QUALITY OF LIFE OF CHILDREN AND ADOLESCENTS WITH FOOD ALLERGY: MAPPING FAQLQ-PF ONTO PAEDIATRIC-SPECIFIC HEALTH STATE UTILITY SCORES

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RATIONALE

- To date, very limited evidence is available regarding the health state utility of children/adolescents with food allergy, which is important in economic evaluations, notably cost-utility analyses (CUA)
- Preference-based health-related quality-of-life (HRQL) instruments are important tools in economic evaluation as they enable calculation of quality-adjusted life years (QALYs), which are calculated as the number of life years affected multiplied by an index of health state utility measured on a 0 (death) to 1 (full health) QALY scale[1,2]
- The food allergy–specific, non-preference–based Food Allergy Quality of Life Questionnaire (FAQLQ) is widely used and previously validated[3-5]; however, unlike generic, preference-based instruments, it cannot be used to generate health state utilities and is not suitable for CUA
- Mapping techniques can be used to create an algorithm to allow a non-preference–based instrument, like the FAQLQ, to be used in the context of CUA

OBJECTIVE

- This study aimed to investigate generic preference-based HRQL instruments in children with food allergy and to develop mapping algorithms that could be used to predict health state utilities from the disease-specific FAQLQ, thereby addressing the gap in the literature on the health state utility of children/adolescents with food allergy

METHODS

Study Design

- Parents/caregivers of children aged 1–17 years with a clinician diagnosis of IgE-mediated food allergy were recruited via the Allergy & Anaphylaxis Australia (A&AA) website from October to December 2019. Mapping algorithms were developed based on a sub-sample of those with children aged 7–17 years old
- For the survey, each participant completed the following:
  - A brief survey on their child's food allergy, including physician confirmation
  - The FAQLQ-patient proxy form (PF) to evaluate their child's HRQL **(Table 1)**
  - Generic, validated, preference-based paediatric instruments (proxy versions) scored using Australian specific tariffs: Assessment of Quality of Life-6D (AQoL-6D) and Child Health Utility 9D (CHU9D) **(Table 1)**

Table 1. HRQL Instruments

SCALE	DESCRIPTION	SCORING
FAQLQ-PF[6]	• 30 items grouped into 3 subscales	• Each item scored from 0 (not at all) to 6 (extremely) • Total mean scores (all 30 times) and mean subscale scores can be calculated
AQol -6D[7]	• 20 items grouped into 6 dimensions	• Each item has 4 to 6 response categories • Preference-based health utility score is derived
CHU9D[8]	• 9 items representing 9 domains	• Each dimension has 5 response levels from least to most severe • Preference-based health utility score is derived

Statistical Analyses

- A dataset with responses to all 3 instruments from the same individual was used to estimate mapping algorithms, which going forward can be used to map data generated from the FAQLQ to health state utilities in order to undertake health economic evaluation
- The FAQLQ-PF items were used as key predictors of a regression framework; stepwise technique was used to select statistically significant ($P<0.05$) predictors to use in estimating final mapping functions for each model
- Three main econometric techniques were considered to explore optimal mapping functions from FAQLQ-PF items onto CHU9D/AQoL-6D utilities:
  - Ordinary least squares (OLS)
  - Beta regression (BETA)
  - Generalised linear model (GLM)
- Optimal statistical analysis methods were based on a series of goodness-of-fit statistics; the 3 key goodness-of-fit indicators were:
  - Mean absolute error (MAE)
  - Concordance correlation coefficient (CCC)
  - Proportion of predicted utilities deviating from observed utilities by absolute error <0.05 ([diff]<0.05]
- Participants were randomly split into an estimation sample and a validation sample for an internal 10-fold cross-validation. Additional validation was conducted on children aged 4–6 years and on a sample of children with peanut allergy
- Statistical analyses were performed using Stata software, version 16

RESULTS

Characteristics of Children With Food Allergy

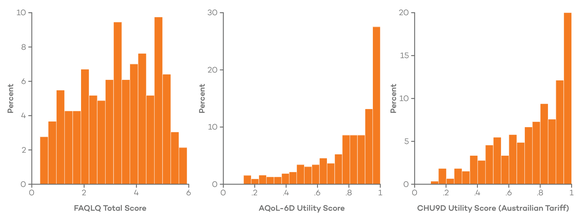
- A total of 432 respondents completed the survey, of which 96% were completed by mothers **(Table 2)**
  - The mean age of the 432 children with food allergy was 7.8 years, with 55% of children being between 7 and 17 years of age
  - Of the 432 children with food allergy, 62% were allergic to peanut, 58% to other nuts, 47% to egg, and 34% to milk/dairy
  - In the total sample, 27% experienced anaphylaxis to peanut and 25% had experienced anaphylaxis to any food in the past 12 months
- The mean total score on the FAQLQ-PF was 3.27 (standard deviation [SD] 1.4) in the whole sample; the mean utility scores on the AQoL6D and CHU9D were 0.78 (SD 0.22) and 0.74 (SD 0.22), respectively, for children aged 4 and older **(Table 2** and **Figure 1)**.

Table 2. Characteristics of Children With Food Allergy

	TOTAL SAMPLE N=432	MAPPING SAMPLE N=238	PROPORTION WITH PEANUT ALLERGY N=267
SOCIODEMOGRAPHIC CHARACTERISTICS, n (%)			
Age distribution			
1–3 years	105 (24.3)	–	61 (22.8)
4–6 years	89 (20.6)	–	52 (19.5)
7–12 years	151 (34.9)	151 (63.4)	99 (37.1)
13–17 years	87 (20.1)	87 (36.6)	55 (20.1)
Female	168 (38.9)	97 (40.8)	92 (34.5)
FOOD ALLERGY BACKGROUND, n (%)			
Physician-diagnosed/ confirmed food allergy	426 (98.6)	235 (98.7)	264 (98.9)
Adrenaline auto-injector prescribed	397 (91.9)	227 (95.4)	254 (95.1)
Anaphylaxis to peanut	117 (27.1)	81 (34.0)	112 (41.9)
Anaphylaxis to any other food	233 (53.9)	143 (60.1)	127 (47.6)
Anaphylaxis to any other food in past 12 months	108 (25.0)	50 (21.0)	70 (26.2)
Number of foods currently avoiding due to allergy	137 (31.7)	76 (31.9)	70 (26.2)
0–2	169 (39.1)	94 (39.5)	113 (42.3)
3–6	46 (10.6)	27 (11.3)	30 (11.2)
7–10	80 (18.5)	41 (17.2)	54 (20.2)
10+	–	–	–
HRQL, MEAN (SD)			
FAQLQ-PF, total score	3.27 (1.43)	3.46 (1.41)	3.20 (1.41)
AQoL-6D utility	0.78 (0.22)	0.78 (0.22)	0.80 (0.21)
CHU9D utility	0.74 (0.22)	0.74 (0.23)	0.76 (0.22)

All quality-of-life measures were proxy assessed; AQoL-6D and CHU9D were proxy reported from year 4 and onwards.

Figure 1. Score Distributions Across the 3 HRQL Instruments in the Total Sample (% of Patients)



Relationship Between FAQLQ and AQoL/CHU9D

- The strength of Spearman's correlation coefficients was consistently stronger between FAQLQ-PF (total score) and AQoL-6D than between FAQLQ-PF and CHU9D utility scores **(Table 3)**
- For the mapping sample (ages 7–17 years), the Spearman correlation between the FAQLQ-PF Total Score and the AQoL-6D was -0.565 compared with -0.453 for the CHU9D

Table 3. Spearman's Correlations Between FAQLQ-PF Scales and AQoL-6D/CHU9D by Age Groups

	AGE: 4–6 YEARS (n=89)		AGE: 7–12 YEARS (n=151)		AGE: 13–17 YEARS (n=87)		AGE: 7–17 YEARS (n=238)	
	AQOL-6D	CHU9D	AQOL-6D	CHU9D	AQOL-6D	CHU9D	AQOL-6D	CHU9D
FAQLQ-PF SCALE								
Total score	-0.444	-0.392	-0.551	-0.451	-0.588	-0.433	-0.565	-0.453
General impact	-0.487	-0.437	-0.588	-0.481	-0.648	-0.493	-0.607	-0.489
Food-related anxiety	-0.346	-0.329	-0.478	-0.414	-0.469	-0.341	-0.479	-0.398
Social & dietary limitations	-0.421	-0.344	-0.464	-0.369	-0.518	-0.367	-0.483	-0.372

Development of Mapping Algorithms Based on the Full Mapping Sample

- Mapping FAQLQ-PF onto AQoL-6D had better performance than mapping onto CHU9D utility scores based on key goodness-of-fit statistics **(Table 4)**
  - Goodness-of-fit statistics of mapping onto the AQoL-6D utility score in the full mapping sample (N=238) demonstrated that OLS and GLM had the best performance
  - For the CHU9D, the beta regression and Tobit regression performed the best of the 5 candidate methods

Table 4. Goodness-of-Fit Statistics—Full Mapping Sample (N=238)

MAPPING ONTO AQoL-6D							
MODEL	**MEAN**	**MIN**	**MAX**	**CORRELATION**	**CCC**	**MAE**	**[DIFF] < 0.05 (%)**
Observed	0.782	0.136	1	–	–	–	–
OLS	0.782	0.485	0.986	0.658	0.587	0.126	31.090
BETA	0.775	0.465	0.920	0.660	0.551	0.131	20.170
GLM-1	0.782	0.401	0.928	0.640	0.582	0.127	24.370
GLM-2	0.782	0.369	0.923	0.640	0.584	0.127	23.110
MAPPING ONTO CHU9D							
MODEL	**MEAN**	**MIN**	**MAX**	**CORRELATION**	**CCC**	**MAE**	**[DIFF] < 0.05 (%)**
Observed	0.739	0.105	1	–	–	–	–
OLS	0.739	0.480	0.911	0.532	0.432	0.156	13.450
BETA	0.764	0.393	0.978	0.543	0.482	0.154	20.590
GLM-1	0.739	0.533	0.941	0.534	0.430	0.156	16.390
GLM-2	0.739	0.508	0.927	0.534	0.434	0.155	16.390
Tobit	0.755	0.463	0.953	0.532	0.460	0.153	19.330

For GLM-1 and GLM-2, family and link were specified (for corresponding family and link functions please see **Table 5** and **Table 6**). The best 2 results for each are in **bold blue type**.

Validation of Mapping Algorithms (data not shown)

- Internal (10-fold) validation results supported the GLM and OLS, in that order, as performing the best for mapping onto the AQoL-6D. When mapping onto CHU9D, although the best method was still beta regression, the second-best method became GLM
- Validation results based on a sample of younger children aged 4–6 years (n=89) demonstrated similar goodness-of-fit statistics when applied to the AQoL-6D and better statistics when applied to the CHU9D, except for the CCC
- In children aged 4–17 years with only peanut allergy (n=206), performance for the AQoL-6D and the CHU9D mapping algorithms was better than the full mapping sample statistics

Optimal Mapping Algorithms

- Estimated regression coefficients for mapping onto AQoL-6D and CHU9D utility scores were calculated **(Table 5** and **Table 6)**; neither age nor gender contributed significantly and were not in included in final mapping algorithms
- The R^2 statistic was substantially larger in the AQoL-6D equation (R^2=0.414) than in the CHU9D equation (R^2=0.276)
- Four items from the FAQLQ-PF were selected in the final mapping functions onto the AQoL-6D: B25 ("because of food allergy, my child is not as confident as other children of his/her age in social situations"); A6 ("because of food allergy, my child experiences physical distress"); B23 ("because of food allergy, my child is more anxious in general than other children of his/her age"); and A7 ("because of food allergy, my child experiences emotional distress")[9]
  - The final mapping algorithm based on OLS was considered the most optimal mapping algorithm, followed by GLM **(Table 5)**

Table 5. Mapping Functions From FAQLQ-PF Onto AQoL-6D

FAQLQ ITEM #	(1) OLS	(2) BETA	(3) GLM-1	(4) GLM-2
B25	-0.030900 (0.008)***	-0.183453 (0.037)***	-0.248144 (0.095)***	-0.217251 (0.082)***
A6	-0.033400 (0.008)***	-0.118127 (0.050)**	-0.244617 (0.110)**	-0.203907 (0.092)**
B23	-0.019246 (0.009)**	–	–	–
A7	–	-0.128434 (0.050)***	–	–
Constant	0.986084 (0.021)***	2.439297 (0.134)***	2.555477 (0.339)***	2.529292 (0.306)***
Scale	–	1.512661 (0.092)***	–	–
Observations	238	238	238	238
R-squared	0.415	–	–	–

Standard errors in parentheses.
***P<0.01, **P<0.05
For GLM-1, family(binomial) and link(logit) were specified; for GLM-2, family(binomial) and link(loglog) were specified.

- For the final mapping function onto the CHU9D, 3 FAQLQ-PF items were selected with the exception of the beta regression estimate: B25; A6; and C29 ("because of food allergy, my child feels concerned by poor labelling on food products")[9]
  - The goodness-of-fit statistics indicated that the mapping algorithm based on beta regression was the optimal mapping algorithm **(Table 6)**

Table 6. Mapping Functions From FAQLQ Onto CHU9D

FAQLQ ITEM #	(1) OLS	(2) BETA	(3) GLM-1	(4) GLMA-2	(5) TOBIT
B25	-0.029486 (0.007)***	-0.288222 (0.044)***	0.054754 (0.015)***	-0.040323 (0.011)***	-0.035296 (0.008)***
C30	–	-0.121722 (0.055)**	–	–	–
A5	–	0.137657 (0.049)***	–	–	–
A13	–	0.132531 (0.052)**	–	–	–
B20	–	-0.194762 (0.064)***	–	–	–
A11	–	-0.310039 (0.073)***	–	–	–
A10	–	0.132178 (0.055)**	–	–	–
A14	–	0.130133 (0.062)**	–	–	–
A1	–	0.176720 (0.074)**	–	–	–
A7	–	-0.139372 (0.065)**	–	–	–
A6	-0.029172 (0.009)***	–	0.055994 (0.019)***	-0.041157 (0.013)***	-0.029927 (0.010)***
C29	-0.013280 (0.007)*	–	0.025142 (0.011)**	-0.018705 (0.009)**	-0.016383 (0.008)**
Constant	0.911375 (0.026)***	2.235939 (0.206)***	1.062207 (0.034)***	-0.075495 (0.029)***	0.953130 (0.028)***
Scale	–	0.965971 (0.094)***	–	–	–
Observations	238	238	238	238	238
R-squared	0.276	–	–	–	–

Standard errors in parentheses.
***P<0.01, **P<0.05, *P<0.1
For GLM-1, family(gaussian) and link(power -1) were specified; for GLM-2, family(gaussian) and link(log) were specified.

CONCLUSIONS

- Eliciting health state utility scores from children and adolescents with food allergy is essential for health economic evaluation
- This study represents the first mapping study to predict paediatric health utility scores from a food allergy HRQL instrument internationally
- Based on our results, mapping FAQLQ-PF onto AQoL-6D would be preferred to mapping onto CHU9D utility scores
- We have successfully generated mapping algorithms, which will facilitate the use of FAQLQ-PF for cost-utility analyses, with a performance comparable to other disease-specific mapping algorithms

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