FOOD ALLERGY QUALITY OF LIFE QUESTIONNAIRES FOR ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE IN CLINICAL FOOD ALLERGY TREATMENT STUDIES: USE OF ITEM RESPONSE THEORY

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RATIONALE

- Peanut allergy (PA) is a common and potentially life-threatening food allergy[1]; the number of children affected by PA has increased significantly over recent decades[2]

- PA is associated with reduced health-related quality of life (HRQL) as a result of high levels of anxiety in social settings, impaired self-management, and stress related to constant vigilance surrounding peanut avoidance[3,4]

- Food allergy quality of life questionnaires (FAQLQ) are the most common instruments used in food allergy research to assess HRQL, including those investigating epicutaneous immunotherapy (EPIT) for PA

- With the increase in trials for potential food allergy treatments, it is important to determine which items within the FAQLQ are most and least useful in this context

- 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 Viaskin Peanut 250 μg (VP250). A statistically significant difference in the 12-month rate of response (percentage of participants meeting a defined eliciting dose to peanut challenge) was observed for participants randomized to VP250 (35.3%) versus placebo (13.6%) (P=.00001); the prespecified criterion (≥15% lower bound of the confidence interval) was not met; tolerability was favorable[5]

OBJECTIVE

- To retrospectively assess which items of the FAQLQ-Child Form (FAQLQ-CF) were most discriminative using item response theory (IRT), which examines the relationships between a response to a questionnaire item and the underlying latent construct (ie, HRQL)

METHODS

Study Design

- A retrospective analysis was conducted to evaluate food allergy HRQL using data from the PEPITES study
  ○ Children with PA (aged 4–11 years) were randomized (2:1) to receive VP250 or placebo patch daily for 12 months
  ○ Participants had peanut-specific IgE level (ImmunoCAP system) >0.7 kU/L, positive peanut skin prick test (SPT), and positive double-blind placebo-controlled food challenge at ≤300 mg peanut protein

- HRQL was assessed at baseline and Month 12 in children ≥8 years of age using the FAQLQ-CF, a multidimensional self-report measure
  ○ FAQLQ-CF consists of 24 items corresponding to 4 factors: Dietary Restriction, Allergen Avoidance, Risk of Accidental Exposure, and Emotional Impact
  ○ Data were collected from all subjects irrespective of treatment received (VP250 or placebo) or treatment outcome

Statistical Analysis

- The observed variables comprised each item of the FAQLQ-CF questionnaire, with food allergy HRQL representing the construct under study

- FAQLQ-CF items were analyzed using IRT via 3 interconnected steps to determine the best items for predicting HRQL: Discrimination, Difficulty, and Item/Test Information Curves

- The discrimination parameter (a) is an index of how well an item in the FAQLQ can differentiate between participants of varying levels of HRQL, with more discriminating items better able to differentiate
  ○ Discrimination classification levels were very high (>1.70), high (1.35–1.69), moderate (.65–1.34), low (.35–.64), very low (.01–.34), and no discrimination (0)

- The difficulty threshold (b) is the value that is associated with a 50% probability of scoring 1 (rather than zero) on an individual item
  ○ Items considered as neither too easy nor too difficult had means across b1–b6 that were between -1.5 and 1.5

- 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 visually assessed, with bell-shaped curves indicating higher information spread across different levels of the latent trait (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

- A total of 165 children completed the FAQLQ-CF at baseline; mean age (SD) was 9.33 (1.1) years and 61.2% of participants were male; 152 children completed the FAQLQ-CF at both baseline and the Month 12 endpoint

Baseline FAQLQ-CF Data

- Baseline FAQLQ-CF discrimination levels were very high (a > 1.7) for 12 items, high (1.35 < a < 1.69) for 7 items, and moderate (0.65 < a < 1.34) for 5 items (Table 1)
  ○ The most discriminative items were Items 19 and 20 from the Emotional Impact factor, which begins with "How frightened are you because of your food allergy"
    ▪ The corresponding question for Item 19 is "...of an allergic reaction?"
    ▪ The corresponding question for Item 20 is "...of eating the wrong food by accident?"
  ○ The items with lowest discrimination were Item 06 (Allergen Avoidance: "...can less easily stay for a meal with someone?"), Item 11 (Risk of Accidental Exposure: "...must watch out when touching certain foods?"), and Item 23 (Emotional Impact: "How disappointed are you when people don't take your food allergy into account?")

- All the items had an acceptable level of difficulty (means across b1–b6= -1.5 to 1.5) (Table 1)

Table 1. FAQLQ-CF Item Parameters (Baseline)

ITEM	DISCRIMINATION LEVELS a	DIFFICULTY MEAN BETWEEN b1–b6
Dietary Restriction		
01	1.836	-.4
02	1.869	-.03
03	1.649	.11
05	1.814	-.31
12	1.663	-.29
18	1.248	.05
Allergen Avoidance		
04	1.73	.04
06	.761	.5
07	1.629	-.05
08	3.087	-.02
09	2.755	-.02
10	1.443	-.72
15	1.534	-.07
Risk of Accidental Exposure		
11	1.223	-.15
13	1.564	-.31
14	2.161	-.47
16	1.275	-.3
17	2.633	-.28
Emotional Impact		
19	2.723	-.87
20	2.504	-.88
21	1.705	-.4
22	2.082	-.27
23	1.234	-1
24	1.55	-.55

Very high discrimination=green, high discrimination=orange, moderate discrimination=yellow; Difficulty b1–b4=threshold, acceptable levels of difficulty in green.

- Item Information Curves showed that all items shared reasonable information with their factors; the total information of each factor suggests a reasonable spread of discrimination across their respective factors (Figure 1)
  ○ Allergen Avoidance was the most informative factor, followed by Emotional Impact

Figure 1. Baseline FAQLQ-CF Test Information Curve

TEST INFORMATION

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

Endpoint (Month 12) FAQLQ-CF Data

- Month 12 FAQLQ-CF discrimination levels were very high (a > 1.7) for 20 items and high (1.35 < a < 1.69) for 4 items (Table 2)
  ○ Similar to baseline, the most discriminative items were Items 19 and 20 from the Emotional Impact factor; Item 10 from the Allergen Avoidance Factor was also highly discriminative ("...hesitate eating certain foods when you don't know if it is safe?")
  ○ Items 1 and 18 (Dietary Restrictions: "...must always watch what you eat?" and "...that you don't know how things taste which you can't eat?"), and Item 6 (Allergen Avoidance: "...can less easily stay for a meal with someone?") were the least discriminative

- All the items presented an acceptable level of difficulty (means across b1–b6= -1.5 to 1.5)

Table 2. Item Parameters of the FAQLQ-CF (Month 12)

ITEM	DISCRIMINATION LEVELS a	DIFFICULTY MEAN BETWEEN b1–b6
Dietary Restriction		
01	1.6	-.23
02	2.213	.12
03	2.012	.37
05	2.298	-.09
12		-.15
18	1.399	.12
Allergen Avoidance		
04	1.843	-.02
06	1.487	.66
07	1.721	.1
08	2.778	.03
09	2.673	.11
10	3.055	-.23
15	2.047	-.01
Risk of Accidental Exposure		
11	1.634	.21
13	2.015	-.13
14	1.831	-.27
16	1.926	-.11
17	2.4	-.05
Emotional Impact		
19	2.819	-.61
20	3.899	-.58
21	2.059	-.03
22	1.823	-.19
23	1.742	-.66
24	1.779	-.12

Very high discrimination=green, high discrimination=orange, moderate discrimination=yellow; Difficulty b1–b4=threshold, acceptable levels of difficulty in green.

- Item Information Curves showed that all items shared reasonable information with their factors; the total information of each of the factors implies that the spread of discrimination was reasonable across their factors (Figure 2)
  ○ Similar to baseline, Allergen Avoidance and Emotional Impact were the most informative factors at endpoint

Figure 2. Month 12 FAQLQ-CF Test Information Curve

TEST INFORMATION

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

FAQLQ-CF Data: Baseline Versus Month 12

- Between baseline and Month 12, 11 items (Items 2, 4, 5, 8, 9, 14, 17, 19, 20, 21, 22) had consistent discrimination levels, with Items 19, 20, 21, and 22 very highly discriminative in both stages; Items 19 and 20 also shared high information with their factors

- All items with moderate discrimination at baseline (Items 6, 11, 16, 18, 23) had an increase in discrimination level at Month 12

- All items had an acceptable level of difficulty at baseline and Month 12

- Item Information Curves showed that all factors presented reasonable information levels across baseline and Month 12 stages; Emotional Impact and Allergen Avoidance were the most informative factors

CONCLUSIONS

- IRT identified the key FAQLQ-CF items that provide valuable information on their factors and food allergy quality of life, the construct under investigation

- At the factor level, Emotional Impact and Allergen Avoidance presented the highest information level on the food allergy quality of life construct

- These findings may 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 PA population in food immunotherapy clinical trials

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