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### ORIGINAL ARTICLE



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# Health-related quality of life of food-allergic children compared with healthy controls and other diseases

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### **Abstract**

**Background:** Food allergy is a potentially life-threatening disease, affecting up to 10% of the pediatric population.

**Objective:** The aim of our study was to assess the health-related quality of life (HRQL) of food-allergic patients compared with the general population and patients with other chronic diseases with dietary or allergic burden, in a cross-sectional study.

Methods: We recruited patients aged 8–17 years diagnosed with food allergy and matched healthy controls recruited in schools. We also included patients with asthma, inflammatory bowel disease, celiac disease, diabetes, obesity, and eating disorders. We used the CHQ-CF87 questionnaire for generic HRQL assessment. Food allergy HRQL was also assessed using specific questionnaires: Food Allergy Quality of Life Questionnaire (FAQLQ) and Food Allergy Independent Measure (FAIM).

Results: One hundred and thirty-five food-allergic children, 255 children with chronic diseases, and 463 healthy controls were included in the analyses. Food-allergic patients had a better HRQL than healthy controls in the Behavior (BE), Bodily Pain (BP),

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Family Activities (FA), and Mental Health (MH) domains and a worse HRQL in the General Health Perception (GH) domain (p = .048). Food-allergic patients exhibited a better HRQL than patients affected by other chronic diseases, notably diabetes. Although an epinephrine autoinjector had been prescribed to 87.4% of the food-allergic children, only 54.2% of them carried it at all times.

**Conclusion:** Food-allergic patients display overall good HRQL compared with the general population and those with other diseases with daily symptoms and treatments, in line with recent improvements in food allergy management.

#### **KEYWORDS**

children, disease-specific questionnaire, food allergy, generic questionnaire, health-related quality of life

### 1 | INTRODUCTION

Food allergy is a public health problem affecting up to 10% of the pediatric population. Unlike patients with other chronic diseases, food-allergic patients do not have daily or chronic manifestations. Symptoms only occur after an accidental exposure, but can be lifethreatening. Food allergy is a source of stress and anxiety for the parents of food-allergic children, compromising their quality of life. <sup>2,3</sup>

Health-related quality of life (HRQL) is a multidimensional concept, which gives insight into the impact of a disease from the patient's perspective and can be helpful in medical decision-making or disease follow-up. 4-6 The first studies comparing HRQL of foodallergic patients with that of those with other chronic diseases (diabetes mellitus, arthritis) emerged in the 2000s.<sup>7,8</sup> These studies mostly used specific, non-validated questionnaires, making the reliability of comparisons problematic. In 2010, Flokstra-de Blok et al.<sup>9-11</sup> compared HRQL of food-allergic patients included prospectively with that of healthy children and children with other chronic diseases included retrospectively from Dutch studies performed up to eight years earlier. Such a study design could not offer optimal comparison between groups. Food-allergic teenagers (13-17 years) had worse HRQL compared with the general population and those with diabetic teenagers but better HRQL than teenagers with asthma. This result is surprising because although food-allergic and diabetic patients share food restriction issues and potentially life-threatening complications, it would seem that diabetic patients experience more daily constraints related to insulin treatment. Moreover, food-allergic children (8-13 years) demonstrated better HRQL than the general population, also an unexpected finding.

In order to assess the reliability of these results, our aim was to compare, using a cross-sectional method, HRQL of food-allergic patients aged 8–17 years firstly with HRQL of a control pediatric population and secondarily with HRQL of patients affected by other comparable chronic diseases (notably asthma and diseases with dietary impact) using a generic questionnaire, CHQ-CF87. We then

### Key message

We showed that health-related quality of life was globally better in children with food allergy than in the general population. In our cohort, food-allergic patients also showed better health-related quality of life than the patients affected by other chronic diseases. This work is original as no cross-sectional studies using validated questionnaires on this subject have been reported to date.

assessed the relevance of using this questionnaire in our allergic population compared with specific questionnaires, and we assessed the risk factors associated with variation of HROL in food allergy.

### 2 | METHODS

### 2.1 | Subjects

The QUALIFE study was a cross-sectional, comparative, controlled, monocentric study. All subjects and their parents provided informed consent before enrollment, and the regional ethics committee approved the trial protocol (*Comité de Protection des Personnes Sud-Méditerranée* V, ID RCB: 2013-A01033-42). The study was registered in ClinicalTrials.gov (NCT02008643).

We included patients aged 8-17 years followed in a tertiary care center in the South of France. We included patients followed for food allergy, asthma, inflammatory bowel disease, celiac disease, type 1 diabetes, obesity, and eating disorders. Patients with the co-occurrence of another somatic or psychiatric disease were excluded, except for food-allergic patients who also had asthma that was controlled for more than one year.

We then recruited healthy controls aged from 8 to 10 years in primary schools, from 11 to 14 years in junior high schools, and from 15 to 17 years in high schools. All schools were located within the

city limits of Nice. Healthy controls were declared by their parents to have no somatic or psychiatric disease.

### 2.2 | Questionnaire assessment

Generic HRQL was assessed using the CHQ-CF87 questionnaire, translated, and validated in French. This questionnaire allows the assessment of eleven dimensions scored between 1 and 100: Behavior (BE); Bodily Pain/Discomfort (BP); Family Activities (FA); Family Cohesion (FC); General Health Perception (GH); Mental Health (MH); Physical Functioning (PF); Role/Social limitations—Behavioral (RB); Role/Social limitations—Emotional (RE); Role/Social limitations—Physical (RP); and Self-Esteem (SE); and one dimension between 1 and 5: Change in Health (CH). Higher scores are correlated with better HRQL.

Specific HRQL in food-allergic patients was assessed using two questionnaires, the Food Allergy Quality of Life Questionnaire—Child Form (FAQLQ-CF) for children aged 8–12 years and the Food Allergy Quality of Life Questionnaire—Teenager Form (FAQLQ-TF) for adolescents aged 13–17 years. <sup>10,11,13</sup> These self-administered questionnaires allow the assessment of a global score and also a score for each domain. <sup>14,15</sup> Scores run from 1 (minimal impairment of HRQL) to 7 (maximal impairment of HRQL).

The Food Allergy Independent Measure (FAIM)—Child Form (8–12 years; FAIM-CF) and Teenager Form (13–17 years; FAIM-TF) questionnaires<sup>16</sup> were also used. This scale measures the child's perception of the severity of his or her disease. A lower score is associated with a lower perceived disease severity.

### 2.3 | Sample size calculation

Sample size calculation was based on CHQ-CF87 results from two studies by Flokstra-de Blok et al.<sup>6,9</sup> in order to ensure adequate study power to compare HRQL between food-allergic and control children (80% power and 5% type 1 error, accounting for a 2:1 inclusion ratio for controls) (data provided by Dr Flokstra-de Blok). The final sample size was 137 food-allergic patients and 500 controls (see details in Supplemental data 1).

### 2.4 | Statistical analysis

The generic HRQL score from CHQ-CF87, in all its dimensions, was compared between food-allergic patients and healthy controls and between food-allergic patients and chronic disease groups using Student's *t*-test (or the Wilcoxon rank sum test where necessary). No adjustment for multiple testing was carried out, and statistical significance was set at 5%, as reported in a previous study<sup>6</sup> (see details in the supplementary data).

Analyses were performed with SAS Enterprise Guide software, version 7.1 (SAS Institute Inc.).

### 3 | RESULTS

### 3.1 | Description of the cohort

From February 2014 to March 2016, 950 children met the inclusion criteria. Of these, 97 were excluded, as reported in the study flow-chart in Figure 1. The final analysis was made on 135 food-allergic children, 255 children with chronic diseases, and 463 healthy controls.

Demographic features of the cohort are described in Table 1. The mean age was similar in the three groups, approximately 11.6 years (range: 8–17 years). Children were comparable for all parameters except sex ratio. Food allergy was associated with asthma in 87 cases (n = 57 in the 8- to 12-year-old group and n = 30 in the 13- to 17-year-old group).

Table 2 describes the clinical manifestations of food-allergic children and their treatments. For a large majority of children, the ingestion of the triggering food-induced anaphylaxis. 64.4% (87/135) of food-allergic patients were also asthmatic. Children had already experienced a mean of five allergic reactions, of which a mean of three reactions occurred after the diagnosis of food allergy. Although an epinephrine autoinjector had been prescribed to 87.4% of the food-allergic children, only 54.2% of these children carried it with them at all times.

### 3.2 | Comparison of HRQL between food-allergic children and healthy controls

The scores for the different domains of the generic CHQ-CF87 questionnaire are presented in Figure 2 and Supplemental data 2. Food-allergic patients had a better HRQL than healthy controls in the domains of BE, BP, FA, and MH. However, their quality of life was significantly worse in the GH domain. Focusing on the 8- to 12-year-old group, food-allergic children had a better quality of life than controls in the BP domain. In the 13- to 17-year-old group, food-allergic children had a better quality of life than controls in the following domains: BE, FC, MH, RB, and RE. Quality of life for food-allergic children was worse in the GH domain.

### 3.3 | Comparison of HRQL between patients with food allergy and with other chronic diseases

The distribution of mean HRQL scores for each group is represented in Figure 3 and Supplemental data 3.

Food-allergic patients presented significantly worse HRQL than asthmatic patients for one domain: CH.

Food-allergic patients presented significantly better HRQL than (1) asthmatic patients in two domains: PF and RP; (2) diabetic patients in five domains: FA, GH, RB, RP, and SE; (3) obese patients in nine domains: BE, FA, GH, MH, PF, RB, RE, RP, and SE; (4) patients with inflammatory bowel disease in four domains:



### Inclusion objective n=1179

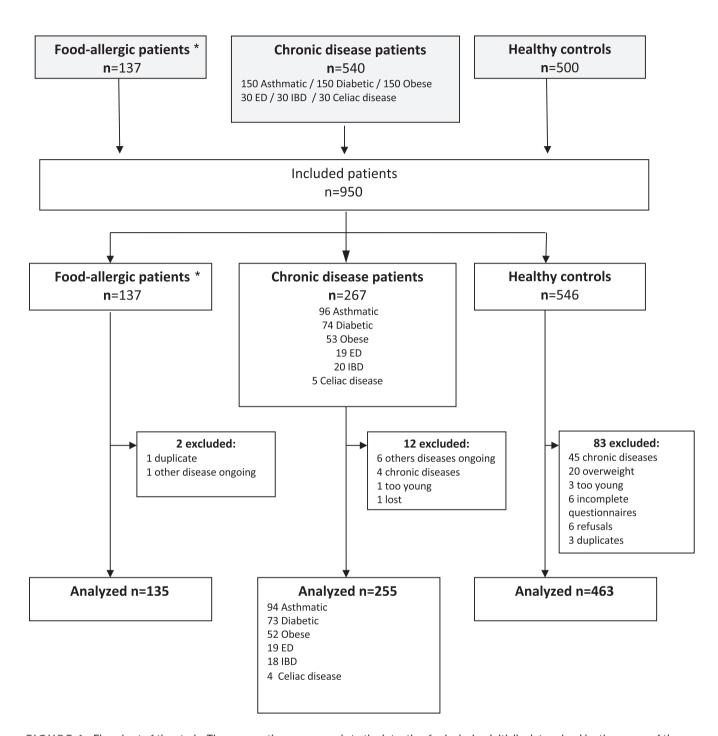


FIGURE 1 Flowchart of the study. The gray section corresponds to the intention for inclusion initially determined by the power of the study. Footnote: ED, eating disorder, IBD, inflammatory bowel disease, \* food-allergic patients with current uncontrolled asthma or severe current atopic dermatitis have not been included

GH, PF, RB, and RE; and (5) patients with eating disorders (ED) in nine domains: BE, FA, FC, GH, MH, PF, RB, RP, and SE. We were not able to compare HRQL in patients with food allergy with that in those with celiac disease because of the small number of patients.

## 3.4 | Correlation with disease-specific HRQL questionnaires in the food-allergic patients

Food Allergy Quality of Life Questionnaire and FAIM scores of foodallergic patients are presented in Table 3 and Supplemental data 4.

**TABLE 1** Demographic characteristics of the cohort

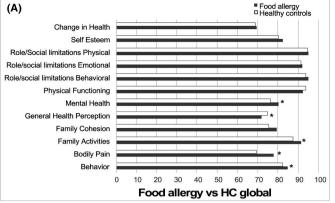
		Total	Food-allergic children	Healthy controls	Chronic diseases
n		853	135	463	255
Age (years)		11.6 (±2.49)	11 (±2.64)	11.6 (±2.29)	12 (±2.69)
Age range	8-12 years	63.70%	67.40%	65.20%	58.80%
	13-17 years	36.30%	32.60%	34.80%	41.20%
Sex	Boys	40.90%	58.50%	30.90%	49.80%
	Girls	59.10%	41.50%	69.10%	50.20%
Weight (kg)		43.95 (±14.58)	40.37 (±13.35)	41.42 (±10.92)	50.24 (±18.37)
Height (cm)		151.2 (±14.26)	146.8 (±14.96)	151.5 (±13.61)	153.2 (±14.56)
Follow-up (years)		6.48 (±3.845)	8.44 (±3.309)	-	5.44 (±3.704)

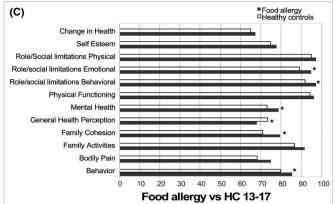
Note: Data are presented as means ( $\pm$ SD) or percentages.

TABLE 2 Description of the food-allergic group

	n	%		Mean	SD
Triggering allergens					
Peanuts	68	50.4	Time between the first reaction and a specialist meeting (months)	10.6	15.25
Nuts	51	37.8	Number of allergen(s) per child	2	1.17
Eggs	37	27.4	Number of food-allergic reactions per child	5	4.3
Cow's milk	27	20	Number of accidental food-allergic reactions per child (after diagnosis)	3	3.8
Kiwi	14	10.4			
Fish	13	9.6	Number of hospitalizations for food-allergic reactions	2	1.7
Goat's milk	8	5.9	Occurring during the previous year	0	0.5
Mustard	6	4.4	Number of hospitalizations in a pediatric care unit	0	0.2
Pine nuts	6	4.4			
Crustaceans	6	4.4		n	%
Legumes	6	4.4	Underwent oral food challenge in a medical environment		
Rosaceae	5	3.7	Yes	85	63
Wheat	5	3.7	No	50	37
Soya	2	1.5	Epinephrine autoinjector		
Other	28	20.7	Yes	118	87.4
Most severe clinical manifestations experienced			No	14	10.4
Anaphylaxis	91	67.4	NA	3	2.2
Angioedema	22	16.3	If yes, is it carried all the time by the child?		
Urticaria	11	8.1	Yes	64	54.2
Anaphylactic shock	5	3.7	No	54	45.8
Digestive manifestations	3	2.2			
Laryngeal edema	2	1.5			
Asthma exacerbation	1	0.7			

Abbreviation: NA, not available.





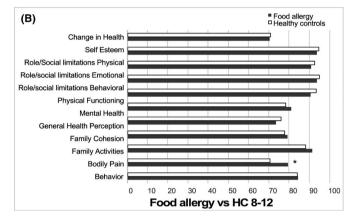


FIGURE 2 Comparison of CHQ-CF87 scores between food allergy and the general population. Histograms comparing CHQ-CF87 domain scores of food-allergic patients with healthy controls in the general population (8–17 years) (A), in the 8- to 12-year-old subgroups (B) and in the 13- to 17-year-old subgroup (C). Food-allergic patients are represented in dark, and the general population is represented in white. A star indicates a significant difference. Footnote: HC, healthy control

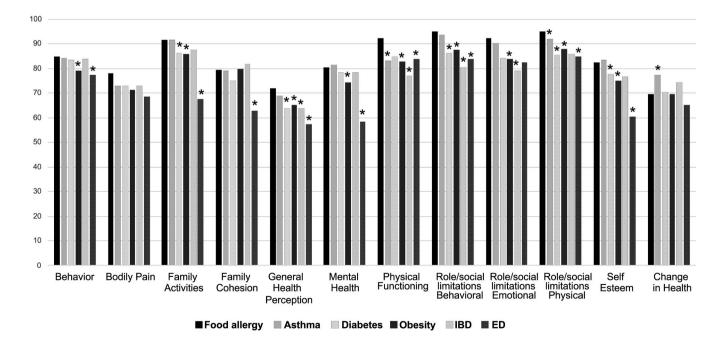


FIGURE 3 Comparison of CHQ-CF87 scores between food allergy and other diseases. Histograms comparing CHQ-CF87 scores for the 12 domains studied of patients with food allergy compared with patients with asthma, diabetes, obesity, inflammatory bowel disease, and eating disorders (in respective order). A star indicates a significant difference. Footnote: ED, eating disorder; IBD, inflammatory bowel disease

TABLE 3 Scores of the FAQLQ-CF and FAQLQ-TF questionnaires in the food-allergic group

FAQLQ-CF	8-12 years old	FAQLQ-TF	13-17 years old
Allergen Avoidance (AA)	3.40 (±1.646)	Allergen Avoidance & Dietary Restrictions (AADR)	3.83 (±1.439)
Risk of Accidental Exposure (RAE)	3.59 (±1.554)	Risk of Accidental Exposure (RAE)	3.39 (±1.491)
Emotional Impact (EI)	4.74 (±1.505)	Emotional Impact (EI)	3.74 (±1.433)
Dietary Restrictions (DR)	3.96 (±1.734)		
Total FAQLQ-CF Score	3.91 (±1.441)	Total FAQLQ-TF score	3.69 (±1.270)

Note: Data are expressed as means ( $\pm$ SD).

Agreement between the generic questionnaire, CHQ-CF87, and the specific questionnaire, FAQLQ, was found for only 20.9% of children (8–12 years old) and 22.7% of teenagers (13–17 years old) (Supplemental data 5).

No ceiling effect was detected for the disease-specific questionnaires. Regarding the generic questionnaire CHQ-CF87, a ceiling effect was seen in half of the domains, especially in the RE, RB, and RP domains. No floor effect was seen in either the disease-specific or generic questionnaires.

### 3.5 | Identification of risk factors associated with HRQL in food-allergic patients

The only factor related to FAQLQ in uni- or multivariate analyses was the asthma comorbidity. Indeed, asthma was associated with a higher FAQLQ-CF, indicating a poorer quality of life, in 8- to 12-year-old children. Conversely, in the 12- to 17-year-old range, asthma was associated with a lower FAQLQ-TF, and thus a better quality of life.

### 3.6 | Comparison with Flokstra-de Blok cohort

Compared with the Dutch cohorts, our food-allergic group had a better generic HRQL in the FA, MH, SE, and BE domains and our control group had a worse HRQL in the BP, BE, FC, PF, and MH domains (Supplemental data 6). Compared with the Dutch cohorts, our food-allergic group had a better specific HRQL in teenagers for global score and for risk of accidental exposure and emotional impact. Our food-allergic children had a better specific HRQL concerning risk of accidental exposure but a worse HRQL concerning emotional impact. (Supplemental data 7).

### 4 | DISCUSSION

We have compared HRQL in food allergy with HRQL in a control population and in other chronic diseases using a validated generic questionnaire and, for the first time on this topic, using a cross-sectional design. Our results show that food-allergic patients had a better generic HRQL than healthy controls in four domains: BP, BE,

MH, and FA. The only generic HRQL impairment for food-allergic patients was found in the GH domain, and this was only for children aged between 13 and 17 years.

These results should be put into context. First, our control group had a worse generic HRQL than the controls reported by Flokstra-de Blok et al. The BP domain, which was particularly impaired, is scored with only two questions, probably leading to problems of misunderstanding, especially for the youngest children for whom only one adult per class was available to explain the items in the control group. A declarative bias of psychological or medical issues, undiagnosed and/or unreported by their families, is also possible. This declarative bias was less prevalent in the other patient groups, where children with comorbidities (e.g., psychological troubles or dyslexia) were excluded from the study by the specialist.

Our food-allergic group could benefit from referral bias as it was recruited in a tertiary center with possible socio-economic differences compared with our randomly selected healthy control population. Nevertheless, in comparison with the food-allergic patients of Flokstra-de Blok et al. mostly recruited also in a tertiary center, our food-allergic group had a better generic quality of life in some CHQ-CF87 domains (FA, MH, SE, BE), and also a better specific HRQL, notably concerning the risk of accidental exposure. This improvement could be explained by the progress made regarding food allergy in recent years. Much effort has been put into reducing the impact of food allergy on daily life. European laws on mandatory nutritional labeling, for example, provide a better visibility of the presence of allergens. Hospital centers have also developed workshops focusing on therapeutic education, enabling children to better cope with their food allergies and to learn how to act in case of accidental exposure. Secondly, only 54.2% of food-allergic patients carried their epinephrine autoinjector at all times. These figures are lower than those reported by Pouessel et al. 17 (77%) and Sicherer et al. 18 (86%). A lower level of epinephrine carriage has been linked to underestimation of the severity of food allergy, which could modify HRQL.<sup>2</sup>

Finally, the generic questionnaire CHQ-CF87 lacks specificity.<sup>4-6</sup> The comparison between CHQ-CF87 and FAIM or FAQLQ showed a weak agreement between generic and disease-specific scales.<sup>4,6,19</sup> These results strengthen the notion that generic questionnaires, even if they allow comparison of HRQL between different diseases, are not fully adapted to catch every aspect of HRQL in food allergy.

Quality of life of children with food allergies should be evaluated using disease-specific questionnaires such as FAQLQ or FAQL-PB.

A secondary objective of this study was the comparison between HRQL in food allergy and HRQL in chronic diseases related to allergic conditions or impacting the diet. Food-allergic patients reported better generic HRQL than all other groups. One exception was for the asthmatic group, for whom the CH score was better, probably because of the strategy of coping that we presented above. Marsac et al.<sup>20</sup> found that asthmatic patients tend to adopt an approach strategy, which means they try to modify stressful events rather than following an avoidance strategy. Patients who had been managing their disease for several years and had adopted an approachcoping strategy had better HRQL scores than the patients who had been recently diagnosed.

Flokstra-de Blok et al.9 found poorer HRQL scores in foodallergic patients than in diabetic patients. Our study showed opposite results, with better HRQL scores in food-allergic than in diabetic patients in four domains. Our results are consistent with other studies, which have reported poor HRQL scores for psychosocial domains<sup>21</sup> and physical domains in diabetic patients.<sup>22</sup> Food-allergic patients had better HRQL scores than obese patients and patients with eating disorders for nine out of twelve domains. Obesity is known to be associated with a poor HRQL in both the physical and psychological domains. 23-25 Few studies have focused on HRQL in children with eating disorders, but it has been shown both in adolescents and in adults that psychosocial outcomes are impaired.<sup>26</sup> Food-allergic patients had better HRQL than patients with inflammatory bowel diseases, especially in the physical domains and in social limitations. Other studies have reported HRQL impacted for physical domains<sup>27</sup> but not for social limitations domains.<sup>28</sup> which differs from our results.

Another secondary objective of this study was to identify the risk factors associated with variation of HRQL in food allergy. Controlled asthma was the only comorbidity allowed in the food-allergic group in our study, as asthma is very frequently associated with food allergy in this age group in a real-life setting.<sup>29</sup> The only risk factor associated with variation of HRQL in food allergy that we highlighted in this context in uni- and multivariate analyses was asthma. Indeed, asthmatic food-allergic patients of 8-12 years old had a worse HRQL than food-allergic patients of the same age, as already published. 30 Food-allergic children tend to develop more anxiety if they also suffer from asthma. 31 Contrarily, asthmatic, food-allergic teenagers had a better quality of life than food-allergic teenagers. This result could be explained by the coping processes developed by teenagers to accept their chronic disease. The type of allergen, clinical manifestations in case of accidental exposure, and prescription of epinephrine autoinjector were not factors associated with worse HRQL, unlike in Piczower et al.<sup>32</sup>

One limit of our study was its monocentric feature, but this may be compensated by the large number of participants included. Targets for inclusion were reached for food-allergic patients and for the general population, allowing sufficient statistical power for the analysis; however, our study lacked sufficient numbers of patients

with some chronic diseases, notably celiac disease. Concerning the food-allergic group, we did not include patients with current uncontrolled asthma or severe current atopic dermatitis in order not to have a cumulative effect of both pathologies at the time point of the questionnaire and to catch the real effect of food allergy on HRQL. Consequently, some food-allergic patients may not have been included. Nevertheless, the large proportion of food-allergic patients with asthma clearly shows that this condition was not really limiting to study inclusion (68.1% of our food-allergic children and 62.6% of our food-allergic teenagers had asthma). Moreover, severe atopic dermatitis remains very unusual (2% of atopic dermatitis in general)-particularly in this age group and even in a group of foodallergic patients. We may assume that there is a declarative bias for the answers from the 8- to 12-year-old patients, but we tried to limit this by allowing parents to help in explaining the questionnaire, without influencing the answers. Concerning the 8- to 12-year-old group in the general population, a clinical research associate was present at the school to help. Statistical differences were possibly not clinically meaningful as there is no minimal clinically important difference (MCID) studied and published in CHQ-CF87. The strengths of our study were first the cross-sectional methodology, the large number of patients, and the clinical relevance of the compared diseases. In addition, we used an internationally validated generic HRQL questionnaire, which is the most reliable type of questionnaire for comparing several diseases.

### 5 | CONCLUSION

Generic health-related quality of life was globally better in children with food allergy than in the general population and than data published 10 years ago in food-allergy. In our cohort, food-allergic patients also showed better HRQL than the patients affected by similar chronic diseases, notably diabetes. Improvements that have occurred in management of food allergy in recent years, including the introduction of food-allergen labeling policies and education programs for patients and carers, have probably helped patients followed in tertiary care centers.

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### **CONFLICT OF INTEREST**

The authors have no conflict of interest to declare.

#### **AUTHOR CONTRIBUTION**

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Visualization (supporting); Writing-original draft (equal); Writingreview & editing (supporting). Eric Fontas: Data curation (lead); Formal analysis (equal); Methodology (lead); Project administration (equal); Resources (lead); Software (lead); Validation (supporting); Writing-review & editing (supporting). Dominique Donzeau: Data curation (supporting); Formal analysis (supporting); Investigation (supporting); Methodology (supporting); Project administration (supporting); Validation (supporting); Writing-review & editing (supporting). Marie Hoflack: Investigation (equal); Methodology (equal); Resources (equal); Validation (supporting); Visualization (supporting); Writing-review & editing (supporting). Frederique Gastaud: Investigation (equal); Methodology (equal); Resources (equal); Validation (supporting); Writing-review & editing (supporting). Elisabeth Baechler: Investigation (equal); Methodology (equal); Resources (equal); Validation (supporting); Writing-review & editing (supporting). Emmanuelle Dor: Investigation (equal); Methodology (equal); Resources (equal); Validation (supporting); Writing-review & editing (supporting). Bruno Descos: Investigation (equal); Methodology (equal); Resources (equal); Validation (supporting); Writing-review & editing (supporting). Valérie Triolo: Investigation (equal); Methodology (equal); Resources (equal); Validation (supporting); Writing-review & editing (supporting). Stéphanie Berthet: Investigation (equal); Methodology (equal); Resources (equal); Validation (supporting); Writing-review & editing (supporting). Carole Bailly-Piccini: Investigation (equal); Methodology (equal); Resources (equal); Validation (supporting); Writing-review & editing (supporting). Mélissa Beguin: Investigation (equal); Methodology (supporting); Validation (supporting); Writing-review & editing (supporting). Bertine MJ Flokstra: Conceptualization (supporting); Formal analysis (supporting); Methodology (supporting); Validation (supporting); Writing-review & editing (supporting). Thierry Bourrier: Conceptualization (supporting); Data curation (supporting); Formal analysis (supporting); Funding acquisition (supporting); Investigation (supporting); Validation (supporting); Writing-review & editing (supporting). Lisa Giovannini-Chami: Conceptualization (lead); Data curation (equal); Formal analysis (equal); Funding acquisition (lead); Investigation (lead); Methodology (equal); Project administration (lead); Resources (equal); Software (equal); Supervision (lead); Validation (lead); Visualization (lead); Writing-original draft (lead); Writing-review & editing (lead).

### PEER REVIEW

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### SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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