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Generic Health-Related Quality of Life of Children With Severe Peanut or Tree Nut Allergy

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ABSTRACT

Aim: Food allergies may decrease health-related quality of life. We assessed health-related quality of life in Finnish children at risk of a severe peanut or tree nut allergy and their parents.

Methods: Study included children aged 3–15 years referred to Tampere University Hospital for suspected severe nut allergy. Eligibility criteria included a history of anaphylaxis and/or molecular immunology testing referring for severe peanut and/or tree nut allergy. Health-related quality of life was assessed with generic questionnaires 15D for adults, 16D for teenagers or 17D for children, with scores compared with age group-matched population references.

Results: A total of 101 children (mean age 7.7 ± 2.9 years) and parent pairs were enrolled. The mean 16D score for 11 teenagers aged 12–15 years and mean 15D score for 101 parents was similar to reference populations; parental distress was borderline statistically worse (0.890 vs. 0.932, $p = 0.013$). The mean 17D score for 90 children aged 3–11 years was significantly higher (0.959 vs. 0.938) than in references ($p < 0.01$).

Conclusion: Children with a suspected severe peanut or tree nut allergy had a comparable health-related quality of life to the reference population. Distress among their parents seemed to be increased, warranting more focus on parental counselling.

Abbreviations: CI, confidence interval; HRQoL, health-related quality of life.

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Summary

- We report health-related quality of life (HRQoL) of children with a suspected severe peanut and/or tree nut allergy as there are no previous reports from Finland.
- A generic HRQoL questionnaire revealed the HRQoL of these children to be comparable with reference populations HRQoL.
- Distress among their parents seems to have increased.
- Further studies using allergy-specific HRQoL questionnaires are needed. Our results warrant more focus on parental counselling.

1 | Introduction

Peanut and tree nut allergies are common in children [1], and both can trigger anaphylaxis [2]. Unlike other major food allergies, such as milk, soy and wheat allergies, peanut and tree nut allergies seldom resolve spontaneously [3], usually affecting people into adulthood. The incidence of peanut allergies has been increasing in children [4], and severe allergic reactions among children may have been increasing in general [5]. During the last decade, there have been changes in the management of nut allergies, with the earlier introduction of peanuts [6] and oral immunotherapy for peanut [7].⁸⁷ However, the current treatment recommendations for children with any severe food allergy remain avoidance of the causative allergen and having an adrenaline autoinjector available [8].

Quality of life or health-related quality of life (HRQoL) has been reported to be decreased among children with a peanut and/or tree nut allergy and their caregivers [9, 10]. However, the impact of nut allergy on HRQoL has been found to vary with age, usage of adrenaline and type of nut [11] and there are significant differences between countries [12]. In an older study from the United States [10], which used two different disease-specific HRQoL instruments, children with PA had lower HRQoL than children with diabetes mellitus. In Greece, where there is a low incidence of food allergy and low public awareness about allergies in general, PA and TNA had only moderate effects on patients' HRQoL [11]. Also, there seems to be substantial heterogeneity between patients as to how PA affects their HRQoL [13]. Many parents have experienced fear and anxiety related to dietary avoidance and allergic reactions, even when a child has never experienced anaphylaxis [14]. Having to carry an adrenaline autoinjector for acute treatment in case of anaphylaxis or a severe allergic reaction can in itself affect HRQoL [15].

Therefore, the aim of this study was to assess the HRQoL of the children at risk of severe peanut or tree nut allergy and their parents.

2 | Materials and Methods

Tampere ALL NUTS is a Finnish ongoing single-centre cohort of children referred to a paediatric allergist consultant at Tampere University Hospital due to suspicion of severe peanut and/or tree

nut allergy. Suspicion of the risk of severe allergy was based on previous severe symptoms or positive molecular immunology test results. The latter were obtained from the children due to previous symptoms, or in some cases due to a severe peanut or tree nut allergy of first-degree relative. The study inclusion criteria were either a history of an anaphylaxis or another severe allergic reaction caused by peanut or tree nut. Other inclusion criteria were a positive molecular immunology test result referring to a severe reaction. A positive test was defined as immunoglobulin E levels > 0.35 kU/L for any of the risk components. Tree nut allergies included in the study were cashew, walnut, hazelnut, pistachio and pecan allergies. The used risk components were Ara h2, Ara h6, Cor a14, Cor a9, Cor a8, Ana o3, Jug r1 and Jug r3. All included patients avoided at least one type of nut.

To be eligible, patients had to be aged 3–15 years and without undiagnosed or uncontrolled asthma. Asthma control was defined as a normal lung function test and lack of exacerbations. Lung function tests, including a free running exercise, were performed on all patients. In children 3–6 years of age, lung function was assessed with impulse oscillometry and in children ≥ 7 years of age with spirometry. If a patient had diagnosed asthma, the same tests were used to assess asthma control.

All patients with referral indications were invited to meet a paediatric allergist at the Allergy Centre of Tampere University Hospital between 2021 and 2024. After referral, the patients had typically waited at least a couple of months before the first assessment at the study clinic. Eligible 101 patients and their parents were given information about the study. Those who gave written consent were included. The study protocol differed from the normal treatment protocol only in the measurement of HRQoL at appointments.

2.1 | Health-Related Quality of Life Measurement

HRQoL was assessed using the questionnaires 15D, 16D and 17D [16], which are generic, comprehensive self-administered instruments. The questionnaire 15D is for adults ≥ 16 years, 16D is for teenagers between 12 and 15 years, and 17D is for children < 12 years. There are 15–17 dimensions in each, assessing different descriptions in health status with ordinal levels from 1 to 5. The single index score (15D, 16D or 17D score) represents overall HRQoL on a scale of 0–1, where 0 = being dead and 1 = full health. The dimension level values are calculated using a set of population-based preference or utility weights. Mean dimension level values are used to draw 15D profiles for groups. We assumed that the minimum clinically important change or difference in any instrument score was the same ± 0.015 established for the 15D score [17]. The specifics of the instruments used are explained with greater detail elsewhere [16].

Depending on a child's literacy skills, as assessed by its family, the 17D was completed by the parents or the child. The 17D includes descriptive pictures to make the questions more comprehensible. The 16D was completed by the teenagers themselves. The 15D was for measurement of the participants' parents' HRQoL. If a patient was accompanied by more than one parent, only one filled out the questionnaire. The parents decided which of them would accompany the child and whether they or the child could complete the questionnaire.

Questionnaires were filled out during the first study appointment held at the Allergy Centre of Tampere University Hospital. The participant demographics, chronic illnesses and allergy history were collected by paediatric allergists through a separate survey during study appointments. Allergy, asthma and anaphylaxis history were confirmed by paediatric allergists.

2.2 | Reference Group

Acquired HRQoL data were compared with age group-adjusted reference population HRQoL data samples gathered in prior studies from Finnish children and adults. These samples include 244 children <12 years of age and 373 teenagers between 12 and 15 years of age [18–20]. Parental HRQoL data were compared with a sample of 1151 adults presenting general Finnish population aged 25–45 years [18], as we lacked information about parents' biological sex and dates of birth. The same 15D for adults, 16D for teenagers and 17D for children were used to measure reference group HRQoL.

Our primary outcome was the HRQoL of children with severe nut allergy compared with the general child population in Finland. The secondary outcome was parents' HRQoL.

2.3 | Statistical Analyses

Independent samples *t*-tests were used to determine whether there were statistically significant differences in the means of the HRQoL variables between the study and reference populations. One of the authors (HS) had access to reference population data, with results of individual samples, to which the study population was compared. Therefore, individual dimension scores, means and standard deviations were available for the reference population as well. *p* values <0.05 in overall scores were considered statistically significant. Due to the high number of dimensions (16–18), *p* <0.01 were considered significant for specific dimensions to reduce the possible risk of the multiple testing problem. Data analyses were performed with SPSS software version 28 (IBM Corp, New York, USA).

2.4 | Ethical Considerations

The protocol for this study was approved by the Institutional Ethics Committee of Pirkanmaa hospital district (registration number ETL R21024). Written consent was given by children mature enough to understand the protocol and by the teenager and the parent who was with the patient at the study appointment. If a referred patient or parent did not give consent for the study, they were invited to the outpatient clinic as usual but not included in the study.

3 | Results

In total, 101 patients (57.4% boys) were enrolled in the study (Table 1), with a mean age of 7.7 years (± 2.92 years). There were 90 children who completed the 17D and 11 teenagers who completed the 16D. All 101 parents completed the 15D.

TABLE 1 | Characteristics of study population by health-related quality of life instrument used.

	16D <i>n</i> = 11 <i>n</i> (%)	17D <i>n</i> = 90 <i>n</i> (%)
Girls	2 (18)	41 (46)
Age (in years, mean)	13.7	6.9
Answered health survey	11 (100)	89 (99)
Asthma	6 (55)	21 (24)
Atopy	8 (73)	65 (73)
Overall IgE sensitivity	9 (81)	69 (77)
Anaphylaxis	6 (55)	43 (48)
Sampson criterion		
Criteria 1	2 (33)	18 (42)
Criteria 2	3 (50)	24 (56)
Criteria 3	0	0
Cause of anaphylaxis		
Peanuts	1 (17)	13 (30)
Cashews	3 (50)	19 (44)
Hazelnuts	0	1 (2)
Walnuts	1 (17)	7 (16)
Pecans	1 (17)	1 (2)

Note: History of asthma, allergy and anaphylaxis was collected and confirmed by the clinician (a parental report was not sufficient). There were two cases of anaphylaxis where the clinician could not determine which Sampson criterion [21] was fulfilled in the diagnosis of anaphylaxis. Also, there were two cases of anaphylaxis where the causative nut could not be determined specifically. For one child, allergy and asthma history were missing. 16D is the questionnaire for teenagers; 17D is the questionnaire for children. Abbreviation: IgE = immunoglobulin E.

A history of atopy was reported by 73% of the study subjects and asthma by 27%. Only 5% of children reported other medical diagnoses, with diabetes mellitus type 1 being the most common with two individuals. Around half of the participants (47%) had a history of anaphylaxis due to either peanuts or tree nuts. A history of anaphylaxis did not affect mean 15D, 16D or 17D scores or any specific dimensions. Allergy and other medical histories were missing for one child. This child was included in the analyses as age and biological sex were known, and HRQoL instruments were properly completed by the child and parent.

3.1 | Results Among Teenagers (16D)

The mean age of teenagers was 13.7 years (± 1.1 years), and 2 of 11 (18%) were girls. Independent samples *t*-tests showed no difference in mean age between the study and reference populations. The mean 16D score among 11 teenagers was 0.955, with the age group-matched population reference score being 0.947 (Figure 1). The difference in the mean score was neither clinically important (-0.008) nor statistically significant

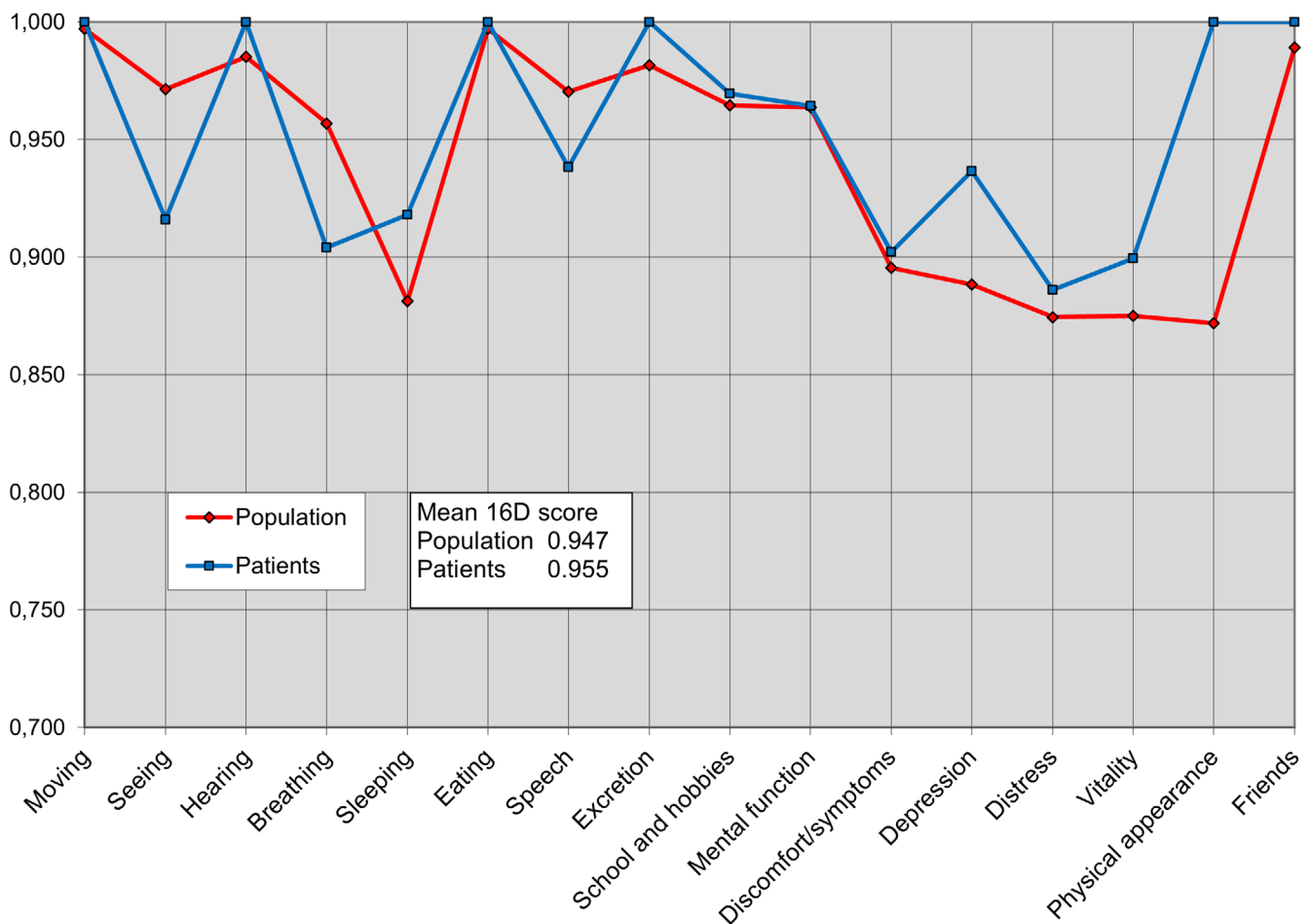


FIGURE 1 | The mean 16D score profiles of the patients aged 12–15 years ($n = 11$) compared with the reference population ($n = 373$).

($p = 0.54$). Statistically significant differences (defined as $p < 0.01$) were observed, all in favour of the study group, with higher scores in the hearing, excretion, and physical appearance dimensions.

3.2 | Results Among Children (17D)

The mean age of 90 (55.4 boys) children was 6.9 years (± 0.4 years). The mean 17D score was 0.95 (95% CI 0.946–0.962) for the study group and 0.938 (95% CI 0.931–0.944) for the reference population. This difference was both clinically important (-0.017) and statistically significant ($p < 0.01$). For specific dimensions (Figure 2) a statistically significant difference ($p < 0.01$) was observed in favour of the study group in hearing, breathing, learning, depression, vitality and physical appearance. The study group had lower values for excretion (0.916 vs. 0.987, $p < 0.01$). The sex of the children did not affect mean 17D scores or any specific dimensions of the instrument.

There was a significant difference in mean age between the study and reference groups (6.9 vs. 9.4 years, $p < 0.01$). Therefore, analyses were also carried out separately for children > 6 years of age ($n = 38$, mean age 8.4 years). The results were similar to those for the entire group, except in excretion, which did not differ from that of the reference group in this age subset.

3.3 | Results Among Parents (15D)

All 101 parents completed the 15D for adults during the study appointments. The mean 15D score was 0.942 for parents and 0.945 for the reference population, and the difference was not significant ($p = 0.59$). The parents were borderline statistically significantly worse off in distress than the references (0.890 vs. 0.932, $p = 0.013$, score difference 0.042). Among parents of children aged 3–11 years, the difference was statistically significant (0.884 vs. 0.932, $p = 0.008$, score difference 0.048). No significant differences were found in other dimensions (Figure 3).

4 | Discussion

In this study of HRQoL of children with a severe peanut and/or tree nut allergy, we identified that HRQoL among children with these allergies was comparable to that of a general reference population. In contrast, parents of the children with peanut or tree nut allergy report greater distress than that of a general reference population.

The mean 17D score HRQoL for children was better in the study population than in the reference population. Although this difference was statistically significant and may be considered clinically important [17], the true difference between groups was

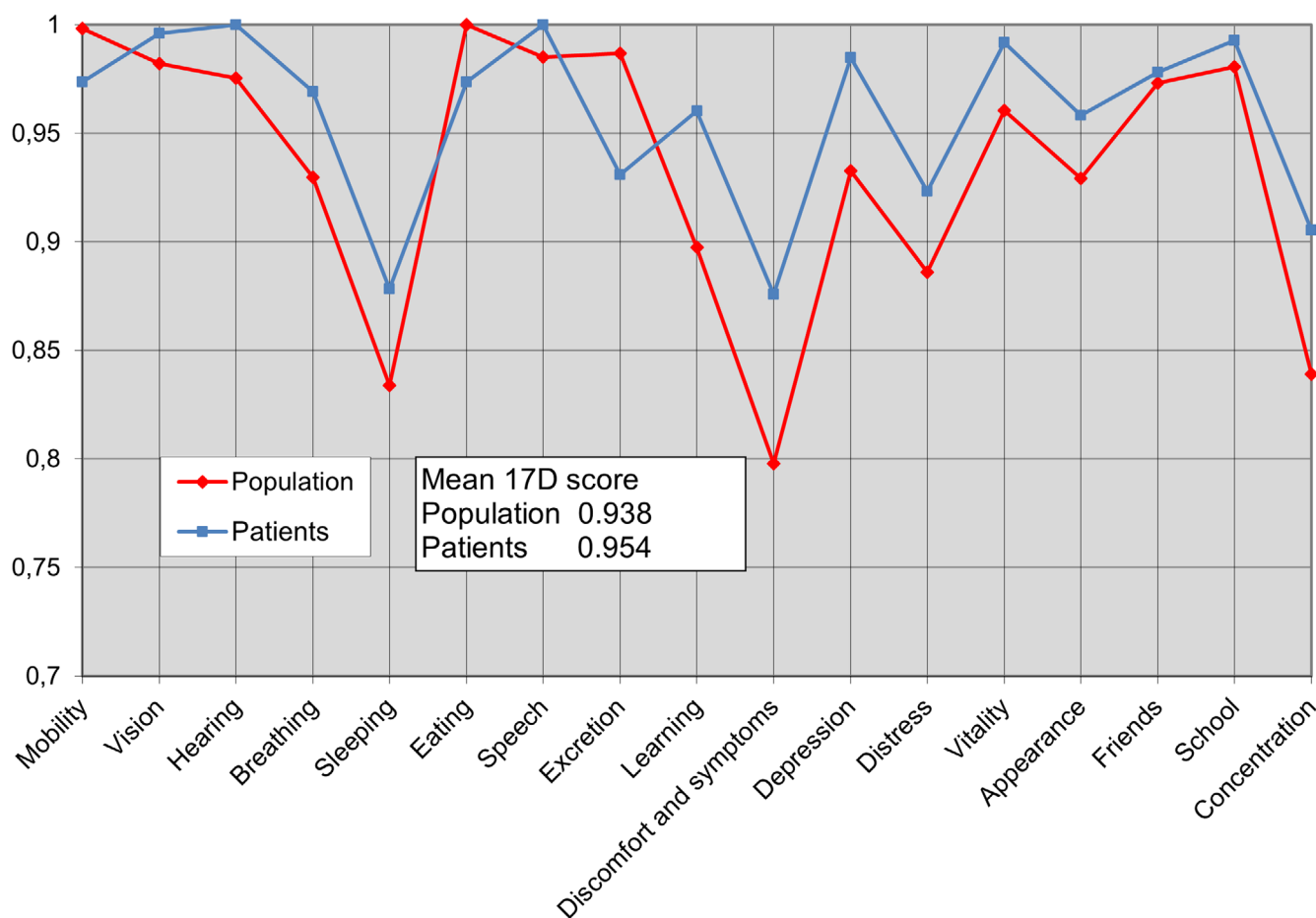


FIGURE 2 | The mean 17D score profiles of the patients aged 3–11 years ($n=90$) compared with the reference population ($n=244$).

small and it is questionable whether the difference was true. It may partly be attributable to the fact that our participants were screened for uncontrolled asthma, while there may be some in the general population references. For teenagers and parents, there were no differences in mean scores. This differs from previous studies, which have repeatedly shown that peanut allergy has a negative effect on HRQoL [9, 10, 14].

There are potential explanations for why generic HRQoL impairment was not observed in the present study. One might be the age of our study group. Participants in our study were younger than those in other peanut allergy HRQoL studies [9]. Some peanut allergy studies have shown older children and teenagers to be at greater risk of HRQoL impairment [9, 11]. As food allergies typically cause symptoms only through contact with the allergen and are asymptomatic when the allergen is avoided, the effect on HRQoL may come from the risk of exposure to the allergen. The concept of risk may be hard for younger children to comprehend, with older children likely to be more aware. The risk of accidental exposure to peanuts or tree nuts in school or day care is very small, as meals offered to children in our region are nut-free. Also, as HRQoL was measured at the first visit to the paediatric allergist after referral, it may be that some children in our study had only been at risk of repeated allergic reactions for a short period of time.

Most other HRQoL studies concern peanut allergies only, whereas our study had a pool of children with peanut and/or

tree nut allergy. There are no high-quality reports on the effects of tree nut allergy on paediatric HRQoL. However, we presume that tree nut allergy has a similar effect on HRQoL as peanut allergy in our study, given that all patients were at risk of severe allergic reaction, with a similar risk of accidental exposure.

Among all parents of children and teenagers with nut allergy, we saw an almost statistically significant increase in parental distress ($p=0.013$). Among parents of children aged 3–11 years, the increase was statistically significant ($p=0.008$). Based on other studies, we know that allergies may cause parental distress or anxiety [9], even where the allergy would not be as severe as in our patients. Our finding may be more revealing, as it comes from a generic HRQoL tool and not from a disease-specific instrument.

Using generic HRQoL instruments allowed us to compare peanut and tree nut allergic children to a general population. Our results indicated no difference in HRQoL. This does not mean that a peanut or tree nut allergy would not affect a child's HRQoL at all. Although the instruments have shown strengths in numerous medical conditions [16, 22], they may be too crude to capture some of the health burden of allergies. Still, another study using generic HRQoL questionnaires reported peanut allergy having a negative effect on adolescent and caregiver HRQoL [9].

Peanut allergy can affect everyday life even when physical symptoms are absent [4]. There may be a constant fear of

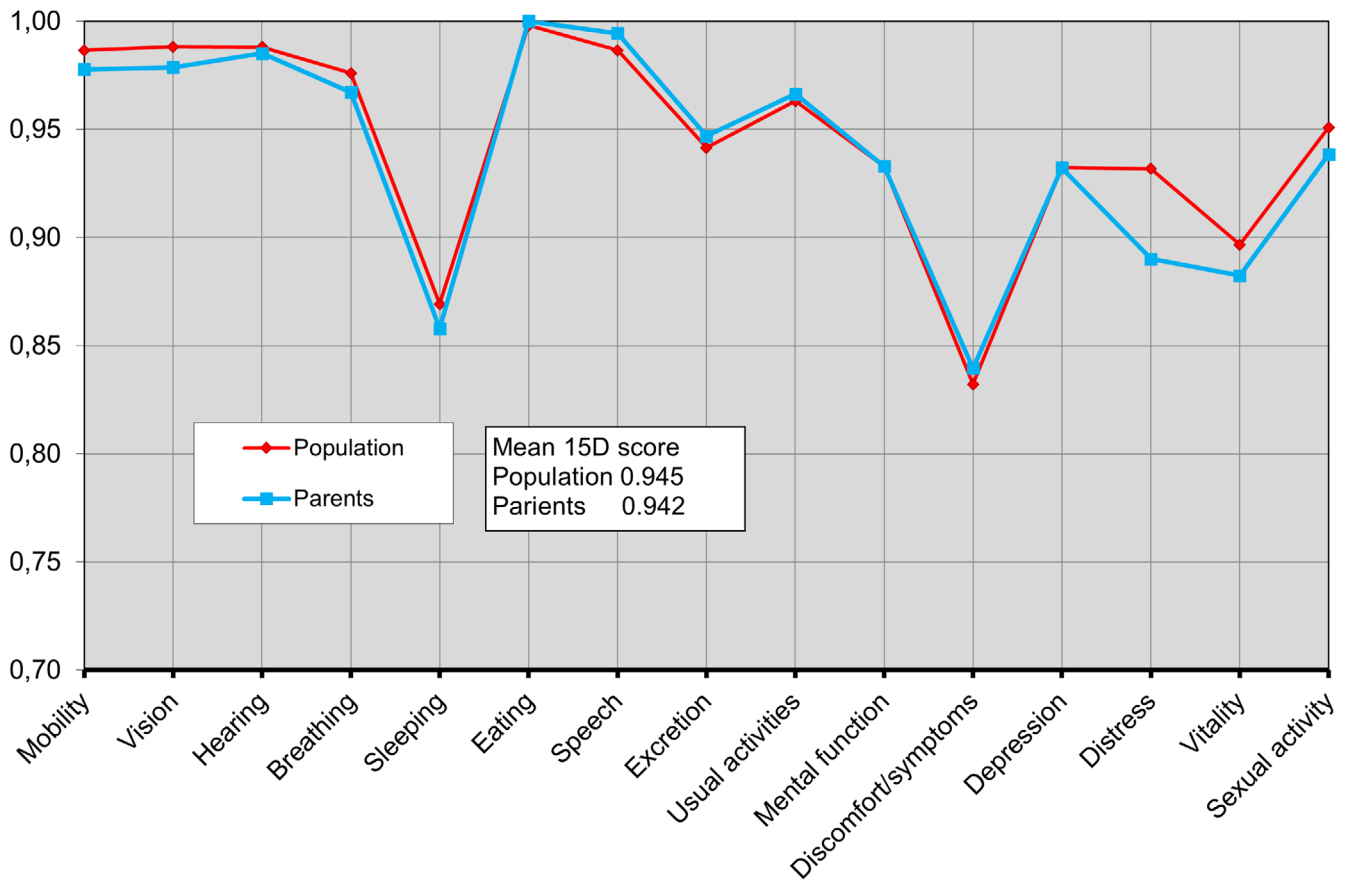


FIGURE 3 | The mean 15D profiles of the parents ($n = 101$) and the reference population ($n = 1151$). The reference population was a general population sample of Finnish adults aged 25–45 years, as parental demographics were not available.

accidental exposure and a need to carry an adrenaline autoinjector. Therefore, more specific tools for screening of HRQoL in children with food allergies are used in some instances, such as assessing the effect of oral immunotherapy on the HRQoL of peanut allergic children. A Norwegian study [23] done with a generic HRQoL instrument found no effect of OIT on HRQoL in children. However, a meta-analysis [24] which only included studies conducted with disease-specific questionnaires found oral immunotherapy and oral food challenges beneficial to HRQoL.

4.1 | Strengths and Limitations

A major strength of our study was the use of validated Finnish HRQoL questionnaires [22], depicting the real effects of peanut and tree nut allergies. Further, we included the children at greatest risk of life-threatening allergic reactions as they had strong susceptibility for a severe nut allergy, with past severe allergic reactions to nuts or molecular immunology testing. Therefore, our study population could be thought of as having the most impaired HRQoL. We are not aware of other HRQoL studies of children with all study participants at risk of severe allergic reactions. Lastly, our study used age group-matched general reference populations. Paediatric PA HRQoL studies with control groups are scarce, as many [13] merely report different risk factors contributing to HRQoL impairment.

We acknowledge the limitations of our study. The sample size was relatively small, especially regarding teenagers, who have been reported to be at greater risk of HRQoL impairment compared to children. If more teenagers had been recruited, there would have been a better statistical power to detect potential differences in the generic HRQoL in relation to nut allergies. Children who completed the 17D were significantly younger than the reference population, which might explain the difference seen in the dimension of excretion, for instance. The lack of information about parental demographics may have resulted in the reference group for parents being incorrectly selected. However, we find the comparison justified, as the HRQoL of parents was closely similar to that of the population in all aspects except distress. Finally, as we are comparing numerous variables, some of which should be completely unaffected by allergy, it may be that some differences between the study and control groups come up by chance. This was tried to be avoided by holding $p < 0.01$ as a threshold of statistical significance.

5 | Conclusion

This study shows that the HRQoL of children with a suspected severe peanut and/or tree nut allergy in our hospital's region seems to be comparable to the general population. This implies that these children are generally otherwise healthy and/

or their health conditions are managed properly. However, it is important to investigate their HRQoL with disease-specific HRQoL instruments to further clarify our results. It is concerning that parental distress of these children seems to be increased, especially when it is observed with a generic HRQoL instrument. More focus should be emphasized to parents when treating children with nut allergies. Parents should be told that no children have died from anaphylaxis in Finland in past years [25] and that severe allergic reactions very seldom cause any sequelae after correct treatment. The representativeness of our results may, however, be limited. They represent nut-allergic children in a relatively small hospital area in a resource-rich setting, where nuts are not part of traditional cuisine, allergen labelling is adequate, and hospital emergency care is near for most people.

Author Contributions

Lasse Saarimäki: conceptualization, investigation, writing – original draft, methodology, validation, visualization, writing – review and editing, formal analysis, project administration, supervision. **Juho E. Kivistö:** conceptualization, writing – original draft, investigation, methodology, writing – review and editing, resources. **Iida Ojaniemi:** investigation, writing – review and editing. **Harri Sintonen:** investigation, methodology, writing – review and editing. **Heini Huhtala:** writing – review and editing, formal analysis, data curation. **Jennifer L. P. Protudjer:** writing – original draft, writing – review and editing. **Sandra Ekström:** writing – review and editing. **Inger Kull:** writing – review and editing. **Jussi Karjalainen:** conceptualization, writing – original draft, writing – review and editing.

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Conflicts of Interest

The authors declare no conflicts of interest.

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