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Title: Valuing child health: an EQ-5D-Y-3L value set for the United States

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Abstract:

OBJECTIVES: To inform value-based pricing and reimbursement in the United States, a value set for the EQ-5D-Y-3L, a measure of child and adolescent health, was developed based on general population preferences elicited from both adults and adolescents.

METHODS: Study design was informed by an international valuation protocol as well as recommendations from US stakeholders. US adults (≥18 years) and adolescents (11-17 years) were asked to complete an online discrete choice experiment (DCE). Adult respondents were subsequently invited to complete composite time trade-off (cTTO) valuation tasks via videoconferencing with a trained interviewer. DCE data were analyzed using latent class models and adjusted mean values for 28 health states from the cTTO tasks were estimated using Tobit models censored at -1 and 0. An adult/adolescent model was estimated by combining information from the best fitting latent-class model and cTTO models to produce a population weighted, latent-class hybrid model with coefficients anchored by a 0 (dead) to 1 (full-health) scale.

RESULTS: The analytic sample included DCE data from 714 adolescents and 1,669 adults, and cTTO data from 200 adults. Estimated utilities for state 33333 to 12111 ranged from -0.004 to 0.972. Pain/discomfort was the most important dimension, followed by worried/sad/unhappy.

CONCLUSIONS: Informed by stakeholder consultation, this US EQ-5D-Y-3L value set was the first to combine adolescent and adult preferences into a single value set. Useful insights for future valuation studies included: 1) How to reconcile diverse stakeholder views, 2) choice of valuation tasks, 3) different framing perspectives for adults and adolescents, 4) weaker preferences for health-state dimensions exhibited by adolescents, and 5) the analytic approach selected to anchor estimates to the QALY scale.

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Introduction

The EQ-5D-Y-3L is a generic measure of health-related quality of life (HRQoL) designed to complement the standard (adult) EQ-5D-3L as a child-friendly instrument for individuals ages 8-15. Since the publication of an international valuation protocol in 2020, investigators around the world have conducted valuation studies to estimate national value sets for the 243 health states described by the EQ-5D-Y-3L, providing utility scores for use in economic evaluations. (1-11)

Informed by valuation exercises in other measures for pediatric populations (12, 13) and a valuation protocol (1), valuation studies for the EQ-5D-Y-3L from other countries have typically elicited preferences from adult respondents via discrete choice experiments (DCE) and composite time trade-off (cTTO) tasks, where tasks are framed from the perspective of a 10-year-old child. Several studies have explored the framing of perspectives used in valuation tasks, ethical arguments for and against the inclusion of adolescents in valuation, and differences in adult and adolescent preferences for EQ-5D-Y-3L health states. (14-18) Compared to cTTO, which includes an element of duration, DCE without duration is a less cognitively demanding elicitation method, contributing to its popularity in valuing children's HRQoL, including directly from children and adolescents. (19-22) In the international valuation protocol for the EQ-5D-Y-3L, DCE responses reflect preferences for the relative importance of attributes and response levels on an unanchored latent scale, while cTTO responses provide a basis for anchoring latent scale DCE values to the 0 (dead) to 1 (full health) scale, which is required for quality-adjusted life-year (QALY) estimation.

Although legislation in the US prohibits the use of QALY thresholds in value assessment of therapies for federal programs (23) , cost per QALY remains an important metric in pricing and value discussions.(24-26) In a roundtable discussion hosted by the investigators to gain insight into methodological issues and to inform the study design, US stakeholders were supportive of the development of a national value set for the EQ-5D-Y-3L (27). They provided input about methodology and normative decision-making to guide the development of a value set that would be fit-for-purpose in the US context. Although it was difficult to reach consensus on some issues, stakeholders found intuitive appeal in a value set including preferences directly from adolescents in addition to adults, weighted to reflect the proportion of adolescents in the US population. (27) Drug development and approvals by the US Food and Drug Administration (FDA) for drug labeling in pediatric populations have accelerated, driven in part by legislative measures such as the Pediatric Research Equity Act that mandates that new drugs and biologics which are likely to be used by children must include pediatric assessments. (28) Considerations of pediatric HRQoL and the values assigned to their health states can be important to support drug labeling claims and pricing and reimbursement discussions for approved drugs. (29)

In the US, there is currently no pediatric-specific measure of HRQoL with a preference-based scoring function to derive utility values. Guided by the international protocol and national stakeholder recommendations, this study aimed to develop a US-specific value set for the EQ-5D-Y-3L representing the views of both adolescents and adults from the general public. The primary objective of this research was to produce a preference-based scoring function based on a robust model to support the use of the EQ-5D-Y-3L in economic evaluations of healthcare interventions in the US.

Method

Study Overview and Ethical Approval

The study design was informed by the international EQ-5D-Y-3L protocol(1) and recommendations from US stakeholders. (27) Data collection occurred from November 2022 to December 2023 through separate surveys designed for adolescent and adult participants. The Institutional Review Board of the University of San Francisco granted ethics approval (#1780). We followed the RETRIEVE checklist to report key elements for studies pertaining to the elicitation of stated preferences for child HRQoL. (30)

Descriptive System

Health states were described using the EQ-5D-Y-3L, an instrument designed for children ages 8-15 years consisting of five dimensions of health: mobility (defined as walking about), looking after myself (defined as washing or dressing), doing usual activities (examples include: going to school, hobbies, sports, playing, doing things with family or friends), having pain or discomfort, and feeling worried, sad or unhappy. Three response levels describe the level of problems in each dimension: “no” (or “not”), “some” (or “a little”), or “a lot” (or “very”). (31) The descriptive system defines 243 unique health states, which can be represented by a five-digit profile ranging from 11111 (no problems in any dimension) to 33333 (the highest level of problems in all dimensions).

Preference elicitation methods

Methods included separate online surveys consisting of DCE or cTTO tasks.(32) DCE surveys were self-completed while cTTO surveys were conducted via online video calls with one of three trained interviewers. In the DCE, respondents were asked to select the health state they preferred in a forced (i.e., no opt-out option) pairwise comparison of two EQ-5D-Y-3L health states. The cTTO compared living 10 years in a suboptimal EQ-5D-Y-3L health state to living up to 10 years in full-health. In the conventional TTO, respondents were asked to consider trading-off time in increments of 0.5-1 year from full-health to find a point of indifference between living 10 years in the specified health state. If a respondent felt that a health state was equivalent to less than 0 years in full-health (i.e., worse than dead (WTD)), the task was modified with 10 additional years of full-health (lead-time TTO). Thus, possible cTTO values ranged from -10 to 10 in 6-month increments, corresponding to utility values from -1 to 1 in 0.5-unit increments. The DCE assessed the relative importance of health state dimensions and levels without a duration component (latent scale), while cTTO provided values on a 0 (dead) to 1 (full-health) scale consistent with QALY estimation in economic evaluations.

Discrete Choice Experiment (DCE)

DCE Survey Design and Procedure

Respondents were first asked to report their own health using the EQ-5D-Y-3L and to provide sociodemographic information – including age, gender, race, ethnicity, and state of residence – to ensure eligibility with recruitment quotas. The DCE design featured 10 blocks, each containing 15 experimental pairs of health states and 3 fixed pairs for quality control (QC) purposes. This design was chosen based on maximization of D-efficiency criteria without specifying priors. (1) Each respondent was randomly assigned to complete one block of tasks, with the order and positioning of health state pairs randomized to reduce framing effects. In each pair, two dimensions overlapped in severity, while the remaining three differed and were presented in bold font. Adolescent respondents (ages 11-17 years) assessed health states from their own perspective (*which health state do you prefer?)*, whereas adults (ages ≥18 years) evaluated health states considering a 10-year-old child's perspective (*which health state do you prefer for a 10-year-old child?).*

DCE Sampling and Recruitment

The target sample comprised approximately 1,500 adults and 700 adolescents, recruited through an online panel survey company, Dynata (https://www.dynata.com). Quota sampling was applied based on age, gender, race, ethnicity, and state of residence to reflect the composition of the US population according to the 2022 American Community Survey in the US Census.(33) English speaking adults (≥18 years of age) and adolescents (11-17 years) residing in the US were eligible to participate. Potential participants were additionally screened for eligibility based on remaining recruitment quotas. Importantly, adolescents provided written assent with a parent or guardian providing written informed consent, and adolescents were instructed to complete the survey independently; adult participants provided written informed consent. Participants who completed the survey without QC violations received incentives from the survey company.

DCE Quality Control

The same three DCE pairs were presented to respondents for QC purposes. QC pairs featured a dominated health state with more severe problems across all dimensions compared to the alternative. Responses were assessed for quality using two criteria: 1) selecting the dominated health state in at least 2 out of 3 QC pairs (dominant pairs violations) and/or 2) completing all DCE tasks in ≤150 seconds (speeding violations). Responses violating either criterion were excluded from analysis. Additionally, CAPTCHA tasks were added to the survey to ensure responses were human-generated.

<u>Composite Time Trade-Off (cTTO)</u>

cTTO Survey Design and Procedure

The cTTO survey featured an orthogonal design with 3 blocks of 10 health states, where the most severe (33333) health state was included in each block, representing a total of 28 health states (34). Tasks were completed from a proxy 1 perspective (*Considering your views for a 10-year-old child).(*35*)* First, respondents reported their own health using the EQ-5D-Y-3L. Interviewers explained the cTTO task, including the lead-time TTO for WTD states, then guided respondents through three practice tasks pertaining to a mild (21121), severe (23332), and intermediate (13211) EQ-5D-Y-3L health state. The 10 experimental states were presented in a random order. Each session concluded with a standard feedback module, where respondents were presented a review of valued health states rank-ordered by decreasing cTTO-derived utility and asked to identify health states they felt were out of order. (36) Respondents were compensated with a digital $40 gift card for their participation.

cTTO Sampling and Recruitment

The target sample included 200 adult respondents, recruited through three strategies: 1) invitations to DCE participants from the online panel company, Dynata; 2) sampling of known acquaintances; 3) ResearchMatch (a national health volunteer registry that was created by several academic institutions and supported by the U.S. National Institutes of Health as part of the Clinical Translational Science Award (CTSA) program; ResearchMatch has a large population of volunteers who have consented to be contacted by researchers about health studies for which they may be eligible). Only adults who first completed the DCE survey without QC violations were eligible to participate in the cTTO survey; therefore, participants recruited through known acquaintances and ResearchMatch were first invited to complete the DCE survey. Quota sampling was not applied for the cTTO survey.

cTTO Quality Control

Interviewers were trained by EuroQol scientific staff using the EuroQol Valuation Technology (EQ-VT) 2.1 platform. (37, 38) Interviewers were trained to instruct, motivate, and probe respondents for understanding of valuation tasks. Respondents were encouraged to think aloud to ensure comprehension and engagement. All interviewers completed pilot surveys prior to beginning data collection. During data collection, Interviewer performance was reviewed with EuroQol scientific staff approximately every 10 completed interviews focusing on three main QC criteria: time spent on cTTO tasks (≥ 3 minutes on explanations; ≥5 minutes on cTTO tasks), whether the lead-time TTO was demonstrated, and whether the worst health state (33333) was assigned a value of ≥0.5 points greater than other health states. Feedback was promptly shared with interviewers to incorporate necessary changes in subsequent interviews.

<u>Statistical Analysis</u>

Overview

Sample characteristics were described using percentages for categorical variables and means for continuous variables. Differences in representation of age groups and gender between the sample and US general population were corrected by weighting analyses. A population-weighted, latent-class hybrid model combining DCE and cTTO data was used to model health state preferences.(39, 40) All analyses were conducted in Stata MP version 14 (StataCorp, College Station, TX).

DCE

To account for unobservable preference heterogeneity in the data, valid adult and adolescent DCE data without QC violations were modeled using latent class models with the 'lclogit2' Stata command. (7, 41). The utility, U, of a health state, j, was modeled according to Equation 1. Each model consisted of a main effect specification with ten independent incremental dummy variables, where estimated coefficients represented the incremental disutility within each of the five dimensions between consecutive levels, starting with level 1 as the reference category, and an intercept, β_0, representing the utility associated with the health state with no problems in any dimension (11111) (Equation 1)

Equation 1: $U_j = \beta_0 + \beta_1 MO2_j + \beta_2 MO3_j + \beta_3 SC2_j + \beta_4 SC3_j + \beta_5 UA2_j + \beta_6 UA3_j + \beta_7 PD2_j + \beta_8 PD3_j + \beta_9 AD2_j + \beta_{10} AD3_j$

Model diagnostics included the mean square error (MSE) and mean absolute error (MAE) to quantify how well modeled probabilities predicted observed choice probabilities. Goodness of fit for each model was assessed by the Bayesian information criteria (BIC). Models were explored specifying between 2 to N number of classes, where the model with N classes showed a worse fit (higher BIC) compared to the preceding model of N-1 classes. The best fitting (lowest BIC) model with N-1 classes was chosen as the final model for further analysis.

The weighting of each class in the selected latent class model was based on the percent class share, adjusted for the relative magnitude of coefficients within each class, to produce a scale-adjusted class share. Additional methodological details are described in the Spanish EQ-5D-Y-3L value set publication. (7)

cTTO

For each of the 28 health states valued through cTTO, the observed mean value was adjusted by applying weights to correct for differences between the sample and US general population in terms of age group and gender. Separate Tobit models censored at values of -1 and 0 were estimated for each health state, with the weighted cTTO value as the dependent variable and a constant as the independent variable. Models were censored at -1 to reflect the lower bound of WTD values in the lead-time TTO task. Models were censored at 0 to account for differences in the proportion of 0 values between the three interviewers (i.e., potential interviewer effects). Models were *not* censored at 1, which represents full health in the cTTO tasks and is the upper bound for health utilities. Health states that were flagged by respondents in the feedback module were excluded from analysis.

Hybrid Model

Information from the DCE and cTTO models were combined in a hybrid model using the hyreg Stata command, adapted to include weighting.(42) Using the best fitting latent-class model for the DCE data, population weights for age group and gender were applied to class grades for individual respondents, similar to the weighting applied to the cTTO values. Since the cTTO survey respondents also completed the DCE survey, class grade weights from the latent class model were carried over to further weight the cTTO values. Weighted hybrid models were estimated per each latent class, using population weights multiplied by the class grades. Since coefficients for each class would be rescaled in the hybrid model estimation, the relative scale of the coefficients for each class was preserved by adjusting using the scale-adjusted class shares (the class shares multiplied by the ratio of the value of the 33333 state within each class and the value of the 33333 state in the overall model).

Following stakeholder recommendations, both adolescent and adult responses were combined in the hybrid model to produce the value set. Additionally, an adult-only hybrid model was estimated for comparison.

Results

<u>Sample Characteristics</u>

The analytic sample for the DCE comprised 714 adolescents and 1,669 adults; 211 adults additionally completed the cTTO, and after exclusions based on interviewer assessment of lack of understanding or engagement, 11 interviews were excluded for a total of 200 adults in the cTTO analytic sample. Adolescents were categorized into two age groups: 11-14 years (45.5%) and 15-17 years (54.5%) (Table 1). Adults were distributed across a broader range of age groups, with the largest proportion aged 65 years or older (32.8%). Among adolescents, 39.6% were female and 60.2% were male. In the adult sample, females constituted 52.7% and males 47.2%. Population weights used to scale down or up each age group by gender ranged from 0.26 (i.e., representation reduced to one quarter) to 2.45 (i.e., representation more than doubled).

Most participants were White (87.0% of adolescents and 8s0.3% of adults). Black or African American participants comprised 6.7% of adolescents and 11.6% of adults. Hispanic ethnicity was reported by

10.6% of adolescents and 10.3% of adults. Of the adult sample, 38.2% reported being a parent or primary caregiver of one or more children. In describing their health at the time of the survey, the most commonly reported health problems were: pain or discomfort (19.5% of adolescents, 46.3% of adults), being worried, sad, or unhappy (29.6% of adolescents, 38.2% of adults), and problems with mobility (11.8% of adolescents, 18.0% of adults).

Modeling Results

After removal of health states flagged in the feedback module, the observed mean utility value based on 190 cTTO observations for the worst health state (33333) was 0.020 (Table 2). Scaling by the population weights, the number of weighted, effective observations ranged from 59 to 224 per health state. The population-weighted, Tobit modeled cTTO values ranged from -0.018 for the 33333 health state to 0.832 for the 31211 health state (the highest valued health state)

The DCE data were modeled by a latent class model representing 5 classes for the adolescent and adult sample (Table 3a). A class with pain or discomfort as the highest utility decrement received the most weight in the hybrid model. As such, the transition from no pain (level 1) to some pain (level 2) had a decrement of 0.115 in the overall model, and from some pain (level 2) to a lot of pain (level 3) had a decrement of 0.172. The utility decrement from not feeling worried (level 1) to feeling a bit worried (level 2) was 0.083, and from a bit worried (level 2) to very worried (level 3) was 0.174. An adult-only hybrid model (Table 3b) was represented by 6 latent classes and had the largest utility decrements associated with having pain or discomfort. Coefficients between the two models were similar, with the largest differences equal to 0.01 points lower in level 3 of having pain or discomfort and level 3 of feeling worried, sad, or unhappy for the adolescent and adult model compared to the adult-only model. Overall, the utility value of the worst health state (33333) was 0.01 points higher in the adolescent and adult model compared to the adult-only model.

The hybrid model featuring adolescents and adults was selected as the US value set (Table 4). In addition to incremental utility decrements, the value set is presented as non-incremental utility decrements, as customary, where each coefficient represents the decrement compared to no problems (level 1) and the state with no problems in any dimension (state 11111) has a utility value of 1.0 (full-health). Thus, EQ-5D-Y-3L health states utilities for a particular health state can be calculated by subtracting the relevant non-incremental decrement for each dimension from 1.0; for example, the health state utility for the state 31332 would be calculated as:

U (32332) = 1 – 0.178 - 0.028 - 0.155 - 0.288 - 0.083 = 0.268

The range of values represented by the value set compared with those for the US EQ-5D-3L (43) shows comparable results (Figure 1). The US EQ-5D-Y-3L features more positive health states, with an approximately 0.10 greater value for the 33333 state and a greater proportion of health states with values of greater than 0.5.

Discussion

This study provides a US model with comprehensive utility estimates for all 243 EQ-5D-Y-3L health states. As recommended by an international valuation protocol, DCE tasks provided information to generate latent scale values, while information cTTO tasks were used to anchor the utilities. Aligning with US stakeholder feedback, a single value set was produced representing both adolescents and adults. The model indicates that members of the US public consider having pain or discomfort as the most important dimensions of health for children and adolescents, followed closely by feeling worried, sad, or unhappy. The resulting value set aligns with guidance for calculating QALYs in cost-utility analyses by providing preference weights from a community-based, societal sample. (44)

This study integrated well-established valuation methods with progressive elements to advance the state of the science of child health valuation. Established elements included the preference elicitation methods, survey platform, data QC, and interviewer training based on protocols by the EuroQol group (1, 32, 38). The international valuation protocol is not prescriptive about modeling approaches, and EQ-5D-Y-3L value sets in other countries have primarily varied in terms of number of included health states (10 vs >10); the modeling of DCE data (conditional or mixed logit models); and the anchoring approach based on cTTO data (anchored to the 33333 health state, mapping, or a hybrid model). In the present study, a latent-class approach was used to model the DCE data (similar to Spain (7)). We leveraged a more complex study design comprising 28 instead of 10 health states in cTTO (similar to The Netherlands(9) and Brazil (11)), facilitating the use of a hybrid model (similar to China (10)). By having the same adults who completed the cTTO also complete the DCE, we could estimate a robust, population weighted, latent-class hybrid model. This model was preferred as means to weight adolescent and adult representation according to their heterogenous preferences and maximize the information gained from the DCE and cTTO tasks. This approach previously explored in the Spanish EQ-5D-Y-3L valuation study, though not selected as the preferred model due to an insufficient number of health states in cTTO. (7)

Other unique elements of this study included proactive stakeholder engagement and the integration of both adolescent and adult perspectives. This approach was implemented to maximize the applicability of the value set to the population it aims to represent and align with expectations of potential value set users. Stakeholders rejected producing multiple models representing multiple US value sets, so an approach to combine adolescent and adult preferences was preferred. (27) There was added complexity and need for innovation introduced from the inclusion of adolescents, both in terms of data collection and in selecting a modeling approach. While quota sampling was strictly enforced at the beginning of the DCE data collection, eligibility requirements were relaxed when certain subgroups, especially of adolescents, could not successfully be recruited from the survey panel. Notably, different framing perspectives were used between adolescent (self) and adult (10-year-old-child) DCE tasks, aligned with previous studies that have explored the inclusion of adolescents in valuing EQ-5D-Y-3L health states (20, 21, 45, 46). This difference in presentation of DCE tasks may have contributed to observed differences in responses between adolescents and adults.

Within the cTTO, some adult respondents found it overwhelming to consider death in relation to a 10-year-old-child. The theoretically validity of using of death as an anchoring point in cTTO is controversial (47). Particularly considering children's health states, this task presentation may not be desirable and can lead to less willingness to trade (i.e., higher cTTO values). (48) Although a thorough comparison of the US EQ-5D-3L(43) and EQ-5D-Y-3L value sets is beyond the scope of this paper, one potentially important consideration for end-users of the value sets is to account for the differences in scale when applying the value sets in longitudinal studies where children age into adulthood and switch from assessments with the EQ-5D-Y-3L to the EQ-5D-3L. While the distribution of health state values between value sets is similar overall, a reluctance to engage with the lead-time (WTD) task for severe child health states may contribute to our findings of a greater proportion of states with values >0.5. The lower bound of the range of US EQ-5D-Y-3L values is approximately 0/dead, which suitably conveys US values of avoidance of children's health states as WTD and could moderate concerns in the current US policy landscape where use of QALYs is criticized as discriminatory (26).

This study's methodological innovations offer a framework for future valuation studies, suggesting that latent class analysis can be effectively used to integrate diverse preferences into a cohesive value set. Although the integration of adolescent preferences into HRQoL valuation may be viewed as critical step towards more inclusive and accurate health assessments, these decisions ultimately rely on many normative, rather than strictly empirical, justifications. (12, 15, 22, 49) Whether – and how – future valuations studies include adolescents should consider the empirical evidence, the local policy context, and input by national stakeholders to guide normative decision making to produce a value set that is fit for purpose. As far as empirical evidence, there is a need for further research into how preference elicitation techniques or the mode of administration (e.g., interviewer assisted) can be most engaging for younger populations to optimize the reliability and validity of their values.

In conclusion, this study makes a significant contribution to the field of health economics by developing a US-specific EQ-5D-Y-3L value set that integrates adolescent and adult preferences. The methodological approach and stakeholder-informed design provide a robust framework for future valuation studies and underscore the inclusion of diverse perspectives in HRQoL assessments. This EQ-5D-Y-3L value set can play a role in measuring health outcomes for children and adolescents and informing treatment availability for pediatric diseases in the US. The value set is available for use by contacting the corresponding author or the EuroQol group.

Table 1: Description of DCE Analytic Sample

Variable		Adolescent DCE n= 714	Adult DCE n= 1669	Percentage of US Population*	Population Weights Applied	
Age Groups (years)					Male	Female
	11-14	325 (45.5%)	NA	5.1%	0.33	0.62
	15-17	389 (54.5%)	NA	3.9%	0.26	0.30
	18-34	-	300 (2.2%)	23.0%	2.42	1.85
	35-44	-	325 (19.5%)	13.2%	0.96	1.31
	45-54	-	344 (20.6%)	12.1%	1.36	0.74
	55-64	-	153 (9.2%)	12.6%	2.45	2.12
	≥ 65	-	547 (32.8%)	17.4%	0.77	0.96
Gender						
	Female	283 (39.6%)	879 (52.7%)	50.4%		
	Male	430 (60.2%)	787 (47.2%)	49.6%		
	Other	3 (0.2%)	3 (0.2%)	-		
Race						
	White	621 (87.0%)	1340 (80.3%)	60.9%		
	Black or African American	48 (6.7%)	194 (11.6%)	12.2%		
	Asian or Pacific Islander	4 (0.6%)	72 (4.3%)	6.1%		
	American Indian/Alaskan Native	21 (2.9%)	10 (0.6%)	1.0%		
	Other	4 (0.6%)	37 (2.2%)	7.3%		
	Two or more races	16 (2.2%)	16 (1.0%)	12.5%		
Hispanic Ethnicity, n(%)		76 (10.6%)	171 (10.3%)	19.1%		
Regional Location, n(%)						
	Midwest	82 (11.5%)	367 (22.0%)	20.6%		
	Northeast	166 (23.3%)	336 (20.1%)	17.1%		
	South	250 (35.0%)	630 (37.8%)	38.6%		
	West	214 (30.0-%)	335 (20.1%)	23.6%		
	Other/Not-specified	2 (0.3%)	1 (0.1%)	-		

Parent or Primary Caregiver of child(ren)		
Yes(n,%)	-	638 (38.2%)
Reported Health with EQ-5D-Y-3L		
Mobility		
No Problems	630 (88.2%)	1368 (82.0%)
Some Problems	44 (6.2%)	248 (14.9%)
A Lot of Problems	40 (5.6%)	53 (3.2%)
Looking after myself		
No Problems	637 (89.2%)	1569 (94.0%)
Some Problems	42 (5.9%)	79 (4.7%)
A Lot of Problems	35 (4.9%)	21 (1.3%)
Usual Activities		
No Problems	619 (86.7%)	1397 (83.7%)
Some Problems	54 (7.6%)	235 (14.1%)
A Lot of Problems	41 (5.7%)	37 (2.2%)
Pain or Discomfort		
No	575 (80.5%)	897 (53.7%)
Some	96 (13.5%)	686 (41.1%)
A Lot	43 (6.0%)	86 (5.2%)
Feeling Worried, Sad, or Unhappy		
Not	503 (70.5%)	1032 (61.8%)
A bit	168 (23.5%)	519 (31.1%)
Very	43 (6.0%)	118 (7.1%)
VAS (mean, SD)	88.2 (12.6)	80.2 (15.9)

**US Population data from the 2022 American Communities Survey from the US Census (33)*

Table 2: cTTO Results

Profile	N	N (population weighted)	Observed mean value (population weighted)	Std Error	Censored value (population weighted)	Std Error
31211	63	71	0.917	0.018	0.832	0.000
22312	58	70	0.844	0.020	0.779	0.000
22112	62	71	0.878	0.029	0.759	0.001
13322	56	63	0.800	0.029	0.736	0.001
31122	62	68	0.808	0.025	0.727	0.001
13222	59	70	0.802	0.030	0.724	0.001
22222	58	68	0.794	0.033	0.715	0.001
21123	54	62	0.744	0.040	0.678	0.001
23112	58	72	0.784	0.050	0.676	0.002
33321	55	65	0.699	0.035	0.639	0.001
31321	57	69	0.730	0.054	0.618	0.002
31312	57	69	0.728	0.057	0.596	0.003
22213	60	66	0.717	0.044	0.590	0.002
12323	61	72	0.638	0.054	0.575	0.002
33221	58	72	0.664	0.057	0.534	0.002
23313	59	67	0.614	0.057	0.526	0.002
21232	62	73	0.512	0.061	0.483	0.002
12132	53	66	0.538	0.073	0.454	0.004
22223	54	66	0.515	0.070	0.445	0.003
32231	60	71	0.507	0.067	0.419	0.003
21231	54	62	0.518	0.076	0.384	0.004
13332	62	71	0.351	0.080	0.278	0.004
32332	54	69	0.333	0.079	0.277	0.004
31233	50	59	0.285	0.076	0.264	0.004
23331	54	59	0.378	0.082	0.252	0.005
33133	63	73	0.237	0.072	0.206	0.003
23333	50	62	0.059	0.084	0.047	0.004
33333	190	224	0.020	0.044	-0.018	0.001

Table 3a: Hybrid Model – Adolescents and Adults (Preferred Model)

		Class 1		Class 2		Class 3		Class 4		Class 5		Class 6		
		Incremental dummies												
EQ-5D-Y-3L dimension	Response Level Transition	Coeff.	Std Error	Coeff.	Std Error	Coeff.	Std Error	Coeff.	Std Error	Coeff.	Std Error	Coeff.	Std Error	OVERALL MODEL
MOBILITY	1 to 2	0.166	0.018	0.056	0.008	0.055	0.006	0.277	0.031	0.097	0.014	0.061	0.010	0.069
	2 to 3	0.187	0.020	0.177	0.010	0.077	0.005	0.225	0.027	0.130	0.015	0.095	0.010	0.109
LOOKING AFTER MYSELF	1 to 2	0.032	0.020	0.008	0.007	0.025	0.005	0.081	0.013	0.015	0.014	0.059	0.009	0.028
	2 to 3	0.095	0.020	0.100	0.008	0.099	0.005	0.054	0.013	0.038	0.014	0.130	0.011	0.099
DOING USUAL ACTIVITIES	1 to 2	0.050	0.018	0.047	0.006	0.060	0.005	0.038	0.011	-0.013	0.013	0.108	0.009	0.060
	2 to 3	0.063	0.019	0.121	0.008	0.098	0.005	-0.014	0.014	0.026	0.013	0.101	0.009	0.095
HAVING PAIN OR DISCOMFORT	1 to 2	0.052	0.018	0.108	0.007	0.135	0.006	-0.007	0.012	0.039	0.012	0.112	0.009	0.115
	2 to 3	0.159	0.023	0.254	0.016	0.169	0.008	0.000	0.012	0.111	0.016	0.143	0.011	0.172
FEELING WORRIED, SAD OR UNHAPPY	1 to 2	-0.001	0.019	0.025	0.006	0.106	0.005	0.046	0.013	0.133	0.016	0.081	0.009	0.083
	2 to 3	0.106	0.019	0.139	0.009	0.193	0.008	0.022	0.013	0.299	0.030	0.163	0.012	0.174
U (33333)		0.090		-0.036		-0.016		0.278		0.125		-0.054		-0.004
Unadjusted Class Share		27.2%		11.9%		32.7%		4.7%		5.4%		18.1%		
Scale-adjusted Class Share		**3.6%**		**18.2%**		**57.7%**		**3.6%**		**3.9%**		**13.1%**		

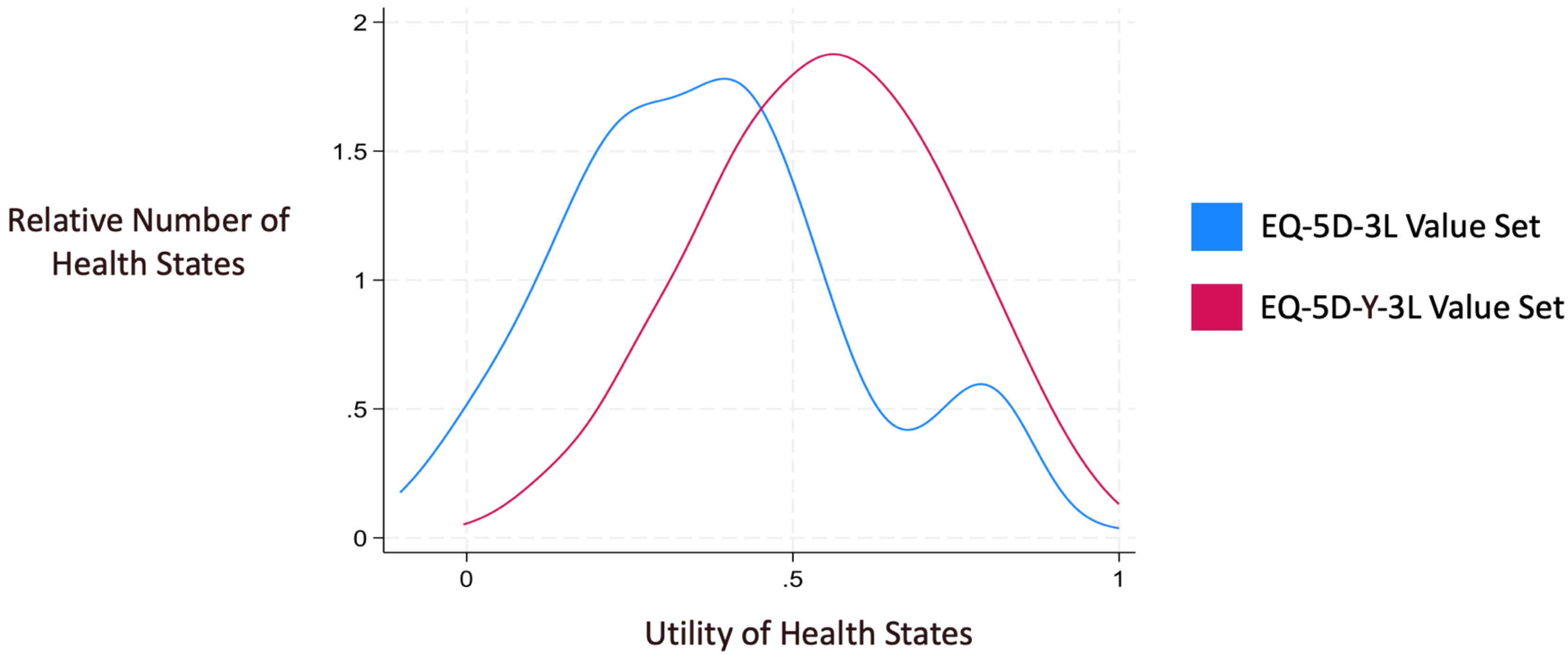
Table 3b: Hybrid Model – Adults Only

		Class 1		Class 2		Class 3		Class 4		Class 5		
		Incremental dummies										
EQ-5D-Y-3L dimension	Response Level Transition	Coeff.	Std Error	Coeff.	Std Error	Coeff.	Std Error	Coeff.	Std Error	Coeff.	Std Error	OVERALL MODEL
MOBILITY	1 to 2	0.137	0.015	0.054	0.007	0.284	0.036	0.058	0.010	0.049	0.009	0.061
	2 to 3	0.153	0.017	0.086	0.006	0.270	0.037	0.090	0.009	0.177	0.011	0.106
LOOKING AFTER MYSELF	1 to 2	0.031	0.017	0.025	0.006	0.051	0.021	0.040	0.009	0.002	0.009	0.024
	2 to 3	0.089	0.017	0.095	0.007	0.097	0.024	0.108	0.010	0.102	0.010	0.098
DOING USUAL ACTIVITIES	1 to 2	0.065	0.015	0.053	0.005	0.022	0.021	0.081	0.008	0.053	0.008	0.058
	2 to 3	0.062	0.016	0.101	0.006	-0.030	0.025	0.100	0.009	0.108	0.009	0.099
HAVING PAIN OR DISCOMFORT	1 to 2	0.091	0.015	0.134	0.007	-0.045	0.024	0.091	0.008	0.115	0.009	0.120
	2 to 3	0.140	0.019	0.178	0.010	-0.001	0.021	0.136	0.011	0.269	0.020	0.182
FEELING WORRIED, SAD OR UNHAPPY	1 to 2	0.023	0.016	0.102	0.006	0.023	0.022	0.101	0.009	0.024	0.008	0.085
	2 to 3	0.129	0.017	0.196	0.011	0.027	0.024	0.217	0.015	0.129	0.011	0.184
U (33333)		0.079		-0.026		0.302		-0.022		-0.028		-0.017
Unadjusted Class Share		23.4%		35.7%		4.2%		24.0%		12.7%		
Scale-adjusted Class Share		**5.2%**		**61.6%**		**0.9%**		**16.8%**		**15.6%**		

Table 4: US EQ-5D-Y-3L Value Set

EQ-5D-Y-3L dimension	Response Level	Utility decrements (non-incremental dummies)	Response Level Transition	Utility decrements (Incremental dummies)
MOBILITY	2	0.069	1 to 2	0.069
	3	0.178	2 to 3	0.109
LOOKING AFTER MYSELF	2	0.028	1 to 2	0.028
	3	0.128	2 to 3	0.099
DOING USUAL ACTIVITIES	2	0.060	1 to 2	0.060
	3	0.155	2 to 3	0.095
HAVING PAIN OR DISCOMFORT	2	0.115	1 to 2	0.115
	3	0.288	2 to 3	0.172
FEELING WORRIED, SAD OR UNHAPPY	2	0.083	1 to 2	0.083
	3	0.257	2 to 3	0.174

Figure 1: Comparison of the US EQ-5D-Y-3L and the Adult EQ-5D-3L* Value Sets



**EQ-5D-3L Value Set from Shaw et al. (43)*

References

1. Ramos-Goñi JM, Oppe M, Stolk E, et al. International Valuation Protocol for the EQ-5D-Y-3L. PharmacoEconomics. 2020; 38: 653-63.
2. Prevolnik Rupel V, Ogorevc M, Greiner W, et al. EQ-5D-Y Value Set for Slovenia. PharmacoEconomics. 2021; 39: 463-71.
3. Shiroiwa T, Ikeda S, Noto S, et al. Valuation Survey of EQ-5D-Y Based on the International Common Protocol: Development of a Value Set in Japan. Medical Decision Making. 2021; 41: 597-606.
4. Dewilde S, Roudijk B, Tollenaar NH, et al. An EQ-5D-Y-3L Value Set for Belgium. Pharmacoeconomics. 2022; 40: 169-80.
5. Fitriana TS, Roudijk B, Purba FD, et al. Estimating an EQ-5D-Y-3L Value Set for Indonesia by Mapping the DCE onto TTO Values. Pharmacoeconomics. 2022; 40: 157-67.
6. Kreimeier S, Mott D, Ludwig K, et al. EQ-5D-Y Value Set for Germany. PharmacoEconomics. 2022.
7. Ramos-Goñi JM, Oppe M, Estévez-Carrillo A, et al. Accounting for Unobservable Preference Heterogeneity and Evaluating Alternative Anchoring Approaches to Estimate Country-Specific EQ-5D-Y Value Sets: A Case Study Using Spanish Preference Data. Value in Health. 2022; 25: 835-43.
8. Rencz F, Ruzsa G, Bató A, et al. Value Set for the EQ-5D-Y-3L in Hungary. PharmacoEconomics. 2022.
9. Roudijk B, Sajjad A, Essers B, et al. A Value Set for the EQ-5D-Y-3L in the Netherlands. PharmacoEconomics. 2022.
10. Yang Z, Jiang J, Wang P, et al. Estimating an EQ-5D-Y-3L Value Set for China. Pharmacoeconomics. 2022; 40: 147-55.
11. Espirito Santo CM, Miyamoto GC, Santos VS, et al. Estimating an EQ-5D-Y-3L Value Set for Brazil. PharmacoEconomics. 2024.
12. Rowen D, Rivero-Arias O, Devlin N, et al. Review of Valuation Methods of Preference-Based Measures of Health for Economic Evaluation in Child and Adolescent Populations: Where are We Now and Where are We Going? Pharmacoeconomics. 2020; 38: 325-40.
13. Stevens K. Valuation of the Child Health Utility 9D Index. Pharmacoeconomics. 2012; 30: 729-47.
14. Devlin N, Pan T, Kreimeier S, et al. Valuing EQ-5D-Y: the current state of play. Health Qual Life Outcomes. 2022; 20: 105.
15. Devlin NJ. Valuing Child Health Isn't Child's Play. Value in Health. 2022.
16. Dewilde S, Janssen MF, Lloyd AJ, et al. Exploration of the Reasons Why Health State Valuation Differs for Children Compared With Adults: A Mixed Methods Approach. Value in Health. 2022.
17. Lipman S, Reckers-Droog V, Kreimeier S. Think of the Children: A Discussion of the Rationale for and Implications of the Perspective Used for EQ-5D-Y Health State Valuation. Value in Health. 2021; 24.
18. Reckers-Droog V, Karimi M, Lipman S, et al. 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.

19. Rowen D, Mukuria C, Powell PA, et al. Exploring the Issues of Valuing Child and Adolescent Health States Using a Mixed Sample of Adolescents and Adults. Pharmacoeconomics. 2022; 40: 479-88.
20. Prevolnik Rupel V, Ramos-Goñi JM, Ogorevc M, et al. Comparison of Adult and Adolescent Preferences Toward EQ-5D-Y-3L Health States. Value Health. 2021; 24: 1350-59.
21. Mott DJ, Shah KK, Ramos-Goñi JM, et al. Valuing EQ-5D-Y-3L Health States Using a Discrete Choice Experiment: Do Adult and Adolescent Preferences Differ? Med Decis Making. 2021; 41: 584-96.
22. Bailey C, Howell M, Raghunandan R, et al. Preference Elicitation Techniques Used in Valuing Children's Health-Related Quality-of-Life: A Systematic Review. Pharmacoeconomics. 2022; 40: 663-98.
23. Protecting Health Care for All Americans Act of 2023, HR 485, 118th Cong (2023). https://www.congress.gov/bill/118th-congress/house-bill/485?s=1&r=1&q=%7B% 22search%22%3A%5B%22Protecting+Health+ Care+for+All+Patients+Act%22%5D%7D. Accessed June 11, 2024. .
24. ICER. 2023 Value Assessment Framework Proposed Changes. June 5, 2023. https://icer.org/wp-content/uploads/2023/06/Proposed-VAF-Changes-For-Public-Comment_For-Publication_06052023.pdf Accessed June 11, 2024.
25. Devlin NJ, Drummond MF, Mullins CD. Quality-Adjusted Life Years, Quality-Adjusted Life-Year-Like Measures, or Neither? The Debate Continues. Value in Health. 2024; 27: 689-91.
26. Willke RJ, Pizzi LT, Rand LZ, et al. The Value of the Quality-Adjusted Life Years. Value in Health. 2024; 27: 702-05.
27. Nazari JL, Pickard AS, Gu NY. Findings from a Roundtable Discussion with US Stakeholders on Valuation of the EQ-5D-Y-3L. Pharmacoeconomics. 2022; 40: 139-46.
28. Food and Drug Administration (FDA). Pediatric Drug Development Under the Pediatric Research Equity Act and the Best Pharmaceuticals for Children Act: Scientific Considerations Guidance for Industry. 2023. https://www.fda.gov/media/168202/download. Accessed June 11, 2024. .
29. US Food & Drug Administration (FDA). New Pediatric Labeling Information Database. Available at: https://www.accessdata.fda.gov/scripts/sda/sdNavigation.cfm?sd=labelingdatabase&displayAll=true. Accessed June 11, 2024.
30. Bailey C, Howell M, Raghunandan R, et al. The RETRIEVE Checklist for Studies Reporting the Elicitation of Stated Preferences for Child Health-Related Quality of Life. PharmacoEconomics. 2024; 42: 435-46.
31. Wille N, Badia X, Bonsel G, et al. Development of the EQ-5D-Y: a child-friendly version of the EQ-5D. Qual Life Res. 2010; 19: 875-86.
32. Stolk E, Ludwig K, Rand K, et al. 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: 23-30.
33. US Census Bureau. 2022 American Community Survey 1-Year Estimates. https://www.census.gov/programs-surveys/acs/data.html. Accessed: June 9th, 2024.
34. Yang Z, Luo N, Bonsel G, et al. Selecting Health States for EQ-5D-3L Valuation Studies: Statistical Considerations Matter. Value in Health. 2018; 21: 456-61.

35. Lipman SA, Essers BAB, Finch AP, et al. In a Child's Shoes: Composite Time Trade-Off Valuations for EQ-5D-Y-3L with Different Proxy Perspectives. Pharmacoeconomics. 2022; 40: 181-92.
36. Wong ELY, Ramos-Goñi JM, Cheung AWL, et al. Assessing the Use of a Feedback Module to Model EQ-5D-5L Health States Values in Hong Kong. Patient. 2018; 11: 235-47.
37. Rowen D, Mukuria C, Bray N, et al. Assessing the comparative feasibility, acceptability and equivalence of videoconference interviews and face-to-face interviews using the time trade-off technique. Social Science & Medicine. 2022; 309: 115227.
38. Ramos-Goñi JM, Oppe M, Slaap B, et al. Quality Control Process for EQ-5D-5L Valuation Studies. Value Health. 2017; 20: 466-73.
39. Andrade LF, Ludwig K, Goni JMR, et al. A French value set for the EQ-5D-5L. Pharmacoeconomics. 2020; 38: 413-25.
40. Nazari J, Ramos-Goni JM, Gu NY, et al. PCR106 Merging Adolescent and Adult Preference Data Into a Potential Latent Scale EQ-5D-Y-3L Value Set: A Latent Class Approach to Analyze Contribution of Each Group to the Preference Weights. Value in Health. 2023; 26: S469.
41. Pacifico D, Yoo Hi. Lclogit: A Stata Command for Fitting Latent-Class Conditional Logit Models via the Expectation-Maximization Algorithm. The Stata Journal. 2013; 13: 625-39.
42. Ramos-Goñi JM, Pinto-Prades JL, Oppe M, et al. Valuation and Modeling of EQ-5D-5L Health States Using a Hybrid Approach. Medical Care. 2017; 55.
43. Shaw JW, Johnson JA, Coons SJ. US valuation of the EQ-5D health states: development and testing of the D1 valuation model. Med Care. 2005; 43: 203-20.
44. Sanders GD, Neumann PJ, Basu A, et al. Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses: Second Panel on Cost-Effectiveness in Health and Medicine. Jama. 2016; 316: 1093-103.
45. Dalziel K, Catchpool M, García-Lorenzo B, et al. Feasibility, Validity and Differences in Adolescent and Adult EQ-5D-Y Health State Valuation in Australia and Spain: An Application of Best-Worst Scaling. Pharmacoeconomics. 2020; 38: 499-513.
46. Kreimeier S, Oppe M, Ramos-Goñi JM, et al. Valuation of EuroQol Five-Dimensional Questionnaire, Youth Version (EQ-5D-Y) and EuroQol Five-Dimensional Questionnaire, Three-Level Version (EQ-5D-3L) Health States: The Impact of Wording and Perspective. Value Health. 2018; 21: 1291-98.
47. Sampson C, Parkin D, Devlin N. Is anchoring at 'dead' a theoretical requirement for health state valuation? Health Econ. 2024.
48. Lipman SA, Zhang L, Shah KK, et al. Time and lexicographic preferences in the valuation of EQ-5D-Y with time trade-off methodology. Eur J Health Econ. 2023; 24: 293-305.
49. Devlin NJ, Pan T, Sculpher M, et al. Using Age-Specific Values for Pediatric HRQoL in Cost-Effectiveness Analysis: Is There a Problem to Be Solved? If So, How? PharmacoEconomics. 2023; 41: 1165-74.