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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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All items of the food allergy quality of life questionnaires are relevant for peanut-allergic patients

To the Editor,

Peanut allergy and the management of peanut allergy may have a considerable impact on health-related quality of life (HRQL). HRQL can be measured by the Food Allergy Quality of Life Questionnaire-Adult Form, Food Allergy Quality of Life Questionnaire-Teenager Form and Food Allergy Quality of Life Questionnaire-Child Form (FAQLQ-AF, FAQLQ-TF and FAQLQ-CF).¹⁻³ The FAQLQs were developed to measure the impact of food allergy on HRQL irrespective of the causative food allergen.¹⁻⁶ The FAQLQs were shown to be valid and responsive instruments.¹⁻⁶ At present, it is unknown whether all items contained in these instruments are relevant for peanut-allergic patients and whether intervention studies on peanut allergy would be better served by the existing FAQLQs in their entirety or by a peanut-specific selection of FAQLQ items. This study aims to identify whether all items of the FAQLQ-CF, FAQLQ-TF and FAQLQ-AF are considered important by peanut-allergic patients and, consequently, whether the FAQLQs are valid in a subgroup of peanut-allergic patients.

The FAQLQ-AF, FAQLQ-TF and FAQLQ-CF are self-reported instruments for measuring the impact of food allergy on HRQL in adults (≥ 18 years of age), adolescents (13-17 years of age) and children (8-12 years of age), respectively.¹⁻³ The FAQLQ-AF contains 29 items, the FAQLQ-TF contains 23 items, and the FAQLQ-CF contains 24 items. Each item is scored on a 7-point scale and ranges from 1 (minimal impairment in HRQL) to 7 (maximal impairment in HRQL). The FAQLQs have been shown to be valid, reliable and responsive instruments.¹⁻⁷

In order to ascertain whether HRQL items of the FAQLQ-CF, FAQLQ-TF and FAQLQ-AF were suitable to peanut-allergic patients, some retrospective analysis was performed using databases generated during the development and validation of the FAQLQs.

Firstly, all patients with a physician-diagnosed peanut allergy were selected from the development database to identify FAQLQ

items that were reported most frequently and had the highest impact scores (ie, overall importance) for peanut-allergic patients (ranging from 1.0 "not" to 5.0 "extremely").¹⁻³ Additionally, the overall importance of each FAQLQ item was compared and correlated (Pearson correlation coefficient) between peanut-allergic patients and non-peanut-allergic patients and tested for significance ($P < 0.05$).

Secondly, the cross-sectional validity¹⁻³ of the FAQLQs was determined in a peanut-allergic subgroup. Spearman correlation coefficients (ρ) were calculated between the FAQLQ mean scores and the Food Allergy Independent Measure (FAIM) mean score. The FAIM is an instrument that measures the patients perceived disease severity and has previously been used successfully in validating the FAQLQs.⁶ Moderate correlation was to be expected (0.40-0.60).¹⁻⁴

Thirdly, the longitudinal validity⁴ of the FAQLQs was determined in a peanut-allergic subgroup. Correlations were calculated between the change in total FAQLQ and the change in total FAIM score of patients who underwent a double-blind placebo-controlled food challenge (DBPCFC) with peanut (longitudinal validity). HRQL was measured 1 month before (baseline) and 6 months after (follow-up) a DBPCFC.

Data were analysed with SPSS software for Windows. Table 1 shows the participant characteristics.

Overall importance analysis showed that all items exceeded the previously used cut-off level of >1.37 in the peanut-allergic subgroup.¹⁻³ Figure 1 shows that peanut-allergic patients reported a higher overall impact than non-peanut-allergic patients ($P < 0.05$). Thus, all items may be considered to be important. The Pearson correlation coefficient between the overall importance of peanut-allergic patients and non-peanut-allergic patients was 0.70, $P < 0.001$ (FAQLQ-AF), 0.71, $P < 0.001$ (FAQLQ-TF) and 0.80, $P < 0.001$ (FAQLQ-CF).

Cross-sectional validity analysis showed that the total FAQLQ score correlated significantly with the total FAIM score in the

TABLE 1 Patient characteristics

FAQLQ analysis	AF			TF			CF		
	1	2	3	1	2	3	1	2	3
Peanut/nonpeanut allergy (n)	32/22	42/30	20/33	36/10	57/17	23/23	33/18	60/20	25/32
Sex m/f, %	37/63	25/75	17/83	47/53	46/54	50/50	61/39	58/42	61/39
Mean age Y (SD)	36.6 (16.5)	37.2 (14.3)	35.8 (14.9)	14.9 (1.5)	14.7 (1.3)	15.2 (1.4)	9.7 (1.3)	10.2 (1.3)	10.4 (1.6)
Multiple food allergies, %	94	71	83	92	84	88	94	75	80
Cardiovascular symptoms, %	31	44	53	36	23	48	39	19	25

Analysis 1: Overall impact analysis: item reduction database.

Analysis 2: Cross-sectional validity analysis: cross-sectional database.

Analysis 3: Longitudinal validity analysis: longitudinal database.

FIGURE 1 Overall importance of the FAQLQ items in adults (A), adolescents (B) and children (C)

peanut-allergic subgroup for children ($\rho = 0.50$, $P < 0.001$), adolescents ($\rho = 0.54$, $P < 0.001$) and adults ($\rho = 0.70$, $P < 0.001$).

Longitudinal validity analysis showed that the changes in FAQLQ and FAIM scores following a DBPCFC were significantly correlated in the peanut-allergic subgroup for adults ($\rho = 0.47$, $P = 0.037$) and adolescents ($\rho = 0.49$, $p = 0.018$). For children, a trend was shown ($\rho = 0.36$, $P = 0.077$).

In this study, we aimed to identify whether all FAQLQ items are important for peanut-allergic children, adolescents and adults and whether future studies would be better served by the existing FAQLQs in their entirety or by a peanut-specific selection of FAQLQ items. We found that all items of the FAQLQ were important for peanut-allergic patients. The overall importance of the FAQLQ items was generally higher for peanut-allergic patients than for non-peanut-allergic patients. Additionally, the FAQLQs were shown to be cross-sectionally valid for measuring HRQL in peanut-allergic adults, teenagers and children and longitudinally valid for measuring HRQL changes over time in peanut-allergic adults and teenagers. For children, a trend was shown. This lack of statistical significance for the FAQLQ-CF may be explained by differences in cognitive abilities and language skills between children, adolescents and adults resulting in more consistent answers and higher correlations for adolescents and adults than for children. Thus, all FAQLQ items are considered important for peanut-allergic patients.

Several instruments have been developed to measure HRQL in food allergy. Only the FAQLQs have been completely validated.¹⁻⁷ As far as we know, no completely validated instrument exists that measures peanut-specific HRQL.

A previous study on HRQL following peanut oral immunotherapy⁸ illustrated that the majority of FAQLQ-CF and FAQLQ-TF items were responsive to change. HRQL improved significantly in 22 of 24 FAQLQ-CF items and in 17 of 23 FAQLQ-TF items. Additionally, the mean improvement in HRQL of all FAQLQ-CF items and 21 of 23 FAQLQ-TF items exceeded the minimal clinically important difference, that is, the minimal change in HRQL that is considered to be clinically important by patients.⁹ These findings support our conclusion that the FAQLQ-CF and FAQLQ-TF items may be longitudinally valid and that an intervention study on peanut allergy may be well-served by the existing FAQLQs.

In conclusion, all items of the FAQLQ-AF, FAQLQ-TF and FAQLQ-CF are considered important for peanut-allergic patients. Additionally, the FAQLQs in their entirety were valid for measuring HRQL in a subgroup of peanut-allergic patients. Consequently, an intervention study on peanut allergy may thus be well-served by using the existing FAQLQs in their entirety.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

Clinical Implications

The items of the FAQLQs may be considered relevant for peanut-allergic patients. Intervention studies on peanut allergy would thus be well-served by using the existing FAQLQs in their entirety.

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Long-term effects upon rituximab treatment of acquired angioedema due to C1-inhibitor deficiency

To the Editor,

Acquired angioedema due to deficiency of C1-inhibitor is a relatively infrequent but serious disorder, resulting in severe, sometimes life-threatening, angioedema.^{1,2} Most cases of acquired C1-inhibitor deficiency are associated with an underlying B-cell disorder, ranging from autoimmune anti-C1-inhibitor antibodies to lymphoproliferative disease with excessive activation of the classic complement pathway due

to anti-idiotypic antibodies directed to monoclonal antibodies produced by the malignant clone with consequent consumption of C1 inhibitor.^{3,4} In view of the central role of B cells in this condition, anti-CD20 treatment seems a rational strategy. Since the initial publication of successful treatment of acquired angioedema due to C1-inhibitor deficiency with rituximab was published in 2005,^{5,6} several case reports have confirmed the efficacy of this approach.⁷⁻⁹ Most reports

FIGURE 1 Effect of the administration of anti-CD20 monoclonal antibodies (rituximab) in ten patients with acquired angioedema due to C1-inhibitor deficiency on plasma levels of C1-inhibitor and C4. Each line represents one patient, and patients are labeled A-J (see table in Data S1). The arrow indicates rituximab treatment, in all patients at the beginning of the observation period and a second cycle in patient F and I, respectively. The striped red line represents the lower level of normal values [Colour figure can be viewed at wileyonlinelibrary.com]