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Peanut allergy impact on productivity and quality of life (PAPRIQUA): Caregiver-reported psychosocial impact of peanut allergy on children

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Abstract

Background: Limited research has examined the impact of peanut allergy (PA) on children using validated instruments to assess psychosocial burden and the factors influencing burden.

Objective: The PAPRIQUA study aimed to assess the caregiver-reported impact of living with PA on children's health-related quality of life (HRQL), correlations between PA severity and child's sex, and associations of caregivers' sex and anxiety with the proxy report of their child's HRQL and to identify significant predictors of a child's HRQL.

Methods: A cross-sectional survey of caregivers of children with mild, moderate and severe PA, based on caregiver perception, was conducted in the United Kingdom. Participants were recruited through a survey recruitment panel; a maximum quota of 20% who rated their child's PA as mild was set to ensure population diversity; however, the quota was not required as few participants considered their child's PA mild. The survey, funded by Aimmune Therapeutics, included sociodemographic and clinical questions, the EQ-5D-Y, Hospital Anxiety and Depression Scale, Food Allergy Quality of Life Questionnaire-Parent Form (FAQLQ-PF) and Food Allergy Independent Measure (FAIM).

Results: One hundred caregivers of children with PA (aged 4-15 years) completed the survey. Child's sex was not associated with proxy-reported burden. For younger children (aged 4-10 years), there was no effect of PA severity; parents of older children (aged 11-15 years) reported low to higher burden for their child on the EQ-5D-Y and FAQLQ-PF dependent upon PA severity. For all measures of child burden except the EQ-5D-Y, two or more reactions in the past 12 months and parental anxiety significantly predicted higher levels of burden for the child ($P < .05$–$P < .001$). Experiencing a life-threatening event in the past 12 months significantly predicted EQ-5D-Y proxy utility ($P < .01$).

Conclusions and Clinical Relevance: Caregivers report that children with PA experience high levels of psychosocial burden, particularly those with more severe PA and a reaction history. Interventions to decrease caregiver anxiety and reaction frequency may help reduce the child's burden. Self-report studies in children with PA would help confirm these findings.

KEYWORDS
food allergy, paediatrics, quality of life

1 | INTRODUCTION

Peanut allergy (PA) affects up to 3% of children in the developed world,[1] although prevalence estimates vary widely, with a recent Clinical Practice Research Datalink (CPRD) study suggesting the prevalence of PA in children in the United Kingdom (UK) is around 0.6%.[2,3] It is not easy to predict how sensitive an individual with PA may be; even ingestion of a small amount of peanut can trigger a reaction.[4]

Although several immunotherapies are under investigation for the prevention and management of PA, there is currently no approved treatment outside of the United States of America.[5,6] As a result, the management of PA currently involves strict avoidance of peanuts and emergency treatment in the case of accidental ingestion.

A recent review found a growing body of evidence that demonstrates that living with food allergy (FA) adversely affects children and families emotionally, socially and financially.[7] In PA specifically, studies have compared the health-related quality of life (HRQL) of children with PA to the HRQL of children with other conditions or healthy siblings. Avery et al (2003), using an unvalidated PA quality of life (QoL) questionnaire and an adapted Vespid Allergy QoL questionnaire, found that children with PA reported poorer QoL, more fear of an adverse event and more anxiety about eating than children with insulin-dependent diabetes.[8] King et al (2009) compared children with PA to their non-PA siblings using the generic Paediatric QoL Inventory (PedsQL) and the Spence Children's Anxiety Questionnaire.[9] They reported that children with PA have significantly greater separation anxiety and poorer QoL in general, in school and in relation to their physical HRQL, compared to their siblings with no PA.

Many factors have been identified as having an influence on HRQL for children with FA. Perceived FA severity and objective indicators of FA severity (history of anaphylaxis, number of symptoms experienced during a reaction) have been found to influence a child's HRQL in FA.[10,11] In addition, having multiple FAs, severe symptoms and maternal depression, stress and anxiety have also been found to negatively impact a child's HRQL.[11-13] No relationship has previously been reported between adrenaline auto-injector (AAI) prescription, reaction severity, or child sex and child HRQL.[10,11,14,15] Conflicting findings on the relationship between children's age and HRQL have been reported, with one study finding that older children (aged 6-12 years) had worse HRQL than children aged up to 5 years[12] and another study showing no significant association between age and HRQL.[11] In PA specifically, one study found that child anxiety and parenting stress (measured using the Parenting Stress Index) predict parent's proxy report of their child's HRQL, and child anxiety, parenting stress, length of diagnosis and AAI experience predict child's self-report of their HRQL.[16] No studies have been identified investigating the relationship between perceived disease severity or child sex and HRQL in PA specifically.

Previous research has suggested that caregivers' sex is associated with their ratings of their child's HRQL. In a study of FA, both parents scored their food-allergic child's HRQL better than the child's own assessment, whereas mother-reported child HRQL was significantly correlated with limitations in the child's social life, and father-reported child HRQL was associated with limitations in the family's social life.[14,15] In a study of families with a child with PA, mothers felt that there was a greater impact on HRQL for their peanut-allergic child, compared to that reported by siblings, fathers or the peanut-allergic children themselves.[9]

Due to the limited PA-specific research exploring factors associated with child HRQL, and limited use of validated FA instruments to assess HRQL in PA, the objectives of this study were to (a) describe the caregiver-reported impact of living with PA on children's HRQL and evaluate the roles of PA severity and child sex; (b) explore how caregivers' sex and anxiety are associated with the proxy report of their child's HRQL; and (c) identify significant predictors of a child's HRQL. This paper reports data from a survey conducted in the UK with parents of children aged 4 to 15 years. Given the age range of the children, the effect of age was also considered by splitting the sample for those aged 4-10 and 11-15 years, reflecting meaningful context changes such as school environment and increased independence.

2 | METHODS

2.1 | Study design

This study used a cross-sectional design to survey caregivers of children and teenagers aged 4 to 15 years to provide reports of their child's HRQL. The study was reviewed and approved by the Freiburg Ethics Commission International (FECI) prior to participant recruitment (FECI code: 017/1938; date: 20/11/2017).

2.2 | Participants

Participants were recruited through a survey recruitment panel. Participants were eligible for the study if they were a parent or primary caregiver of a child (aged 4-15 years) with medically diagnosed PA who had experienced at least one reaction to peanuts in their day-to-day life (other than a food challenge). Participants were also asked to rate the severity of their child's PA using categories of mild, moderate or severe. In order to ensure diversity in the severity of PA in the sample, a quota was set for a maximum of 20% of participants who perceived the severity of their child's PA as mild and a minimum of 80% who perceived their child's severity as moderate to severe. At least 25% of the moderate/severe samples were required to have used an AAI, and a minimum of 10% were required to have experienced a life-threatening event. However, in the end, the sample quotas were achieved without the need to enrich or limit any numbers. All participants came from the UK.

2.3 | Procedures and measures

Eligible participants were informed that the study involved completing an online survey, was expected to take up to 30 minutes, and would be about their and their child's experiences of living with PA. Participants were asked to read the information provided, and if interested in participating were asked to give their consent online prior to completing the online survey. Participants received nominal reimbursement for participating in the study.

The survey consisted of sociodemographic questions about the caregiver and their child and clinical questions about the child's PA. Clinical questions included the caregiver's perception of the severity of their child's PA (mild, moderate or severe), how their child was diagnosed, caregiver's confidence in managing their child's reactions to PA (not at all confident to very confident), the number of reactions to peanut their child has experienced in the last 12 months and their lifetime, the type of treatment received in the last 12 months and their lifetime, and whether their child ever experienced a life-threatening reaction to peanut. The survey also included proxy-reported measures of child HRQL (Proxy EQ-5D-Youth version, Food Allergy Quality of Life Questionnaire-Parent Form [FAQLQ-PF]), caregiver and child expectation of outcome questions (Food Allergy Independent Measure-Parent Form [FAIM-PF]), and caregiver anxiety and depression (Hospital Anxiety and Depression Scale [HADS]).

The EQ-5D-Y (proxy 1)[17] is a validated generic health status measure.[18] Participants report their child's current health on five dimensions (mobility, self-care, pain and discomfort, usual activities, anxiety and depression) from no problems to extreme problems. The responses are converted into a single index value where a score of 1 represents full health and a score of 0 represents dead. As there are currently no value sets for use in children and teenagers, the UK value set was applied to score the instrument.[19] Participants also rated their child's current health on a 0-100 visual analogue scale (VAS). To the best of our knowledge, this is the first study to show proxy-reported impacts of PA on the EQ-5D-Y.

The FAQLQ-PF[20] is a 30-item questionnaire assessing three domains (emotional impact, food anxiety, and social and dietary limitations). Each item is scored on a 7-point scale ranging from 0 (no impact) to 6 (extreme impact); each domain is scored as an average of the items with the total score representing the mean of the domain scores. The instrument has been validated with internal consistency of $\alpha = 0.91$ (age 6-12) for the total score and $\alpha = 0.90$-0.94 for the domains (age 6-12).[20] In a study of child-parent pairs, the FAQLQ-PF correlated moderately with the FAQLQ-CF (ICC = 0.57; $P < .001$),[21] a self-report instrument for children aged 8-12 years, which is validated for patients with PA.[22] The children's self-report scores were higher (worse) than those reported for them by their parents ($P < .001$).[21]

The FAIM-PF[23] is usually used in conjunction with the FAQLQ and consists of eight items in total, four items related to the parent's self-reported perception of their child's likelihood of allergic reaction events (accidentally ingesting the food to which they are allergic, having a severe reaction, dying from their FA, effectively treating themselves when needed) and the same four items related to the parent-reported perception of their child's beliefs. Each item is answered on a seven-point scale, with FAIM scores ranging from 1 (low perceived disease severity) to 7 (high perceived disease severity). Total FAIM scores were significantly correlated with FAQLQ scores for corresponding age groups, and with DBPCFC scores in peanut-allergic adults and teenagers, with a trend for children.[22] The FAIM-PF was well correlated with the FAIM Child Form (FAIM-CF) in child-parent pairs (ICC = 0.80; $P < .001$).[21]

The HADS[24] is a 14-item measure of anxiety and depression used in both hospital and community settings. The questionnaire gives clinically meaningful results as a psychological screening tool and can assess the symptom severity and "caseness" of anxiety disorders and depression in patients with illness and the general population. HADS provides separate scores for anxiety and depression domains. Scores for each domain range from 0 to 21, with scores of 0-7 indicating "normal" or no anxiety or depression, 8-10 indicating mild, 11-14 indicating moderate and 15-21 indicating severe anxiety or depression; scores of ≥11 indicate probable "caseness."[24] Population norms related to the proportion of people reporting probable clinical caseness in the UK (based on adults aged 25-65 years) have also been estimated at 12.5% (males) and 19% (females), with averages for males and females of 15.8% for anxiety and 6.9% for depression.[25] The HADS has been validated many times in different populations, with internal consistency for the anxiety scale ranging from $\alpha = 0.68$-0.93 (mean: 0.83) and the depression scale ranging from $\alpha = 0.67$-0.90 (mean: 0.82).[26]

2.4 | Analysis

Demographic and clinical characteristics were analysed using descriptive statistics. The FAQLQ-PF and HADS were scored according

to their published scoring instructions.[20,24] The EQ-5D-Y was scored using the UK EQ-5D-3L adult value set.[19] Pearson's, point biserial and Spearman's correlations were conducted as appropriate (based on scale response type and sample distribution) to explore relationships between variables. Correlations were interpreted in line with Cohen's guidelines: small, 0.10-<0.30; moderate, 0.30-<0.50; and large, 0.50.[27] To explore the impact of different variables on child burden, two-way analyses of variance (ANOVAs) and Kruskal-Wallis tests were conducted. To further explore which variables significantly predicted child burden, multivariate ordinary least squares linear regression models were conducted, with each of the FAQLQ-PF domains and total score included as dependent variables in separate models. The number of reactions in the past 12 months and number of reactions in the child's lifetime were included as categorical variables in the regression analysis: 0, 1, 2 or more reactions in the past 12 months, and 0-2, 3-5 and 6 or more reactions in their lifetime. Results of statistical tests were considered statistically significant if *P*-values were equal to or below .05. All analyses were conducted using STATA (version 16.0).

3 | RESULTS

The demographics and clinical characteristics of the participants and their children with PA are displayed in Table 1. The survey was completed by 100 caregivers of a child with PA; the sample contained male (45%) and female (55%) caregivers, and female (42%) and male (58%) children with PA. Caregivers had a mean age of 39 years (standard deviation [SD]: 7.6; range 21-65) and their children had a mean age of 10 years (SD: 3.4; range: 4-15); nearly a quarter of children had other food allergies in addition to PA and almost three-quarters had been prescribed an AAI. Both parent and child samples had a high proportion of allergic rhinitis (parents: 22%; children: 36%), asthma (parents: 20%; children: 34%) and skin disorders (parents: 17%; children: 26%).

3.1 | Impact of PA on children's HRQL

Summaries of the impact of PA on the HRQL of children with PA, based on proxy-reported generic (EQ-5D) and FA-specific outcome measures (FAQLQ and FAIM) for the sample as a whole and by age and severity groups, are presented in Figure 1 and Table 2. All of the health outcome measures were significantly correlated with each other (*r*'s = .30-0.68, *P*'s < .01, excluding domains of the same measure), indicating medium to large effect sizes.[26] The EQ-5D-Y mean scores show a lower mean utility value and VAS for the severe group (index: 0.768; VAS: 78.5) compared to mild (index: 0.863; VAS: 81.7) or moderate (index: 0.909; VAS: 82.0). No population norms are available for the EQ-5D-Y; however, the population norm for young adults (aged 18-24 years, EQ-5D-3L) is 0.940.[28] Therefore, the proxy-reported utility for the sample as a whole (0.873) is lower than the norm for young adults.

TABLE 1 Parent and child demographic and clinical background

Characteristic	Parents (N = 100)	Children (N = 100)
Age, years		
Mean (SD)	39.49 (7.59)	9.82 (3.42)
Minimum-Maximum	21-65	4-15
Sex, n		
Female	55	42
Comorbidities, n		
Allergic rhinitis	22	36
Asthma	20	34
Diabetes type 1/2	2/4	3/2
Eating disorders	7	6
Skin disorders	17	26
Stress	13	5
Other	2	4
None of the above	37	28
Other food allergies, n (%)		
Yes	-	24 (24.0)[a]
No	-	76 (76.0)
If Yes: Food allergy, n (%)		
Celery	-	2 (8.3)
Cow milk/dairy products	-	6 (25.0)
Egg	-	11 (45.8)
Fish/shellfish etc	-	1 (4.2)
Soya beans/other legumes	-	1 (4.2)
Other nuts	-	11 (45.8)
Other	-	5 (21.0)
Prescribed an AAI, n		
Yes	-	71
Experienced life-threatening event (lifetime, n)		
Yes	-	34
Number of reactions (lifetime)		
Mean (SD)	-	12.0 (28.2)[b]
Median		5
Proxy-reported severity, n		
Mild	-	13
Moderate	-	66
Severe	-	21

Abbreviations: AAI, adrenaline auto-injector; N, sample size; SD, standard deviation.

[a]38% among those with caregiver proxy-reported severe peanut allergy.

[b]If two outliers are excluded (192 and 206 reactions) the mean (SD) is 8.2 (8.6).

When considering age group, Figure 1 shows the younger age group consistently tracking below the EQ-5D utility population norm, showing a non-linear relationship with severity. The older age group only drop below population norms in the severe group and show a clear linear

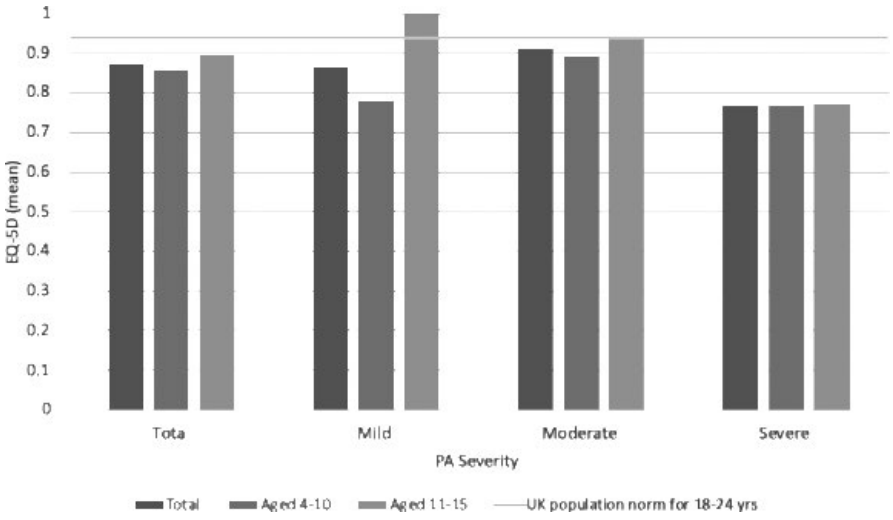

FIGURE 1 EQ-5D-Y index by PA severity for the total sample and each age group. PA, peanut allergy; UK, United Kingdom

association between PA severity and HRQL. This was supported by Kruskal-Wallis test results showing a significant main effect of severity on EQ-5D-Y utility, showing that there was a significant difference in utility depending on the level of severity. While significant for the sample as a whole ($X^2 = 6.469$, $P < .05$), when considering age group, it can be seen that this effect is driven by the older population (aged 11-15 years: $X^2 = 7.802$, $P < .05$). For the younger group, there was no significant difference in utility depending on proxy-rated severity of PA (aged 4-10 years: $X^2 = 1.565$, $P = .457$). The EQ-5D VAS did not show a significant effect of PA severity for either group.

The FAQLQ total and domain scores also followed the same pattern with regard to the proxy-reported severity of PA (Table 2). The FAQLQ results show a similar burden profile, insofar as the total age group means are similar, but reflect the parents of younger children reporting a more consistent level of moderate (FAQLQ scores of 3-4) burden. For the younger age group, there was no main effect of PA severity (aged 4-10 years: $X^2 = 1.032$-1.600; P's $> .05$), showing no difference in the FAQLQ scores in relation to severity rating, whereas the parents of older children report low to higher burden dependent upon PA severity (FAQLQ scores of 2-5) with a significant main effect of PA severity on all FAQLQ domains (aged 11-15 years: $X^2 = 7.707$-10.309; P's $< .05$). The FAIM total score did not significantly differ across levels of PA severity for either age group. The sex of the child was not significantly associated with any outcome measures or proxy-reported PA severity (all r's $< .13$, all P's $> .05$). Similarly, there were no main effects of sex or interaction effects between sex and severity in the inferential analyses.

3.2 | Relationship between caregiver sex and anxiety and proxy report of child's HRQL

Descriptive statistics of the child HRQL outcomes by caregiver sex and HADS "probable clinical anxiety" are presented in Table 3. This shows that greater PA burden, as measured by the EQ-5D-Y, FAQLQ and FAIM, was reported amongst children whose caregivers had "probable clinical anxiety." Caregiver sex was not significantly associated with caregiver "probable clinical anxiety" caseness ($X^2 = 0.718$; $P > .05$) or mean anxiety score as measured using the HADS ($r = .07$, $P > .05$) or significantly correlated with any of the child proxy-reported outcome measures (EQ-5D-Y, FAQLQ-PF, FAIM) (Appendix S1; r's $= .02$-0.13, P's $> .05$). However, caregiver mean anxiety was significantly associated with all child proxy-reported outcome measures, with moderate effect sizes (r's $= .30$-0.55, P's $< .01$). Relatedly, caregiver's mean anxiety was significantly associated with the number of life-threatening events their child had experienced in the past 12 months ($r = .25$, $P < .05$) and the number of reactions their child had experienced in their lifetime ($r = .23$ and $r = .24$, P's $< .05$, respectively). Furthermore, only caregivers with children considered to have moderate or severe PA reported levels of probable clinical anxiety higher than UK population norm values (33% versus 15.8%, respectively).[25]

Results from ANOVAs exploring main effects and interactions showed a main effect of caregiver anxiety on EQ-5D-Y-VAS ($F = 8.33$, $P < .01$), FAQLQ-PF-Total ($F = 24.02$, $P < .001$), FAQLQ-EI (FAQLQ-Emotional Impact; $F = 28.61$, $P < .001$), FAQLQ-FA (FAQLQ-Food Anxiety; $F = 17.99$, $P < .001$), FAQLQ-SDL (FAQLQ-Social and Dietary Limitations; $F = 20.14$, $P < .001$) and FAIM-CF (FAIM child version; $F = 7.87$, $P < .01$) but not on EQ-5D-Y utility ($F = 3.67$, $P > .05$). Having included the significant main effect of anxiety and interaction term, thus reducing error variance, the ANOVAs also showed that male caregivers reported that their children experience greater PA burden with a significant main effect of sex on FAQLQ-PF-Total ($F = 4.75$, $P < .05$), FAQLQ-EI ($F = 6.25$, $P < .05$) and FAQLQ-FA ($F = 4.14$, $P < .05$). There was no significant sex by anxiety interactions; the effect of caregiver anxiety on their child's proxy-reported QoL did not differ by sex.

3.3 | Predictors of HRQL in children with PA

Caregiver anxiety, caregiver confidence, PA severity, life-threatening events and number of reactions were significantly correlated with several measures of child burden (Appendix S1). Other potential predictors (AAI use, child's sex) were not significantly associated

TABLE 2 Proxy-reported measures of child PA burden by child age and PA severity

	Total Sample		Aged 4-10 Years		Aged 11-15 Years	
Outcome	**N**	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**Mean (SD)**
EQ-5D Utility						
Total	100	0.873 (0.231)	60	0.858 (0.258)	40	0.896 (0.189)
Mild	13	0.863 (0.354)	8	0.778 (0.439)	5	1.000 (0.000)
Moderate	66	0.909 (0.165)	43	0.892 (0.187)	23	0.939 (0.109)
Severe	21	0.768 (0.292)	9	0.766 (0.337)	12	0.771 (0.269)
EQ-5D VAS						
Total	100	81.3 (15.9)	60	81.2 (17.2)	40	81.4 (14.0)
Mild	13	81.7 (16.3)	8	79.8 (19.7)	5	84.8 (9.5)
Moderate	66	82.0 (15.5)	43	81.3 (16.6)	23	83.5 (13.4)
Severe	21	78.5 (17.4)	9	82.0 (19.6)	12	75.9 (16.0)
FAQLQ Total						
Total	100	3.37 (1.57)	60	3.32 (1.52)	40	3.45 (1.66)
Mild	13	2.73 (1.43)	8	3.15 (1.40)	5	2.06 (1.32)
Moderate	66	3.21 (1.55)	43	3.23 (1.51)	23	3.17 (1.66)
Severe	21	4.28 (1.38)	9	3.88 (1.68)	12	4.58 (1.09)
FAQLQ-Emotional Impact						
Total	100	3.14 (1.60)	60	3.07 (1.58)	40	3.24 (1.66)
Mild	13	2.47 (1.25)	8	2.88 (1.24)	5	1.80 (1.03)
Moderate	66	2.99 (1.62)	43	2.97 (1.60)	23	3.02 (1.69)
Severe	21	4.03 (1.45)	9	3.72 (1.74)	12	4.27 (1.21)
FAQLQ-Food Anxiety						
Total	100	3.72 (1.65)	60	3.61 (1.60)	40	3.88 (1.72)
Mild	13	3.07 (1.61)	8	3.44 (1.58)	5	2.48 (1.64)
Moderate	66	3.56 (1.62)	43	3.53 (1.57)	23	3.64 (1.76)
Severe	21	4.61 (1.47)	9	4.18 (1.86)	12	4.93 (1.07)
FAQLQ Social Dietary Limitations						
Total	100	3.40 (1.63)	60	3.42 (1.55)	40	3.38 (1.78)
Mild	13	2.80 (1.63)	8	3.26 (1.64)	5	2.07 (1.49)
Moderate	66	3.22 (1.59)	43	3.36 (1.55)	23	2.97 (1.66)
Severe	21	4.33 (1.48)	9	3.84 (1.57)	12	4.70 (1.35)
FAIM Total						
Total	100	3.78 (0.894)	60	3.80 (0.979)	40	3.75 (0.76)
Mild	13	3.63 (1.10)	8	3.75 (1.17)	5	3.45 (1.07)
Moderate	66	3.69 (0.84)	43	3.74 (0.95)	23	3.60 (0.58)
Severe	21	4.17 (0.87)	9	4.17 (0.98)	12	4.17 (0.83)

Abbreviations: FAIM, Food Allergy Independent Measure; FAQLQ, Food Allergy Quality of Life Questionnaire; N, sample size; SD, standard deviation; VAS, visual analogue scale.

with outcome assessments. Multivariate regression models for each outcome assessment are presented in Appendix S2 (only significant predictors rather than all predictors in the models are shown). As the number of reactions in the "past 12 months" and in the child's "lifetime" and life-threatening events are not independent of each other, these were run in separate models. The regression models show that for all measures of PA burden except the EQ-5D-Y proxy utility, the experience of two or more reactions in the past 12 months, and parental anxiety, are significantly associated with increased burden, after controlling for other covariates. Lower caregiver confidence was also significantly associated with increased burden for the EQ-5D-Y proxy VAS and FAQLQ-PF Social and Dietary Limitations domain. Having experienced a life-threatening event in the past 12 months was the only significant independent predictor of EQ-5D-Y proxy utility ($B = -0.146$, $P < .01$). This predictor was not significant for any other outcomes. When entered into the regression models, child's age group, severity group and the age × severity interactions were not significant predictors for any outcomes.

TABLE 3 Descriptive statistics of child HRQL outcomes by caregiver sex and HADS "probable clinical" anxiety

	HADS Probable Anxiety	
	No (N = 69)	Yes (N = 31)
Outcome/Sex	M (SD)	M (SD)
EQ-5D-Y Utility		
Male (N = *45*)	0.925 (0.147) N = *33*	0.839 (0.146) N = *12*
Female (N = *55*)	0.887 (0.274) N = *36*	0.780 (0.285) N = *19*
EQ-5D-Y-VAS		
Male	81 (15)	77 (11)
Female	88 (11)	72 (23)
FAQLQ Total		
Male	3.1 (1.4)	4.9 (0.8)
Female	2.8 (1.4)	4.0 (1.8)
FAQLQ-Emotional Impact		
Male	2.8 (1.3)	4.9 (0.9)
Female	2.5 (1.3)	3.8 (1.9)
FAQLQ-Food Anxiety		
Male	3.6 (1.6)	5.0 (0.7)
Female	3.1 (1.5)	4.4 (1.8)
FAQLQ-Social and Dietary Limitations		
Male	3.1 (1.5)	4.9 (0.9)
Female	2.9 (1.5)	4.0 (1.7)
FAIM Total		
Male	3.6 (0.9)	4.4 (0.6)
Female	3.6 (0.8)	4.1 (1.0)

Abbreviations: FAIM, Food Allergy Independent Measure; FAQLQ, Food Allergy Quality of Life Questionnaire; HADS, Hospital Anxiety and Depression Scale; M, mean; N, sample size; SD, standard deviation; VAS: visual analogue scale.

When the regression models were repeated with "lifetime" life-threatening events and reactions, the pattern of significant results was the same for almost all the FAQLQ outcomes, with six or more reactions in a lifetime replacing the significant two or more reactions in the past 12 months; however, the beta coefficients were lower (B = 0.735, 0.874, 0.876 for Total, EI and FA, respectively; all *P*'s < .05). For the FAQLQ-SDL domain, the number of "lifetime" reactions was not significant but having had a life-threatening event in their lifetime was (B = 0.612, $P < .05$). For FAIM, the number of "lifetime" reactions was not significant, but HADS anxiety caseness remained significant. For the EQ-5D-Y-VAS the pattern of results was the same for "lifetime" reactions as it has been for reactions in the "past 12 months" (six or more "lifetime" reactions was significant; B = −8.811, $P < .05$). In the EQ-5D-Y Utility model, "lifetime" reactions was a significant predictor (B = −0.123, $P < .05$) and life-threatening events also became significant (B = −0.109, $P < .05$).

4 | DISCUSSION

This survey describes the caregiver-reported burden experienced by children with PA in the UK. In line with recent findings, a child's sex was not associated with proxy-reported child burden,[12] demonstrating that male and female children experience a similar level of psychosocial burden due to their PA. Increased PA severity, however, was significantly associated with increased burden among the older children; younger children appear to have a similar level of burden overall, with less variability due to severity of PA. This finding is in line with expectations, given the more uniform impact on a young person, for whom the presence of the PA may have similar effects regardless of severity, whereas an older child may be given more freedom and autonomy and be more able to evaluate a situation based on their and their caregiver's perception of their PA severity.

Caregiver anxiety was significantly correlated with almost all proxy-reported measures of child impact, partially supporting previous research finding maternal anxiety is significantly associated with child's proxy-reported HRQL in FA.[11,13] However, while caregiver sex was also significantly associated with child's PA burden for almost all FAQLQ outcomes, our findings suggest that male caregivers report higher levels of burden experienced by their child than female, whereas previous research has found mothers reported greater burden for their child than fathers reported.[9] It is possible that this novel finding is due to previous studies lacking male caregivers in their sample; alternatively, this may reflect the increase in shared parenting and greater involvement of males in childcare. Rates of anxiety were consistent across caregiver sex, so the higher burden reported by males was not due to the fact males were more anxious.

Relatedly, caregiver anxiety was associated with the child's PA reaction history, and "probable clinical" anxiety was only reported at levels above UK population norms amongst caregivers reporting their child had moderate/severe PA. Given the cross-sectional nature of this study, it is not possible to establish whether the caregiver's anxiety was caused by their child's experiences with PA, or if their anxiety led to higher levels of PA burden being reported. Given the association between caregiver anxiety and objective markers of peanut allergy severity, the former seems likely, but longitudinal research would be required to confirm this definitively.

When controlling for multiple predictors of the child's HRQL outcomes, caregiver anxiety and the experience of two or more reactions in the past 12 months were the most consistent independent predictors of child HRQL. While the descriptive results showed increased HRQL burden with increased PA severity, and significant correlations between severity and HRQL measures, severity was not a significant independent predictor in the multivariate regression models. This may be due to the association between the child's PA severity and caregiver anxiety. The only significant predictor of child proxy-reported EQ-5D-Y utility was the objective severity indicator of having experienced a life-threatening event. There are

currently no published normative values for the EQ-5D-Y; however, there is a published normative value of 0.940 for young adults in the UK (aged 18-24 years), and the proxy-reported utilities in the current study are lower (0.873 overall) for children than the norm for young adults. Further, the results reported here are in line with previously reported utilities for children with FA. Protudjer et al (2015) reported an overall proxy-reported EQ-5D-Y utility of 0.873, compared to 0.875 reported here; likewise, their adolescent utility values also reflected better HRQL (0.91) than the child utility values (0.84).[29] Based on review of the literature, this study is the first to report caregiver-reported impacts of PA on the EQ-5D-Y, and thus may provide a benchmark for future studies using this instrument in caregivers of subjects with PA.

Some limitations should be considered when interpreting the results from this study. All data generated in this study relied upon parent-proxy reports of child HRQL. Previous studies in FA have found that parents reported significantly better HRQL for their child than the children themselves reported[14,15,30]; therefore, the results of the current study may underestimate the burden experienced by children with PA. In addition, self-reported data are subject to recall bias and inaccuracy. As discussed above, the study also used a cross-sectional design, so it is not possible to establish cause and effect and it is unknown whether caregiver anxiety influences their proxy report of their child's HRQL or whether caregiver perception of their child's burden causes their anxiety. The FAQLQ-PF was developed for children aged 0 to 12 years; as 28 participants in this study had a child aged 13-15 years, it is unclear how this may have affected the FAQLQ-PF results. Additionally, like with many studies that collect data using online methods, this study did not have clear access to response rate data which unfortunately is a common issue. Finally, the sample is quite small, data collection was only conducted in the UK, and some of the analyses may be underpowered. Future research could extend the sample size, traceability of responses and the recruitment to other countries. The inclusion of parent-child dyads and a longitudinal design in future research could assess any potential differences between parent-proxy reports and child self-reports, and begin to unpick the relationship between caregiver anxiety and child burden in PA.

This study demonstrated the caregiver-reported burden experienced by children with PA in the UK, and to our knowledge is the first to report caregiver-reported impacts of PA on the widely used EQ-5D-Y. The results showed that male and female children experience a similar level of psychosocial burden due to their PA. For older children, increased PA severity is associated with increased burden, whereas younger children experience a consistently high level of burden unrelated to their PA severity. Caregiver anxiety and sex were significantly associated with many proxy-reported measures of child impact, with male caregivers reporting more burden experienced by their child than female caregivers, using disease-specific measures. It is clear that further research in a larger sample could explore and validate this finding. Research could also explore whether children with PA in other countries experience a similar level of burden. Caregiver anxiety was also associated with the child's PA reaction history and severity of PA, suggesting the elevated burden reported by caregivers with anxiety may be due to the child's experiences rather than their own anxiety. This issue would benefit from further research to investigate whether reducing caregiver anxiety may reduce the perceived burden of PA on the child's life.

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CONFLICT OF INTEREST

SA, KG, JdV and RCK report consulting for Aimmune Therapeutics. AV and RR are employees of Aimmune Therapeutics.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study captured in the current article are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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