ISPOR issue panel: Developing Preference-Based Health-Related Quality-of-Life Instruments for Young Children and Infants: What's the Best Way to Proceed?

Novel Strategies for Assessing Preferences for Pediatric Health States

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Utility Measurement in Children

- Generic health-related quality of life
  - Value of preference-based measure for understanding preferences and HRQoL impacts
- Calculation of QALYs as a universal measure for cost-utility analysis
- Guidelines promote CUA for decision-making:

> "*In the reference case, the economic evaluation should be a cost-utility analysis (CUA) with outcomes expressed as quality-adjusted life-years (QALYs). Any departure from this approach should be clearly justified." (CADTH 2017)*

- Several direct choice methods and indirect instruments available to elicit utilities

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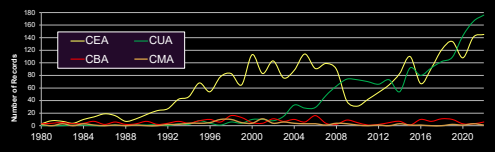
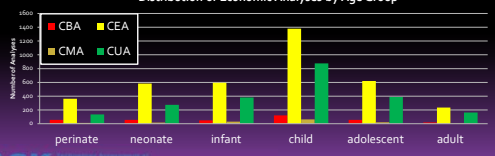
Pediatric Economic Evaluation 1980-2020 (n=4711)



Distribution of Economic Analyses by Age Group



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Scope of Pediatric Utility Estimation

- PEDE (1980-2022): 1,649 CUA papers reported 4,540 pediatric utility weights
- Kwon et al., *Qual Life Res* 2019:
  - From 1990-2017, 335 pediatric CUAs studies used 23 valuation methods and 12 respondent types
  - 34% of study samples that used indirect methods applied childhood-derived tariffs
  - Over time, significant increase in use of childhood-specific and adult-specific indirect valuation methods

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Indirect Utility Elicitation Instruments for Young Children and Toddlers

Instrument	Age group (years)	Child-specific QoL attributes?	Whose preferences used to derive underlying weights?
17D	8-11	Yes	Parents
CHU-9D	7-11	Yes	Adolescents/students; General adult population
HUI2/3	5-8	No	Parents; General adult population
EQ-5D-Y	3-7	No	General adult population
HuPS	2-5	Yes	Parents
EQ-TIPS (TANDI)	0-3	Yes	N/A
IQI	0-1	Yes	Parents; General adult population

From: Kwon et al. *PharmacoEconomics* 2022. https://doi.org/10.1007/s40273-021-01128-0

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Child-specific Instrument: CHU-9D

- Descriptive system
  - Developed in children
  - 9 dimensions: worried, sad, pain, tired, annoyed, schoolwork, sleep, daily routine, activities
- Preference weights
  - Sample of UK adult population: adult preferences using SG
  - Sample of Australian adolescent population valuing health states using BWS
- Self-completed by child
- Present state (no recall)

Stevens KJ. *Qual Health Res.* 2010

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CHU9D and HUI Health Utilities in Pediatric Crohn's Disease (CD) and Ulcerative Colitis (UC)

			CHU9D Utility (Adult Tariffs)	CHU9D Utility (Youth Tariffs)	HUI2 Utility	HUI3 Utility
CD	Males (n = 127)	Mean (SD)	0.862 (0.122)	0.773 (0.203)	0.885 (0.152)	0.821 (0.220)
		Median (IQR)	0.880 (0.148)	0.810 (0.232)	0.926 (0.136)	0.879 (0.230)
		Range (minimum to maximum)	0.380–1.000	0.052–1.000	0.174–1.000	−0.160–1.000
	Females (n = 72)	Mean (SD)	0.838 (0.112)	0.721 (0.200)	0.855 (0.155)	0.791 (0.216)
		Median (IQR)	0.866 (0.163)	0.757 (0.274)	0.907 (0.177)	0.846 (0.224)
		Range (minimum to maximum)	0.558–1.000	0.167–1.000	0.266–1.000	0.081–1.000
UC	Males (n = 35)	Mean (SD)	0.869 * (0.115)	0.778 * (0.210)	0.854 (0.200)	0.799 (0.212)
		Median (IQR)	0.885 (0.154)	0.810 (0.311)	0.937 (0.189)	0.879 (0.264)
		Range (minimum to maximum)	0.567–1.000	0.230–1.000	0.212–1.000	0.232–1.000
	Females (n = 51)	Mean (SD)	0.806 * (0.129)	0.675 * (0.216)	0.791 (0.214)	0.706 (0.251)
		Median (IQR)	0.826 (0.174)	0.686 (0.296)	0.868 (0.222)	0.748 (0.307)
		Range (minimum to maximum)	0.480–1.000	0.174–1.000	0.257–1.000	0.011–1.000

* p = 0.02 (statistically significant difference between sexes), SD = standard deviation, IQR = interquartile range.

Bashir et al., *Children* 2021. https://doi.org/10.3390/children8050343

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Health-related quality of life in neonates and infants: Theoretical construct

From: Oliveira et al. *Qual Life Res.* 2020 https://doi.org/10.1007/s11136-020-02432-6

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Which to Choose?

- Several alternative approaches
  - choice of instrument: HUI3, CHU-9D, EQ-5D-Y, others
  - choice of respondent: proxy (true) vs. adult/parent rater
- Increasing the number of options available is good for research…but raise issues of poor correlation and construct validity
- Universality of QALY outcome is eroded with multiple measures → Inconsistent funding decision-making

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Alternative: Family Perspective

- Interdependency of HRQoL within a family
- Value of reporting HRQoL effects on caregivers and other family members
- Emphasis on individual preferences for health state valuation assumes the respondent is autonomous

Adapted from Basu A & Meltzer D. *J Health Econ.* 2005; 24:751-773

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Family Perspective

Lamsal *et al.*:

- Systematic reviews of methods used in 1) pediatric and 2) maternal-perinatal CUAs to include family spillover effects

1. Pediatric (*PharmacoEconomics* 2023 doi: 10.1007/s40273-023-01331-1):
   - 29 CUAs included quality-of life spillover effects in family members
2. Maternal-perinatal (manuscript under review):
   - 45 CUAs included health outcomes of both mother and neonate

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Approaches to Integrating HRQoL of Family Members

- Child's health state utility reduced by disutility of caregiving (NICE HST8, 2018)
- Child's health state utility reduced by disutility of caregiving, with models including both child and caregiver health states (NICE, HST2 2015)
- QALYs calculated and reported separately for children and family members (Chatterton 2019)
- QALYs calculated and reported separately for children and family members and also summed (Tubeuf 2019)
- Family perspective via discrete choice experiments with attributes reflecting family effects

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Active Research in Pediatric Preference-based HRQoL

- EuroQoL EQ-5D-Y-3L, -5L
- PedsQL mapping (DeLuca, others)
- Whose values? (Xie, *Qual Life Res* 2024)
- PEDE Project

QUOKKA: paediatric multi-instrument comparison (P-MIC) study

TORCH: Tools for Outcomes Research to measure and value Child Health

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Next Steps

- Validation studies for reworded, recalibrated and new instruments
- Comparative performance research
- Additive or multiplicative models for combining family members' utilities; statistical household functions
- Discrete choice methods to derive utilities for pediatric health state incorporating attributes relevant to family
- Health economic guidelines must be updated to reflect methodologic challenges and guide alternative approaches

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