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Quality of life improves significantly after real-world oral immunotherapy for children with peanut allergy

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ABSTRACT

Background: Peanut oral immunotherapy (POIT) is a novel and active form of treatment for patients with peanut allergy, with multiple research studies supporting its efficacy and safety. However, there are limited data available on changes in patients' quality of life (QoL) after successful desensitization. The Food and Drug Administration in the United States recently approved the first POIT drug for commercial use.

Objective: To evaluate the QoL of patients with peanut allergy receiving POIT in a real-world academic setting.

Methods: Twenty-one patients aged 4 to 17 years with a physician-established diagnosis of peanut allergy were offered POIT. Quality-of-life scores were assessed with the use of a validated Food Allergy Quality of Life questionnaire. Changes in quality-of-life scores were measured for each patient before and after POIT. The Wilcoxon signed-rank test was used to compare the distributions of scores before and after therapy.

Results: We noted a statistically significant drop (reflecting improvement in the QoL) in the overall Food Allergy Quality of Life score (median 3.70 vs 2.97, $P = .049$) between baseline and successful desensitization to 300-mg peanut protein. In addition, the Social and Dietary Limitations subscale score (median 4.33 vs 2.89, $P = .02$) and the Food Allergy Independent Measure score (median 3.17 vs 2.22, $P = .001$) also improved significantly after therapy.

Conclusion: We report a significant improvement in the overall QoL before and after POIT treatment, with fewer concerns about accidental exposures and severity of allergic reactions as well as fewer limitations in dietary choices and social interactions.

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Introduction

Food allergies are common, affecting 1 in 13 children in the United States.¹ This poses a significant burden on children with food allergies and their families with reported physical and emotional impact.² Children with food allergies are required to avoid their food triggers; unfortunately, this can be difficult when

eating outside the home or traveling.^{3,4} In addition, food labels can often be misleading⁵⁻⁷ and accidental exposures may result in severe allergic reactions.⁸ The risk of a severe reaction creates fear and significant anxiety in the daily lives of children with food allergies and is often associated with limitations in their social interactions.^{9,10} The burden of food allergy is therefore apparent in many aspects of the patient's life and can significantly affect daily quality of life (QoL). In an effort to measure QoL in patients with food allergy and their family, multiple disease-specific instruments have been developed.¹¹⁻¹³ Children with food allergies have worse QoL compared with children with other chronic diseases, such as type 1 diabetes. The main reasons for this include fear of accidental exposure to the allergenic food and life-threatening reactions.¹⁴

The natural resolution of peanut allergy mostly occurs in the preschool age for a reported 20% of children.^{15,16} Peanut oral immunotherapy (POIT) is a novel and active form of treatment for patients with peanut allergy, with multiple research studies

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supporting its efficacy and safety, including a recent phase 3 trial.^{17–23} There are a few published studies that focus on the changes in QoL after oral immunotherapy (OIT), with some of these supporting improvement in patient QoL after successful desensitization.^{24–26}

The aim of our prospective cohort study was to examine changes in the QoL of patients with peanut allergy undergoing POIT and to evaluate the safety of clinical POIT in a real-world academic setting.

Methods

Study Design

We designed our study as an open, prospective cohort to examine changes in the QoL of patients with peanut allergy participating in POIT. We also evaluated the safety of clinical POIT in a real-world academic setting. Patient enrollment commenced in 2018, and this study presents data, collected prospectively, from a group of 21 children who have completed peanut immunotherapy. Approval from the institutional review board (Baylor College of Medicine IRB) was obtained for prospective data collection, analysis, and publication.

Patient Selection

A total of 21 patients aged 4 to 17 years with a physician-established diagnosis of peanut allergy seen consecutively in our pediatric allergy clinics were offered the option of participating in POIT. Children with previous anaphylaxis to peanut (not requiring intensive care unit admission) and those with well-controlled asthma and well-controlled allergic rhinitis were included. Exclusion criteria for participating were as follows: (1) severe or uncontrolled asthma; (2) emergency department admission owing to asthma within the last 12 months; (3) systemic oral corticosteroid therapy within the last 12 months; (4) severe atopic dermatitis (defined as patients who have more than 20% skin involvement and have not been responsive to first-line treatment, or patients who require ongoing or frequent treatment with high-potency topical glucocorticoids²⁷); (5) uncontrolled allergic rhinitis; (6) chronic undiagnosed gastrointestinal symptoms (eg, chronic abdominal pain with no clear diagnosis); (7) eosinophilic esophagitis (EoE); and (8) any other nonatopic chronic illness (eg, immune deficiency, malignancy, diabetes). Children with well-controlled chronic urticaria were included.

Procedures

A pediatric allergist discussed the intervention at length with parents and eligible patients, outlining the advantages and disadvantages of POIT and providing relevant written information. Families were given at least 7 days to consider participation, and patients were enrolled consecutively. Informed consent was obtained from the parents or guardians of all patients who agreed to undergo POIT.

Baseline peanut-specific IgE, Ara h 2, and peanut skin prick test (SPT) were performed on all patients before commencing POIT and were repeated halfway and at the end of therapy. Baseline spirometry was also performed for all patients older than 6 years. We limited enrollment to 21 subjects to monitor the patients closely and allow for potential extra appointments in the clinic if needed.

Our protocol consisted of slow up-dosing, once every 4 weeks (usually ± 2 weeks) in the clinic setting. The starting dose was 2-mg peanut protein, and the target maintenance dose was 300-mg peanut protein. Our detailed buildup protocol is shown in Table 1. For the first 5 doses, peanut powder was used; whereas for the

Table 1
Buildup Protocol

Week #	Material used	Dose increase	Approximate ^a peanut protein dose, mg
0	Peanut flour (JIF), 4 mg flour	Starting dose	2
4	Peanut flour (JIF), 10 mg flour	Increased $\times 2.5$	5
8	Peanut flour (JIF), 20 mg flour	Increased $\times 2$	10
12	Peanut flour (JIF), 50 mg flour	Increased $\times 2.5$	25
16	Peanut flour (JIF), 95 mg flour	Increased $\times 2$	50
20	½ Bamba	No increase	50
24	1 Bamba	Increased $\times 2$	100
28	1½ Bamba or 1 Peanut M&M	Increased $\times 1.5$	150
36	1 Peanut M&M and ½ Bamba	Increased $\times 1.3$	200
40	3 Bamba or 2 Peanut M&Ms	Increased $\times 1.5$	300

^aAllowing for variations in measurement and product variability.

remaining 4, a combination of choice between Bamba and peanut M&Ms was offered. In cases of severe allergic reactions, dose modifications were performed, and additional visits were scheduled. Materials used included peanut powder (*Jif* peanut powder, J.M. Smucker Company, Orrville, Ohio) and *Bamba* (Osem Group, Israel), peanut M&Ms (Mars Inc, Virginia). In terms of product measuring, parents were asked to rate the ease of measuring on a scale of 0 to 10, with 0 representing “very easy” and 10 “very hard.” Patients were asked to rate taste acceptability of different peanut products on a scale of 0 to 10, with 0 representing “disliked the taste” and 10 “loved the taste.”

All patients were observed for 2 hours after consuming the peanut dose. Exercise was not permitted for the 2-hour observation period in the clinic and at home. Between clinic visits, patients ingested a daily dose at home. Dedicated dietetic support was provided in every clinic visit and was also available via a telephone consultation or e-mail correspondence outside the clinic visits. Patient feedback was collected prospectively on taste acceptability of products used as well as ease of measurement and administration. All patients were provided with an updated Food Allergy Action Plan and education on how to treat any allergic reactions. Epinephrine auto-injector training was offered in every clinic visit to parents, patients, and any other caregiver involved in caring for the child with peanut allergy (eg, grandparents, nannies).

A physician was accessible 24 hours a day, 7 days a week, via a dedicated OIT pager for urgent queries or advice. For nonurgent queries, a dedicated clinic nurse and a physician were available during the usual working hours (8 AM to 6 PM). Patients were provided with written instructions on how to manage daily dosing including when to hold doses and call the allergist. Dietetic instructions on dose measurement and administration were provided separately. Symptoms and management of allergic reactions during clinic up-dosing visits were recorded in the patient's medical chart. Caregivers were provided with a daily symptom diary to record any allergic reactions occurring at home as well as any missed doses. Symptoms were graded according to the World Allergy Organization Subcutaneous Immunotherapy Reaction Grading system²⁸ (eTable 1).

The quality-of-life scores were measured with the use of a validated QoL questionnaire before commencing POIT and at the completion of the program. The questionnaires were scored using a 6-point Likert scale. Patients or their parents were invited to complete the Food Allergy Quality of Life Questionnaire – Parent Form (FAQLQ-PF)¹¹ for children aged 4 to 12 years or the Food Allergy Quality of Life Questionnaire – Teenager Form (FAQLQ-TF)¹³ for adolescents aged between 13 and 17 years. Informed consent was obtained. The parental form was completed by the main caregiver of the child with food allergy (proxy report), allowing parents to report QoL from the child's perspective. The teenage form was completed by the teenager with food allergy (self-report).

The Food Allergy QoL Questionnaires include various subscales such as emotional impact, food anxiety, and social and dietary limitations (SDL). These subscales can be combined to average an overall FAQLQ score. The Food Allergy Independent Measure (FAIM) score can also be assessed from the questionnaire. The FAIM score reflects concerns about accidental exposure and allergic reaction severity. Higher scores are interpreted as worse QoL.

Data Analysis

Descriptive statistics were used for analysis. Categorical variables were described as means and percentages (sex, symptoms). Continuous data (age, specific IgE, SPT) were described as median and interquartile range (IQR). A Fisher's exact test was performed using GraphPad Prism version 7.0 for Windows (GraphPad Software, La Jolla, California, <http://www.graphpad.com/>). *P* values of less than .05 were considered statistically significant. The change in QoL scores were plotted for each patient, and the Wilcoxon signed-rank test was used to compare the distributions for QoL scores before and after POIT.

Results

Demographics

A total of 21 patients underwent POIT between June 2018 and August 2019. Demographics and characteristics of our patient population are presented in Table 2. The median age of our cohort was 8 years. Most patients had atopic dermatitis and allergic rhinitis, and almost half also had asthma. Two-thirds of patients had another food allergy, mostly tree nut allergy (Table 2).

Quality-of-Life Changes After POIT

Table 3 compares scores before and after POIT. We noted a statistically significant drop (reflecting improvement in QoL) in the overall Food Allergy QoL score (median 3.70 vs 2.97, *P* = .049) between baseline and successful desensitization to 300-mg peanut protein. Other scores that improved significantly after POIT was the SDL score (median 4.33 vs 2.89, *P* = .02) and the FAIM score (median 3.17 vs 2.22, *P* = .001). All other scores were not significantly different after POIT: emotional impact score (*P* = .14), food anxiety

score (*P* = .68), Food Allergy Health score (*P* = .17), and risk score (*P* = .18) (see Table 3).

Effectiveness of POIT

Of the 21 patients enrolled in the POIT program, 20 (95%) reached the target maintenance dose of 300-mg peanut protein. The median duration of buildup was 283 days (range 225–414) (Table 4). Median SPT decreased from median 13 mm (baseline) to 6 mm (mid-POIT) to 5 mm (end of POIT up-dosing). Peanut-specific IgE increased from median 17.7 (baseline) to 22.75 (mid-POIT) to 23.10 kU/L (end of POIT up-dosing). Ara h 2 initially increased from 16.30 (baseline) to 17.45 (mid-POIT) and subsequently decreased to 9.89 kU/L (end of POIT up-dosing).

Safety of POIT

In 5 of our patients, POIT was completed without any allergic reactions. For the remaining 16 patients, a total number of 79 allergic reactions (79 of 21, 3.8% allergic reactions per patient) were noted (Table 5). Eleven of these (14%) occurred during a clinic up-dosing and 68 (86%) occurred at home. Symptoms included oral itching, abdominal pain, nausea, vomiting, hives, and dysphagia. Of 79, 19 (24%) allergic reactions were treated with antihistamines, and in 2 patients (2.5%), epinephrine was administered (Table 6). Following treatment of the abovementioned allergic reactions with a single dose of epinephrine, symptoms resolved, and no patients needed administration of more than 1 epinephrine dose. There were no biphasic reactions.

Overall, a total number of 5668 doses of peanut were administered, with allergic reactions occurring at 1.3% of all doses. We observed grade 1 reactions in less than 1% of the total doses administered and grade 2 reactions in less than 0.5% of the total of POIT doses administered. Epinephrine was used in 0.03% of all POIT doses (Table 7). Most grade 1 allergic reactions self-resolved within a few minutes without treatment.

One patient discontinued owing to EoE concerns. The patient had received POIT for 283 days, reaching the dose of 100 mg, when she reported a sudden onset of dysphagia and difficulty swallowing for 4 consecutive days. Thereafter, POIT was discontinued with full resolution of symptoms over the next 5 days. A referral to gastroenterology was made. Endoscopy and biopsy were performed 4 months later, with no abnormal findings reported. For this patient, POIT was not reattempted.

Six patients (29%) received daily antihistamines alongside POIT due to perennial allergic rhinitis (in 5 patients) and well-controlled chronic urticaria (in 1 patient). Of the patients receiving daily antihistamines, 4 (57%) experienced allergic reactions during POIT, whereas 3 patients did not experience any reactions at all during up-dosing.

Discontinuation and Dropout Rate

The discontinuation rate was 5% (1 patient) in our cohort, as discussed above. There were no dropouts. Adherence to treatment was very good, with only 111 missed doses of a total of 5668 doses administered (2% missed doses overall) (see Table 4). Reasons for the missed doses included the following: (1) forgotten dose (*n* = 33, 0.58% of total doses); (2) travel, holiday, or camp (*n* = 27, 0.47% of total doses); (3) illness (*n* = 22, 0.44% of total doses); (4) sporting or social event (*n* = 12, 0.21% of total doses); and (5) other (*n* = 14, 0.24% of total doses).

Dietetic Information

We noted that 57% of our patients took their dose in the morning and 43% in the afternoon or evening once school and other activities were finished for the day (Table 8). The most popular

Table 2
Baseline Characteristics of the Patient Cohort

Characteristic	Median	IQR
Age (y) at entry into POIT	8	5–9
Age (y) at index reaction	2	1–2.6
Baseline peanut SPT	13	10–18
Baseline peanut-specific IgE	17.7	1.2–9.9
	<i>N</i> = 21	%
Sex		
Male	14	67
Female	7	33
Atopic comorbidities	21	100
Atopic dermatitis	17	81
Asthma	9	43
Allergic rhinitis	16	76
Other food allergies	16	76
Tree nuts	15	71
Egg	1	5
Fish	2	10
Cow's milk	1	5
Shellfish	1	5
Sesame	1	5
Chickpeas or lentils	1	5
Family history of atopy	18	86
Sibling with peanut allergy	4	19

Abbreviations: IgE, immunoglobulin E; IQR, interquartile range; POIT, peanut oral immunotherapy; SPT, skin prick test.

Table 3

QoL Scores at Baseline and After Completion of the POIT Program (Wilcoxon Signed-Rank Test)

Score	Baseline				After OIT				P value
	N	Median	Min	Max	N	Median	Min	Max	
EI score	19	3.50	1.80	6.85	19	2.69	1.46	4.62	.14
FA score	16	4.00	1.00	7.00	16	3.19	2.14	5.00	.68
SDL score	19	4.33	1.67	7.00	19	2.89	1.89	5.60	.02
FAH score	2	4.33	4.33	4.33	2	3.67	3.67	3.67	.17
Risk score	2	4.81	4.50	5.13	2	3.44	2.75	4.13	.18
Total score	19	3.70	2.50	6.93	19	2.97	1.93	4.97	.049
FAIM score	18	3.17	1.78	5.00	18	2.22	.67	3.78	.001

Abbreviations: EI, emotional impact; FA, food anxiety; FAH, food allergy health; FAIM, Food Allergy Independent Measure; OIT, oral immunotherapy; QoL, quality of life; SDL, social and dietary limitations.

vehicle for mixing the peanut powder was applesauce (57%), followed by chocolate pudding (19%), fruit smoothie (14%), yogurt (9%), and ice cream (5%).

Peanut powder was scored with a median of 5, but there was high variability in rating (IQR: 3–10). Bamba scored a median of 4.5 but with much lower variability (IQR: 1–6). Peanut M&Ms (chocolate-covered) achieved the highest score for taste acceptability with a median of 8 (IQR: 5–10).

Table 4

Total Number of POIT Doses Administered, Total Days of POIT, Missed Doses per Subject and Reasons for Missed Doses Are Shown

Subject #	Total number of POIT doses (n = 5668)	Total days on POIT	Number of missed home doses	Reasons for missed doses
1	245	250	5	2: GI illness 1: Received vaccination 2: AR flare
2	248	249	1	Holiday
3	283	288	5	Illness
4	275	288	13	7: Summer camp 6: Forgot
5	225	225	0	N/A
6	239	240	1	Forgot
7	270	272	2	Traveling (on flight)
8	313	333	20	11: Sport competition days 9: EoE-like symptoms
9	248	251	3	Forgot
10	285	291	6	4: Illness 2: Forgot
11	283	283	0	N/A
12	283	283	0	N/A
13	391	414	22	7: Forgot 5: Illness 10: Camp/holidays
14	253	256	3	Illness
15	244	244	0	N/A
16	259	262	3	1: Illness 2: Skipped after allergic reaction
17	242	242	0	N/A
18	282	288	6	1: Illness 3: Holidays 1: Forgot 1: Travel (on flight)
19	282	288	6	2: Illness 2: Holidays 1: Forgot 1: Travel (on flight)
20	234	243	9	7: Forgot 1: Illness
21	284	290	6	1: Social event 5: Forgot 1: Illness

Abbreviations: AR, allergic rhinitis; EoE, eosinophilic esophagitis; GI, gastrointestinal, N/A, not applicable; POIT, peanut oral immunotherapy.

Discussion

To our knowledge, we are the first group to report real-world data, collected prospectively, on the QoL impact following POIT within a large pediatric academic center in the United States. Our patients showed significant improvement in QoL scores following completion of POIT; specifically, better scores were reported for overall QoL, SDL, and FAIM scores.

We are the first group to show a direct correlation between successful OIT peanut in a real-world setting and improvement in the FAIM score, which reflects concerns about accidental exposure and disease severity. It is not surprising that children with a peanut allergy who have been successfully desensitized have fewer concerns about unintentional exposures and severity of allergic reactions as a result of cross-contamination. It is also important to highlight that these findings only reflect changes in QoL for the up-dosing period of POIT (which is the hardest, in terms of frequency of treatment-related allergic reactions), and we suspect that even more significant improvements are likely to be seen in longer-term POIT maintenance. Future studies will be able to examine long-term QoL changes.

Changes in QoL after POIT are currently an area of intense interest. Previous research studies support our findings in clinical practice.^{24,25} A randomized controlled trial of POIT in 99 children in the United Kingdom showed significant QoL improvement after successful desensitization. Blumchen et al²⁵ also reported significant improvement in QoL in 62 children undergoing low-dose peanut OIT in a multicenter, double-blind, randomized placebo-controlled trial. Epstein-Rigbi et al²⁹ showed that the QoL of 191 children with food allergy improved significantly upon reaching OIT maintenance, with additional improvement 6 months later. The caregivers' QoL also improved in a trial of multiallergen food immunotherapy.^{30,31}

The QoL represents an important patient-centered outcome of therapy. Research studies focus on well-selected patients and rigorously controlled settings, but real-world, broader populations

Table 5

Number of Allergic Reactions per Patient During POIT

Allergic reaction	Patients (N = 21)	% (As a proportion of 21 patients)
No allergic reactions seen	5	24%
Patients experiencing allergic reactions	16	76%
Total number of allergic reactions	N = 79	% (As a proportion of 79 allergic reactions)
Grade 1	53	67%
Grade 2	26	33%
Grade 3	0	0
Grade 4	0	0
Grade 5	0	0

Abbreviation: POIT, peanut oral immunotherapy.

Table 6
Treatment of Allergic Reactions During POIT

Treatment of allergic reactions	Allergic reactions (N = 79)	Proportion of allergic reactions, %
Antihistamines	19	24%
Epinephrine	2	2.5%
Inhaled bronchodilator	0	0
Oral steroids	0	0
No treatment (self-resolved)	58	73%

Abbreviation: POIT, peanut oral immunotherapy.

often present different challenges in research implementation and must be studied. Patient uptake of a new intervention, adherence, and patient-desired outcomes are all important challenges in translational research. We believe that there is a need for more pragmatic trials that evaluate results in real-life environments as suggested by others, too.^{32–34} Successful POIT programs are likely to evolve and integrate patient acceptance, compliance, and flexibility while focusing on patient-reported outcome measures (such as QoL changes) to ensure viability in widespread practice. Patient-reported goals and barriers to new treatments are also key when research is brought from the “bench to the bedside.”^{35,36}

Our work showed a high rate of successful treatment completion with 95% of our patients reaching the target maintenance dose. In terms of safety, 2 of our patients (10%) required the administration of epinephrine. We did not encounter any grade 3 or 4 reactions in our patient group compared with other groups.³⁷ Our improved safety data may be due to the slower up-dosing protocol used (once-monthly up-doses instead of twice-monthly or biweekly) or differences in age of participants (preschoolers may be more susceptible to severe reactions) and will need to be validated in larger population samples. We identified a single patient with EoE-like symptoms whose biopsy result was negative and did not reveal EoE. A meta-analysis has reported a rate of 2.7% of OIT patients developing EoE; but for some, this was not a biopsy-confirmed diagnosis.³⁸

We believe that encouraging shared decision making and preparing families for a long-term rather than a “quick-fix” process contributed significantly to the high therapy adherence and low discontinuation rate in our cohort. A recent study reported that when advising patients that non-life-threatening symptoms during OIT can signal desensitization (rather than these symptoms being classified as “unfortunate side effects”), families were less anxious, less likely to skip doses, and had better outcomes during POIT (including fewer symptoms and a greater increase in IgG4 levels).³⁹

A multidisciplinary team approach is invaluable in this form of treatment. Our dietitians played a key role in advising patients on dose measurement and administration, and most patients described this process as easy. We identified applesauce, chocolate pudding, and fruit smoothie as the most popular vehicles for mixing the peanut powder, with most patients consistently using 1 specific vehicle and a few alternating between different vehicles for

Table 7
Allergic Reactions During POIT Described as Percentage of Total Doses Administered

Allergic reaction	Number of allergic reactions	Total doses, % (N = 5668)	Total in-clinic doses, % (n = 190)	Total home doses, % (n = 5478)
Allergic reactions	79	1.3%	5.8%	1.2%
Grade 1	53	0.93%	4.8%	0.8%
Grade 2	26	0.46%	1%	0.4%
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade 5	0	0	0	0
Epinephrine use	2	0.03%	0.5%	0.02%

Abbreviation: POIT, peanut oral immunotherapy.

Table 8
Dietetic Information

Dietetic information	Median	IQR
Rating of ease of measurement and administration ^a for		
Peanut powder	3	2–7
Peanut puff (Bamba)	0.5	0–1
Child rating of taste acceptability ^b for		
Peanut powder	5	3–10
Peanut puff (Bamba)	4.5	1–6
Peanut M&M	8	5–10
	N	%
Timing of dose administration:		
AM (morning)	12	57%
PM (afternoon)	9	43%
Vehicle used for mixing the peanut flour		
Applesauce	12	57%
Chocolate pudding	4	19%
Fruit smoothie	3	14%
Yogurt	2	9%
Ice cream	1	5%

Abbreviation: IQR, interquartile range.

^aScale used: 0 to 10 (0: very easy, 10: very hard to measure).^bScale used: 0 to 10 (0: disliked taste, 10: loved taste).

variety. It has been noted that patients with food allergy often have an aversion to the food they react to, so we did not expect any of the children to be enthusiastic about the taste. We suspect that the low number of missed doses (2% of all doses administered) is likely the result of our robust dietetic support. Other explanations could include a highly motivated population or underreporting of missed doses in the patient diaries.

Most of our patients decided to maintain the 300-mg dose in the long term. This dose has been shown to be protective of allergic reactions owing to cross-contamination, and children with peanut allergy and their families reported a direct improvement in QoL once they achieved this maintenance dose. Specifically, raising the baseline threshold of reactivity from 100 mg to 300 mg after immunotherapy reduces the risk of experiencing allergic reactions to trace exposure by more than 95%. Further increase in threshold to 1000 mg is associated with an additional quantitative benefit in risk reduction.^{40,41} Five patients (24%) decided to keep increasing the peanut dose to achieve this added benefit and potentially also introduce peanut-containing foods into their diet.

Our study adds to the limited available data on QoL changes, real-world POIT patient experience, and outcomes. We report a significant improvement in the overall QoL before and after POIT treatment, with fewer concerns about unintentional exposures and severity of allergic reactions, and fewer limitations in dietary choices and social interactions. In addition, we showed POIT to be safe in a real-world setting with the use of a slow up-dosing protocol.

Strengths of our work include an accurate assessment of changes in QoL following POIT in a real-life clinical setting; a slow up-dosing protocol with flexibility in appointment frequency; and inclusion of a wide age range of unselected, pediatric, patients allergic to peanut. In addition, all data were collected systematically and prospectively, and our patients benefited from ongoing multidisciplinary team support.

The limitations of this study include a less rigorous protocol than that of a clinical trial and a lack of a control group. Our study was also limited by a small sample size. We are aware that there is potential variability in allergen levels between commercial products and between doses in a real-life setting, as mentioned in previous published work from other investigators. In addition, all our data were collected from a population of a single, albeit large, tertiary academic center, which may be different from populations derived from community settings.

Supplementary Data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.anai.2020.03.028>.

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Supplementary Data

eTable 1: World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System

World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System (see text)				
Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
<i>Symptom(s)/ sign(s) of one organ system presentⁱ</i>	<i>Symptom(s) sign(s) of more than one organ system present</i>	<u>Lower respiratory</u>	<u>Lower or Upper reeptratory</u>	Death
<u>Cutaneous</u>	or	Asthma (e.g., 40% PEF or FEV1 drop,	Respiratory fajure with or without loss of consciousness	
Generalized pruntus, urticaria.	<u>Lower respiratory</u>	NOT responding to an inhaled bronchodilator)	or	
Hustling or sensalkm c4 heat or warmth ⁱⁱ	Asthma cough, wheezng shortness of breath (e.g. less than 40% PEF or FEV1 drop, responding to an inhaled bronchodilator)	or	<u>Cardiovascular</u>	
or		<u>Upper respiratory</u>	Hypotension with or without loss of consciousness	
Angioedema (not laryngeal. tongue or uvular)	or	Laryngeal. uvula or tongue edema wen or without stridor		
Or	<u>Gastrointesteial</u>			
<u>Upper respiratory</u>	Abdominal cramps. vomiting. or diarrhea			
Rhinitis (e.g., sneezing, rhinorrhea. nasal pruritus and/or nasal congestion)	or			
or	<u>Other</u>			
Throat-clearing (itchy throat)	Uterine cramps			
or				
Cough perceived to come from the upper airway, not the lung, larynx, or trachea				
or				
<u>Conjunctival</u>				
Conjunctival erythema, pruritus or tearing				
<u>Other</u>				
Nausea, metallic taste, or headache				

Referenced from: Cox L, Larenas-Linnemann D, Locky RF, Passalacqua G.

Speaking the same language: The World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System. J Allergy Clin Immunol. 2010;125(3):569-574, 574.e1-574.e7.