Reintroduction of food in adults: frequencies of introduction and influencing factors after a negative oral food challenge.

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ABSTRACT

Title: Reintroduction of food in adults, frequencies of introduction and influencing factors after a negative oral food challenge.

Background: The self-reported point prevalence of food allergy is 6%. An oral food challenge (OFC) is the golden standard to diagnose a food allergy. If patients have negative OFC's, they could reintroduce the food in their daily-diet. Not all patients succeed, which can result in unnecessary mental, financial or physical problems. Currently frequencies and influencing factors for food reintroduction in adults are unknown.

Aim: Identify the frequency and influencing factors for the reintroduction of food in adults after a negative OFC.

Methods: Quantitative prospective, pre-post-test design. Adult patients with ≥ 1 negative OFC for a specific food. Patients received regular after-care during introduction and completed five questionnaires: demographics, food habit (FHQ), Food Allergy Quality of Life – Adult Form (FAQLQ-AF) and STATE-TRAIT Anxiety Inventory (STAI). Reintroduction frequencies were analysed using descriptive statistics. The FAQLQ-AF and STAI were analysed using a T-test and a Wilcoxon signed-rank test to evaluate differences over time. Influencing factors (age, gender, education level, asthma, allergic rhinitis, atopic dermatitis and oral food technique) were analysed using univariate analysis.

Results: Ninety-seven patients who underwent 118 provocations were included. After 1-2 weeks, 85 reintroductions (84%) following a reintroduction scheme succeeded. After six months, 18 (35.3%) reintroductions in daily life succeeded. The FAQLQ-AF showed overall significant increase of quality of life (QoL) over time and in patients who succeeded. The STAI showed no significant difference. No influencing factors were found affecting reintroduction.

Conclusion: Reintroduction frequencies are comparable with other studies. QoL improved over time. No significant influencing factors were found.

Implications of key findings: More data are necessary to evaluate influencing factors and, consequently, patient care.

Key words: adult, food allergy, oral food challenge, reintroduction, healthcare evaluation

INTRODUCTION

A food allergy is defined as an allergic reaction to a specific food.[1] A meta-analysis, partially executed in adults, defines the self-reported point prevalence at 6% and point prevalence of food challenge confirmed in 1%.[2] The most common food allergies include peanuts, nuts, eggs, fruits/vegetables and milk.[1,3] Symptoms involve a large spectrum of reactions including skin, mucosal, gastrointestinal, respiratory and circulatory problems.[4,5] Patients with a food allergy have to avoid the food in daily life. They also have to carry an emergency kit consisting of antihistamines, adrenalin, corticosteroid and inhaled B2-angonist with them to treat unexpected allergic reactions.[4]

Patients with a food allergy may experience disadvantages ranging from mental health to financial issues.[6] They may experience a continuous fear of eating the allergenic food, which can result in anxiety and decrease their quality of life (QoL).[7] In some cases, a food allergy results in an incomplete diet and, consequently, vitamin deficiency.[8] Because of the high percentage of inaccurate self-reported food allergies, proper diagnosis of a food allergy by a healthcare professional is important.[2]

There are various tests to diagnose a food allergy. A serum food-specific IgE (blood test) or skin prick test[4] are easy and cheap methods. The most reliable test is an oral food challenge (OFC). This can be performed in an open or blinded manner.[4,9] If the result is negative, patients can reintroduce the food in their daily life. This can prevent unnecessary elimination of the food, costs and anxiety and improve QoL. However, some adult patients fail to reintroduce the food and continue an avoidant diet.

In children, failure frequency for reintroduction can be up to 25%.[10–13] Currently, frequencies of reintroduction in adults are unknown. In children, factors influencing reintroduction. [11,14] Include, elimination diet for more than three other foods, a minimum of two years of elimination, the presence of symptoms during reintroduction, family members with allergies and a fear of reintroducing the food.[11,14] The influencing factors for reintroduction in adults are also unknown.

Due to the disadvantages of patients remaining on an inappropriate diet and a high number of failed reintroductions, experts at a Dutch academic hospital developed a local evidence-based protocol to improve after-care during reintroduction at home. This protocol is defined as usual care for patients after an OFC. It consists of a reintroduction scheme and multiple phone consultations after a negative OFC to support patients during reintroduction. To improve patient care and provide more insight into the reintroduction of food after a negative OFC in adult patients, information about the frequency and influencing factors is required.

AIM

The aim of this study is to identify the frequency of reintroduction and gain insight into factors that influence the frequency of reintroduction of food in adults after a negative OFC.

METHODS

Design

This quantitative prospective pre-post-test study was executed in patients referred to the allergology outpatient clinic of the Utrecht University Medical Centre (UMCU) with a self-reported food allergy undergoing an OFC. The pre-post-test design was suitable, as a patient's daily food habits and anxiety levels can change before and after an OFC. Furthermore, the local protocol supported patients before and during the reintroduction over a period of six months. Data was collected at three time points: before the OFC, after 1-2 weeks and six months post-OFC. During these six months, the patients received regular after-care (Figure 1). This study had two main outcomes: frequencies of reintroduction and influencing factors affecting the frequency of reintroduction. The research was part of a larger study concerning all patients taking part in an OFC, including those with positive OFCs.

Population and domain

The domain of this study consisted of patients with a self-reported food allergy who were referred for an OFC and who obtained negative results ≥ 18 years. Consecutive sampling was used. Patients were included if they received after-care according to the local evidence-based protocol and literate in Dutch.

There is not enough evidence concerning the frequency of reintroducing food in adults to calculate a sample size. For this reason, the number of patients needed to include a representative sample of the population undergoing an OFC at the Department of Dermatology and Allergology of the UMCU was calculated. This department performs 85 OFCs annually and approximately 60 of those patients have a negative OFC. Using the Raosoft®[15] sample size calculator, with an error of 5% and a confidence interval of 95%, the recommended sample size was 53 patients with a negative OFC every year. As such, a sample size of 106 patients over a two-year period was suitable.

Data collection

Data was collected from September 2014 until March 2017. Before an OFC, the patient completed three questionnaires: a demographic questionnaire, the Food Allergy Quality of Life –

Adult Form (FAQLQ-AF) and the STATE-TRAIT Anxiety Inventory (STAI). After 1-2 weeks, reintroduction at home according to the introduction scheme was evaluated by means of phone consultations. Six months post-OFC or, in case the patient received multiple OFCs, six months after the last OFC the patient completed three questionnaires: a food habit questionnaire (FHQ), the FAQLQ-AF and the STAI. Furthermore, patients' hospital records were used to extract data about age, sex and OFC technique (open, double-blind placebo-controlled or single-blind placebo controlled).

Looking at the outcome, the measures were reintroduction frequencies derived from phone consultations and the FHQ. Based on the literature, reintroduction success after six months was defined. A reintroduction was successful if the patient is using the pure food, is using the food as an ingredient or has used the food in composite dish in a restaurant and eats it at least once a month. Influencing factors were derived from the demographic questionnaire, patients' hospital records, the FAQLQ-AF and the STAI.

The questionnaires will be explained in more detail below. The demographic questionnaire consisted of 13 multiple-choice questions developed by the principal investigator (AV). The questions were about the patient's age, education level and medical history, such as asthma, allergic rhinitis and atopic dermatitis. Not all patients who had complaints related to asthma, allergic rhinitis or atopic dermatitis were officially diagnosed. Based on questions asked in the demographic questionnaire, definitions of diagnoses were therefore developed in consultation with a pulmonologist and a dermatologist. For definitions of diagnoses, see Table 1.

The FHQ consisted of 20 multiple-choice questions developed by the principal investigator (AV) and face validity was confirmed by experts (a dermatologist, nurse scientist, clinical nurse specialist and dietician). The questions investigated patients' habits of reading food labels, their use of the food product at home and outdoors, and the frequencies of use of the food. Patients with multiple OFCs, completed a separate questionnaire for each OFC.

The FAQLQ-AF[16] consisted of 35 Likert scale questions, ranging from 0 (not at all) to 6 (very severe), about health-related quality of life (HRQL). The questions were divided into four domains: risk of accidental exposure (RAE), emotional impact (EI), allergen avoidance and dietary restrictions (AADR) and food allergy-related health (FAH). The FAQLQ-AF has internal consistency (Cronbach's alpha 0.97).[16]

The STAI[17] consisted of 40 Likert scale questions, ranging from 1 (not at all) to 4 (a lot), about anxiety levels. The questions were divided into two domains: state-anxiety (SA) (how threatening an individual perceives his or her environment to be related to food) and trait-anxiety (TA) (the

individual's capacity to perceive normal situations). The STAI has internal consistency in the general population (Cronbach's alpha state for state anxiety is 0.95 and 0.91 for trait anxiety).[17]

Procedures

Outpatients referred for an OFC were, with their physicians' agreement, contacted by phone, whereupon they received a verbal explanation of the study. Interested patients received an information letter and signed an informed consent form. The OFC and after-care are the usual care all patients receive (Figure 1). The OFC consists of hospitalisation for one or two separate days. During these days, patients eat food open or blinded. Objective and subjective symptoms are observed and discussed with the patient. If no symptoms occur, the food challenge is negative and patients receive a reintroduction scheme. To be sure of no delayed symptoms, patients are called the day after. The first step in the reintroduction schedule at home consists of increasing the amount of the food every half hour. During a phone consultation after 1-2 weeks, the reintroduction and potential allergic reactions are discussed. If the patient fails to reintroduce the food, the reason for this and the patient's needs are discussed. If the patient reintroduces the food without symptoms, the patient receives advice to start reintroduction in daily life. After six months, the final phone consultation is conducted to evaluate the reintroduction in the patient's daily diet.

Data analysis

Data were analysed using the quantitative analysis software package SPSS statistics version 22 (IBM analytics corporation, Armonk, New York, USA[18]).

Patients characteristics and OFC characteristics were derived from the demographic questionnaire and patients' hospital records. Both datasets consisted of ordinal data and were analysed using descriptive statistics.

Reintroduction frequencies were derived from phone consultations after 1-2 weeks and an FHQ after six months. Both datasets consisted of ordinal data and were analysed using descriptive statistics.

Influencing factors were derived from the demographic questionnaire, patients' hospital records, the FAQLQ-AF and the STAI. The FAQLQ-AF was normally distributed and analysed using the T-Test.[19,20] Four separate analyses were performed: 1) an overall analysis including all patients who completed both questionnaires, using a paired sample T-Test; 2) patients who succeeded and completed both questionnaires, using a paired sample T-Test; 3) patients who failed and completed both questionnaires, using a paired sample T-Test.; and 4) differences

between success and failure, using a sample-independent T-Test. The STAI was not normally distributed and was analysed using the Wilcoxon rank test.[19,20] Four separate analyses were performed. These are comparable to the FAQLQ analyses described above.

The influencing factors derived from the demographic questionnaire and patients' hospital records (age, gender, education level, asthma, allergic rhinitis or atopic dermatitis and OFC technique) were analysed using univariate analysis.[19,20] Because the influencing factors were analysed on patient level and not on reintroduction level, evaluations of success and failure were based on the first provocation. A p of <0.05 is considered significant.

Ethical issues

The study was carried out in compliance with the protocol and principles of the Declaration of Helsinki (version 7, 2013)[21] and in accordance with Dutch Law for the protection of personal information (WBP).[22] This study was part of a larger study concerning all patients who had undergone an OFC. The Medical Ethics Review Committee (MERC) of the UMCU confirmed that the Medical Research Involving Subjects Art (WMO) does not apply to the larger study and this substudy.[21] The study presented no physical or mental risks to participants and patients did not receive incentives or compensation. All patients signed an informed consent form. The database was kept in a locked room at the Department of Dermatology and Allergology at UMCU. Only the research team worked with the anonymised data.

RESULTS

Patient characteristics

In total, 198 patients (with positive and negative OFCs) signed the informed consent form and completed baseline questionnaires. The majority was female (60%) and the mean age was 33.7 years (range: 18–70 years). For this sub study, only patients with a negative OFC (N = 97) were were included, the majority of which were female (64%), with a mean age of 33.6 years (range: 18–70) and a medium level of education (54%) (high school or middle-level applied). A diagnosis of asthma was found in 44 patients (54%), allergic rhinitis in 53 (65%) and atopic dermatitis in 49 (60%).

Forty-five (46%) patients had multiple negative OFCs (one to four). In total, 97 patients completed 118 OFCs. Some of the food types that OFCs were performed for were nuts (39%) and fruit (12%). Nuts, the most frequently reported allergens, were divided into three categories: hazelnuts (54%), almonds (11%) and walnuts (15%). Other OFCs (9%) consisted for example of gelatine, cinnamon and pork.

Frequency of reintroduction

In total, 97 patients (representing 118 OFCs) were allowed to reintroduce a specific food. Table 3 shows the reintroduction frequencies. After 1-2 weeks, 85 reintroductions (84%) were successful and 16 (16%) failed. Reasons for failure were; not fully completed the scheme (N=9) or mild symptoms (N=7). In 17 reintroductions, the data at 1-2 weeks were missing, due to no clear reason (N = 12), the patient not answering the phone (N = 3) and the patient not yet having reached the post-reintroduction time point of 1-2 weeks (N = 2). After six months, 33 reintroductions had succeeded (64.7%) and 18 (35.3%) had failed. In 67 reintroductions, the patients had not yet reached the post-reintroduction time point of six months.

Furthermore, the study identified if patients who had succeeded or failed after 1-2 weeks did the same after six months. Twenty-eight reintroductions (74%) remained successful over time and three reintroductions (60%) remained a failure. Ten reintroductions (26%) that had succeeded after 1-2 weeks failed after six months, and three (60%) that had failed after 1-2 weeks succeeded after six months.

Health-related quality of life

The FAQLQ-AFs before the OFC and six months after reintroduction were compared to evaluate changes in the patients' HRQL. N = 43 completed both questionnaires. Table 4 shows the FAQLQ-AF scores. The overall FAQLQ-AF scores show a significant mean difference between pre-OFC and six months after OFC in all four domains (AADR p = 0.00, EI p = 0.00, RAE p = 0.00 and FAH p = 0.00) and the total score (p = 0.00). This represents an increase in HRQL. A subdivision between successful and failed reintroductions showed that patients who succeeded experienced a significant difference in HRQL on three of the four domains (AADR p = 0.00, EI p = 0.00 and FAH p = 0.00) and the total score (p = 0.00). In RAE, there was no significant difference (p = 0.11) in patients who succeeded in the reintroduction. No significant difference in the four domains and the total score was found in patients who failed (AADR p = 0.17, EI p = 0.47, RAE p = 0.92, FAH p = 0.17 and total score p = 0.20).

Lastly, the differences between the mean paired success rate and the mean paired failure rate were identified. Three of the four domains and the total score (AADR p0.02, EI p0.01, RAE p0.07 and total score p0.01) were significantly different. FAH (p0.16) was not significantly different.

Anxiety

The STAIs before the OFC and six months after reintroduction were compared to evaluate changes in patients' anxiety levels. N = 43 completed both questionnaires. Table 4 shows the STAI scores. The STAI showed no significant difference in both domains (SA p0.22, TA 0.89). In both domains no significant difference was found in patients who succeeded (SA p0.22, TA 0.72) or failed (SA p0.91, TA p0.81). Lastly, the differences between the mean paired success rate and the mean paired failure rate were identified. In both domains no significant difference was found (SA p0.39, TA p0.60).

Factors that influence reintroduction

Patient and OFC characteristics were analysed to identify influencing factors. Table 5 shows the univariate analyses. At the univariate level, all patient and OFC characteristics were not significantly related to reintroduction frequencies (age P = 0.98, gender P = 0.28, education level P = 0.28, asthma P = 0.80, allergic rhinitis P = 0.40, atopic dermatitis P = 0.51 and oral food technique P = 0.38).

DISCUSSION

This study identified the frequencies of reintroduction and influencing factors in adult patients after a negative OFC. After 1-2 weeks (reintroduction scheme), a frequency of reintroduction success of 84% and failure frequency of 16% were found. After six months (in daily life) reintroduction success decreased to 65% and the failure frequency increased to 35%. The overall HRQL, measured through FAQLQ-AF between pre-OFC and six months after OFC, showed a significant improvement. A division between success and failure showed that the HRQL in patients who succeeded in the reintroduction after six months improved significantly. No differences in HRQL were found in patients who failed after six months. No significant differences were found in anxiety levels pre-OFC and after six months. No significant influencing factors were found related to reintroduction frequencies.

This study has some limitations. First, a suitable sample size of 106 patients over a two-year period was calculated. However, the results were based on a smaller sample (N = 97) and not all patients achieved the time point of six months (N = 44). This could affect reliability, especially regarding influencing factors. It is recommended that these analyses be repeated if more data becomes available. Secondly, two different methods (a phone consultation and a questionnaire) of data collection were used. Bothe were based on self reported data, which was hard to

objectivities. The may has contributed to information bias. Thirdly, there was not a large amount of data available, some patients had not yet reached the time point. It is recommended that data collection be continued and that these analyses be repeated when more data are available. Despite these three limitations, this study showed initial findings for patients with a negative OFC.

The results of this study can be compared to other studies. The patient characteristics (gender, age, asthma, allergic rhinitis and atopic dermatitis) are in line with similar studies in patients (adults or children) with a food allergy.[23,24] Versluis et al.[23] found relatively higher frequencies of medication (antihistamine) use (60%) in comparison to this study (34%). Versluis et al.'s[23] reports on other medication (systemic corticosteroids and/or immunosuppressive drugs [9%] and inhaled betamimetics [24%]) are in line with this study (corticosteroid 9% and inhalation 25%). This can be explained by the difference in study populations, namely the population of patients who are in the diagnostic process versus patients who have already been diagnosed.

The current study found a success frequency of 84.1% and a failure frequency of 15.9% after 1-2 weeks. After six months, the overall success frequency decreased to 64.7% and the failure frequency increased to 35%. Reintroduction frequencies in adult patients are unknown. Valk et al. investigated reintroduction frequencies in children (N=188) and found a success frequency of 56% (daily diet), a success frequency of 16% (partial introduction) and a failure frequency of 28%. Erp et al.[11] investigated reintroduction frequencies in children (N=103) post-OFC and found a success frequency of 68% and a failure frequency of 33% (daily diet). The frequencies for reintroduction in adults after six months are in line with reintroduction frequencies in children. Erp et al. provided children after an OFC an introduction scheme. This scheme is comparable with the one adults use during 1-2 week introduction in this study. A frequency of 46%[11] children confirmed (retrospectively) that they used a this introduction scheme. In comparison to this study (84%), this is relatively low. The reason for this difference is unclear. To conclude frequencies of reintroduction in adults in daily life are comparable with the frequencies in children. The successful use of a reintroduction scheme after 1-2 weeks in adult patients is relatively higher than in children.

Flokstra et al[6]. and Velde et al[24]. reported a significant improvement in HRQL after six months, measured with the FAQLQ-AF, in child, adolescent and adult with a negative OFC. This is in line with the overall significant improvement in HRQL found in this study. Additionally, the current study showed that HRQL measured through FAQLQ-AF was not significantly different over time in patients who failed in the reintroduction. There is no literature available about the difference in HRQL between patients who succeeded and those who failed. Anxiety levels were

not significantly different. The questionnaire manual[25] provided normal scores for adults of a Dutch city, namely a mean STAI score of 38 and an STAI trait score of 39. Patients in this study reported a mean STAI state score of 33 and an STAI trait score of 33, which indicate lower anxiety levels. The small sample size may have affected this. To conclude, an improvement can be detected from pre-OFC to after six months in the overall HRQL group and in patients who succeeded in the reintroduction. Anxiety levels are relatively low in comparison to adults in a population register of a Dutch city.

Finally, this study did not find influencing factors concerning reintroduction frequencies. To determine influencing factors a univariate analysis was done instead of a multivariate analysis. Erp et al. found refusal (45%) and symptoms after ingestion of peanuts (33%) as the most important reasons for failure among children who started reintroduction. It is recommended that the data be reanalysed when more results are available and that a multivariate analysis be performed.

Based on the findings described above, recommendations can be made for daily practice. Experts at an academic hospital in the Netherlands developed an evidence-based protocol to improve after-care during reintroduction at home. This study, wherein patients received the usual care in accordance with this local protocol, showed that more than half of the patients succeeded in completing the reintroduction scheme. Reintroduction frequencies after six months were comparable with studies which used this protocol partly or not at all. It is recommended that this protocol be evaluated as soon as more data are available and that the analysis be repeated.

It is recommended that further investigation be undertaken to determine why patients failed at reintroduction. Patients completed the questionnaires, but an additional qualitative study is recommended. To minimalize information bias, the use of a questionnaire to evaluate the use of the reintroduction scheme after 1-2 weeks is recommended in future research. This study was part of a larger study concerning all patients taking part in an OFC. The larger study will also focus on patients' purposes for reintroducing the food after a negative OFC. This will provide insight into whether a patient is willing to reintroduce the food, and in what amount, before starting reintroduction and when evaluating after six months.

CONCLUSION

The aim of this study was to identify the frequency and influencing factors for the reintroduction of food in adults after a negative OFC. The reintroduction success frequency was up to 65% and the failures frequency up to 35% in adults with a negative OFC after six months. This finding is in

line with reintroduction frequencies in children after a negative OFC. The patients received after-care during reintroduction, consisting of a reintroduction scheme and multiple phone consultations. This study did not find that influencing factors (age, gender, education level, asthma, allergic rhinitis, atopic dermatitis and OFC technique) affected reintroduction frequencies. It is recommended that this study be repeated with more patients in order to evaluate the local evidence-based after-care protocol.

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FIGURES AND TABLES

Figure 1, Oral food challenge (OFC) usual care and study procedure.

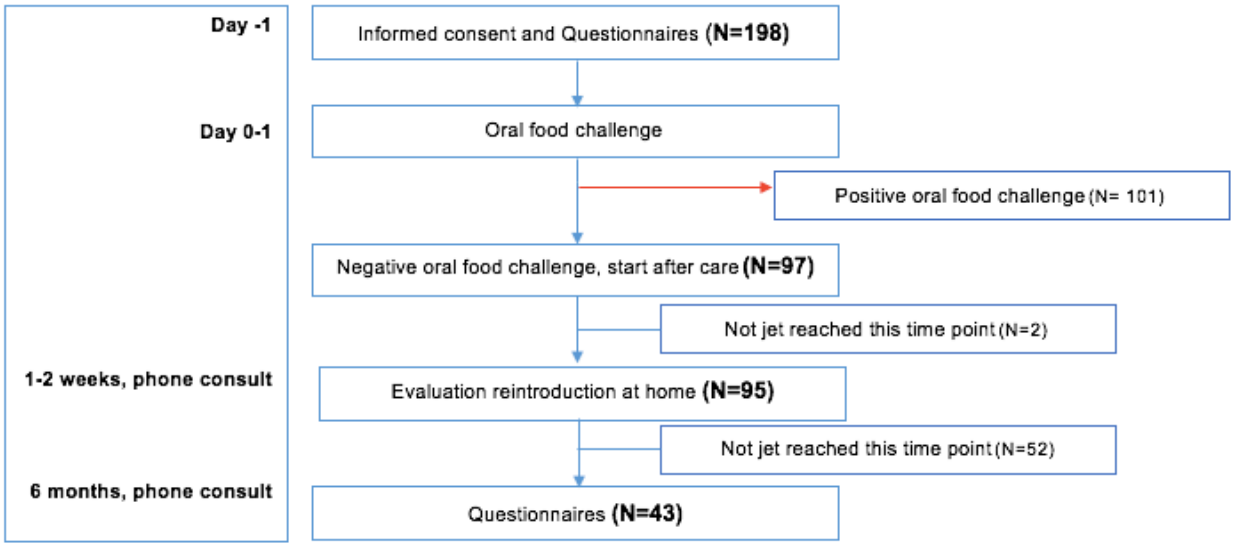

Table 1, Definitions of diagnosis	
Asthma	The patient reported asthma diagnosis **OR** two or more related criteria (coughing, short of breath or wheezing
Allergic rhinitis	The patient reported rhinitis diagnosis **OR** a patient has a positive sensibilisation (skinpricktest, immunoCAP or ISAC) **AND** in combination with complaints during a specific season* **AND** one or more related criteria (watery eyes, sneezing, runny nose, stuffy nose, red eyes, per orbital edema, burning eyes). *Tree and grass season was set from January until August, mugwort pollen season was set in August and dust mites season was set the whole year.
Atopic dermatitis	A patient reported Atopic dermatitis **OR** itchy skin **AND** one or more related criteria (dry skin, history of asthma or Allergist rhinitis).

Table 2, Characteristics of patients	
	Patients with a negative OFC (N=97) N (%)
Sex	
Female	N = 62 (63.9%)
Age (mean and min-max)	33.6 (18-70)
Education level[1] (missing N=17)	
Low	N = 5 (6,3%)
Medium	N = 43 (53.7%)
High	N = 31 (38.7%)
Other	N = 1 (1.3%)
Asthma (missing N=16)	N = 44 (54%)
Allergic rhinitis (missing N=16)	N = 53 (65%)
Atopic dermatitis (missing N=16)	N = 49 (60%)
Allergy repressive medication use	
Antihistaminic daily use and in case needed	N = 36 (34.6%)
Corticosteroid daily use (tablet)	N = 9 (9.3%)
Inhalation (without inhalation corticosteroid)	N = 24 (24.7%)
Characteristics of negative food challenges N=118	
Amount of negative food challenges per patient (mean and min-max)	1.4 (1-4)
Oral food challenge technique (missing 17)	
Open	N = 44 (43.6%)
Double blind placebo controlled food challenge	N = 46 (45.5%)
Single blind placebo controlled food challenge	N = 11 (10.9%)
Food challenged	N = 118 OFC
Nuts	N = 46 (39.0%)
Hazelnut	N = 25 (54.4%)[2]
Almond	N = 5 (10.9%)[2]
Walnut	N = 7 (15.2%)[2]

Other nuts	N = 9 (19.6%)[2]
Fruits	N = 15 (12.7%)
Peanuts	N = 16 (13.6%)
Cow milk	N = 7 (5.9%)
Wheat	N = 6 (5.1%)
eggs	N = 5 (4.2%)
fish	N = 4 (3.4%)
celery	N = 2 (1.7%)
sesame	N = 2 (1.7%)
Soya	N = 2 (1.7%)
Vegetable[3]	N = 2 (1.7%)
shellfish	N = 1 (0.8%)
Other	N = 10 (8.5%)

1. Education levels: low: elementary education; medium: high school or middle-level applied education; high: higher professional or academic education
2. percentage calculated of total amount of nuts (N=46)
3. Excluding celery

Table 3, Result of reintroduction over time

1-2 weeks [1]		**6 months** [2]		**Overall 6 months**[2]	
Reintroduction success	N = 85 (84.1%)	Reintroduction Success	N = 28 (73.7%)	Reintroduction success	N = 33 (64.7%)
		Reintroduction Failure	N = 10 (26.3%)		
		missing	N = 47		
Reintroduction failure	N = 16 (15.8%)	Reintroduction Success	N = 2 (25%)	Reintroduction failure	N = 18 (35.3%)
		Reintroduction Failure	N = 6 (75%)		
		missing	N = 8		
missing[3]	N = 17	Reintroduction Success	N = 3 (60%)	missing[3]	N = 67
		Reintroduction failure	N = 2 (40%)		
		missing	N = 12		
Total OFC	118	**Total OFC**	N = 118	**Total OFC**	N = 118

1) 1-2 weeks' data originating from phone visit evaluating if patients did the introduction increasing dose schema at home, recorded in patient hospital records.

2) 6 months' data originating from FHQ 2

3) missing: data is missing or patients did not yet reached this time point

Table 4, Food allergy quality of life – Adult form and STATE-TRAIT Anxiety Inventory questionnaire										
	Food allergy quality of life – Adult form N=44[1]									
	Overall			success			failure			Success/failure
	Mean Pre-challenge (SD)	Mean post-challenge (SD)	Mean paired difference (p)	Mean Pre-challenge (SD)	Mean Post-challenge (SD)	Mean paired difference (p)	Mean Pre-challenge (SD)	Mean Post-challenge (SD)	Mean paired difference (SD)	Difference between success and failure (p)
Domain: Allergen avoidance & dietary restrictions	4.16 (1.42)	3.36 (1.58)	0.80 (p0.00)	4.08 (1.35)	3.00 (1.51)	1.08 (p0.00)	4.25 (1.48)	3.95 (1.59)	0.30 (p0.17)	0.77 (p0.02)
Domain: Emotional impact	4.47 (1.23)	3.73 (1.62)	0.73 (p0.00)	4.40 (1.27)	3.33 (1.67)	1.07 (p0.00)	4.51 (1.15)	4.33 (1.43)	0.17 (p0.47)	0.89 (p0.01)
Domain: Risk of accidental	4.36 (1.34)	3.90 (1.62)	0.46 (p0.00)	4.03 (1.20)	3.32 (1.69)	0.71 (p0.11)	4.82 (1.35)	4.79 (1.24)	0.03 (p0.92)	0.69 (p0.07)
Domain: food allergy related health	4.26 (1.50)	3.40 (1.66)	0.86 (p0.00)	4.36 (1.52)	3.23 (1.65)	1.13 (p0.00)	4.13 (1.49)	3.61 (1.60)	0.52 (p0.17)	0.61 (p0.16)

Total score	4.30 (1.21)	3.61 (1.47)	0.70 (p0.00)	4.18 (1.17)	3.20 (1.49)	0.98 (p0.00)	4.46 (1.20)	4.24 (1.31)	0.22 (p0.20)	0.76 (p0.01)
STATE-TRAIT Anxiety Inventory N=44[3]										
	overall			Success			failure			Success/failure
	Median Pre-challenge (range)	Median post-challenge (range)	P value	Median Pre-challenge (range)	Median post-challenge (range)	Median difference (P value)	Median Pre-challenge (range)	Median post-challenge (range)	Median difference (P value)	Median difference[2] (p)
State anxiety related to food	33.3 (20-66)	30.8 (20-72)	2.5 (p0.51)	30.9 (20-66)	28.6 (20-54)	2.3 (p0.35)	33.2 (20-55)	33.5 (20-72)	-0.3 (p0.58)	2 (p0.39)
Trait anxiety related to food	32.8 (19-56)	33.1 (19-66)	-0.3 (p0.75)	31.2 (21-52)	31.7 (19-50)	-0.5 (p0.97)	34.2 (20-52)	34.7 (20-66)	-0.5 (p0.52)	0 (p0.65)

1. FAQLQ-AF data was normal distributed so analysed using T-Test
2. STAI data was not normal distributed so analysed using Wilcoxon signed rank test

Table 5, Univariate analysis, influencing factors introduction failure or success after 6 months on first challenge				
Categorical data; Pearson Chi-Square				
	Success N= 24[1]	Failure N= 20[1]	Pearson chi-Square* or Mann-Whitney	Asymp sig (2-tailed)
Age (mean, range)	36.8 (18-67)	37.7 (19-70)	239.0*	0.981
Gender (N, %)				
Female	17 (70.8%)	11 (55%)	1.182	0.277
Male	7 (29.2%)	9 (45%)		
Education [2] (N, %) (missing N=4)				
Low	2 (8.3%)	0 (0%)	3.826	0.281
Intermediate	13 (54.2%)	13 (81.2%)		
High	8 (33.3%)	3 (18.8%)		
Other	1 (4.2%)			
Asthma (N, %) (missing N=4)	13 (54.2%)	8 (50%)	0.067	0.796
Allergic rhinitis/conjunctivitis (N, %) (missing N=4)	18 (75%)	10 (62.5%)	0.714	0.398
Atopic dermatitis (N, %) (missing N=4)	16 (66.6%)	9 (56.3%)	0.444	0.505
Oral food challenge technique (N, %) (missing N=4)				
Open	13 (59.1%)	9 (47.4%)	3.064	0.382
DBPCFC	8 (36.4%)	7 (36.8%)		
EBPCFC	1 (4.5%)	3 (15.8%)		

1. Total N=44 varies between 40-44 due to missing value
2. Education levels: low: elementary education; medium: high school or middle-level applied education; high: higher professional or academic education