Testing two alternative TTO methods for valuation of EQ-5D-Y health states by trading life years in adulthood

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Abstract

Introduction:

One drawback of the current cTTO method for the Y valuation is that it works by asking respondents to consider shortening a 10-years-old child's life for better health. Although it is hypothetical, the cTTO task could be upsetting and abhorrent to some respondents. Also, there is concern that adult respondents are unwilling to trade child life years, and consequently many studies reported cTTO values of Y valuation studies higher than the cTTO values of corresponding adult states. In order to overcome this potential issue, we conceptualized, and pilot tested two alternative TTO variants named the Parent TTO (PTTO) and lag-time TTO (LTTO). Both methods ask respondents to trade adult life years. We hypothesized that they have higher acceptability and would generate lower values compared to cTTO.

Method:

We collected PTTO and LTTO data for the 10 health states included in the EQ-5D-Y valuation protocol from a general population sample in China. The data collection was piggybacked on the China EQ-5D-Y valuation study, using three interviewers with experience using EQ-VT (two interviewers participated in the China Y study, one interviewer participated in two methodological study). For comparison, the cTTO data, including cTTO values, feedback questions and time etc. were drawn from the China EQ-5D-Y study. We compared the methods in terms of acceptability (using three feedback questions: easy to understand, easy to tell the difference, easy to make the decision), feasibility (time to complete the practice task, time to value the 10 states) and characteristics of TTO values (mean and data distributions).

Results:

In total, 304 participants were included (cTTO: 100; LTTO: 102; PTTO: 102) in this study. On a 5-point Likert scale, the mean score of the 'easy to understand' question was 1.18 (SD: 0.58), 1.45 (SD: 0.91) and 1.65 (SD:

1.02) for cTTO, LTTO and PTTO respectively. The mean score of the ‘easy to differentiate’ question was 1.45 (SD: 0.91), 1.94 (SD: 1.08) and 1.86 (SD: 1.24) and the mean score of the ‘difficult to decide’ question was 3.61 (SD: 1.29), 2.97 (SD: 1.33) and 3.02 (SD: 1.50) respectively. The mean (SD) time spent on the wheelchair example was 276.34 (147.51), 350.33 (140.28) and 454.44 (139.92) seconds for cTTO, LTTO and PTTO, respectively. The mean (SD) time spent on valuing each of the 10 states was 102.97 (29.48), 134.66 (49.69), 141.72 (47.07). The mean (SD) TTO values of all 10 states were 0.463 (0.494), 0.387 (0.555) and 0.123 (0.710). All tests were significantly different when using cTTO method as references, except that the mean value comparison between cTTO and LTTO. LTTO and PTTO showed clear clusterings at 0 and -1 respectively; PTTO had more values on the negative value range.

Discussion:

By designing and testing these two alternative TTO methods to trade-off life adult years, we found participants did not find the TTO tasks more acceptable and feasible, but these two methods do produce values that are more similar to the EQ-5D-5L values. We also found the TTO values may be affected by the parental status and age of the respondents suggesting that researchers to pay attention to the sample representativeness when conducting an EQ-5D-Y valuation study.

1. **Introduction**

The composite time trade-off (cTTO) was first developed for valuation of EQ-5D-5L, where it is used together with discrete choice experiments (1). It is also adopted in the recently published EQ-5D-Y valuation protocol (2). In contrast to its use in valuing 5L, in the Y valuation task, respondents are asked to value health states for a hypothetical 10-year-old child, instead of themselves. Moreover, the role of cTTO in valuation of EQ-5D-Y is different: DCE data are the principal means by which preferences over the descriptive system are obtained and cTTO data are collected from a smaller, separate sample, in order to anchor DCE values, in contrast to the pivotal role of cTTO in EQ-5D-5L valuation. This changed role of cTTO is because studies found that cTTO values of EQ-5D-Y health states are high (relative to values for corresponding adult EQ-5D states), which could hamper the identification of modelling coefficients. It has been observed that respondents are reluctant to trade life years for quality of life when the person being considered in cTTO tasks is a child (1, 2). As a result, the values for EQ-5D-Y states are significantly higher than those of their EQ-5D-3L counterparts (3-6). The higher values raise the concern about sensitivity. If the values for a large number of mild to moderate EQ-5D-Y health states are compressed into a narrow range near the top end, the quality of life gain or loss generated from transitions between those health states could be underestimated or even distorted. Similarly, if the minimum values for the EQ-5D-Y are higher than adult instruments (for example, if there are few or no values < 0) then improvements in severe health problems may also generate fewer QALY gains in children than adults. Therefore, the strategy adopted by the current EQ-5D-Y valuation protocol (3) is to use DCE to determine the relative value of health states and then use cTTO values for moderate to severe health states (e.g., 33333) to anchor the DCE values via hybrid modelling or mapping approaches to a 0 to 1 scale.

The major drawback of the current cTTO method for the valuation of EQ-5D-Y valuation is that it requires respondents to make decisions about shortening a 10-years-old child's life. Although it is a hypothetical scenario, the cTTO task could be upsetting and abhorrent to some respondents, posing a potential ethical issue. The experience could also impair data quality by adding to respondent burden or triggering drop-out or undesirable behaviours such as disengagement and satisficing (7, 8). Moreover, in the current lead-time TTO part of the task (used to obtain values < 0), the impaired health states being valued are no longer occurring in childhood but during adulthood (i.e., a hypothetical 10-year-old is imagined to have 10 years in full health as a 10-20 year old (the lead time) + 10 years in the EQ-5D-Y state being valued, which occurs at 20-30 years old).

In search for better valuation methods for valuation of EQ-5D-Y health states using the cTTO method, we conceptualized two alternative TTO variants for valuing Y states. The first one is called Parental TTO (hereafter referred as PTTO), which was used in the study by Lavelle et al in obtaining parents' preference regarding Autism Spectrum Disorders (11). The second one is the lag-time TTO (hereafter referred as LTTO), which was used in a previous study exploring different methods to anchor the latent DCE Y values (12) and was compared with lead-time TTO in previous studies (4, 5). We described both methods in further detail below.

The aim of this project was to develop and test the two alternative TTO methods for the valuation of EQ-5D-Y health states. We hypothesized that by designing and framing the question in these different ways, we could potentially obtain TTO values for EQ-5D-Y with better characteristics i.e. are more similar to values for adult EQ-5D instruments than those obtained for the EQ-5D-Y using the cTTO approach. As a secondary aim, we aimed to examine the effect of parental status on TTO values and whether the effect differs between these TTO methods.

2. Method:

We collected PTTO and LTTO data for the same 10 health states included in the EQ-5D-Y valuation protocol from a general population sample in China. The data collection was piggybacked on the China EQ-5D-Y valuation study, to capitalise on the experience of interviewers with use of the EQ-VT. For comparison, the cTTO data - including cTTO values, feedback questions and time taken, were drawn from the China EQ-5D-Y study. We compared all three methods in terms of acceptability (three default feedback questions: easy to understand, easy to tell the difference, easy to make the decision), feasibility (time to complete the practice task, time to value the 10 states) and the characteristics of TTO values (mean and data distributions). Before formal testing of both methods, we will first pilot tested them using a think-aloud approach to refine the design.

Parental TTO

Figure 1 shows the TTO task of the PTTO. In general, both Life A and Life B consist of the life of both a child and a parent/caregiver. The task requires respondents to consider whether, as the parent/caregiver of a child, they would trade off his or her own life years to avoid the child being in the impaired health state described in Life B. Therefore, in Life A, the life of the parent can be shortened but the life of the child remains 10 years (in full health) throughout the task. It should be noted that for the purposes of this study, the respondents are asked to imagine being a parent, so the participants of this PTTO are not limited to respondents with children.

In order to understand whether some young and elderly respondent have problems with this hypothetical situation of imagining having a 10-year-old child, we used a think-aloud approach in the pilot study and, based on the insights that emerged from piloting, implemented the following rule for different participants. For those participants who are under 30, we defined them as the brother/sister of the child; for those between 30 and 60, we defined them as the parent of the child; for those above 60, we defined them as the grandparent of the child. In the task, they were asked to imagine they were the only legal caregiver of the child. See the screenshots of PTTO in Appendix 1.

Lag-time TTO

The lag-time TTO resembles the design of the cTTO method with only one difference: the order of the full health and impaired health states in the task are reversed. In this study the lag-time TTO replaced lead time TTO in the composite TTO, rather than being used as a 'separate' TTO method. That is, in the WTD part, life B begins with being in the impaired state for 10 years and followed by a healthy 10 years. In the history of EQ-5D health state valuation method development, both lag-time TTO and lead-time TTO have been tested and explored as standalone TTO methods to obtain values both < 0 and > 0 (i.e., not used in a composite way with conventional TTO method) and have shown similar performance (13). Recently. this method has been adopted in the study of Shah et al in exploring methods to anchor the latent EQ-5D-Y values (12). In that study, this lag-time TTO produced similar values for 33333 from the child perspective and adult perspective. This suggests the potential feasibility and validity of this method, but in that study the method was only used to value 33333 (4). How the values of other states distribute when valued by LTTO is unknown.

Health state selection

To examine the acceptability, feasibility and distribution of the values obtained through the two new TTO variants, we decided to use the 10 states from the EQ-5D-Y valuation protocol (3) for this study. These 10 states formed one block of health states and were valued by all participants using either the LTTO or PTTO method. These 10 states have a good coverage of severity levels and the details of how these states were chosen was described elsewhere.

Interviewers, sampling and interview procedure

For collecting PTTO and LTTO data, we recruited three interviewers. All three interviewers had experience conducting cTTO interviews, specifically, two interviewers participated in the China EQ-5D-Y valuation study and one participated in two methodological EQ-5D-5L valuation studies. All interviewers received training of using these two variants, thus knowing the difference between these methods and cTTO method. The interviewer scripts were adapted from standardized EQ-5D-Y valuation interview script for cTTO. The age of the child to be considered was 10 years old for all three TTO methods. Notably, the perspective from which the PTTO valuation takes was dependent on the age of the respondent: as noted earlier, participants who are under 30 were asked to take the perspective of the brother/sister of the child; those 30-60 years were asked to take the perspective of the parent of the child; and those over 60 years, the grandparent of the child. In contrast, both cTTO and LTTO had a fixed perspective of valuing for a 10-year-old child without specifying the relationship between the respondent and the imagined child. The survey tool of these two variants were developed by a single company and graphical design followed the EQ-VT survey tool.

We used quota sampling method and used the same quota criteria as set in the China EQ-5D-Y study. In total, four quota criteria were used to achieve sample representativeness, that is gender, age, education level and residency type (urban, rural). Data collection was conducted in Chongqing and Guizhou, which were both included in the EQ-5D-Y study. For each variant, we aimed to interview 100 members of the general public and the total sample size was 200. The cTTO data used to compare with the data generated by LTTO and PTTO was drawn from China EQ-5D-Y valuation study. We used the snowball sampling method for this study, three interviewers recruited respondents through their acquaintances and rolling out to others. Individuals who 1) gave informed consent, 2) met the four quota criteria and 3) did not participate in the earlier cTTO study of EQ-5D-Y were interviewed. The study was approved by the Guizhou Medical University Ethic Committee (Approval number: GMUEC-2021-002).

We followed the quality control (QC) procedure as used in the EQ-5D-Y study. All three interviewers used the PTTO method first and each of them conducted 34 interviews followed by another 34 interviews using LTTO method. There were three sections in the interview, 1) basic demographic questions and self-report health using EQ-5D-Y, 2) TTO tasks including valuing 3 wheelchair examples and 3 practice states and 10 EQ-5D-Y states, 3) debriefing questions and customized questions asking participant's child status (do you have children, how many, how old are they, what are their genders etc.) and their comments on the TTO method.

cTTO data

The cTTO data was drawn from the China EQ-5D-Y valuation study (n=412) and the data collected in Guizhou and Chongqing (n=100) were used for comparative purposes as the other two new TTO methods were also collected in these two regions. Note in the China EQ-5D-Y study, the study design included the 10 states from the protocol and 18 states drawn from an orthogonal design. When blocking, all states were randomly assigned to three blocks. As we only needed the cTTO data of the 10 protocol states for this study, this resulted the number of observations for the cTTO arm (n=27 to 36) was less than the numbers of other two arms. The acceptability and feasibility analyses were not affected by this blocked design, but this affected the comparison analysis of TTO values as the number of observations was lower for the cTTO arm. To address this, we therefore also report all cTTO values of these 10 states from the China EQ-5D-Y study.

Data analysis

We examined the acceptability, feasibility and TTO data characteristics of these two TTO methods and the cTTO method as a comparator.

Acceptability of the TTO methods was assessed in terms of three debriefing questions (easy to understand the task, easy to tell the difference between two health states, easy to make the decision), the qualitative comments provided by respondents were analyzed and summarized. The responses of debriefing questions were tested using paired Kruskal-Wallis rank test among the three TTO methods.

Feasibility was assessed in terms of time spent on the wheelchair example as this is the most important step to respondents' learning about how the TTO task worked. Mean time and iterative moves spent on formal tasks were also used. Difference was tested using paired unequal variance t-test among the three TTO methods.

The characteristics of the TTO values elicited from each respondent were examined in terms of the number of unique values, range, mean and logical consistency on individual level, and data distribution on aggregate level. Number of unique values was defined as the number of different indifference points used by a respondent to end the task. Methods with more unique values suggest better discriminative ability and are preferred. Range was defined as the maximum value minus the minimum value. For all three TTO methods, the theoretically possible value range is 2 (i.e., the lowest value a respondent can assign a state, by design of all three of these tasks, is -1). Methods with larger value range suggest better discrimination between mild and severe states and are preferred. We defined logical consistency as a better health state having a higher value than a worse health state when one health state is better than the other in at least one dimension and no worse in any dimension (e.g., 11223 and 12345). We counted the number of participants who made inconsistent (defined as value difference larger than 0) and severe inconsistent (defined as value difference larger than 0.5) responses.

The distributional characteristics were assessed at the group level, using histograms with a particular focus on the magnitude of 'spikes' e.g., at 1, 0.5, and 0. In addition, we visually examined whether these two variants produced negative values with better distributional properties than the cTTO method. Previous studies (of both adult EQ-5D and EQ-5D-Y) have shown that the cTTO method produces a limited number of values between 0 and -0.5 and demonstrated a limited sensitivity to health severity (6). The sensitivity of negative values was tested by regressing the level sum score (LSS) onto negative TTO values. We also assessed the number of switches between BTD and WTD parts used for each TTO method.

To assess how parental status affect the TTO values, we first compared the mean TTO values between respondents with children vs respondents without children using student's t-test with unequal variance. Second, we estimate a random effects linear model by entering the TTO values as the dependent variable and 'having children' as independent variable controlling for gender, age, education level, residency type of the respondents. Given the possibility that three TTO methods could produce different values, we conducted these two analyses separately for each method.

3. Results:

In total, 304 participants were included (cTTO: 100; LTTO: 102; PTTO: 102) in this study. Table 1 shows that sample characteristics were very similar across three arms.

Table 1. Sample characteristic, reported by method

Variable	sub-groups	n		
		cTTO n=100	LTTO n=102	PTTO n=102
Gender	Female	48	50	51
	Male	52	52	51
Age group	18-29	26	26	27
	29-39	20	21	21
	39-49	22	21	22
	49-59	14	16	14
	>60	18	18	18
Residency type	Urban	65	68	69
	Rural	35	34	33

Education level	Primary school	34	37	36
	Middle high school	42	41	43
	High school or professional high school	14	16	14
	University or above	10	8	9
No. of child	None	16	18	19
	1	34	26	24
	2	33	36	38
	3	12	19	16
	>=4	5	3	5
EQ VAS	mean, sd	82.37, 9.46	81.35, 8.93	85.62, 8.49

*All sample characteristics did not differ at the significance level of 0.05 across the three arms.

Task acceptability and feasibility

On a 5-point Likert scale, the mean score of the 'easy to understand' question was 1.18 (SD: 0.58), 1.45 (SD: 0.91) and 1.65 (SD: 1.02) for cTTO, LTTO and PTTO respectively. The mean score of the 'easy to differentiate' question was 1.45 (SD: 0.91), 1.94 (SD: 1.08) and 1.86 (SD: 1.24) and the mean score of the 'difficult to decide' question was 3.61 (SD: 1.29), 2.97 (SD: 1.33) and 3.02 (SD: 1.50) respectively. For the first two questions, higher score indicates lower acceptability and for the third task, lower score indicates lower acceptability. cTTO showed better results for all three debriefing questions when compared with two new variants, but the results were not significantly different between these two variants (Kruskal-Wallis rank test, p=0.05). Table 2 shows the distributions of response to the three debriefing questions. The time taken in the wheelchair example, mean time and mean iterative moves of completing 10 TTO tasks are shown in Table 2. cTTO was the lowest for all three measures. PTTO had longer time for both wheelchair example and formal tasks, but LTTO had a higher number of iterative moves.

Table 2. Feasibility and acceptability results of three arms

Acceptability	Likert scale, 1= agree, 5= disagree	cTTO, n=100	LTTO, n=102	PTTO, n=102
Easy to understand	1	88	63	63
	2	9	22	22
	3	0	14	8
	4	3	3	7
	5	0	0	2
Easy to differentiate	1	75	47	59
	2	14	27	18
	3	2	17	12
	4	9	9	6
	5	0	2	7

Difficult to decide	1	5	20	23
	2	23	16	18
	3	11	28	20
	4	28	23	16
	5	33	15	25
Feasibility				
Time of wheelchair example	Mean, sd	276.34, 147.51	350.33, 140.28	454.44, 139.92
Time per valuation task	Mean, sd	102.97, 29.48	134.66, 49.69	141.72, 47.07
Iterative moves per valuation task	Mean, sd	13.48, 5.79	15.33, 2.98	14.79, 4.20

TTO value

As explained in the method section, the cTTO data had fewer observations (n=390) due to the study design of the EQ-5D-Y valuation study of China. Other two arms both had 102 observations for the 10 EQ-5D-Y states (n=1,020). The mean (SD) TTO values of all 10 states were 0.463 (0.494), 0.387 (0.555) and 0.123 (0.710) for the cTTO, LTTO and PTTO respectively. The differences in TTO values were significant among all three arms: PTTO had the lowest values and cTTO had the highest values. Both of the two new TTO methods had more inconsistent respondents, had more unique values and a longer value range.

Table 3. TTO values of each state, reported by arms

Health state values				
Profile	cTTO* n=27 to 36	LTTO n=102	PTTO n=102	cTTO* n=134 to 148
11112	0.954, 0.087	0.940, 0.059	0.863, 0.169	0.924, 0.123
11121	0.928, 0.086	0.888, 0.086	0.799, 0.239	0.888, 0.131
21111	0.959, 0.082	0.920, 0.077	0.840, 0.234	0.921, 0.107
22223	0.691, 0.148	0.627, 0.159	0.277, 0.485	0.596, 0.358
22232	0.593, 0.268	0.529, 0.250	0.229, 0.470	0.510, 0.330
31133	0.417, 0.337	0.220, 0.356	-0.128, 0.563	0.342, 0.400
32223	0.570, 0.292	0.424, 0.249	0.102, 0.489	0.543, 0.329
33233	0.291, 0.395	-0.172, 0.467	-0.511, 0.522	0.260, 0.401
33323	0.308, 0.388	-0.142, 0.480	-0.545, 0.525	0.220, 0.458
33333	-0.011, 0.527	-0.362, 0.491	-0.694, 0.469	-0.088, 0.505
TTO value characteristics				
No. of respondents made Inconsistency	20	25	29	148
No. of respondents made severe inconsistency	0	2	4	20
No. unique values	7.15, 1.62	8.39, 1.46	7.65, 1.49	7.14, 1.68
Value range	0.97, 0.52	1.35, 0.48	1.61, 0.47	1.03, 0.492
Switch between BTD and WTD, percentage	17.69%	25.29%	40.00%	21.74%

*cTTO of the first column was collected in the same region with LTTO and PTTO. cTTO of the last column was the full data of the China EQ-5D-Y study.

By arm, the data distribution of all TTO values were plotted in Figure 1. Overall, the three TTO methods produced quite different TTO value distributions. The cTTO arm had clustering at 1 and a less smooth overall distribution on the positive side; the LTTO had the smoothest distribution among the three methods and did not show any clear clustering or gaps; the PTTO had clustering at -1, but the rest of the distribution was similar to the LTTO distribution. The percentage of negative observations were 15.13%, 20.20% and 36.08% for cTTO, LTTO and PTTO respectively. The percentage of negative observations on the upper end (>=-0.5 & <0) were 8.46%, 11.76%, 10.10% respectively. Figure 2 shows the boxplots of mean TTO values by LSS for each of the three methods. This clearly shows both new TTO methods produced lower values for each LSS group, with PTTO having the lowest values among three methods. By regressing LSS on negative values, the regression coefficient was 0.002 (P-value: 0.346), -0.056 (P-value: 0.002) and -0.057 (P-value: 0.000) for cTTO. LTTO and PTTO methods respectively. Only cTTO did not show a significant relationship between values and severity. The insignificant result remains when all cTTO values of these 10 states in the China EQ-5D-Y study were used for this analysis.

Figure 1. Data distributions of three arms

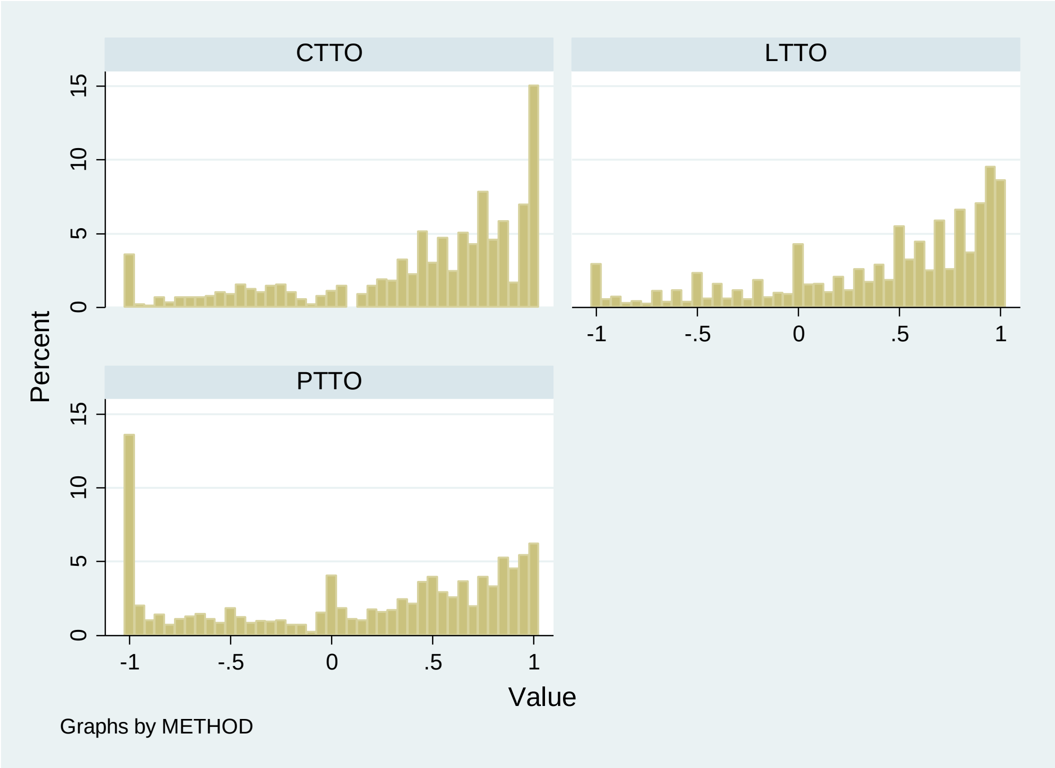


Figure 2. Boxplot of mean TTO values by LSS and method

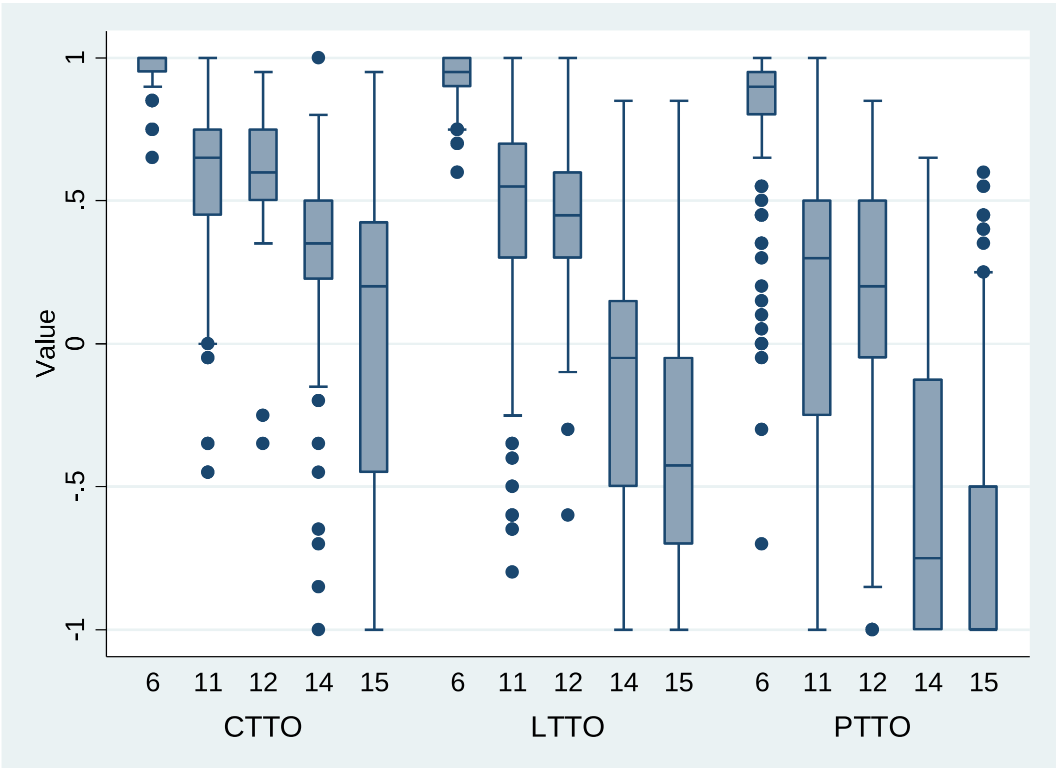


Table 4 shows the effects of parental status on TTO values. The effects differed by three methods. T-tests suggested respondents who are parents gave higher values using cTTO method, but lower values using PTTO method, compared to respondents who are not parents. When controlling for other demographical variables, only parental status and age group had a significant effect on TTO values. Again, being a parent resulted in higher TTO values for the cTTO method, but not for LTTO and PTTO. Respondents from different age groups gave different values using LTTO and PTTO methods, but an opposite effect. In the LTTO arm, the group > 60 years (who took the ‘grandparent’ perspective) had higher values when compared with the group < 30 years (who were asked to take the brother/sister perspective). In the PTTO arm, the 30-60 years and >60 years group both had lower values when compared with the <30 years group.

Table 4. Effects of parental status on TTO values, by method

			cTTO	LTTO	PTTO
T-test	A parent		0.440, 0.014	0.397, 0.019	0.097, 0.025
	Not a parent		0.331, 0.028*	0.341, 0.043	0.237, 0.048*
Random effects linear model	A parent (ref: not a parent)		0.095, 0.053#		
	Age groups (ref:<30)	30-59			-0.304, 0.093*
		>60		0.162, 0.087#	-0.345, 0.115*

* indicates significant at 0.01 level, # indicates significant at 0.10 level

4. Discussion:

Our study highlighted the use of two alternative TTO methods for valuing EQ-5D-Y states. An important concern about EQ-5D-Y values produced using the cTTO is that the relatively high values could hamper the model estimation, and limit comparability of values and QALY estimates between children and adults. The two methods tested in this study demonstrated a clear advantage by addressing the first concern as they both produced lower values. However, judging from the three debriefing questions results, our study did not support the use of these two methods as they had lower acceptability and feasibility. Nevertheless, these two alternative methods were less acceptable and feasible but negated better TTO data in terms of the number and distribution of negative values (in the sense of the distribution of values being more similar to those of adult EQ-5D values). Importantly, the negative values produced by these two new variants were significantly correlated with health state severity, but not for cTTO method. Obviously, one needs to interpret this cautiously as there is a clear value judgement, that is, the distribution of values for EQ-5D-Y should look like the distribution of values for adult EQ-5D instruments. In terms of consistency in application to QALY estimation, having comparable characteristics is a good thing. However, whether one can use EQ-5D as a ‘gold standard’ for child/adolescent instrument is in doubt.

Neither of the two methods demonstrated better acceptability and feasibility. This provides some support for the continued use of the current cTTO method for valuing EQ-5D-Y health states. Given the life in PTTO consists of a life for a child and a life for a parent, it is not surprising to see the task took more time in both the wheelchair example and the valuation tasks. Nevertheless, the time spent on the task of the LTTO method was still longer than the counterpart of the cTTO method. One possible explanation is that in both new methods, respondents were more likely to enter the WTD scenario, which procedure requires more iterative moves and time, especially for very low negative values.

In contrast to the inferior acceptability and feasibility results, both the LTTO and PTTO methods showed better value distributions and characteristics. LTTO performed the best in terms of data distribution as it did not have clear spikes and the proportion of negative value was higher than the cTTO method. PTTO also had a nice distribution except a clear spike at -1 can be seen, a characteristic that has also been reported in some EQ-5D-5L valuation studies (7-9). This suggests that in the PTTO there are people who would have given up even more of their time if it had been possible. In addition, respondents provided more distinct values using both LTTO and PTTO methods. The larger value range of these two methods also suggested better sensitivity of these two methods, i.e., assigning higher values for better state and lower values for worse state, when compared to cTTO method. Indeed, the negative values obtained through these two methods arguably demonstrated better relationship with health state severity. This was not observed in the cTTO data and this problem of cTTO has been examined in previous EQ-5D studies (10-12). Ascertaining the reasons for the better performance of LTTO and PTTO in generating informative negative values than cTTO is beyond the scope of this study. However, the better performance is likely attributable to improved task difficulty and sensibility. cTTO is inconsistent in the target for valuation of health states considered better and worse than dead. For better than dead states, it is 10 years of life starting from the age of 10 years; for worse than dead states, it is 10 years of life starting from the age of 20 years. Using this design, respondents valued two different health states, which could be the reason for the poor validity of the negative cTTO values. The LTTO does not suffer from this issue. The selection of cTTO over LTTO for use in the international EQ-5D-Y valuation protocol is made in order to make it consistent with EQ-5D-5L valuation protocol. This is at the cost of sacrificing the sensibility of the valuation task for EQ-5D-Y. If the cTTO and LTTO values are similar, this decision is well justifiable since the TTO values are used to anchor or map DCE data in Y value set studies. However, the cTTO and LTTO values presented in Table 4 are dramatically different, suggesting that the choice between the two TTO variants is likely to make a significant difference in the estimated value sets. The current EQ-5D-Y valuation study protocol allows respondents to imagine the 10-year-old child for valuation as any person, real or imagined, with or without relationship. This leads to both within- and between-respondent variations and may contribute to data variability. The PTTO stipulates the relationship between respondents and the child for evaluation, which may help reduce data variability and improve the validity of the negative values.

Being a parent was associated with higher cTTO values, but this association was not obvious for LTTO values. This difference could be due to insufficient statistical power as the number of (% of the whole sample) participants who did not have children were only 18 (17.65%) for the LTTO. In contrast, respondents as an actual parent gave lower values using PTTO method, though the effect disappeared when controlled for other demographic variables. Similar to the sample of LTTO, only 19 (18.63%) participants did not have children in the PTTO sample. Moreover, the effect of age on cTTO/LTTO and PTTO differed. With PTTO method, respondents aged 60 years or above (asked to undertake the tasks imagining themselves to be a grandparent of a 10-year-old child) tended to give lower values, but tended to give higher values with LTTO method and similar values with the cTTO method. The differing effects of parenthood were not surprising (13). Parenthood made respondents feel it harder to trade their children's lives in cTTO (thus higher values) but more willing to sacrifice their own lives in PTTO (thus lower values). It is interesting that the effect of parenthood did not attenuate in PTTO where all respondents including those without parental experience were asked to take the perspective of a parent/grandparent. The differing effects of age on cTTO/LTTO and PTTO might suggest different mechanisms. It seems that old age had no or a small effect on the tendency of trading a child's life in cTTO but it significantly increased the willingness of respondents to trade their lives for their grandchildren's health. This is not unreasonable because older people might perceive their life as less precious than that of their own grandchild compared to younger people, particularly in the Chinese culture. These results suggested that PTTO values are more sensitive to sample characteristics than cTTO.

There were some limitations of our study. The first limitation is that each respondent only saw one TTO method. By analyzing the comments given by respondents, we noticed that most comments were about TTO task difficulty and health states being abstract and not easy to differentiate. Future research could use a cross-over design to directly compare how general public feels about these two methods, in comparison with the cTTO method. Some respondents expressed the view that being a parent could impact the values and that this task maybe upsetting for others, but our study design did not allow directly participants to compare and judge whether trading off adult's life years is more acceptable than trading off children's life years. Another limitation of this study is the study design included 10 health states, which does not support estimating a 10-parameter main-effects value set. It is therefore not clear whether the five dimensions were valued similarly across methods. In another word, since both alternative methods trade-off life years in adult time, it is likely participants place different weights onto the five dimensions compared to trade-off life years in adolescent time. Last but not least, the perspective from which adult respondents were asked to value EQ-5D-Y health states using PTTO was different than that which was used in eliciting the cTTO and LTTO data. By imagining to be the caregiver of the 10-year child in PTTO task, participants should have felt more accountable to make decisions for this child. This context makes the PTTO task more like the EQ-5D-5L valuation task as the decision is made from a first person perspective. The perspective from which adults are asked to state their preferences is known to exert an effect on values. As both perspective and methods differed, this limits our ability to attribute differences in results only to the methods. However, this does not affect comparisons drawn between the LTTO and PTTO results, which used the same perspectives.

5. Conclusions:

By designing and testing these two alternative TTO methods to trade-off life adult years, we found participants did not find the TTO tasks more acceptable and feasible, but these two methods do produce values that are more similar to the EQ-5D-5L values. We also found the TTO values may be affected by the parental status and age of the respondents suggesting that researchers to pay attention to the sample representativeness when conducting an EQ-5D-Y valuation study.

6. References:

1. Dewilde S, Janssen MF, Lloyd AJ, Shah K. Exploration of the Reasons Why Health State Valuation Differs for Children Compared With Adults: A Mixed Methods Approach. Value in Health. 2022.
2. Reckers-Droog V, Karimi M, Lipman S, Verstraete J. Why Do Adults Value EQ-5D-Y-3L Health States Differently for Themselves Than for Children and Adolescents: A Think-Aloud Study. Value Health. 2022.
3. Ramos-Goni JM, Oppe M, Stolk E, Shah K, Kreimeier S, Rivero-Arias O, et al. International Valuation Protocol for the EQ-5D-Y-3L. Pharmacoeconomics. 2020.
4. Devlin N, Buckingham K, Shah K, Tsuchiya A, Tilling C, Wilkinson G, et al. A comparison of alternative variants of the lead and lag time TTO. Health Econ. 2013;22(5):517-32.
5. Augustovski F, Rey-Ares L, Irazola V, Oppe M, Devlin NJ. Lead versus lag-time trade-off variants: does it make any difference? Eur J Health Econ. 2013;14 Suppl 1:S25-31.
6. Gandhi M, Rand K, Luo N. Valuation of Health States Considered to Be Worse Than Death-An Analysis of Composite Time Trade-Off Data From 5 EQ-5D-5L Valuation Studies. Value Health. 2019;22(3):370-6.
7. M. Versteegh M, M. Vermeulen K, M. A. A. Evers S, de Wit GA, Prenger R, A. Stolk E. Dutch Tariff for the Five-Level Version of EQ-5D. Value in Health. 2016;19(4):343-52.
8. 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.
9. Luo N, Liu G, Li M, Guan H, Jin X, Rand-Hendriksen K. Estimating an EQ-5D-5L Value Set for China. Value Health. 2017;20(4):662-9.

10. Yang Z, Rand K, Luo N. Censoring negative time trade-off values at zero improves modelling results a call to reconsider worse-than-death valuation? . 2019 EuroQol Plenary Meeting dicussion paper; Brussels, Belgium2019.

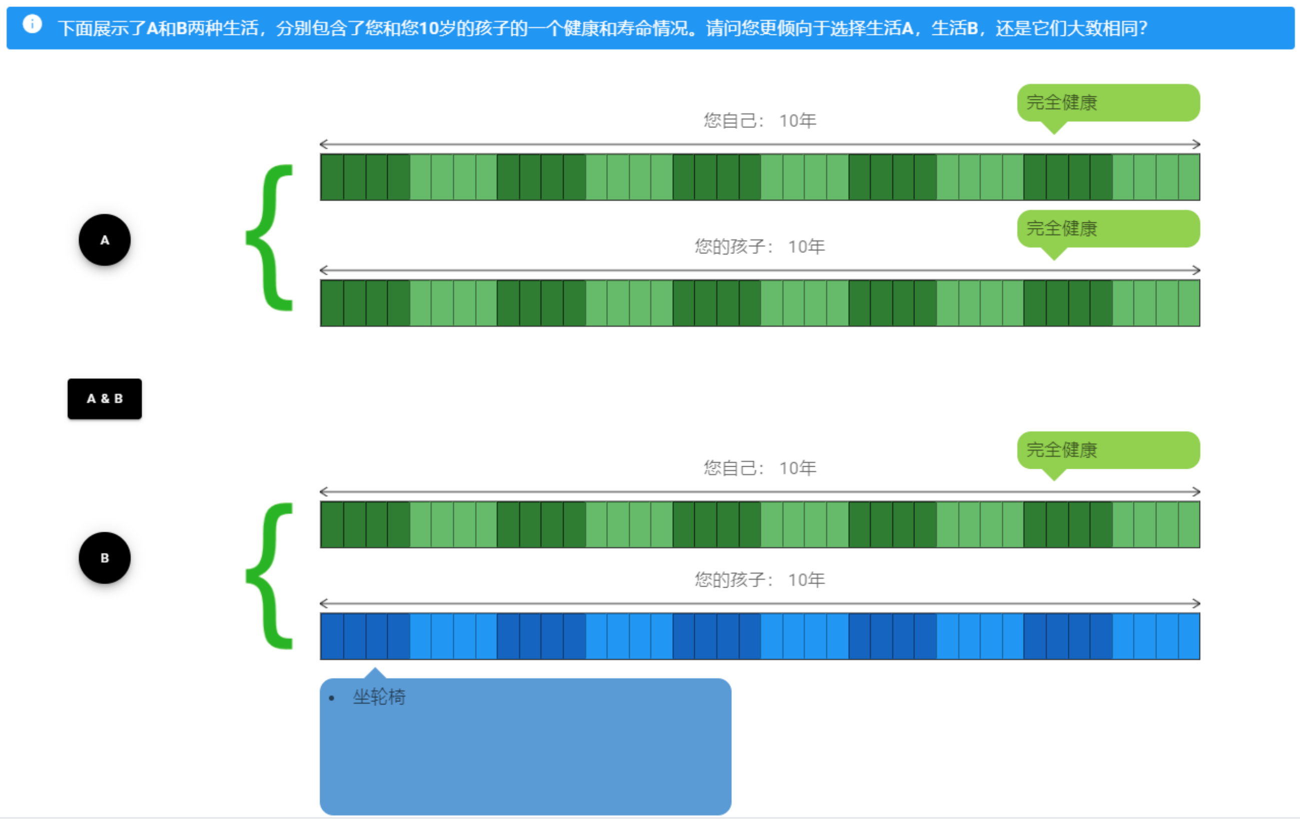
11. M G, Rand-Hendriksen K, Luo N. Valuation of Health States Considered to Be Worse Than Death-An Analysis of Composite Time Trade-Off Data From 5 EQ-5D-5L Valuation Studies. Value Health. 2019;22(3):6.

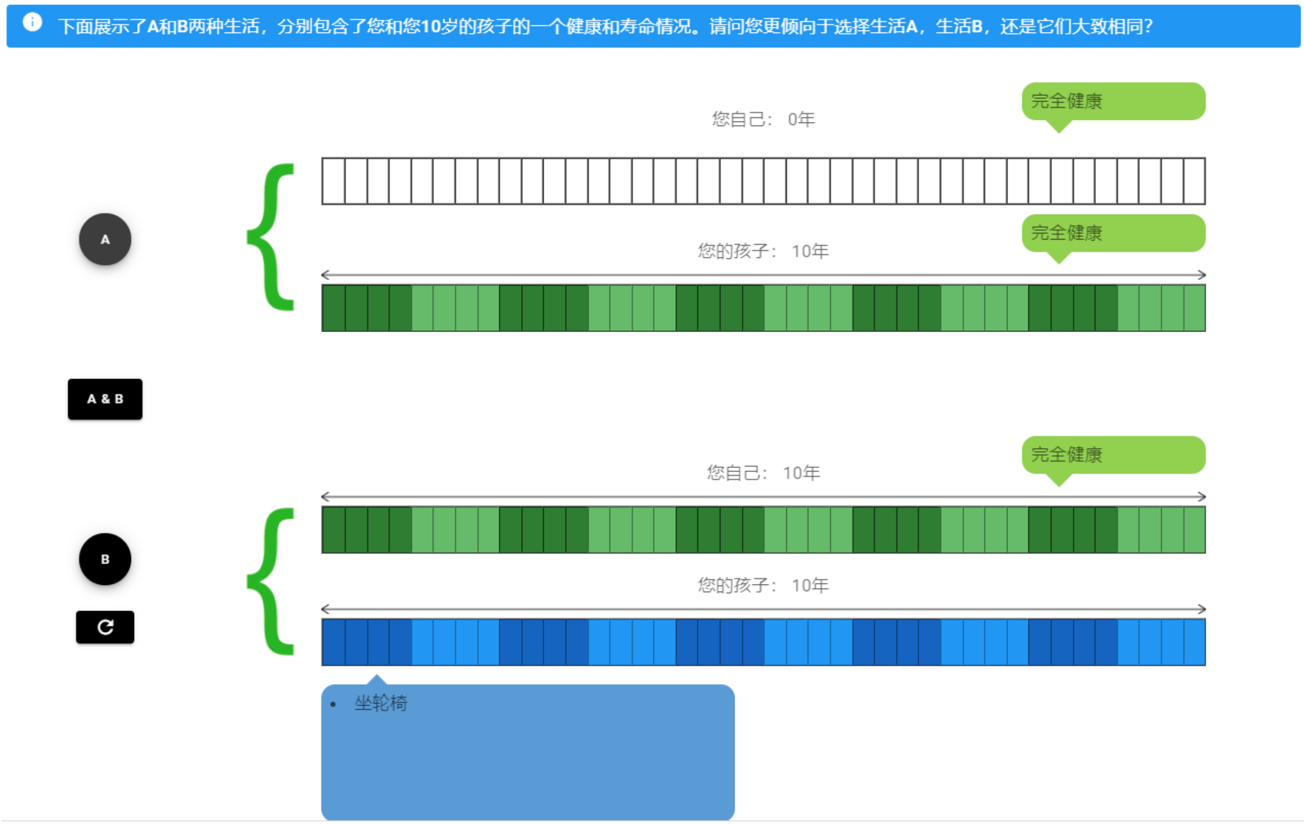
12. Rand-Hendriksen K, Augestad LA, Dahl FA, Kristiansen IS, Stavem K. A shortcut to mean-based time tradeoff tariffs for the EQ-5D? Med Decis Making. 2012;32(4):569-77.

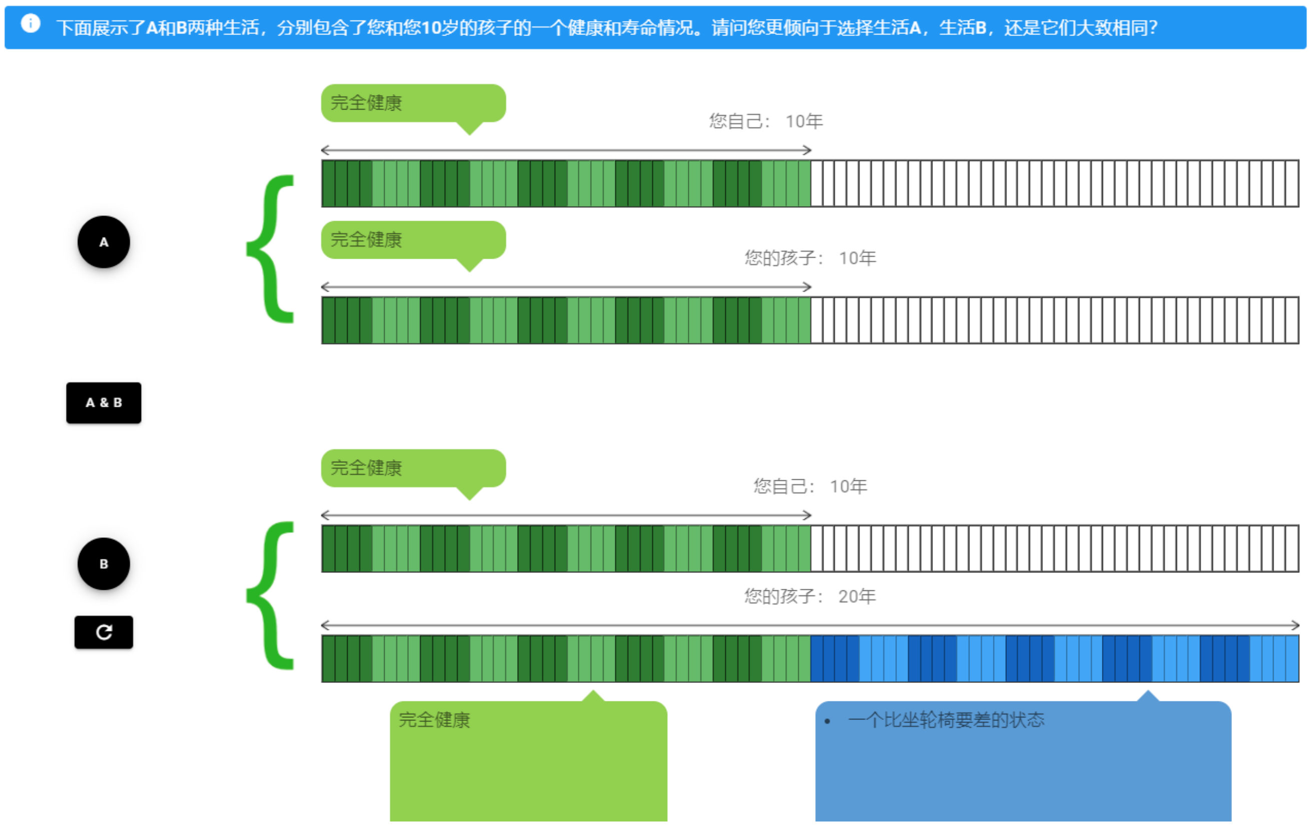
13. Reckers-Droog V, Karimi M, Lipman S, Verstraete J. Why Do Adults Value EQ-5D-Y-3L Health States Differently for Themselves Than for Children and Adolescents: A Think-Aloud Study. Value in Health. 2022.

7. Appendix:

Appendix 1. Screenshots of PTTO (in Chinese). In sequence, first figure shows the staring point, second figure shows sorting question, third figure shows the starting point of WTD scenario




下面展示了A和B两种生活，分别包含了您和您10岁的孩子的一个健康和寿命情况。请问您更倾向于选择生活A，生活B，还是它们大致相同?
完全健康
您自己：0年
A
完全健康
您的孩子：10年
A & B
完全健康
您自己：10年
B
您的孩子：10年
坐轮椅


下面展示了A和B两种生活，分别包含了您和您10岁的孩子的一个健康和寿命情况。请问您更倾向于选择生活A，生活B，还是它们大致相同?
完全健康
您自己：10年
A
完全健康
您的孩子：10年
A & B
完全健康
您自己：10年
B
您的孩子：20年
完全健康
一个比坐轮椅要差的状态