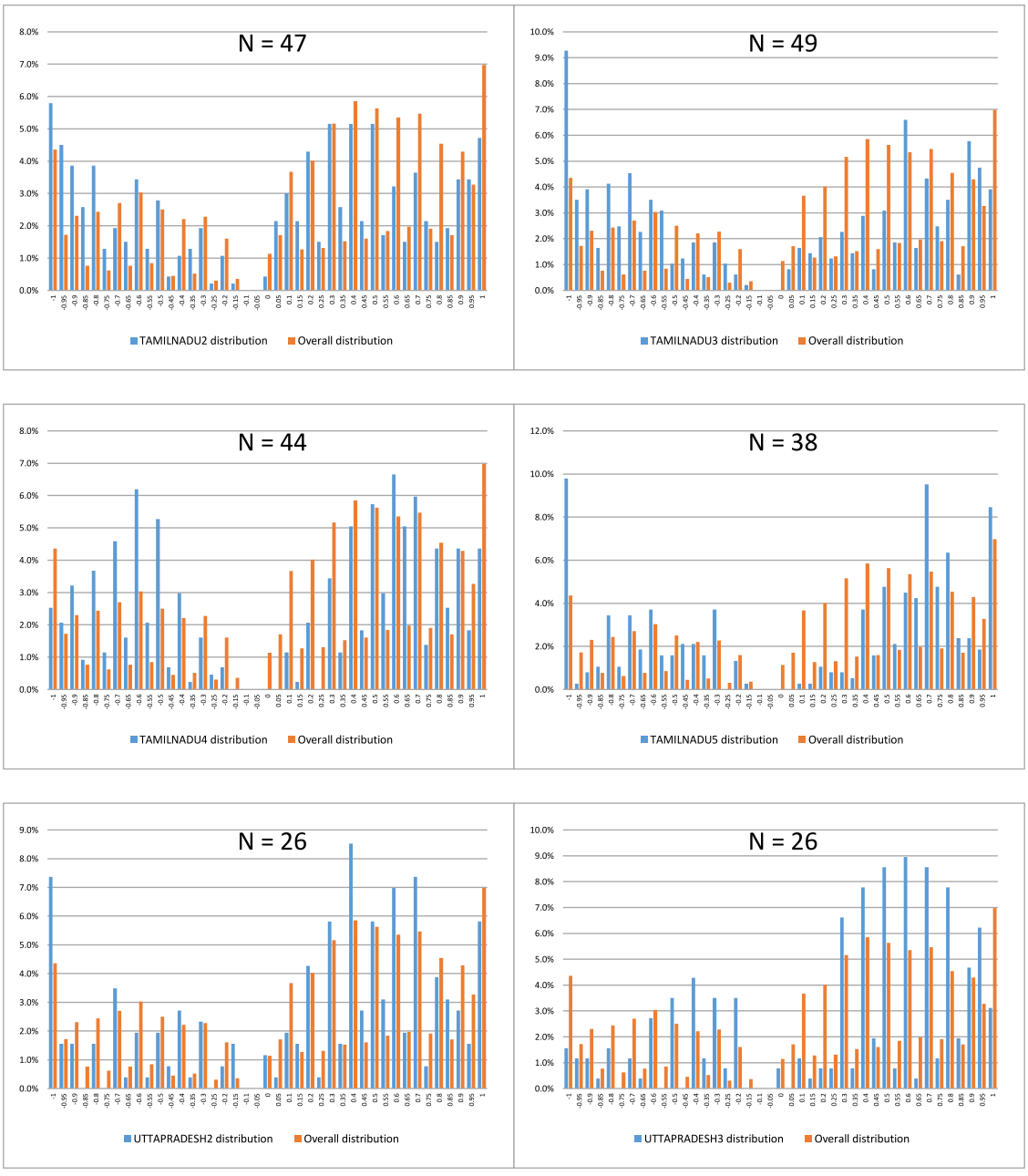
Interviewer	Total Obs.	% Obs. at 1	% Obs. at 0	% Obs. at 0.5	% Obs. at -0.5	% Obs. at -1	Shanon Index	MSE
CHANDIGARH1	1632	4.2%	5.4%	0.9%	0.6%	1.6%	4.49	0.01791
CHANDIGARH2	1631	9.4%	4.5%	1.5%	1.3%	1.7%	4.90	0.01132
CHANDIGARH5	1591	8.8%	5.4%	4.1%	3.6%	1.9%	4.69	0.01658
GUJARAT2	1856	6.5%	4.8%	0.0%	3.9%	6.3%	4.85	0.01224
GUJARAT3	1792	2.5%	5.7%	0.1%	8.9%	3.5%	4.69	0.01759
GUJARAT5	677	10.5%	6.8%	1.3%	4.9%	8.0%	4.50	0.01519
ODISHA2	1311	6.6%	3.8%	6.2%	4.5%	4.8%	4.95	0.01871
ODISHA4	1263	12.0%	1.5%	0.0%	0.8%	0.6%	4.51	0.01903
ODISHA5	1323	2.8%	6.4%	0.5%	0.4%	0.1%	4.80	0.01840
TAMILNADU2	1114	4.2%	5.4%	0.4%	3.1%	5.7%	5.04	0.00961
TAMILNADU3	1153	5.6%	4.1%	0.0%	1.4%	10.4%	4.90	0.01656
TAMILNADU4	1145	4.2%	4.4%	0.0%	4.8%	2.0%	4.85	0.01070
TAMILNADU5	1162	7.5%	4.6%	0.0%	1.9%	8.7%	4.87	0.01478
UTTAPRADESH 2	1330	5.0%	5.6%	0.0%	4.5%	2.0%	4.91	0.01238
UTTAPRADESH 3	1373	4.7%	6.2%	0.0%	3.9%	0.5%	4.75	0.01209
UTTAPRADESH 4	1213	5.9%	6.1%	0.2%	4.4%	0.4%	4.64	0.01317

UTTAPRADESH 5	1213	7.4%	3.9%	0.0%	4.7%	0.0%	4.94	0.01190
ODISHA3	1175	8.4%	1.4%	0.1%	0.7%	4.9%	4.74	0.01871

The presence of interviewers' effect in the data was 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 'zero' in the TTO tasks, health states given value of 'less than zero' in the TTO tasks, and proportion of non-traders (individual 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 was interpreted by comparing the data of a specific interviewer with the pooled data from all interviewers (Figure-15). Any interviewer reflecting interviewers' effect was assisted by the investigators and trainers via phone and video calls during the conduct of next round of pilot interviews.

Figure 15: TTO value distribution for each interviewer.





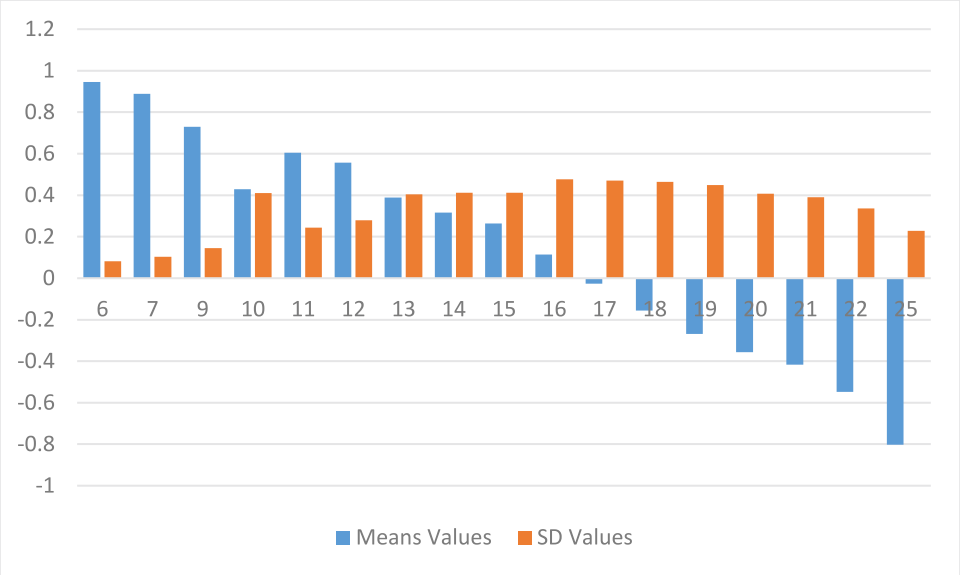
These figures show the TTO value distribution for each interviewer. The overall distribution is also shown in this figure, for comparison purposes.

After assessing the protocol compliance and interviewer's effect in the data, the face validity of the collected data was also checked after every round of interviews. This face validity was checked primarily with the help of two indicators (Figure 16-17):

1. Assessment of mean TTO values by level sum score

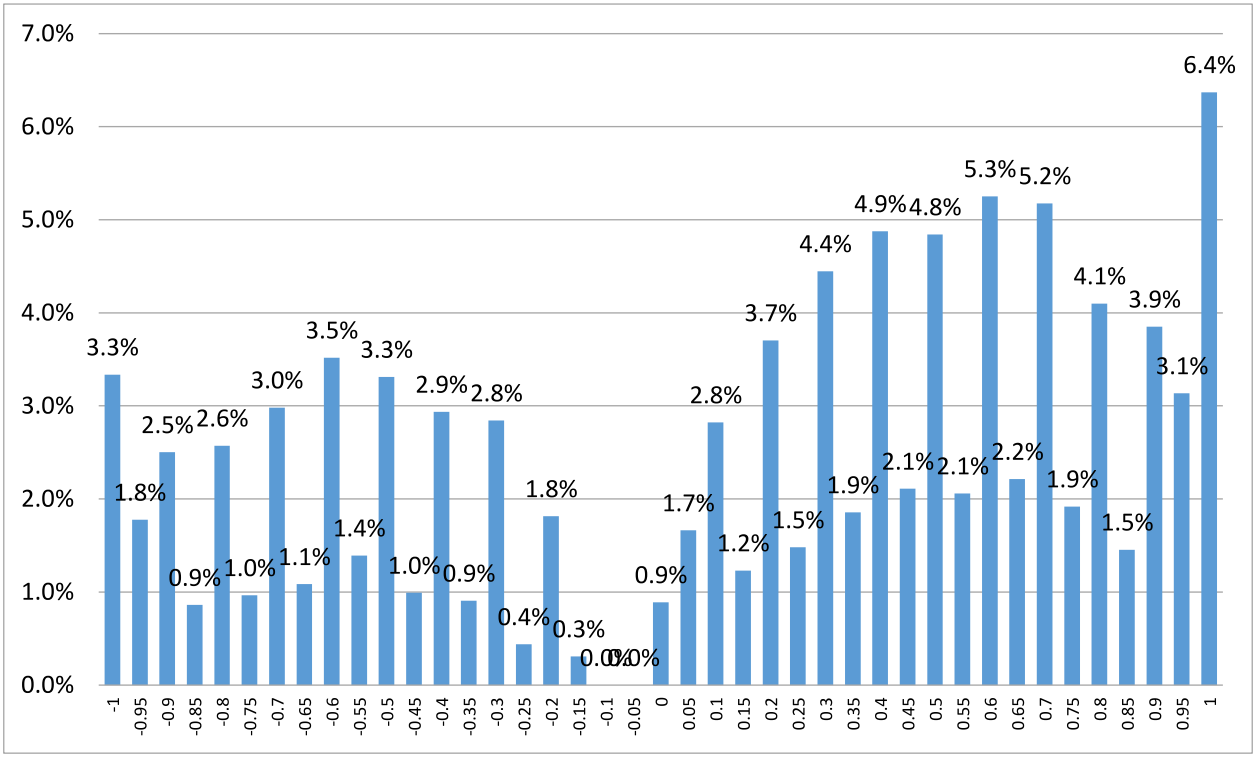
2. Overall TTO value distribution

Figure 16: Mean TTO value, by level sum score



This figure shows the mean (and standard deviation) TTO value observed, by level sum score, across all interviewers. The level sum score is a proxy for severity and is calculated by summing the five- dimension levels for each health state. We would expect health states with lower level sum scores (e.g. 21111: 2+1+1+1+1=6) to have higher mean values that those with higher level sum scores (e.g. 55555: 5+5+5+5+5=25). This excludes the wheelchair example and practice TTO tasks.

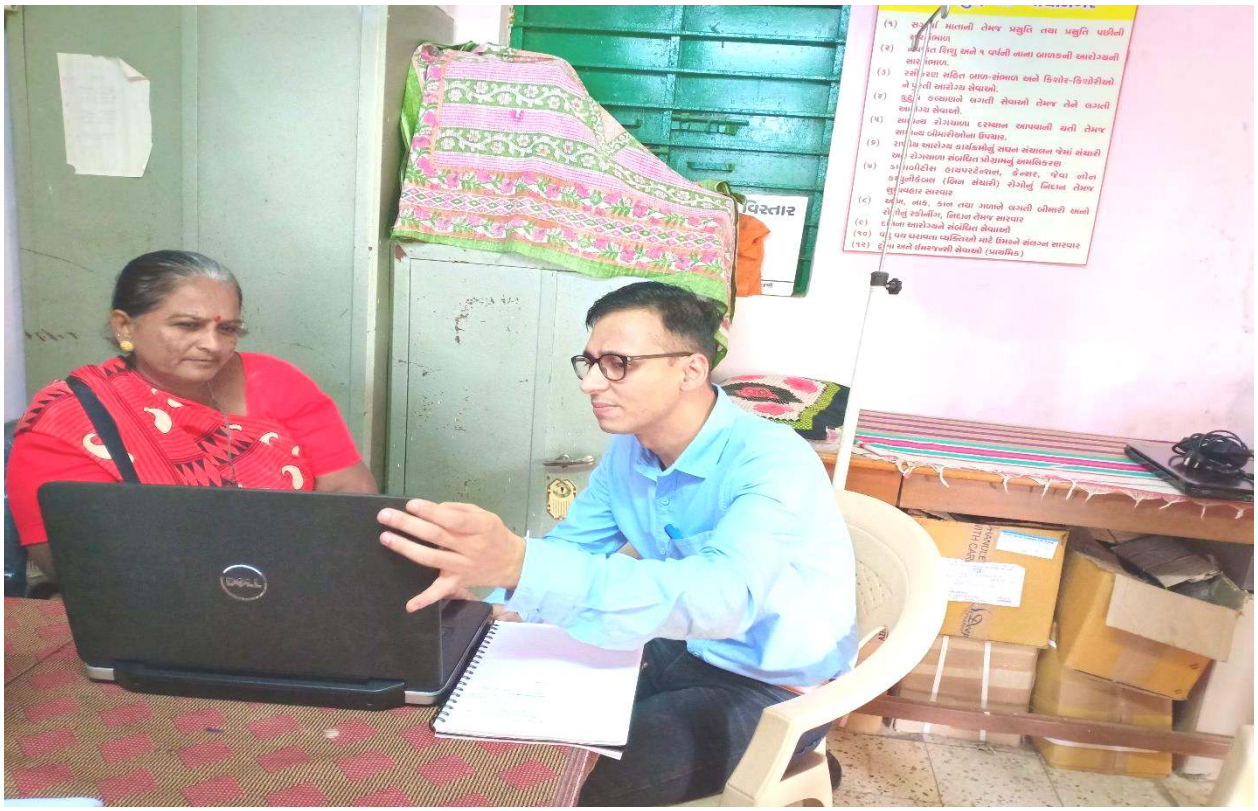
Figure 17: Overall TTO value distribution

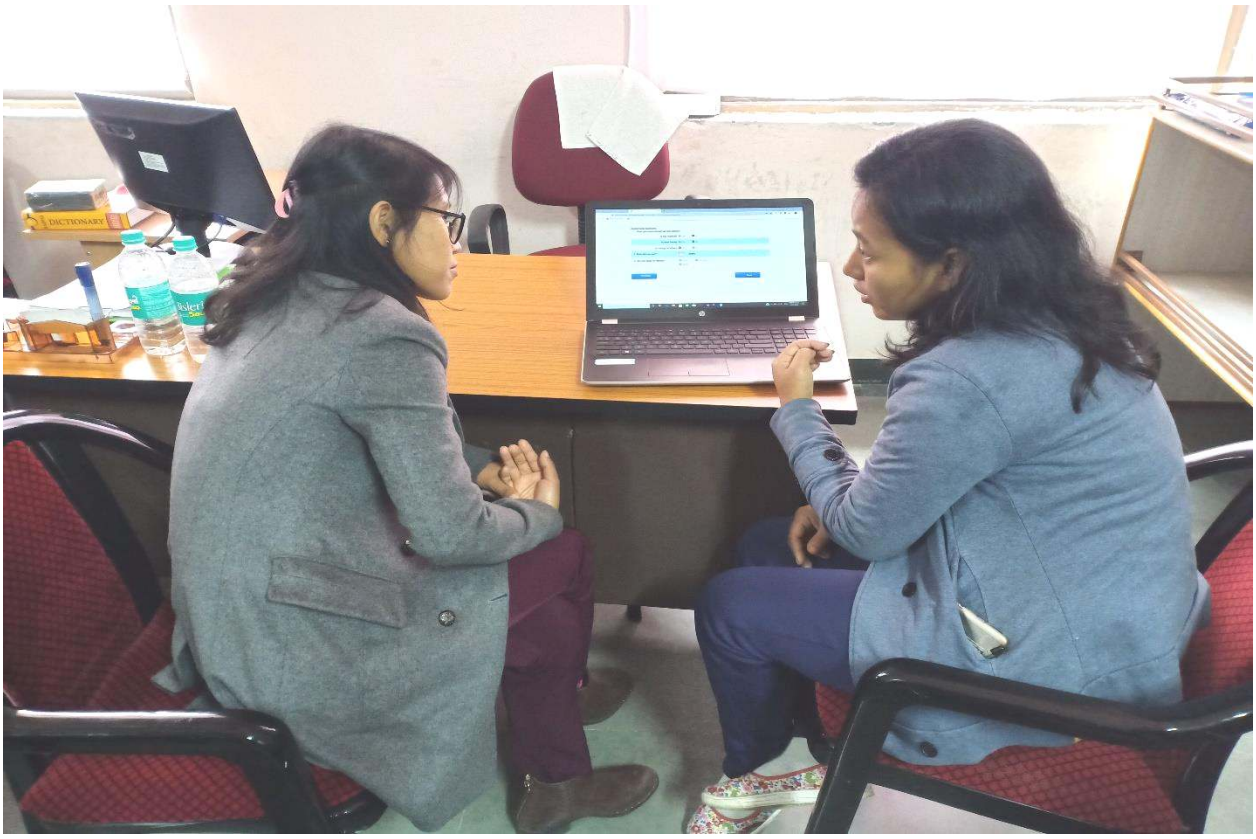


This figure shows the 5L TTO value distribution for all health states. For example, the rightmost bar shows the proportion of observations of values greater than 0.95 and less than or equal to 1.0. This excludes the wheelchair example and practice TTO tasks.

During the process of QC, it was also observed whether the interviewer is influencing respondent by its interviewing style, shortening the task due to laziness, or facing difficulty in explaining WTD element of the c-TTO task. Personalized feedback was provided to interviewers to overcome any such difficulty. Poor performing interviewers were retrained using online platforms. The interviewers were allowed to start the real data collection once they had achieved a stable performance on the QC protocol. This QC check and personalized feedback process was constantly followed throughout the process of real data collection.

Figure 18: Interviewers conducting interviews in field using EQ-VT software





Ethical considerations

All interviews were conducted with care and sensitivity and with respect for participants' ethnicity, religion, language, sexual orientation or literacy level. Participants were presented the study's participant information sheets, and their signatures were obtained on the informed consent forms after explaining the same to the participants. All participants were 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. Each participant was interviewed within one visit. 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.

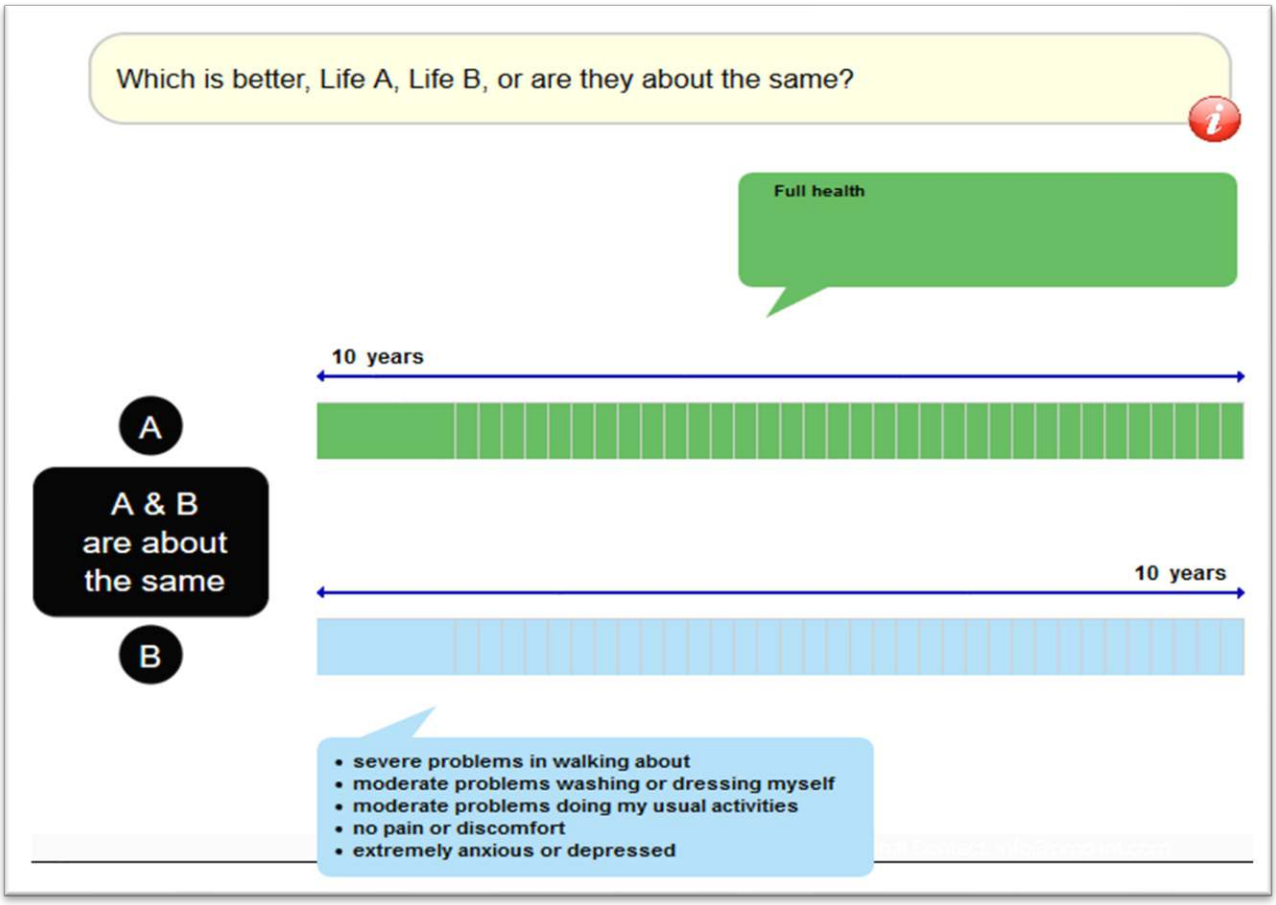
Valuation Methods: Data Analysis for the generation of Value Set

Recording the data

To develop the EQ-5D-5L value-set for India, the participants were interviewed in a face to face setting using CAPI (computer assisted personal interviewing) technique. The EuroQol Group's Valuation Technology (EQ-VT) software generated by the EuroQol Group was used for this purpose. Each respondent was asked to complete socio-demographic details and self-reported health questionnaire using EQ-5D-5L and the EuroQol visual analogue scale (EQ-VAS). TTO valuation was done using 10 composite TTO (c-TTO) tasks and 7 discrete choice experiment (DCE) tasks.

In the standard design of c-TTO, there are 10 blocks of health states. Each block contains 10 health states which includes one anchor state (55555). The blocks used for interview were randomly selected by the EQ-VT software. In TTO valuation, the respondent was asked to indicate the amount of time he/ she is willing to give up to attain perfect health. The respondent was asked to imagine two alternative health states (life A and life B) described on screen and express the preference using TTO (Figure-19).

Figure 19: The process of TTO preference elicitation using EQ-VT

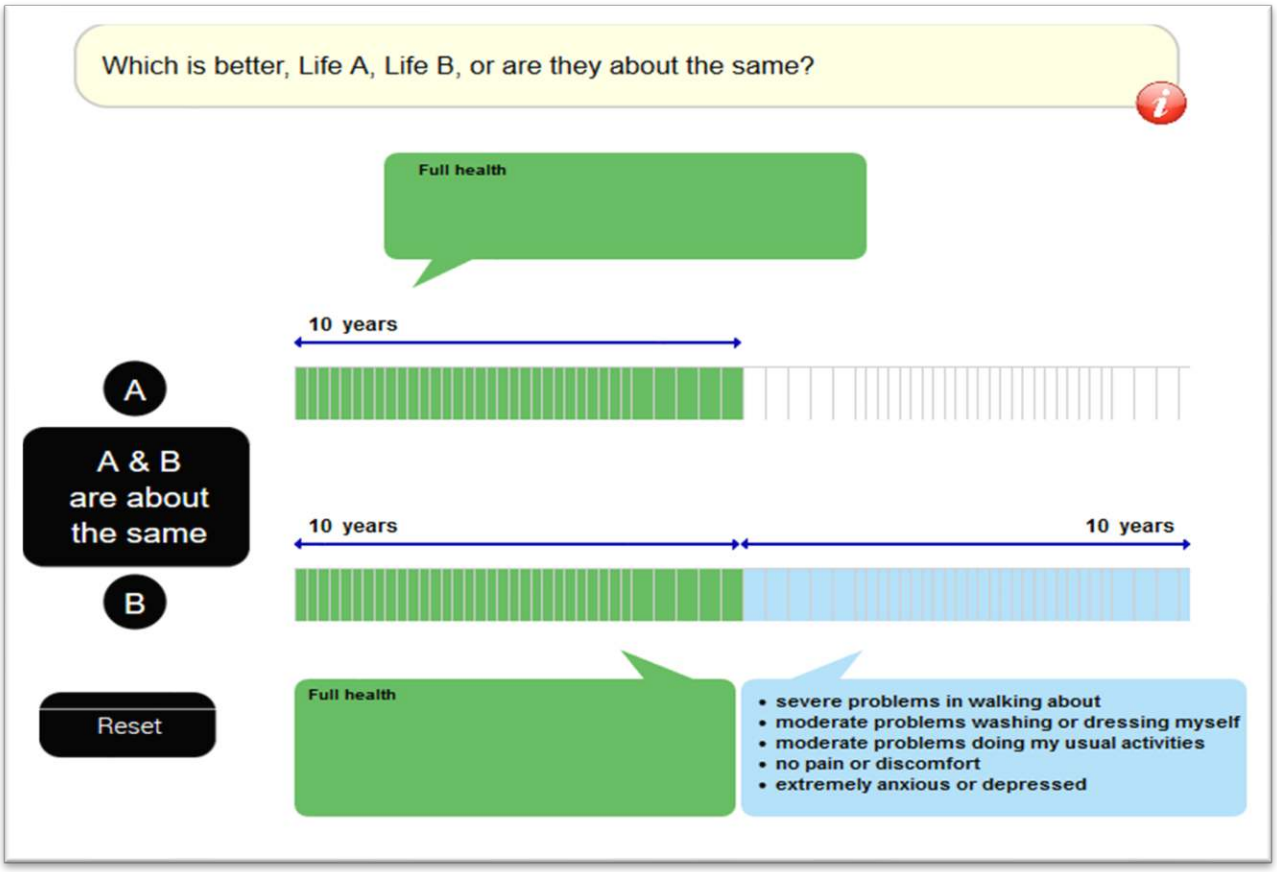


The respondents were asked whether they prefer to live for 10 years in perfect health (life A) or 10 years in some inferior health state (life B). It was explained to the respondents that at the end of the stated time, there would be an immediate painless death in both the lives. As a rational choice, the respondents would prefer good health (life A) over the state of inferior health (life B) when the time available in both the alternatives is equal (10 years). Thereafter, the time available in life B was kept constant at 10 years, while the time available in life A was decreased sequentially, and the respondent was asked to select the better alternative between life A and life B. Thereby, the respondent was 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 was done till 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 was 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 prefers to die immediately rather than living in that health state. These health states are known as worse than dead (WTD), and their valuation was done with the help of composite TTO (c-TTO). The c-TTO approach begin with the conventional TTO for all health states, followed by a lead time TTO (LT-TTO) in the scenario where the participants' response indicated the health state to be worse than dead (WTD). The c-TTO involved adding healthy life years ('lead time') before both the alternatives (life A and life B) being compared. This allowed the respondent to trade-off these additional years when he or she considers the health state in life B to be worse than dead. As per the EuroQol group's recommendations, a lead time of 10 years was used (Figure-20).[28]

Figure 20: The process of composite time-trade off (c-TTO) preference elicitation using EQ-VT



The value of health was be calculated as x/t for better than dead health states and (x-10)/t for worse than dead 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, i.e., 10 years.[29] This being a cognitively demanding exercise, first a small training exercise using an example of 'being in a wheelchair' as life B was performed with the respondent to make sure the respondent understands the concept of TTO.[29] The concept trading-off the time in both 'better than dead' and 'worse than dead' health states was explained in this exercise. This was 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 got over, the respondents were assigned a block of 10 health states, on which the valuation exercise was done.

In the Discrete Choice Experiment (DCE) task, the respondents were presented with two different health states in which the levels, but not the order of the attributes, were differed and the respondents were asked to choose one amongst the two. The 196 pairs of DCE health states were distributed over 28 blocks thus resulting in seven pairs per respondent.[31] These DCE task blocks were balanced in terms of their severity, which was calculated as the sum of the level scores on all dimensions.

Modeling

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

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

where Y_{it} refers to the TTO values dependent variable, μ_{0i} was the individual specific error component and ε_{it} refers to the combined time series and cross-section error component, i indicating the respondent, and t accounting for the panel structure of the dataset (because

there are 10 cTTO 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

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

which is similar for SC, UA, PD and AD, leading to a total of 20 regressors plus the constant. The tobit model assumed a latent variable Y_{it}^{*} underlying the observed Y_{it} cTTO values. This matched with the censored cTTO data, which by nature of the applied cTTO task was left-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 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}^{*} was linear. The DCE data were modeled under random utility using the conditional logit model. The model included the same 5 parameters as the cTTO 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 had 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.

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

where *js* is the choice alternative in the choice sets.

As both TTO and DCE data provide information about the values of health states, we also implemented a hybrid modelling approach that made 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.[32-40] The hybrid model combined the likelihood functions of a linear model for the c-TTO data and a logit model for the DCE data. As the coefficients were estimated from a conditional logit and expressed on a latent arbitrary utility scale, we used a rescaled parameter θ, which assumed that the c-TTO model coefficients are proportional to 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 196 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.

Sensitivity Analysis

A sensitivity analysis was conducted to explore the mechanism through which presence of severely inconsistent responses impacts the modeling of c-TTO results. All c-TTO responses were removed for respondents who valued state 55555 higher than any other state. A pair of c-TTO responses was considered logically inconsistent if the observed values of two states, state A and state B, contradicted 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 was then considered as logically inconsistent. Considering, however, that many

inconsistencies may occur as a result of random error, the "seriousness" of the inconsistencies was evaluated by the size of utility difference between two states. Random error always occurs and is typically not considered a sufficient reason for exclusion. For this reason, the sensitivity analysis excluded only a subset of inconsistent responses.

DCE responses were considered to be problematic if the responses of the respondent follow a particular pattern (e.g. AAAAAA, BBBBBB, ABABABAB etc.) Regression was re-performed 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 were calculated by multiplying the EQ-5D scores of the respondent selected for the model (N=2409) with the coefficients of the preferred regression model. In the original study protocol, it was estimated to include responses of 2700 individuals (from six states), however, due to COVID pandemic, only 2409 individuals (from five states) could be interviewed. Hence, the current set of reference values have been generated on the basis of N=2409 respondents.

Prospective areas of research

Over the last several years, a lot of formal studies tried to create methodological convergence in the valuation work.[26-28, 32] 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 increases 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, and second, how many observations per health state are required to obtain sufficiently stable (reliable) states (Figure-2).

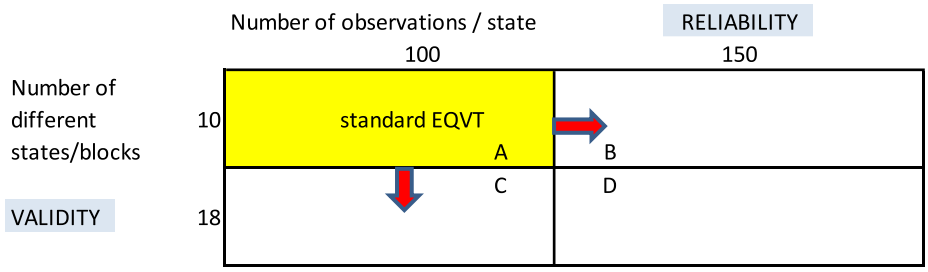
In contrast to the conventional EQ-VT protocol, which is optimized for a sample size of around 1000, the current study aims to collect data from 2700 respondents. This offers an opportunity to add more health states and assess the additional value of using a richer number of health states in predicting 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, i.e, 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.[28] 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.[31, 41] 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.[41] 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, when the remaining data for the study will be collected, this would be used 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, eight additional blocks have been added, consisting of 64 new health states. This selection was guided by added-value considerations, taking the initial ten 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, mean square error) 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 analyze results of different n=10 block drawings by assigning some imbalance of domain/level indicator.

As define in figure 21, 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:

Figure 21: Analytical strategy to assess the increased validity and reliability of the extended EQVT design



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 standard error of the mean) of health states with 'known' higher random error, such as with large stress. We will compare results obtained with standard 100 to 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 socio demographic variables like age, gender etc. by using scatter plot with calculated R square value (correlation coefficient) or Wilcoxon match pair signed rank test (Non-parametric test).

The Indian EQ-5D-5L Value Set

Overview

We describe the sample characteristics including self-reported health on the EQ-5D-5L descriptive system and the EQ-VAS using percentages for discrete variables and means and standard deviations for continuous variables. In this investigation we used TTO (specifically c-TTO) and DCE. TTO has limitations such as loss of aversion, but also has advantages as the TTO-based value sets are anchored on a scale of (0) death to (1) full health. DCE is not exempt from limitations, as lexicographic behavior from respondents has been widely reported in the literature. It is also noticeable that DCE, in its present form, where time is not incorporated in health state presentations, does not anchor value sets on a (0) death to (1) full health scale. Therefore, DCE produces value sets on an arbitrary scale based on the relative distances between health states. However, both techniques attempt to measure health states preference, but using different underlying assumptions, and seem to not share the same limitations. Therefore, the data obtained from these two elicitation methods could be seen as complementary, not necessarily competing with each other. Hence, we chose the solution of combining DCE with c-TTO in a 'hybrid model', imposing the (0) death to (1) full health scale as determined by c-TTO.

To illustrate how the hybrid model combined c-TTO and DCE responses in this study, we also present the results from the models estimated from each c-TTO and DCE separately, with the same assumptions as those used for the hybrid model. We used the 20-parameter main effects model, which estimates four parameters for the five levels of each of the five

dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each coefficient represents the additional utility decrement of moving from one level to another. Hence, the overall decrement of moving from 'no problems' to 'unable/extreme problems' is calculated as the sum of the coefficients of 'no problems to slight problems', 'slight problems to moderate problems', 'moderate problems to severe problems', and 'severe problems to unable/extreme problems'. Presenting the TTO, the DCE and the hybrid model also allows us to compare the value distribution in the form of the correlations between the predicted values of the models, and we can compare the weights of the individual dimensions. This gives information about construct validity in the form of 'convergent validity', or 'concordance'. c-TTO data were modelled using the response values as dependent variables and the health states as explanatory variables. This was achieved by the implementation of a Tobit model (hyreg with ll() option), which assumes a latent variable Y*it underlying the observed Yit of C-TTO values when there is either left- or right-censoring in the dependent variable. The C-TTO data, in particular the lead-time C-TTO for WTD health states, is by nature censored at -1 [ll(-1) option on hyreg command]. This means that observed preference values were valued by the C-TTO method at -1, despite the latent preferences of respondents possibly including values lower than -1. The Tobit model accounts for this censoring by estimating the latent variable Y*it, which can take on predicted preference values extrapolated beyond the range of the observed values. Variance of C-TTO data is not homogeneous among health states; this led us to model C-TTO data as heteroskedastic data. We used the hetcont() option of the hyreg command. The dummy variables included in the hetcont() option were the same as those included in the main model, that is, the 20 dummies that specified the main effects model. DCE (forced pair

comparisons in our case) responses were modelled as a conditional logistic regression model including the same 20 dummy parameters as those used for the c-TTO data. Nevertheless, we did not use the coefficients estimated from a conditional logit model because they were expressed on a latent arbitrary utility scale. We rescaled the DCE coefficients using the same parameter h that was estimated in the hybrid model. This rescaling assumes that the C-TTO model coefficients are proportional to the DCE model coefficients.

Sample Characteristics

In total, 2409 respondents who were approached after the retraining of the interviewers completed the interview. Reasons for interview failure were refusal to participate, conflicting schedules, discontinuation of the interview at the respondent's request, and discontinuation of the interview by the interviewer's decision because of the respondent's lack of understanding. The detailed sample characteristics have been presented in Table-7.

Table 7: Sample characteristics

Characteristics	Study sample (N=2311)
	n (%)
Residence	
Urban	724 (31.3)
Rural	1587 (68.7)
Gender	
Female	1178 (51.0)
Male	1133 (49.0)
Age	
17-19	97 (4.2)
20-29	625 (27)
30-39	518 (22.4)
40-49	467 (20.2)
50-59	326 (14.1)
60-69	188 (8.1)
70+	90 (3.9)
Education	
Illiterate	250 (10.8)
Primary	296 (12.8)
Middle	395 (17.1)
Matric	438 (19.0)
Senior Secondary	405 (17.5)
Graduate and above	527 (22.8)
Religion	
Hindu	2046 (88.5)
Muslim	119 (5.2)
Christian	115 (5.0)
Others	31 (1.3)

Self-reported health status of the Indian population

Table 8 shows that the highest proportion of health problems was reported in the pain/discomfort dimension (54.78% reported 'any problems') and the lowest in the self-care dimension (14.54%). From the final sample, 582 (25.18%) reported no health problems on any dimension ('11111').

Table 8: Health states as reported by the participants of the study

	EQ-5D-5L descriptive system with scores in %				
	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 as reported by the respondents					
	Mean	**SD**	**25th percentile**	**Median**	**75th percentile**
EQ-VAS score	75.18	16.416	65.0	80.0	90.0

Data Characteristics

The 2311 respondents provided 23110 c-TTO observations (respondents valued 10 health states each). Accordingly, the c-TTO dataset contained 23110 observations. Of these, 17161 (24.6%) observations relayed the value 0, and another 13170 (18.85%) were negative values. The 150 observed mean C-TTO values ranged from -0.803 for state '55555' to 0.963 for state '11112'. The mean observed values were negative for 49 health states out of 150 used in the C-TTO design. The DCE dataset comprised 16177 observations (all respondents completed seven paired comparisons).

Modelling Results

There were 780 (33.8%) left-censored c-TTO observations: when respondent gave the lowest possible value (-1) for a health state in the c-TTO task. The Tobit c-TTO model results were logically consistent. Conditional logistic regression was used to model the DCE responses that were also logically consistent. c-TTO and DCE predicted values for 3125 health states were correlated, as Fig. 22-A shows (r = 0.991, p value\0.0001). Table 9 shows that both sets of coefficients were in relative agreement; that is, the most important dimension was mobility and the least important was pain/discomfort. The hybrid model, which utilized both c-TTO and DCE data, was also in relative agreement with both c-TTO and DCE models. Figure 22-B, 22-C show a positive correlation of hybrid predicted utility with models predicted from C-TTO (r = 0.730, p\0.0001) and DCE (r = 0.731, p\0.0001). The hybrid model with main effects was logically consistent (Table 9). 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 0.983. The minimum value was -0.923 for the ‘55555’ health 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 two models regarding mobility appearing as the most important dimension and pain/discomfort as the least important. To obtain utility for an EQ-5D-5L health state, for instance ‘12345’, the following calculation based on the hybrid model (final value set) is needed: Utility weight (‘12345’) = 1 - no problems in MO (0) - no problems to slight problems in SC (0.051) - no problems to slight problems in UA (0.045) - slight problems to moderate problems in UA (0.043) - no problems to slight problems in PD (0.051) - slight problems to moderate problems in PD (0.074) - moderate problems to severe problems in PD (0.264) - no problems to slight problems in AD (0.016) - slight problems to moderate problems in AD (0.046) - moderate problems to severe problems in AD (0.101) - severe problems to extreme problems in AD (0.083) = 0.226. Note that each coefficient represents the additional utility decrement of moving from one level to another.

Table 9: Estimation results for C-TTO model, DCE rescaled model, and hybrid model

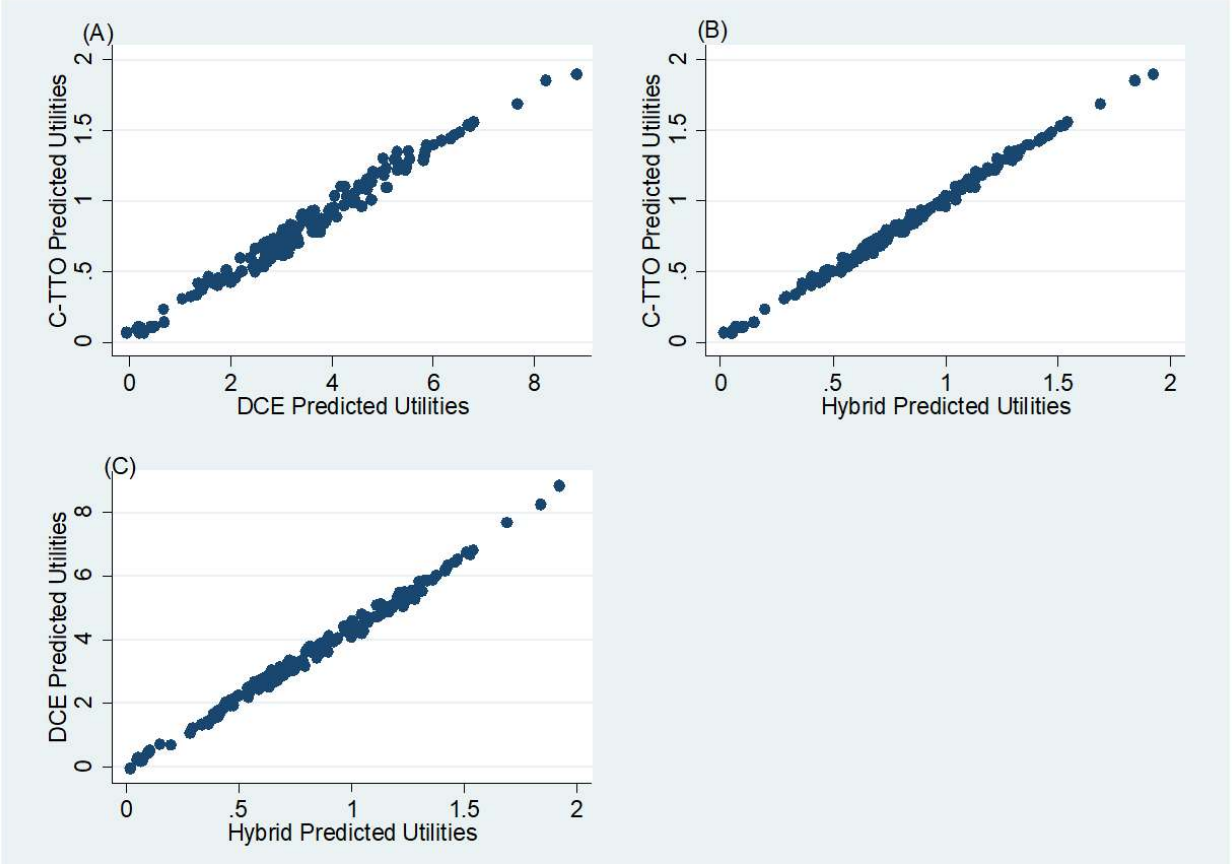
Independent variables of the model	C-TTO Tobit model censored at -1			DCE conditional logistics model			Hybrid model censored c-TTO values at -1 (Final value set)		
	Coeff.	**(SE)**	**P-value**	**Coeff.**	**(SE)**	**P-value**	**Coeff.**	**(SE)**	**P-value**
Mobility (MO)									
No problems to slight problems	0.034	(0.007)	0.000	0.267	(0.037)	0.000	**0.050**	**(0.006)**	**0.000**
Slight problems to moderate problems	0.039	(0.008)	0.000	0.209	(0.042)	0.000	**0.049**	**(0.006)**	**0.000**
Moderate problems to severe problems	0.175	(0.009)	0.000	0.648	(0.043)	0.000	**0.155**	**(0.007)**	**0.000**
Sever problems to unable	0.107	(0.008)	0.000	0.742	(0.043)	0.000	**0.133**	**(0.006)**	**0.000**
Self-care (SC)									
No problems to slight problems	0.033	(0.008)	0.000	0.280	(0.038)	0.000	**0.051**	**(0.006)**	**0.000**
Slight problems to moderate problems	0.092	(0.009)	0.000	0.218	(0.041)	0.000	**0.079**	**(0.006)**	**0.000**
Moderate problems to severe problems	0.180	(0.009)	0.000	0.713	(0.043)	0.000	**0.171**	**(0.007)**	**0.000**
Sever problems to unable	0.050	(0.008)	0.000	0.581	(0.042)	0.000	**0.078**	**(0.006)**	**0.000**
Usual activities (UA)									
No problems to slight problems	0.030	(0.008)	0.000	0.202	(0.037)	0.000	**0.045**	**(0.006)**	**0.000**
Slight problems to moderate problems	0.042	(0.008)	0.000	0.197	(0.040)	0.000	**0.043**	**(0.006)**	**0.000**
Moderate problems to severe problems	0.169	(0.009)	0.000	0.582	(0.043)	0.000	**0.153**	**(0.007)**	**0.000**
Sever problems to unable	0.040	(0.008)	0.000	0.599	(0.042)	0.000	**0.082**	**(0.006)**	**0.000**
Pain/discomfort (PD)									
No problems to slight problems	0.043	(0.007)	0.000	0.234	(0.040)	0.000	**0.051**	**(0.006)**	**0.000**
Slight problems to moderate problems	0.071	(0.009)	0.000	0.346	(0.041)	0.000	**0.074**	**(0.006)**	**0.000**
Moderate problems to severe problems	0.295	(0.009)	0.000	0.998	(0.042)	0.000	**0.264**	**(0.007)**	**0.000**
Sever problems to unable	0.182	(0.009)	0.000	1.049	(0.047)	0.000	**0.194**	**(0.007)**	**0.000**

Anxiety/depression (AD)									
No problems to slight problems	0.029	(0.008)	0.000	-0.050	(0.040)	0.214	**0.016**	**(0.006)**	**0.005**
Slight problems to moderate problems	0.044	(0.009)	0.000	0.200	(0.042)	0.000	**0.046**	**(0.007)**	**0.000**
Moderate problems to severe problems	0.110	(0.008)	0.000	0.441	(0.043)	0.000	**0.101**	**(0.007)**	**0.000**
Sever problems to unable	0.091	(0.007)	0.000	0.390	(0.042)	0.000	**0.083**	**(0.006)**	**0.000**
AIC	19520.38			16798.85			**41149.52**		
BIC	19698.10			16967.37			**41502.68**		
Examples of estimated utilities values									
U(12121)	0.889						**0.897**		
U(31111)	0.891						**0.901**		
U(41111)	0.716						**0.746**		
U(51111)	0.609						**0.613**		
U(12345)	0.176						**0.223**		
U(34521)	0.263						**0.224**		
U(55555)	-0.891						**-0.923**		

AIC Akaike information criteria, BIC Bayesian information criteria, c-TTO composite time trade-off, DCE discrete choice experiments, SE standard error

The full Indian EQ-5D-5L value set, containing utility scores for all 3125 health states, has been made available as a separate Microsoft Excel file.

Figure 22: Comparison of C-TTO and DCE rescaled predicted utilities. b Comparison of C-TTO and hybrid predicted utilities. c Comparison of DCE rescaled and hybrid predicted utilities.



Conclusion

This study is the largest EQ-5D-5L valuation study conducted so far. Also, this study is the first attempt to develop a country specific EQ-5D-5L value-set in the South Asia.[42] India's large geographic expanse and profound linguistic and cultural variations permit the interpretation of this study as a multi-country study. Assuming intense communication between the six regional teams, and a strong common flavor in the on- field data collection and identical analysis protocols, the obtained data permit an analysis on the psychometric impact of culture/ language alone, all other things equal. Although the Indian value- set generated as a part of this study will be fairly generalizable to the adjacent countries, the state specific value- sets can also be used by the countries having similar socio- cultural settings. For examples, value- set generated using the preferences of the respondents of Tamil Nadu can be fairly generalized to Sri Lanka.

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 health technology assessments 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.

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References

1. Wiseman V, Mitton C, Doyle-Waters MM, et al. Using Economic Evidence to Set Healthcare Priorities in Low-Income and Lower-Middle-Income Countries: A Systematic Review of Methodological Frameworks. Health Econ. 2016;25 Suppl 1(Suppl Suppl 1):140–61.
2. Bollyky TJ, Templin T, Cohen M, Dieleman JL. Lower-Income Countries That Face The Most Rapid Shift In Noncommunicable Disease Burden Are Also The Least Prepared. Health Aff. 2017;36(11):1866–75.
3. Downey L, Mehndiratta A, Grover A, Gauba V, Sheikh K, Prinja S, et al. Institutionalising health technology assessment: establishing the Medical Technology Assessment Board in India. BMJ Glob Health. 2017 Jun 26;2(2):e000259.
4. Prinja S, Downey LE, Gauba VK, Swaminathan S. Health Technology Assessment for Policy Making in India: Current Scenario and Way Forward. PharmacoEconomics - Open. 2018;2(1):1-3.
5. MacQuilkan K, Baker P, Downey L, Ruiz F, Chalkidou K, Prinja S, et al. Strengthening health technology assessment systems in the global south: a comparative analysis of the HTA journeys of China, India and South Africa. Global health action. 2018 Jan 1;11(1):1527556.
6. World Health Organization. WHO | Health technology assessment. [online] Available at: https://www.who.int/medical_devices/assessment/en/ [Accessed 16 May 2019].
7. Drummond M, Sculpher M, Claxton K, Stoddart G, Torrance G. Methods for the economic evaluation of health care programmes. 4th ed. New York: Oxford University Press; 2015.
8. Jakubczyk M, Golicki D, Niewada M. The impact of a belief in life after death on health-state preferences: True difference or artifact?. Qual Life Res. 2016;25(12):2997-3008.
9. Dolan P, Roberts J. To what extent can we explain time trade-off values from other information about respondents?. Soc Sci Med. 2002;54(6):919-29.
10. Kind P, Dolan P. The effect of past and present illness experience on the valuations of health states. Med Care. 1995; 33(4 Suppl): AS255-63.
11. Roudijk B, Donders ART, Stalmeier PFM; Cultural Values Group. Cultural Values: Can They Explain Differences in Health Utilities between Countries?. Med Decis Making. 2019;39(5):605-16.
12. Jain S, Rajshekar K, Sohail A, Gauba VK. Department of Health Research-Health Technology Assessment (DHR-HTA) database: National prospective register of studies under HTAIn. Indian J Med Res. 2018 Sep;148(3):258-61. doi: 10.4103/ijmr.IJMR_1613_18.
13. Department of Health Research, Ministry of Health and Family Welfare, Government of India. Health Technology Assessment in India: A Manual. New Delhi: Department of Health Research; 2018.
14. Rajsekar K. [Personal Communication]. Indian reference case for undertaking economic evaluation for Health Technology Assessment in India. New Delhi: Department of Health Research, Ministry of Health and Family Welfare, Government of India; 2018.
15. Prinja S, Chauhan AS, Angell B, Gupta I, Jan S. A Systematic Review of the State of Economic Evaluation for Health Care in India. Appl Health Econ Health Policy. 2015 Dec;13(6):595-613.
16. Oremus M, Tarride JE, Clayton N, Raina P. Health utility scores in Alzheimer's disease: differences based on calculation with American and Canadian preference weights. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2014;17(1):77-83.
17. Chevalier J, de Pouvourville G. Valuing EQ-5D using time trade-off in France. Eur J Health Econ. 2013;14(1):57–66.
18. GSDP at constant (2004-05)prices (2004-05 to 2014-15), NITI Aayog, National Institution for Transforming India [Internet]. NITI Aayog. National Institution for Transforming India, Government of

India; [cited 2018Aug24]. Available from: http://niti.gov.in/content/gsdp-constant-2004-05prices-2004-05-2014-15.
19. Registrar General & Census Commissioner of India. SRS Bulletin 2014. [Internet]. Sample Registration System. New Delhi: Registrar General of India; 2014. (Accessed 24 August 2018). Available at: http://censusindia.gov.in/vital_statistics/SRS_Bulletins/SRS%20Bulletin%20-Sepetember%202014.pdf.
20. Reserve Bank of India. Handbook of Statistics on the Indian Economy 2018-19. [Internet] New Delhi: Reserve Bank of India. [Cited on 5 September 2020] Available from: https://rbidocs.rbi.org.in/rdocs/Publications/PDFs/0HB2018-19A91A298806164470A2BCEF300A4FE334.PDF.
21. Registrar General and Census Commissioner of India. Estimates of Mortallity Indiacators. [Internet]. New Delhi: Vital statistics division, Ministry of Home Affairs, Government of India; 2013. [Cited on 5 September 2020]. Available from: https://www.censusindia.gov.in/vital_statistics/SRS_Report_2017/11.%20Chap%204-Estimates%20of%20Mortality%20Indicators-2017.pdf

22. National Statistical Office. Key Indicators of Household Social Consumption on Education in India. NSS 75th Round [Internet]. New Delhi: Ministry of Statistics and Programme Implementation, Government of India; 2019. [Cited on 5 September 2020] Available from: http://www.mospi.gov.in/sites/default/files/NSS75252E/KI_Education_75th_Final.pdf.
23. Oxford Poverty and Human Development Initiative. Global Multidimansional Poverty Index. [Internet]. Available at: https://ophi.org.uk/multidimensional-poverty-index/.
24. Henderson RH, Sundaresan T. Cluster sampling to assess immunization coverage: a review of experience with a simplified sampling method. Bull World Health Organ. 1982;60:253-60.
25. Purba FD, Hunfeld JA, Iskandarsyah A, et al. Employing quality control and feedback to the EQ-5D-5L valuation protocol to improve the quality of data collection. Qual Life Res. 2017;26(5):1197–1208.
26. Ramos-Goñi JM, Oppe M, Slaap B, Busschbach JJ, Stolk E. Quality Control Process for EQ-5D-5L Valuation Studies. Value Health. 2017;20(3):466–73.
27. Stolk E, Ludwig K, Rand K, van Hout B, Ramos-Goñi JM. Overview, Update, and Lessons Learned From the International EQ-5D-5L Valuation Work: Version 2 of the EQ-5D-5L Valuation Protocol. Value Health. 2019;22(1):23–30.
28. Oppe M, Devlin NJ, van Hout B, Krabbe PF, de Charro F. A program of methodological research to arrive at the new international EQ-5D-5L valuation protocol. Value Health. 2014;17(4):445–53.
29. Oppe M, Rand-Hendriksen K, Shah K, Ramos-Goñi JM, Luo N. EuroQol Protocols for Time Trade-Off Valuation of Health Outcomes. Pharmacoeconomics. 2016;34(10):993-1004. doi:10.1007/s40273-016-0404-1.
30. Olariu E, Paveliu MS, Baican E, Oluboyede Y, Vale L, Niculescu-Aron IG. Measuring health-related quality of life in the general population and Roma communities in Romania: study protocol for two cross-sectional studies. BMJ Open. 2019 Aug 18;9(8):e029067.
31. Oppe M, van Hout B. The “power” of eliciting EQ-5D-5L values: the experimental design of the EQVT. Rotterdam: EuroQol Research Foundation; 2017 October. EuroQol Working Paper Series, No. 17003.
32. Purba FD, Hunfeld JAM, Iskandarsyah A, et al. The Indonesian EQ-5D-5L Value Set. Pharmacoeconomics. 2017;35(11):1153–65.
33. Wong ELY, Ramos-Goñi JM, Cheung AWL, Wong AYK, Rivero-Arias O. Assessing the Use of a Feedback Module to Model EQ-5D-5L Health States Values in Hong Kong. Patient. 2018;11(2):235-47.

34. Ludwig K, Graf von der Schulenburg JM, Greiner W. German Value Set for the EQ-5D-5L. Pharmacoeconomics. 2018;36(6):663-74.
35. Hobbins A, Barry L, Kelleher D, Shah K, Devlin N, Goni JMR, et al. Utility Values for Health States in Ireland: A Value Set for the EQ-5D-5L. Pharmacoeconomics. 2018;36(11):1345-53.
36. Lin HW, Li CI, Lin FJ, Chang JY, Gau CS, Luo N, et al. Valuation of the EQ-5D-5L in Taiwan. PLoS One. 2018;13(12):e0209344.
37. Golicki D, Jakubczyk M, Graczyk K, Niewada M. Valuation of EQ-5D-5L Health States in Poland: the First EQ-VT-Based Study in Central and Eastern Europe. Pharmacoeconomics. 2019;37(9):1165-76.
38. Ferreira PL, Antunes P, Ferreira LN, Pereira LN, Ramos-Goñi JM. A hybrid modelling approach for eliciting health state preferences: the Portuguese EQ-5D-5L value set. Qual Life Res. 2019;28(12):3163-75.
39. Andrade LF, Ludwig K, Goni JMR, Oppe M, de Pouvourville G. A French Value Set for the EQ-5D-5L. Pharmacoeconomics. 2020;38(4):413-25.
40. Welie AG, Gebretekle GB, Stolk E, Mukuria C, Krahn MD, Enquoselassie F, et al. Valuing Health State: An EQ-5D-5L Value Set for Ethiopians. Value Health Reg Issues. 2019;22:7-14.
41. Yang Z, Luo N, Bonsel G, Busschbach J, Stolk E. Effect of Health State Sampling Methods on Model Predictions of EQ-5D-5L Values: Small Designs Can Suffice [published correction appears in Value Health. 2019 Jun;22(6):750]. Value Health. 2019;22(1):38-44.
42. EQ-5D 5L Valuation: Standard value sets [Internet]. Available from: https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/valuation-standard-value-sets/

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