EVALUATION OF PSYCHOMETRIC PARAMETERS OF FOOD ALLERGY QUALITY-OF-LIFE QUESTIONNAIRES WITH ITEM RESPONSE THEORY FOR THE ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE DURING FOOD ALLERGY TREATMENTS

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RATIONALE

- Peanut allergy (PA) is associated with reduced health-related quality of life (HRQL),[1,2] typically measured in food allergy research with the Food Allergy Quality of Life Questionnaire (FAQLQ)[3]
- Measurement properties of a scale can affect the interpretation of clinical trials because change scores are used to evaluate efficacy of interventions
- It is important to understand the measurement properties of a scale as precisely as possible to assess HRQL longitudinally and identify between-group differences
- Datasets from 2 clinical trials were used to retrospectively evaluate psychometric properties of the FAQLQ:
  - The Peanut EPIT™ Efficacy and Safety study (PEPITES) was a global phase 3, pivotal, double-blind, placebo-controlled trial evaluating the safety and efficacy of epicutaneous immunotherapy (EPIT) for peanut allergy (Viaskin Peanut 250 µg [VP250]) in children aged 4–11 years[4]
  - The Open-Label Follow-Up Study-Viaskin Peanut's Efficacy and Safety (OLFUS-VIPES) trial of up to 24 months on EPIT (VP250) was an extension of the VIPES phase 2b, randomized, controlled trial assessing the optimal dose, safety, and efficacy of 12 months of daily peanut EPIT in peanut-allergic subjects aged 6–55 years[5]

OBJECTIVE

- To assess the difficulty, information value, and discriminative ability of each item of the FAQLQ-child form (CF) and parent proxy form (PF) using item response theory (IRT) and FAQLQ assessments from the EPIT clinical trials to improve future assessment of HRQL during food allergy treatment

METHODS

HRQL Assessment

- HRQL was assessed at baseline and Month 12 (endpoint) in PEPITES in all enrolled children aged 4–12 years and at baseline, Month 12, and Month 24 (endpoint) in OLFUS-VIPES in participants of all ages using the age-appropriate FAQLQ
  - FAQLQ-CF assessed 24 items across 4 factors (Dietary Restriction, Allergen Avoidance, Risk of Accidental Exposure, Emotional Impact) and was completed by children aged ≥8 years
  - The FAQLQ-PF assessed 30 items across 3 factors (Food-related Anxiety, Social and Dietary Limitations, Emotional Impact) and was completed by caregivers of all participants
  - Additionally, the FAQLQ-Teenager Form (TF) was completed by participants aged 13–17 years and the FAQLQ-Adult Form (AF) was completed by those aged ≥18 years *(data not shown)*

Statistical Analyses

- Observed variables included each item of the FAQLQ questionnaires, and HRQL represented the construct under study
- FAQLQ items were analyzed using IRT via 3 interconnected steps to determine the best items for predicting HRQL:
  1. The **Discrimination** parameter (a) is an index of how well an item in the FAQLQ can differentiate between participants with varying levels of HRQL. The higher the value, the higher the discrimination differentiating ability
     - Discrimination classification levels were: very high (>1.70), high (1.35–1.69), moderate (0.65–1.34), low (0.35–0.64), very low (0.01–0.34), and no discrimination (0)
  2. The **Difficulty Threshold** (b) is the value that is associated with a 50% probability of scoring 1 (rather than 0) on an individual item
     - Items with means between −1.5 and 1.5 across b1-b6 were considered as neither too easy nor too difficult
  3. **Item/Test Information Curves** evaluate how much information an item shares with the total information of the measure. Items with a higher curve are more informative, indicating higher measurement precision, less measurement error, and higher reliability of the scale
     - Curves were assessed visually, with bell-shaped curves indicating higher information spread across different levels of HRQL
- All data were analyzed using R software to evaluate the psychometric properties of discrimination, difficulty thresholds, and information curves for both the individual items and factors, using the multidimensional item response theory (MIRT) package

RESULTS

Participants

Table 1. Number of Participants Completing the FAQLQ-CF or -PF at Baseline and Study Endpoint

STUDY	BASELINE, n	ENDPOINT, n
PEPITES		
Children	165	152
Parents	324	307
OLFUS-VIPES		
Children	82	48
Parents	84	50

FAQLQ-CF: Discrimination and Difficulty

- In PEPITES, discriminative ability was consistent between baseline and endpoint for 11 items (**Table 2**)
  - The greatest discrimination was demonstrated with items 19 and 20 (Emotional Impact Factor), and reflected fear of an allergic reaction and fear of eating the wrong food by accident
  - All items had an acceptable level of difficulty
- Results for OLFUS-VIPES were consistent with those of the PEPITES study (**Table 3**)
  - Emotional Impact (items 19 and 20) had the greatest discriminative ability

Table 2. PEPITES: Item Parameters of the FAQLQ-CF (Baseline and Endpoint)

ITEM	DISCRIMINATION LEVELS (a)		DIFFICULTY (MEAN BETWEEN b1-b6)	
	BASELINE	ENDPOINT	BASELINE	ENDPOINT
Dietary Restriction				
01	1.836	1.6	-0.4	-0.23
02	1.869	2.213	-0.03	0.12
03	1.649	2.012	0.11	0.37
05	1.814	2.298	-0.31	-0.09
12	1.663	1.852	-0.29	-0.15
18	1.248	1.399	0.05	0.12
Allergen Avoidance				
04	1.73	1.843	0.04	-0.02
06	0.761	1.487	0.5	0.66
07	1.629	1.721	-0.05	0.1
08	3.282	2.778	-0.02	0.03
09	2.755	2.673	-0.02	0.11
10	1.443	3.055	-0.72	-0.23
15	1.534	2.047	-0.07	-0.01
Risk of Accidental Exposure				
11	1.223	1.634	-0.15	0.21
13	1.564	2.015	-0.31	-0.13
14	2.161	1.831	-0.47	-0.27
16	1.275	1.926	-0.3	-0.11
17	2.633	2.4	-0.28	-0.05
Emotional Impact				
19	2.723	2.819	-0.87	-0.61
20	2.504	3.899	-0.88	-0.58
21	1.705	2.059	-0.4	-0.03
22	2.082	1.823	-0.27	-0.19
23	1.234	1.742	-1	-0.66
24	1.55	1.779	-0.55	-0.12

Very high discrimination=green, high discrimination=orange, moderate discrimination=yellow, low discrimination=gray. Difficulty (mean between b1-b6), acceptable levels of difficulty in green.

Table 3. OLFUS-VIPES: Item Parameters of the FAQLQ-CF (Baseline and Endpoint)

ITEM	DISCRIMINATION LEVELS (a)		DIFFICULTY (MEAN BETWEEN b1-b6)	
	BASELINE	ENDPOINT	BASELINE	ENDPOINT
Dietary Restriction				
01	2.130	1.862	-0.02	0.22
02	1.416	2.845	0.19	0.3
03	1.342	2.324	0.31	0.77
05	2.036	2.203	0.01	0.29
12	1.010	1.467	-0.35	0.55
18	2.094	1.067	0.11	0.61
Allergen Avoidance				
04	2.093	1.203	0.23	0.48
06	1.360	2.73	0.66	0.92
07	1.337	1.629	0.50	0.75
08	2.429	2.332	0.32	0.45
09	2.678	2.164	0.35	0.47
10	1.758	2.165	-0.18	-0.11
15	1.696	1.644	0.06	0.54
Risk of Accidental Exposure				
11	2.076	0.611	0.26	1.21
13	1.363	1.046	-0.03	0.63
14	2.132	0.924	-0.10	0.61
16	1.506	3.777	-0.08	0.37
17	2.149	2.193	-0.29	0.42
Emotional Impact				
19	3.890	4.024	-0.61	-0.09
20	4.479	8.074	-0.72	-0.08
21	2.362	2.404	-0.11	0.01
22	1.462	1.215	-0.25	0.29
23	1.568	1.24	-0.56	0.03
24	1.743	1.183	-0.45	0.23

Very high discrimination=green, high discrimination=orange, moderate discrimination=yellow, low discrimination=gray. Difficulty (mean between b1-b6), acceptable levels of difficulty in green.

FAQLQ-PF: Discrimination and Difficulty

- In PEPITES, the greatest levels of discrimination were shown by Food-related Anxiety factor items 17, 20, and 21 ("concerned about being always cautious around food," "concerned about accidentally eating an ingredient to which they are allergic," and "worried about eating with unfamiliar adults/children," respectively) (**Table 4**)
- Results of OLFUS-VIPES were similar to those of the PEPITES trial with items 17, 20, and 21 performing consistently from baseline to endpoint (**Table 5**)

Table 4. PEPITES: Item Parameters of the FAQLQ-PF (Baseline and Endpoint)

ITEM	DISCRIMINATION LEVELS (a)		DIFFICULTY (MEAN BETWEEN b1-b6)	
	BASELINE	ENDPOINT	BASELINE	ENDPOINT
Food-related Anxiety				
01	2.595	2.387	0	0.14
04	2.212	2.198	-0.24	-0.12
05	1.891	1.96	0.16	0.39
16	3.4	3.16	0.57	0.68
17	3.017	3.058	-0.22	-0.15
20	3.663	3.727	-0.15	-0.04
21	3.269	3.489	0.16	0.15
29	1.396	1.599	0.81	0.68
Social and Dietary Limitations				
03	1.945	1.989	0.08	0.07
08	1.202	1.117	0.89	1.06
12	2.59	2.191	-0.48	-0.43
13	1.938	2.164	-0.17	-0.1
14	2.296	2.108	-0.25	-0.07
15	2.305	2.257	-0.21	-0.24
18	3.415	3.18	-0.12	-0.1
22	2.768	3.382	0.25	0.23
Emotional Impact				
02	2.023	1.834	0.13	0.25
06	1.892	1.934	1.31	1.45
07	2.848	2.905	0.51	0.55
09	2.2	1.909	0.79	0.93
10	2.194	2.101	0.66	0.71
11	2.331	2.156	0.08	0.22
19	2.154	2.241	0.42	0.46
23	2.251	2.687	0.54	0.61
24	1.595	1.661	-0.22	-0.09
25	2.008	2.171	1.04	1.12
26	1.415	1.326	-1.48	-1.69
27	1.896	2.316	1.32	1.27
28	2.148	1.772	0.18	0.26
30	2.489	2.35	0.29	0.38

Very high discrimination=green, high discrimination=orange, moderate discrimination=yellow, low discrimination=gray. Difficulty (mean between b1-b6), acceptable levels of difficulty in green.

Table 5. OLFUS-VIPES: Item Parameters of the FAQLQ-PF (Baseline and Endpoint)

ITEM	DISCRIMINATION LEVELS (a)		DIFFICULTY (MEAN BETWEEN b1-b6)	
	BASELINE	ENDPOINT	BASELINE	ENDPOINT
Food-related Anxiety				
01	2.145	2.733	-0.31	-0.3
04	2.72	2.129	-0.84	-0.58
05	1.859	2.39	0.2	-0.03
16	2.653	3.718	0.5	0.22
17	2.912	3.142	-0.39	-0.44
20	2.517	3.04	-0.39	-0.37
21	3.002	3.604	-0.14	-0.26
29	1.092	1.315	0.78	0.45
Social and Dietary Limitations				
03	1.547	2.459	-0.06	0.01
08	0.997	0.887	0.8	0.68
12	2.076	1.903	-0.15	-0.14
13	1.486	1.843	0.1	0.22
14	2.777	1.566	0.09	-0.17
15	2.49	1.778	-0.1	0
18	3.69	2.95	-0.08	-0.2
22	3.077	5.608	0.25	0.24
Emotional Impact				
02	1.69	1.779	0.22	0.11
06	1.405	1.542	1.42	0.84
07	2.206	1.933	0.38	0.5
09	2.352	0.758	0.93	1.43
10	2.351	1.225	0.73	0.5
11	2.096	1.302	0.23	0.02
19	2.159	3.314	0.48	0.27
23	2.088	2.244	0.55	0.26
24	1.143	1.895	-0.73	-0.46
25	1.592	3.426	0.9	0.58
26	0.81	1.907	-3.44	-1.45
27	1.979	3.144	1.39	0.81
28	1.534	2.747	0.14	-0.15
30	2.488	3.416	0.45	0.31

Very high discrimination=green, high discrimination=orange, moderate discrimination=yellow, low discrimination=gray. Difficulty (mean between b1-b6), acceptable levels of difficulty in green.

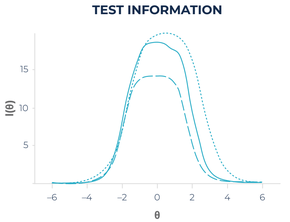
FAQLQ-CF and FAQLQ-PF Item Information Curves

- In PEPITES, the results of the FAQLQ-CF suggest a reasonable spread of discrimination across their respective factors (**Figure 1**)
  - Allergen Avoidance and Emotional Impact were the most informative factors at baseline and endpoint
  - On the FAQLQ-PF, Emotional Impact and Food-related Anxiety were the most informative factors (**Figure 2**)
- In OLFUS-VIPES, results on the FAQLQ-CF were similar to those of the PEPITES trial – Allergen Avoidance and Emotional Impact were the most informative factors (**Figure 3**)
  - On the FAQLQ-PF, Emotional Impact and Food-related Anxiety were again the most informative factors (**Figure 4**)

Figure 1. PEPITES: FAQLQ-CF Test Information Curves – Total Information of Each Factor at Endpoint

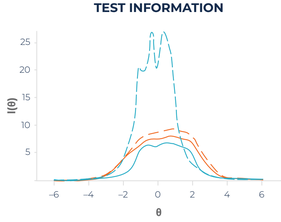
Lines: orange=Dietary Restriction; orange dashed=Allergen Avoidance; blue=Risk of Accidental Exposure; blue dashed=Emotional Impact.

Figure 2. PEPITES: FAQLQ-PF Test Information Curves – Total Information of Each Factor at Endpoint



Lines: complete=Food-related Anxiety; dashed=Social and Dietary Limitations; dotted=Emotional Impact.

Figure 3. OLFUS-VIPES: FAQLQ-CF Test Information Curves – Total Information of Each Factor at Endpoint



Lines: orange=Dietary Restriction; orange dashed=Allergen Avoidance; blue=Risk of Accidental Exposure; blue dashed=Emotional Impact.

Figure 4. OLFUS-VIPES: FAQLQ-PF Test Information Curves – Total Information of Each Factor at Endpoint

Lines: complete=Food-related Anxiety; dashed=Social and Dietary Limitations; dotted=Emotional Impact.

CONCLUSIONS

- IRT identified the key FAQLQ items that provide valuable information on their factors and on HRQL, the construct under investigation
- At the factor level, Emotional Impact and Allergen Avoidance on the FAQLQ-CF presented the highest information level on the HRQL construct. On the FAQLQ-PF, Emotional Impact and Food-related Anxiety provided the most information
- Results from PEPITES dataset were replicated in the OLFUS-VIPES dataset, providing confirmatory evidence of findings
- Together, these findings provide a basis from which to select the most sensitive items to streamline the food allergy quality-of-life assessment process and to create a more sensitive assessment for a peanut allergy population in food immunotherapy clinical trials

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