

Health-Related Quality of Life in Children With Food Allergy and Their Parents: A Systematic Review of the Literature

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■ Abstract

Background: Health-related quality of life (HRQoL) in food-allergic children and their parents can be assessed using generic and specific questionnaires.

Objectives: We investigated whether HRQoL scores in food-allergic children and their parents were similar to normative data and whether they were correlated.

Methods: We searched PubMed, Scopus, and the New York Academy of Medicine Grey Literature Report site. Electronic searches were supplemented by perusal of the references of the papers retrieved.

Results: Seventeen studies were eligible. Two studies compared total HRQoL scores for children with food allergy and normative data and found no significant differences. Six studies compared HRQoL questionnaire subdomain scores for children with normative data, and 4 studies compared the same scores for parents with normative data. Children with food allergy scored worse in subdomains including bodily pain, physical functioning, mental health, general health, and emotional, social, and psychological quality of life. However, they performed better in physical health, and had fewer limitations in schoolwork due to behavioral problems. Parents performed better in subdomains such as physical and environmental health, social and psychological health, and family cohesion but scored worse on social health, overall quality of life, emotional health, impact on parental time, and limitations in usual family activities. Statistically significant results for these subdomains were not invariably corroborated by subsequent studies. No study provided data on the correlation between children's HRQoL and that of their parents.

Conclusions: HRQoL of food-allergic children and their parents may differ from that of the normative population in certain subdomains. However, the evidence was not sufficient to draw robust conclusions.

Key words: Child. Adolescent. Parents. Food hypersensitivity. Questionnaires. Quality of life.

■ Resumen

Antecedentes: La calidad de vida relacionada con la salud (CVRS) en niños y sus padres, con alergia a alimentos, ha sido evaluada mediante cuestionarios genéricos y específicos.

Objetivos: Hemos investigado las puntuaciones en CVRS en niños con alergia a alimentos y en sus padres y evaluado si diferían o no del patrón de poblaciones normales, y si tenían algún tipo de correlación.

Métodos: Se realizó una búsqueda en las bases de datos Pubmed, Scopus, y New York Academy of Medicine Grey Literature Report site. Estas búsquedas electrónicas se complementaron con las referencias obtenidas de la lectura detallada de estos originales obtenidos en la búsqueda electrónica.

Resultados: Se incluyeron finalmente 17 estudios. Dos estudios compararon la puntuación total obtenida en los cuestionarios de CVRS y no encontraron diferencia entre los niños con alergia alimentaria y los obtenidos en población sana. Seis estudios compararon también los subdominios de los cuestionarios entre niños con alergia alimentos y población normal de referencia y otros cuatro estudios compararon estos subdominios entre padres y niños con alergia a alimentos y población normal de referencia. Los niños con alergia a alimentos presentaban peores puntuaciones en diversos dominios, incluyendo dolor corporal, calidad de vida emocional, social y psicológica, función física, salud mental y salud general. Sin embargo tenían mejores puntuaciones en los dominios salud física y menores limitaciones en el trabajo escolar. Los padres de niños con alergia alimentaria tuvieron mejores puntuaciones en los dominios salud física y ambiental, salud psicológica, dominio social y cohesión familiar, pero puntuaron peor en los dominios salud social, salud emocional, impacto en

tiempos de dedicación como padres y en el dominio de limitación de actividades familiares habituales. La significación estadística de todas estas diferencias no era igual ni se corroboraba en todos los estudios. Ningún estudio proporcionó las posibles correlaciones entre las puntuaciones de padres e hijos en los cuestionarios de CVRS.

Conclusiones: La CVRS de los niños con alergia a alimentos y la de sus padres podría diferir de la de poblaciones normales en algunos dominios. Sin embargo, la evidencia en la literatura es capaz de avalar conclusiones sólidas en este sentido.

Palabras clave: Niños. Adolescente. Padres. Hipersensibilidad a alimentos. Cuestionarios. Calidad de vida.

Introduction

The frequency of food allergy has increased during the last few decades and may affect up to 6% of children in developed countries [1-3]. Avoidance of food allergens has been the only proven effective therapy; emergency treatment has kept morbidity low and mortality rare [4,5].

Studies suggest that food allergy can affect several aspects of health-related quality of life (HRQoL) for children, adolescents, and their families [6-9] because the risk of allergic reaction limits children in their autonomous social activities [9,10-13]. Food-hypersensitive adolescents are absent from school more often and less self-confident [14]. Parents may be affected by health and nutritional concerns and frustration caused by taking time-consuming precautionary measures [10,15]. More food allergies in a child may be correlated with worse HRQoL [9,11]. Investigators report improvement in HRQoL as an outcome for assessing the effectiveness of various interventions in food-allergic children under the assumption that these children and their families have poorer HRQoL than the general population [2]. However, no systematic examination has determined whether there is consistent evidence to support this assumption.

HRQoL in food-allergic children can be assessed using both generic and specific questionnaires. Generic HRQoL questionnaires compare patients with the healthy population or patients with different diseases, but they are not sufficiently sensitive to assess specific problems and cannot separate the impact on HRQoL of the disease in question from the impact of comorbid conditions [3,16]. Disease-specific HRQoL instruments are considered more sensitive than generic instruments because they focus on the domains most relevant to the disease, they detect clinically important changes in the patient's HRQoL, and the scores are used as an outcome measure [14]. However, they cannot compare patient HRQoL across different diseases [17]. Since 2008, specific tools have been developed and validated to enable children and teenagers with food allergy to report on their own HRQoL or parents to report on their child's HRQoL from the child's perspective [18-22].

We analyzed generic and disease-specific questionnaires to identify studies that evaluated HRQoL in food-allergic children or their parents and investigated whether the child or parents' HRQoL scores differed from normative data. We also examined the correlation between HRQoL scores in food-allergic children and the parents' scores.

Material and Methods

Search Algorithm

We searched PubMed and Scopus (from inception to April 2012) using the following algorithm: "food hypersensitivity" [MeSH] OR "food hypersensitivity" OR "nut hypersensitivity" OR "peanut hypersensitivity" OR "egg hypersensitivity" OR "milk hypersensitivity" OR "food allergy" OR "nut allergy" OR "peanut allergy" OR "egg allergy" OR "milk allergy" AND ("quality of life" OR "quality of life" [MeSH]). In order to locate work from noncommercial publishers, we also used the key words included in the algorithm above to search the New York Academy of Medicine Grey Literature Report site (<http://www.greylit.org/home>). Electronic searches were supplemented by perusal of the references of the retrieved papers. We did not search the websites of conference proceedings, since research reports and abstracts from meetings do not generally undergo extensive peer review and, therefore, the quality of the data presented cannot be guaranteed.

One investigator (ZM) performed all the initial searches, and a second investigator (AT) confirmed the results. Potential discrepancies were resolved by consensus.

Eligibility Criteria

We included studies in English and in French whose population comprised food-allergic children aged up to 18 years or their parents for whom HRQoL had been assessed and the HRQoL results were reported separately for children or parents, regardless of how food allergy had been diagnosed. If children with comorbidities or allergies other than food allergy were also included, we accepted the study only if it reported separate data on HRQoL for children with food allergy or their parents. If a study included both children and adults with food allergy, we included it when it provided the data on children separately.

We accepted studies based on generic or disease-specific validated questionnaires that clearly stated that they evaluated HRQoL. We considered questionnaires to be validated when psychometric characteristics (ie, validity and reliability) had been reported. We accepted questionnaires validated by other researchers or adapted from validated questionnaires. We excluded questionnaires that were designed to measure outcomes related to but not directly assessing HRQoL, such as impact on family.

We excluded studies without primary data and papers that may have analyzed relevant HRQoL data but whose results

could not be retrieved even after we contacted the authors. If a study was reported in multiple papers, we included the article or the articles that provided complete information on the study.

Data Extraction

Data were extracted using predefined forms. One investigator (ZM) extracted the data. Another investigator (AT) confirmed the extracted data. Discrepancies were resolved by consensus.

Extracted items included name of first author, year of publication, country, study design, and the HRQoL instrument that was used. For children and parents separately, we recorded sample size, percentage of males, and age as reported in the study. For children, we also recorded the definition used to diagnose food allergy, whether the time since diagnosis was reported, and whether comorbidities were described. We also noted whether HRQoL was completed by the children or by their parents as proxies. For parents, we also extracted whether socioeconomic status or educational level were reported.

Finally, we extracted the HRQoL score as reported separately for children and parents. We recorded both composite scores and subdomain scores for each questionnaire. If the HRQoL was evaluated for multiple groups of children or parents in a study, we recorded HRQoL for each group separately.

Our assessment of the quality of reporting was based on guidelines for reporting survey research and observational studies included [23,24]. We recorded several items: whether authors had adequately reported sample size and power calculations; population characteristics; definition of food allergy for children; HRQoL instruments used, how they were administered, and who completed them; presentation of composite and subdomain score results and whether adjustments were made for multiple comparisons; and whether factors that could have influenced HRQoL for allergic children or their parents were described and considered by the investigators in the analyses.

We conducted our systematic review according to the standards for reporting meta-analyses of observational studies in epidemiology as described in the MOOSE statement [25].

Results

Eligible Studies

Our search yielded 440 abstracts from PubMed or Scopus and 3 reports from the New York Academy of Medicine Grey Literature Report site. We excluded 355 articles based on the title or abstract and 3 reports that were not relevant to our research questions. We retrieved 85 full-text articles, of which we excluded 67 articles. Thus, we finally included 18 eligible papers on 17 studies [2,3,7,9,15,26-38] (Figure).

Characteristics of Eligible Studies

The studies were conducted between 2000 and 2012. Twelve studies recruited their participants in Europe, 4 in

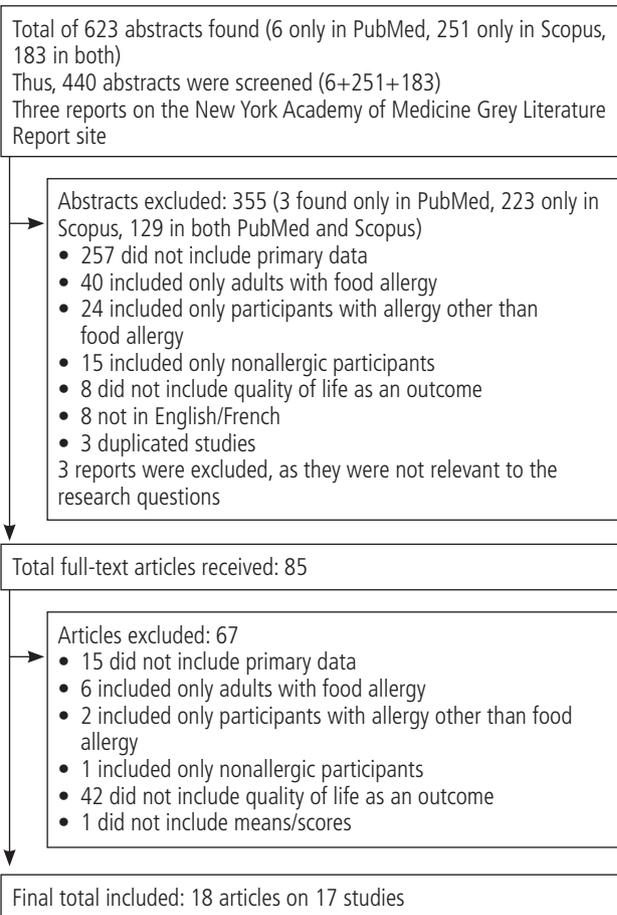


Figure. Flow diagram of the study selection process.

North America, and 1 in China (Table 1). Seven studies were designed as surveys (response rate ranging from 50.5% to 97%), 6 were cross-sectional questionnaire studies, 3 were case-control studies, and 1 was a birth cohort. Seven studies evaluated HRQoL only in children, 2 only in parents, and 8 in both children and their parents. The sample size for children ranged between 20 and 271 (median [IQR], 153 [56-205]). The sample size for parents ranged between 29 and 253 (median, 60 [42-141]).

Population Characteristics

The mean age for children ranged between 1.94 and 15.3 years, and the percentage of boys between 17% and 67% (median, 57% [53%-60%]) (Table 1). The parents' age was not mentioned in any of the studies.

Nine studies reported on children's comorbidities [2,7,9,27,30,31,33,36,38]. The type of allergy symptoms was reported in 11 studies [2,3,7,15,29,30,32,35-38], the type of food allergies in 14 [2,3,7,15,26,27,29-31,33-37], the frequency of allergic episodes in 1 [32], and the severity of food allergy in 4 [7,29,30,37]. Seven studies reported the parent's level of education [27,29-31,34,36,38], and 4 reported socioeconomic status [29,34,36,38].

Table 1. Characteristics of Eligible Studies

Publication	Study Design	Sample Size: Children/ Parents ^a	Children's Mean (SD) Age, y	Boys, %	Food Allergy Definition
Knibb et al 2012 [33] UK	Case-control	103/103 (m)	11.7 (3.0)	56	Physician-diagnosed based on positive skin prick test and/or specific IgE to peanuts or tree nuts
Roy and Roberts 2011 [34] USA	Cross-sectional questionnaire study	48/51	8.1 (1.8)	50	Physician-diagnosed peanut allergy
Van der Velde et al 2011 [35] The Netherlands	Cross-sectional questionnaire study	74/74	10.4 (1.6)	62	Physician-diagnosed
Van der Velde et al 2011 [36] The Netherlands	Cross-sectional questionnaire study	70/70	15.3 (1.2)	43	Physician-diagnosed based on positive skin prick test or food specific serum IgE or food challenge (70%). Patient reported as physician-diagnosed food allergy (30%)
Valentine and Knibb 2011 [37] UK	Cross-sectional questionnaire study	34/29	9 (1.2)	50	Physician-diagnosed based on positive skin prick test or food challenge
Komulainen 2010 [38] Finland	Survey	104/104	1.9 (0.8)	67	Parent-reported
Flokstra de Blok et al 2010 [3,28] The Netherlands	Survey	153 (79 children, 74 adolescents) /ND	12.4 (2.6) (for both children and adolescents)	52	Confirmed by positive double-blind placebo-controlled food challenge (25%) Physician-diagnosed based on history and positive skin prick or blood test (22%) Patient reported as physician-diagnosed food allergy (53%)
Cummings et al 2010 [2] UK	Cross-sectional questionnaire study	41/41 (m)	10.9 (3.1)	56	Physician-diagnosed based on positive skin prick test or food specific serum IgE
Dunngalvin et al 2009 [29] US	Case-control	65/65 (m)	6.7 (3.6)	60	Physician-diagnosed based on positive skin prick test or food-specific serum IgE
Leung et al 2009 [31] China	Survey	197/197	4.2 (6.9)	54	Parent-reported
King et al 2009 [30] UK	Cross-sectional questionnaire study	46/92 (b)	9.8 (ND) Range, 8-12	65	Physician-diagnosed based on history and positive skin prick test or food specific serum IgE
Ostblom et al 2008 [32] Sweden	Birth cohort	212 / 212 ^b	9.0 ^c	58	Parent-reported
Marklund et al 2006 [7] Sweden	Survey	134/134	12.5 (2.6)	17	Parent-reported
Marklund et al 2004 [15] Sweden	Survey	271/NA	ND ^d	ND	Patient-reported
Avery et al 2003 [26] UK	Case-control (pilot study)	20/NA	9.0 (ND) Range, 7-12	45	Allergy clinic medical records reporting patients' allergic reaction to peanuts
Sicherer et al 2001 [9] US	Survey	253/253	10.8 Range, 5-18	59	Members of the Food Allergy and Anaphylaxis Network

Continuation

Publication	Study Design	Sample Size: Children/ Parents ^a	Children's Mean (SD) Age, y	Boys, %	Food Allergy Definition
Primeau et al 2000 [27] Canada	Survey	153/153	6.4 (4.0)	60	History of allergic reaction after exposure to peanut and positive skin prick test or peanut specific serum IgE

Abbreviations: NA, not applicable; ND, no data.

^a(m), only the mother of each child completed the HRQoL questionnaire; (f), only the father of each child completed the HRQoL questionnaire; (b), both mother and father of each child completed the HRQoL questionnaire; if no (m) or (f) or (b) either mother and or father of each child completed the HRQoL questionnaire.

^bNumeric data on HRQoL are given for 203 out of the 212 children with pronounced food hypersensitivity and their parents.

^cIn this cohort all children were 9 years old.

^dOut of 1488 adolescents who completed the quality of life questionnaire in this study, 271 (19%) reported food hypersensitivity. For the total sample (1488 adolescents), mean age (16.2 years) and age range (13-21 years) were given; however, for the subgroup of 271 hypersensitive children age was not reported.

Methods for Diagnosis of Food Allergy in Children

Methods for diagnosis of food allergy were heterogeneous (Table 1). Diagnosis was based on the physician's assessment and positive skin prick test or food specific serum/blood IgE results in 9 studies [2,27,29-33,36,37]. Four studies accepted parent-reported diagnosis [7,31,32,38], and another used patient-reported diagnosis [15]. In one study, the diagnosis was based on the medical records of the allergy clinic [26], and in another, members of the Food Allergy and Anaphylaxis Network were recruited [9]. One study used the patient-reported diagnosis in 53% of the participants, a positive skin prick test result or food-specific serum IgE in 22%, and a positive double-blind, placebo-controlled food challenge result in 25% [3,28].

Quality of Life in Children

Fifteen studies reported HRQoL for 24 groups of children (Table 2). The total HRQoL score for children was reported in 8 studies [2,3,26-29,33,34,37], total HRQoL scores for children with food allergy and normative data [34] or data from a control group [37] were compared in 2 studies, 6 provided formal comparisons between HRQoL questionnaire subdomain scores and normative data [2,3,9,28,30,34], and 1 compared HRQoL questionnaire subdomain scores with control group data [37].

Roy and Roberts [34] found that parents replying on behalf of their children reported poorer emotional health ($P < .001$) but better physical health ($P < .001$) than the normative data. Van der Velde et al [35] correlated the child and parent proxy reports and found that the total score for the Food Allergy Quality of Life Questionnaire Child Form (FAQLQ-CF) was significantly higher than the total score for the Food Allergy Quality of Life Questionnaire Parent Form (FAQLQ-PF) ($P < .001$). Additionally, all domain scores of the FAQLQ-CF were significantly higher than the domain scores of the FAQLQ-PF. In contrast, no significant differences were detected between the total score on the Food Allergy Quality of Life Questionnaire Teenager Form and that of the Food Allergy Quality of Life Questionnaire Parent Form Adolescent ($P = .103$); however, the correlation between them was moderate

to good [36]. Valentine and Knibb [37] found that children with food allergy had better physical functioning ($P < .05$) than the control group. Flokstra de Blok et al [28] reported that food-allergic children and adolescents experienced fewer limitations in schoolwork due to behavioral problems ($P < .05$ and $P < .01$, respectively); however, food-allergic adolescents reported more bodily pain ($P < .05$) and poorer overall health ($P < .01$).

Cummings et al [2] found that children with nut allergy had poorer total HRQoL ($P = .046$) and poorer emotional health ($P = .004$), social health ($P = .043$), and psychological health ($P = .006$). King et al [30] reported that children with peanut allergy had poorer emotional health ($P < .05$) and psychological health ($P < .05$) [30]. Ostblom et al [32] assessed 3 separate groups of children (group A, food-related symptoms affecting the lower airways; group B, food-related symptoms at least once a month; group C, at least 2 different symptoms). For all groups, the children with food hypersensitivity had significantly worse physical functioning ($P < .001$), more school/ social limitations due to physical problems ($P < .001$), more social limitations ($P < .05$), more pain ($P < .05$), and poorer mental health ($P < .01$) and general health ($P < .001$) than children with no allergic diseases. Sicherer et al [9] showed that parental perception of children's general health ($P < .001$) and mental health ($P < .001$) was worse than US normative data [9]. Finally, Primeau et al [27] reported that 53% of children were below the population average in the subdomain scores.

Quality of Life in Parents

Ten studies reported HRQoL for 13 groups of parents (Table 3). Three studies reported a total HRQoL score [2,33,38]. There were no comparisons between total HRQoL scores for parents and normative data. Four out of the 9 studies provided formal comparisons between scores in HRQoL questionnaire subdomains for parents of food-allergic children and normative [2,9,30] or control data [37]. Valentine and Knibb [37] found that parents of food-allergic children had worse social relationships and overall quality of life than the control group ($P < .05$). Cummings et al [2] reported better scores in

Table 2. Quality of Life for Children With Food Allergy

Study	Instrument/ Score Direction	Sample Domain, Score Range [Worst, Best]	QoL Score, mean (SD)		P Value	
			Study Participants	Normative Data ^a		
Knibb et al 2012 [33]	PedsQL/generic	<i>31 food-challenged children</i> Total [0, 100]	77.7 (9.7)	ND	ND	
		<i>50 non-food-challenged children</i> Total [0, 100]	78.7 (12.2)	ND	ND	
	Avery questionnaire [25]/ disease specific	<i>31 food-challenged children</i> Total [100, 25] <i>50 non-food challenged children</i> Total [100, 25]	47.2 (8.5) 51.1 (7.4)	NA NA	NA NA	
Roy and Roberts 2011 [34]	PedsQL/generic	<i>48 peanut-allergic children</i> • Physical functioning [0, 100] • Psychosocial health [0, 100] • Emotional functioning [0, 100] • Social functioning [0, 100] • School functioning [0, 100] Total [0, 100]	88.1 (11.7) 79.1 (13.0) 73.9 (16.0) 82.3 (15.6) 81.3 (14.9) 82.4 (11.7)	87.8 (13.1) 81.8 (14.0) 79.2 (18.0) 85.0 (16.7) 81.3 (16.1) 83.9 (12.5)	.29 .15 .02 .24 .99 .36	
		<i>51 proxy parents of peanut-allergic children</i> • Physical functioning [0, 100] • Psychosocial health [0, 100] • Emotional functioning [0, 100] • Social functioning [0, 100] • School functioning [0, 100] Total [0, 100]	90.0 (11.6) 79.5 (12.0) 70.5 (15.7) 84.4 (14.4) 83.5 (14.0) 83.1 (10.5)	84.1 (19.7) 81.2 (15.3) 81.2 (16.4) 83.1 (19.7) 78.3 (19.6) 82.3 (15.6)	<.001 ^b .30 <.001 ^b .50 <.01 .57	
Van der Velde et al 2011 [35]		FAQLQ-CF/ disease-specific	<i>74 food-allergic children</i> • Allergen avoidance [7, 1] • Risk of accidental exposure [7, 1] • Emotional impact [7, 1] • Dietary restrictions [7, 1] Total [7, 1]	3.4 (1.4) 3.8 (1.6) 4.1 (1.6) 3.7 (1.4) 3.7 (1.3)	NA	NA
		FAQLQ-PF/ disease-specific	<i>74 proxy parents of food-allergic children</i> • Emotional impact [7, 1] • Food anxiety [7, 1] • Social and dietary limitations [7, 1] Total [7, 1]	2.6 (1.0) 3.0 (1.2) 2.5 (1.3) 2.7 (1.0)	NA	NA
Van der Velde et al 2011 [36]		FAQLQ-TF/ disease-specific	<i>70 food-allergic adolescents</i> • Allergen avoidance/dietary restrictions [7, 1] • Risk of accidental exposure [7, 1] • Emotional impact [7, 1] Total [7, 1]	3.9 (1.5) 3.7 (1.6) 3.7 (1.6) 3.8 (1.4)	NA	NA
		FAQLQ-PFA/ disease-specific	<i>70 proxy parents of food-allergic adolescents</i> • Dietary restrictions [7, 1] • Food anxiety [7, 1] • Social restrictions [7, 1] • Emotional impact [7, 1] Total [7, 1]	4.2 (1.4) 3.8 (1.1) 3.2 (1.3) 3.1 (1.2) 3.6 (1.1)	NA	NA
Valentine and Knibb 2011 [37]	PedsQL™/ generic	<i>34 food-allergic children</i> • Physical functioning [0, 100] • Psychosocial health [0, 100] • Emotional functioning [0, 100] • Social functioning [0, 100] • School functioning [0, 100] Total [0, 100]	93.7 (7.4) 78.1 (11.8) 70.1 (14.5) 83.8 (15.4) 80.3 (14.5) 83.5 (8.9)	87.1 (10.5) 76.6 (13.5) 70.7 (14.8) 82.9 (14.5) 76.1 (16.9) 80.2 (11.4)	<.05 NS NS NS NS NS	

Continuation

Study	Instrument/ Score Direction	Sample Domain, Score Range [Worst, Best]	QoL Score, mean (SD)		P Value
			Study Participants	Normative Data ^a	
Flokstra de Blok et al 2010 [3,28]	CHQ-CF87/ generic	<i>79 food-allergic children</i>			
		• Physical functioning [0, 100]	96.0 (8.2)	98 (4)	ND
		• Role functioning-emotional [0, 100]	94.9 (14.3)	94 (15)	ND
		• Role functioning-behavior [0, 100]	95.0 (12.7)	93 (11)	.005
		• Role functioning-physical [0, 100]	94.9 (14.2)	97 (9)	ND
		• Bodily pain [0, 100]	76.8 (24.7)	82 (18)	ND
		• General behavior [0, 100]	84.0 (12.5)	85 (9)	ND
		• Mental health [0, 100]	78.5 (13.1)	81 (12)	ND
		• Self-esteem [0, 100]	79.4 (13.8)	77 (12)	ND
		• General health [0, 100]	72.0 (19.2)	78 (14)	ND
		• Family activities [0, 100]	86.9 (14.7)	ND	ND
		• Family cohesion [0, 100]	80.9 (18.6)	75.7 (23.1)	ND
Total [0, 100]	ND	ND	ND		
	CHQ-CF87/ generic	<i>74 food-allergic adolescents</i>			
		• Physical functioning [0, 100]	94.4 (10.5)	98 (4)	ND
		• Role functioning-emotional [0, 100]	91.4 (18.4)	94 (15)	ND
		• Role functioning-behavior [0, 100]	94.3 (15.4)	93 (11)	.013
		• Role functioning-physical [0, 100]	92.9 (20.9)	97 (9)	ND
		• Bodily pain [0, 100]	70.0 (23.3)	82 (18)	.020
		• General behavior [0, 100]	80.6 (10.4)	85 (9)	ND
		• Mental health [0, 100]	74.6 (13.7)	81 (12)	ND
		• Self-esteem [0, 100]	70.8 (14.4)	77 (12)	ND
		• General health [0, 100]	64.4 (18.8)	78 (14)	<.001
		• Family activities [0, 100]	84.8 (16.1)	ND	ND
		• Family cohesion [0, 100]	73.4 (21.3)	75.7 (23.1)	ND
Total [0, 100]	ND	ND	ND		
	FAQLQ-CF/ disease-specific	<i>79 food-allergic children</i>			
		• Allergen avoidance [7, 1]	3.6 (1.6)	NA	NA
		• Risk of accidental exposure [7, 1]	4.2 (1.7)		
		• Emotional impact [7, 1]	4.0 (1.7)		
		• Dietary restrictions [7, 1]	4.2 (1.6)		
Total [7, 1]	4.0 (1.4)				
	FAQLQ-TF/ disease-specific	<i>74 food-allergic adolescents</i>			
		• Allergen avoidance [7, 1]	4.0 (1.4)	NA	NA
		• Risk of accidental exposure [7, 1]	4.2 (1.3)		
		• Emotional impact [7, 1]	4.4 (1.5)		
		Total [7, 1]	4.2 (1.2)		
Cummings et al 2010 [2]	Avery questionnaire [25]/disease-specific	<i>41 nut-allergic children</i> Total [100, 25]	50.6 (8.4)	NA	NA
	PedsQL/generic	<i>41 nut-allergic children</i>			
		• Physical functioning [0, 100]	84.1 (10.8)	84.4 (17.3)	.855
		• Psychosocial health [0, 100]	75.7 (13.6)	82.1 (15.7)	.006
		• Emotional functioning [0, 100]	71.2 (19.8)	81.0 (19.5)	.004
		• Social functioning [0, 100]	81.3 (16.5)	86.8 (17.5)	.043
		• School functioning [0, 100]	74.6 (14.3)	78.2 (20.7)	.127
		Total [0, 100]	78.8 (11.7)	82.8 (15.0)	.046
Dunngalvin et al 2009 [29]	FAQLQ-PF/ disease-specific	<i>16 parents of children (0-3 years old)</i> <i>who declined to take part in clinical studies</i> Total [6, 0]	3.2 (3.4)	NA	NA
		<i>7 parents of children (0-3 years old)</i> <i>who agreed to take part in clinical studies</i> Total [6, 0]	3.4 (3.5)	NA	NA

Continuation

Study	Instrument/ Score Direction	Sample Domain, Score Range [Worst, Best]	QoL Score, mean (SD)		P Value	
			Study Participants	Normative Data ^a		
Dunngalvin et al 2009 [29]	FAQLQ-PF/ disease-specific	<i>17 parents of children (4-6 years old) who declined to take part in clinical studies</i>				
		• Emotional impact [6, 0]	3.1 (2.4)	NA	NA	
		• Food anxiety [6, 0]	3.6 (3.1)			
		• Social and dietary limitations [6, 0]	3.0 (2.2)			
		Total [6, 0]	3.3 (4.1)			
		<i>13 parents of children (4-6 years old) who agreed to take part in clinical studies</i>				
		• Emotional impact [6, 0]	3.2 (3.1)	NA	NA	
		• Food anxiety [6, 0]	3.7 (2.3)			
		• Social and dietary limitations [6, 0]	3.2 (3.8)			
		Total [6, 0]	3.5 (4.3)			
		<i>7 parents of children (7-12 years old) who declined to take part in clinical studies</i>				
		• Emotional impact [6, 0]	3.5 (2.5)	NA	NA	
		• Food anxiety [6, 0]	3.3 (3.4)			
		• Social and dietary limitations [6, 0]	4.1 (2.6)			
		Total [6, 0]	3.5 (3.8)			
		<i>5 parents of children (7-12 years old) who agreed to take part in clinical studies</i>				
		• Emotional impact [6, 0]	3.4 (3.5)	NA	NA	
		• Food anxiety [6, 0]	3.5 (4.2)			
		• Social and dietary limitations [6, 0]	3.9 (2.5)			
		Total [6, 0]	3.7 (4.2)			
King et al 2009 [30]	PedsQL/ generic ^c	<i>46 peanut-allergic children</i>				
		• Physical functioning [0, 100]	86.3 (14.2)	84.4 (17.3)	NS	
• Psychosocial health [0, 100]		78.0 (13.5)	82.1 (15.7)	<.05		
• Emotional functioning [0, 100]		76.1 (15.7)	81.0 (19.5)	<.05		
• Social functioning [0, 100]		83.4 (16.6)	86.8 (17.5)	NS		
• School functioning [0, 100]		74.2 (16.0)	78.2 (20.7)	NS		
		Total [0, 100]	81.1 (12.9)	82.8 (15.0)	NS	
	Avery questionnaire [25]/disease- specific ^c	<i>46 peanut-allergic children</i> Total [100, 25]	51.1 (7.5)	NA	NA	
Ostblom et al 2008 [32]	CHQ-PF28/ generic	<i>32 parents of children with food hypersensitivity and food-related symptoms affecting the lower airways</i>				
		• Physical functioning [0, 100]	88.1 (ND)	ND	<.001	
		• Role-social/emotional, behavioral [0, 100]	83.3 (ND)	ND	<.05	
		• Role functioning-physical [0, 100]	81.2 (ND)	ND	<.001	
		• Bodily pain [0, 100]	78.8 (ND)	ND	<.05	
		• General behavior [0, 100]	64.3 (ND)	ND	ND	
		• Mental health [0, 100]	69.8 (ND)	ND	<.01	
		• Self-esteem [0, 100]	75.8 (ND)	ND	ND	
		• General health [0, 100]	62.3 (ND)	ND	<.001	
		• Change in health [0, 100]	58.6 (ND)	ND	ND	
		<i>70 parents of children with food hypersensitivity and food-related symptoms at least once each month</i>				
		• Physical functioning [0, 100]	91.0 (ND)	ND	<.001	
		• Role-social/emotional, behavioral [0, 100]	89.2 (ND)	ND	<.05	
		• Role functioning-physical [0, 100]	86.8 (ND)	ND	<.001	
		• Bodily pain [0, 100]	72.1 (ND)	ND	<.05	
		• General behavior [0, 100]	65.3 (ND)	ND	ND	
		• Mental health [0, 100]	71.1 (ND)	ND	<.01	
		• Self-esteem [0, 100]	79.0 (ND)	ND	ND	
		• General health [0, 100]	72.8 (ND)	ND	<.001	
		• Change in health [0, 100]	56.7 (ND)	ND	ND	

Continuation

Study	Instrument/ Score Direction	Sample Domain, Score Range [Worst, Best]	QoL Score, mean (SD)		P Value
			Study Participants	Normative Data ^a	
Ostblom et al 2008 [32]	CHQ-PF28/ generic	<i>101 parents of children with food hypersensitivity and at least two different reported symptoms</i>			
		• Physical functioning [0, 100]	90.0 (ND)	ND	<.001
		• Role-social/emotional, behavioral [0, 100]	87.8 (ND)	ND	<.05
		• Role functioning-physical [0, 100]	86.5 (ND)	ND	<.001
		• Bodily pain [0, 100]	77.7 (ND)	ND	<.05
		• General behavior [0, 100]	64.8 (ND)	ND	ND
		• Mental health [0, 100]	68.2 (ND)	ND	<.01
		• Self-esteem [0, 100]	77.6 (ND)	ND	ND
		• General health [0, 100]	67.5 (ND)	ND	<.001
	• Change in health [0, 100]	56.4 (ND)	ND	ND	
Marklund et al 2006 [7]	CHQ-PF28/ generic	<i>220 parents of food hypersensitivity Children</i>			
		• Physical functioning [0, 100]	87.6 (20.2)	ND	ND
		• Role-social/emotional, behavioral [0, 100]	90.2 (20.0)	ND	ND
		• Role functioning-physical [0, 100]	86.9 (24.9)	ND	ND
		• Bodily pain [0, 100]	74.8 (23.0)	ND	ND
		• General behavior [0, 100]	68.1 (17.0)	ND	ND
		• Mental health [0, 100]	72.0 (15.3)	ND	ND
		• Self-esteem [0, 100]	77.7 (17.4)	ND	ND
		• General health [0, 100]	70.9 (23.4)	ND	ND
		• Physical summary measure [0, 100]	49.8 (11.7)	ND	ND
		• Psychosocial summary measure, [0, 100]	49.6 (9.4)	ND	ND
Marklund et al 2004 [15]	SF-36/ generic	Results are given only in the graph	ND	ND	ND
Avery et al 2003 [26]	Avery questionnaire [25]/ disease specific	<i>20 peanut-allergic children</i> Total [100, 25]	54.9 (ND)	NA	NA
	Adapted from VQLQ/ disease specific for vespid Allergy	<i>20 peanut-allergic children</i> Total [0, 100]	54.3 (ND)	NA	NA
Sicherer et al 2001 [9]	CHQ-PF50/ generic	<i>253 parents of food-allergic children</i>			
		• Physical functioning [0, 100]	95.7 (ND)	96.5 (ND)	.53
		• Role-social/emotional, behavioral [0, 100]	92.8 (ND)	92.5 (ND)	.79
		• Role functioning-physical [0, 100]	91.3 (ND)	93.6 (ND)	.06
		• Bodily pain [0, 100]	79.2 (ND)	81.7 (ND)	.07
		• General behavior [0, 100]	78.3 (ND)	75.6 (ND)	.02
		• Mental health [0, 100]	75.1 (ND)	78.5 (ND)	.0001
		• Self-esteem [0, 100]	80.2 (ND)	79.8 (ND)	.75
• General health [0, 100]	59.3 (ND)	73.0 (ND)	<.0001		
Primeau et al 2000 [27]	CHQ-PF50/ generic	<i>153 parents of peanut-allergic children</i> Total [0, 100]	50.5 (7.5)	ND ^d	ND
	VAS adapted from the EuroQoL-5D/ generic	<i>153 parents of peanut-allergic children</i> Total [100, 0]	37.3 (ND)	ND	ND

Abbreviations: CHQ, Child Health Questionnaire; CHQ-CF, Child Health Questionnaire Child Form; EuroQoL-5D, European Quality of Life questionnaire – 5 Domains; FAQLQ-CF, Food Allergy Quality of Life Questionnaire Child Form; FAQLQ-PF, Food Allergy Quality of Life Questionnaire Parent Form; FAQLQ-PFA, Food Allergy Quality of Life Questionnaire Parent Form–Adolescent version; FAQLQ-TF, Food Allergy Quality of Life Questionnaire Teenager Form; NA, not applicable; ND, no data; NS, nonsignificant; PedsQL, Paediatric HRQoL Inventory; QoL, quality of life; SF-36 Short-Form 36 Health Survey; VAS, visual analog scale; VQLQ, Vespider Allergy Quality of Life Questionnaire.

^aNormative data: Roy et al, 2011: 5079 healthy US children aged 2-16 years, 8713 parents of US children aged 2-16 years; Valentine and Knibb, 2011: control group of 14 children without food allergy recruited via advertisements at universities in the East Midlands and out of school clubs in the UK; Flokstra de Blok et al, 2010: 281 children without chronic diseases aged 9-17 years; Cummings et al, 2010: 699 healthy US children aged 5-16 years; Ostblom et al, 2008: from population with no current report of food hypersensitivity or any other allergic disease (normative data scores are given only in bar chart; however, numeric P-values for their comparison with the study population corresponding scores are provided); King et al, 2009: 699 healthy US children aged 5-16 years; Marklund et al, 2006: from general US child population sample; Sicherer, 2001: from US population sample

^bFor Roy and Roberts, 2011, statistically significant comparisons correspond to a P value \leq .008

^cParents completed the Avery scale and PedsQL as a proxy measure for the child with peanut allergy.

^dIn this study, 53% of children were below the population average.

Table 3. Quality of Life for Parents of Children With Food Allergy

Study	Instrument	Sample Domain, Score Range [Worst, Best]	QoL Score, mean (SD)		P Value
			Study Participants	Normative Data ^a	
Knibb et al 2012 [33]	FAQL-PB /disease specific	<i>Mothers of 31 food-challenged children</i> Total [119, 17]	47.1 (15.5)	NA	NA
		<i>Mothers of 50 non-food-challenged children</i> Total [119, 17]	57.7 (21.4)	NA	NA
	WHOQOL-BREF/ generic	<i>Mothers of 31 food-challenged children</i> • Psychological health [0, 100] <i>Mothers of 50 non-food-challenged children</i> • Psychological health [0, 100]	69.4 (13.5) 67.3 (13.2)	ND ND	ND ND
Valentine and Knibb 2011 [37]	WHOQOL-BREF/ generic	<i>29 parents of food-allergic children</i> • Physical health [4, 20]	17.2 (1.9)	18.0 (1.2)	NS
		• Psychological health [4, 20]	15.7 (1.5)	15.8 (1.3)	NS
		• Social relationships [4, 20]	14.5 (3.2)	16.5 (2.8)	<.05
		• Environmental health [4, 20]	15.8 (1.7)	15.5 (1.5)	NS
		• Overall QoL [1, 5]	4.1 (0.6)	4.5 (0.5)	<.05
		• Satisfaction with health [1, 5]	4.0 (0.8)	4.3 (0.6)	NS
		Total [0, 100]	ND	ND	ND
Komulainen 2010 [38]	FAQL-PB/disease- specific	<i>104 parents of food-allergic children</i> Total [119, 17]	2.8 (1.9) ^b	NA	NA
		Cummings et al 2010 [2]	FAQL-PB/disease- specific	<i>41 mothers of nut-allergic children</i> Total [119, 17]	56.3 (25.4)
WHOQOL-BREF/ generic	• Physical health [4, 20]			16.8 (2.4)	15.8 (3.8)
	• Psychological [4, 20]		14.7 (2.1)	14.7 (3.4)	.959
	• Social relationships [4, 20]		15.2 (3.2)	14.2 (3.5)	.060
	• Environmental [4, 20]		16.1 (2.3)	14.1 (2.3)	<.001
	• Overall QoL [1, 5]		4.1 (0.6)	ND	ND
• Overall health QoL [1, 5]	3.6 (1.1)		ND	ND	
Total [0, 100]	70.3 (9.1)	ND	ND		
Leung et al 2009 [31]	FAQL-PB/ disease-specific	<i>197 parents of children with adverse food reactions</i> Total [119, 17]	Median 0.1 ^c (IQR, 0.02-0.3)	NA	NA
		King et al 2009 [30]	WHOQOL-BREF/ generic	<i>46 mothers of peanut-allergic children</i> • Physical health [4, 20]	16.7 (2.0)
• Psychological [4, 20]	14.6 (2.1)			14.7 (3.4)	NS
• Social relationships [4, 20]	15.6 (2.3)			14.2 (3.5)	<.05
• Environmental [4, 20]	15.9 (2.1)			14.1 (2.3)	<.05
• Overall QoL [1, 5]	4.3 (0.6)			NA	NA
• Satisfaction with health [1, 5]	3.9 (0.9)			NA	NA
Total [0, 100]	ND			ND	ND
<i>46 fathers of peanut-allergic children</i> • Physical health [4, 20]	17.5 (1.7)		15.8 (3.8)	<.05	
• Psychological [4, 20]	15.9 (1.7)		14.7 (3.4)	<.05	
• Social relationships [4, 20]	15.5 (2.8)		14.2 (3.5)	<.05	
• Environmental [4, 20]	16.1 (2.1)		14.1 (2.3)	<.05	
• Overall QoL [1, 5]	4.2 (0.6)		ND	ND	
• Satisfaction with health [1, 5]	4.0 (0.7)		ND	ND	
Total [0, 100]	ND		ND	ND	
Ostblom et al 2008 [32]	CHQ-PF28/ generic	<i>32 parents of children with food hypersensitivity and food-related symptoms affecting the lower airways</i> • Parental impact-emotional [0, 100]	77.3 (ND)	ND	<.001
		• Parental impact-time [0, 100]	85.3 (ND)	ND	ND
		• Family activities [0, 100]	88.7 (ND)	ND	ND
		• Family cohesion [0, 100]	58.4 (ND)	ND	ND
		Total [0, 100]	ND	ND	ND

Continuation

Study	Instrument	Sample Domain, Score Range [Worst, Best]	QoL Score, mean (SD)		P Value
			Study Participants	Normative Data ^a	
		<i>70 parents of children with food hypersensitivity and food-related symptoms at least once each month</i> <ul style="list-style-type: none"> • Parental impact-emotional [0, 100] • Parental impact-time [0, 100] • Family activities [0, 100] • Family cohesion [0, 100] 	78.3 (ND)	ND	<.001
		<i>101 parents of children with food hypersensitivity and at least 2 different reported symptoms</i> <ul style="list-style-type: none"> • Parental impact-emotional [0, 100] • Parental impact-time [0, 100] • Family activities [0, 100] • Family cohesion [0, 100] 	88.9 (ND)	ND	ND
			86.8 (ND)	ND	ND
			73.1 (ND)	ND	ND
		<i>220 parents of children with food hypersensitivity</i> <ul style="list-style-type: none"> • Parental impact-emotional [0, 100] • Parental impact-time [0, 100] • Family activities [0, 100] • Family cohesion [0, 100] 	75.6 (ND)	ND	<.001
			90.2 (ND)	ND	ND
			88.8 (ND)	ND	ND
			67.1 (ND)	ND	ND
Marklund et al 2006 [7]	CHQ-PF28/generic	<i>220 parents of children with food hypersensitivity</i> <ul style="list-style-type: none"> • Parental impact-emotional [0, 100] • Parental impact-time [0, 100] • Family activities [0, 100] • Family cohesion [0, 100] 	81.9 (20.4)	ND	ND
			90.4 (17.3)	ND	ND
			85.5 (19.2)	ND	ND
			68.8 (25.3)	ND	ND
Sicherer et al 2001 [9]	CHQ-PF50/generic	<i>253 parents of food-allergic children</i> <ul style="list-style-type: none"> • Parental impact-emotional [0, 100] • Parental impact-time [0, 100] • Family activities [0, 100] • Family cohesion [0, 100] 	68.1 (ND)	80.3 (ND)	<.0001
			85.2 (ND)	87.8 (ND)	.04
			73.9 (ND)	89.7 (ND)	<.0001
			79.3 (ND)	72.3 (ND)	<.0001
Primeau et al 2000 [27]	CHQ-PF50/generic	<i>153 parents of peanut-allergic children</i> <ul style="list-style-type: none"> • Parental impact-emotional [0, 100] • Parental impact-time [0, 100] • Family activities [0, 100] • Family cohesion [0, 100] 	ND	ND	ND
			ND	ND	ND
			ND	ND	ND
			ND	ND	ND

Abbreviations: QoL, quality of life; SD, standard deviation; IQR, interquartile range; ND, no data; NA, not applicable; FAQL-PB, Food Allergy Quality of Life- Parental Burden questionnaire; WHOQOL-BREF, World Health Organization Quality of Life Scale (brief version); CHQ-PF Child Health Questionnaire Parent Form

^aNormative data: Valentine and Knibb, 2011: control group of 13 parents of children without food allergy recruited via advertisements at universities in the East Midlands and school clubs in the UK; Flokstra de Blok et al, 2010: parents of 281 children without chronic diseases aged 9-17 years; Cummings et al, 2010: from the UK adult healthy population adjusted for age and sex; King et al, 2009: from the UK adult healthy population adjusted for age and sex; Sicherer et al 2001: from a US population sample.

^bTotal score was calculated after the provision of additional data by the authors.

^cMedian (IQR) corresponds to the minimal clinically important difference.

physical health ($P=.015$) and environmental health ($P<.001$) for mothers than UK normative data [2]. King et al [30] found that both mothers and fathers reported better physical, social, and environmental health ($P<.05$). Cummings et al also found that fathers reported better psychological health ($P<.05$). In contrast, Ostblom et al [32] found that parents of children with food hypersensitivity scored worse on parental emotional impact ($P<.001$) than parents of children with no allergic diseases. In their comparison with US normative data, Sicherer et al [9] showed that parents had a worse score on the parental emotional impact subscale ($P<.0001$), on the subscale for parental impact on time ($P<.04$), and on the subscale for limitations in usual family activities ($P<.0001$). The family cohesion subscale score was also worse ($P<.0001$).

Discussion

Few studies have assessed HRQoL in children and adolescents with food allergy and their parents. Formal comparisons with normative data were reported only for subdomains in the studies that used generic HRQoL instruments. Populations with food allergy scored worse in specific HRQoL subdomains such as bodily pain, physical functioning, mental health, general health, and, emotional, social, and psychological health. Children with food allergy performed better in physical health and had fewer limitations in schoolwork due to behavioral problems. Parents performed better than the normative population in subdomains including physical and environmental health, social and psychological

health, and family cohesion, but worse on social health, overall quality of life, emotional health, impact on parental time, and limitations in usual family activities. Significant subdomain differences were not supported by all the studies.

Studies directly comparing HRQoL for children or adolescents and their parents with normative data were limited. Owing to the diversity of HRQoL instruments, a quantitative synthesis of subdomain scores would be difficult to interpret and was also discouraged by the fact that many studies with generic instruments did not report the total HRQoL score for normative data. Data supporting a potential association between the HRQoL of children and that of their parents were also insufficient to be combined for a formal correlation test, since total HRQoL scores were not reported for parents in most of the studies, either by a generic or a disease-specific questionnaire.

Significant differences in certain subdomains were reported by several studies; however, these results were not consistently reported by all the studies that examined the same HRQoL subdomain, and, therefore, should be interpreted with caution. Additional studies with sufficient sample size are needed to confirm these results. Furthermore, children and parents may not always perceive a statistically significant difference in HRQoL score as a clinically important difference. The minimal clinically important difference (MCID) model has been proposed to facilitate identification of differences in the interpretation of HRQoL scores by interpreting changes in scores over time or differences in scores between patients [16]. One study did report the results as the MCID, although it did not use the MCID to interpret changes in score but as a benchmark of good or bad HRQoL [31].

It is also unclear whether a significant difference can be attributed to food allergy or not. Generic questionnaires do not separate the impact of the disease in question on HRQoL from the impact of comorbid diseases [39,41]. HRQoL measured using generic instruments tends to ignore limitations of lifestyle and the psychological burden of diseases such as food allergy [28]. Therefore, generic questionnaires could tend to show that HRQoL for persons with the disease remained unaffected. It is encouraging that food allergy-specific tools in Europe and in the US have recently been developed and validated [16,18,19,21,42,43].

The study populations may not be representative of all children with food allergy. For example, members of the Food Allergy and Anaphylaxis Network [9] might be more concerned about their child's food allergy or may not be negatively affected if a factor such as good social support network is present. Unfortunately, HRQoL questionnaires cannot identify whether good HRQoL can be attributed to an external support system. Regular feedback by peer groups may lower the burden of the disease and contribute to equally good or even better HRQoL than normative data [9]. Similarly, patients with physician-diagnosed food allergy who are receiving medical care and advice and—potentially—support from a dietician might report a different HRQoL compared with those not receiving this support.

Our review is subject to several limitations. First, a limited number of studies had small sample sizes. Second, our search may have missed some articles. However, our search based on the New York Academy of Medicine Grey Literature Report

site and on the references of the retrieved papers did not yield additional data. Third, power calculations were invariably lacking; therefore, the significance or lack of significance for an association may be due to chance. Fewer significant results may also have been reported if adjustments to multiple comparisons are considered; however, adjustments were generally not described. Fourth, in addition to the diversity of HRQoL instruments, the definition of food allergy was also heterogeneous. In several studies, the diagnosis was not based on specific serum IgE or food challenge. This may have affected the robustness of the results, since the participants in several studies may not have confirmed food allergy. Fifth, parents in some studies completed the questionnaires for children's HRQoL; however, since child and parent proxy reports on the child's HRQoL are only moderately correlated, parent proxy HRQoL may not have clearly reflected the child's perception [35-36]. Sixth, the possible score range varied (ie, 0 to 100, 25 to 100, 17 to 119, 0 to 6, and 1 to 7). Unless scores are standardized, they do not allow for direct comparisons. Seventh, most studies did not report potential factors that may have influenced HRQoL for allergic children, such as the type or the amount of food that could have caused an allergic reaction, the severity of the child's symptoms, the number of foods to which the child was allergic (single or multiple allergies), or the time since the diagnosis. Eighth, several of the analyses omitted gender differences, comorbidities, and potential cultural and socioeconomic modifiers. Finally, publication bias in favor of studies that report significant differences cannot be excluded.

In conclusion, the HRQoL of children or adolescents with food allergy and of their parents may differ in specific subdomains of generic HRQoL instruments when compared with normative data. However, the results found were limited and were not invariably corroborated by subsequent studies. Future studies need to consider the quality of the study design by ensuring adequate sample size, use of validated questionnaires, robust methods of evaluating food allergy, reporting of clinically meaningful results, and adjustment for potential confounding factors.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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