Development, validation and outcome of health-related quality of life questionnaires for food allergic patients
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Introduction: the impact of food allergy on quality of lifes

Aims and outline of this thesis

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Chapter 1

Introduction

Food is an essential element in our lives; it is essential for staying alive and it is an important part of our cultural identity. For patients with a food allergy some sources of food may be fatal. Consequently, the lives of these patients may be seriously disrupted by the continuous vigilance required to avoid foods to which they are allergic.

Adverse food reactions or hypersensitivities include any abnormal reaction resulting from the ingestion of food and might be the result of food intolerance (nonallergic food hypersensitivity) or food allergy. Food intolerance is a non-immunologic response, such as may be seen in certain metabolic disorders (e.g., lactase deficiency). Food allergy is an adverse immunological reaction that may be due to IgE- or non-IgE-mediated immune mechanisms and the symptoms may involve the skin, gastrointestinal tract, respiratory tract, and cardiovascular system. Although any food may provoke a reaction, relatively few foods are responsible for the vast majority of food allergic reactions: milk, egg, peanuts, tree nuts, fish and shellfish.

Prevalence of food allergy

The prevalence of food allergy is the greatest in the first few years of life. It has been estimated that up to six per cent of children less than three years of age experience food-induced allergic disorders. Most children outgrow their sensitivity and approximately two per cent of the adult population experience food-induced allergic disorders. Although it was once thought that peanut, tree nut and seafood allergies were never outgrown, it has become apparent that clinical tolerance develops in about 20% of young children with peanuts allergy. However, many studies show that food allergy prevalence is increasing in most Western countries. The prevalence of peanut allergy was found to have doubled in American children less than five years old in a five-year period. Emergency room visits due to food allergy have increased by a factor of six in the United Kingdom. This increase in prevalence of food allergy is also accompanied by an increase of anaphylaxis caused by food allergy, which is potentially fatal.

Management of food allergy

Tools for diagnosis and management of food allergy have not changed much in the past two decades. The diagnosis includes clinical history, physical examination, tests for specific IgE antibody to suspected foods, elimination diets and oral food challenges. The management includes restriction diets and provision of medications such as epinephrine for emergency treatment. Once properly diagnosed by double-blind placebo-controlled food challenges (DBPCFC), strict avoidance of the implicated food or foods is the only proven form of treatment. In addition, proper patient education about their allergy, avoidance strategies and dealing with reactions in cases of accidental exposure, allows patients to control their disease as much as possible. In many patients clinical tolerance will develop over time, and
therefore follow-up food challenges are often indicated. Promising new methods for diagnosing food allergy such as individualised analysis of allergenic epitope recognition patterns and novel strategies for treatment, including immunotherapy, are under development but are not yet commonly available.

**Health-related quality of life**

Quality of life has various meanings, which encompasses factors such as financial security, freedom, spiritual contentment, quality of environment, health, and the way these factors interrelate. It has been defined by the World Health Organisation (WHO) as 'the individual’s perception of their position of life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.' A simpler definition of quality of life is 'the subjective value a person places upon satisfaction with his or her own life.' The component of overall quality of life that pertains to an individual’s health is called health-related quality of life (HRQL) and may be defined as ‘the effects of an illness and its consequent therapy upon a patient, as perceived by the patient’. HRQL incorporates the definition of health of the WHO; 'a state of complete physical, mental, and social well-being and not merely the absence of disease and infirmity.' HRQL can be seen as a multidimensional concept that includes physical status and functional abilities, psychological status and well-being, social and professional interaction, and the patient’s health perception. It is important to understand that a similar level of objective clinical impairment may have a different impact on HRQL in different patients because individuals vary in their tolerance level. In addition, unlike objective clinical measures, HRQL focuses on the patient’s perspective of their disease and measures the impairments that patients consider to be important.

**Impact of food allergy on quality of life**

There is no cure currently available for patients with food allergy. Food allergic patients must carefully avoid the causal foods every day, and this is a great burden to themselves and their families. Despite taking precautions, accidental exposure may occur and for some patients this may be fatal. Once a patient has experienced anaphylaxis, there is a great risk that he or she will experience recurrence. This may create an additional burden of fear. In daily life, food allergic patients are burdened with a variety of tasks, including careful label reading of manufactured products, obtaining information about cross-contamination of foods with allergens, avoiding accidental exposures that may occur and limiting common social activities associated with eating.

Joshi et al. found that most parents of children on restricted diets are unable to identify common allergenic food ingredients. Only seven per cent of the parents correctly identified milk, 22% correctly identified soy protein and 54% correctly identified peanut. Most parents correctly identified wheat and egg. These findings strongly support the need for improved labelling and education for patients and parents about reading labels. These recommendations are in accordance with the
findings of Gowland. She discusses food allergen avoidance from the patient’s viewpoint and states that the vigilance required to avoid food allergens depends on information that is often hidden or misleading. This uncertainty may lead to stress and social exclusion. In order to reduce the allergen risk and in addition to improve the quality of life of food allergic patients, Gowland states that there should be clear food allergen labelling on manufactured products. Moreover, there should be integration of food allergy into all primary professional training for cooks, caterers and all those who prepare food for the public. And finally, there should be clear allergen management in food hygiene controls for all food businesses.

Accidental exposure to allergenic food often occurs outside the home and it accounts for the majority of deaths reported from food allergy. In Britain 14% of food allergic patients reported reactions in restaurants and in the United States almost 14% of self-selected registered peanut and/or tree nut allergic patients reported reactions in restaurants or other food establishments. Establishments commonly reported in the latest study were Asian food restaurants (19%), ice cream shops (14%), and bakeries / doughnut shops (13%). Among meal courses, desserts were a common cause (43%). In most of the cases (78%) someone in the establishment knew that the food contained peanut or tree nut as an ingredient; in 50% of these incidents the food item was ‘hidden’ in sauces, dressing etc. In 22% of the cases, exposure resulted from contamination caused primarily by shared cooking or serving supplies. These data show that patients with a food allergy are faced with a number of challenges when eating in restaurants and other food establishments. Given the effort required to avoid accidental exposures and the inherent uncertainty of success, living with a food allergy may be expected to have a negative influence on the quality of life.

Why measure HRQL?
HRQL measurements offer the opportunity to study the impact of disease from the patient’s perspective. Measurement of an objective disease parameter provides information to clinicians, but are of limited interest to patients. These measures are often poorly correlated with areas in which patients are most interested and familiar, such as functional capacity and well being. Moreover, two patients with the same objective clinical impairment may have very different degrees of impairment in their HRQL. For example, two patients with the same severe reaction to peanut following accidental exposure may have different social function and well-being. Although some patients may continue going to social events without anxiety, others may stay at home and feel isolated. Therefore, HRQL instruments allow quantification of differences between patients with similar objective disease burdens.

HRQL measurements also offer the opportunity to study the effect of a treatment from the patient’s perspective. HRQL instruments allow quantification of changes within patients over time due to diagnostic or therapeutic interventions. Especially in allergic diseases where mortality is low, HRQL issues are of importance in the management of patients. This is also true in food allergy, especially in cases
where patients only intermittently have symptoms and need to undertake extensive measures in order to prevent exposure to foods to which they are allergic.

These considerations explain why measuring HRQL is important in general and especially in patients with food allergy. It gives clinicians additional information about the impact of disease from the patient’s perspective and it can be used for measuring clinical effectiveness of management strategies.

**Approaches to study quality of life**

**Types of HRQL instruments**
There are two major types of HRQL instruments used in clinical trials and practice: generic and disease-specific questionnaires. Generic instruments can be used to evaluate and compare different disease states, treatment interventions and populations. The disadvantages of generic instruments are that they are by design comprehensive, so they may not focus adequately on problems specific to a particular disease. Furthermore, they may not be responsive enough to detect small but clinically meaningful changes in HRQL in a given disease state.

Disease-specific instruments are more responsive than generic instruments and they can by targeted to a specific population, disease, or function. This allows evaluation of HRQL restricted solely to the disease studied. These disease-specific instruments are much more likely than generic instruments to detect clinically important changes in patients’ impairments. However, disease-specific instruments do not allow comparison between different diseases.

In some situations both generic and disease-specific instruments are of value and can be used in combination to compare populations (generic) and identify specific areas of problems within patient groups (disease-specific).

**Structure and administration of HRQL instruments**
HRQL questionnaires are made up of items, grouped into a number of domains. A domain refers to a set of HRQL behaviours or experiences that one is trying to measure. HRQL questionnaires can be self-completed, or may be administered by a face-to-face or telephone interview. In some cases a surrogate responder such as a parent, completes the questionnaire. A face-to-face interview maximises the rate of response, minimises missing items and errors of misunderstanding, but requires more resources and training of the interviewer and may reduce willingness to acknowledge problems. Telephone interviews, are less resource intensive than face-to-face interviews. On the other hand, there is a greater likelihood of low response rates, missing items and misunderstanding, if questionnaires are self-completed. Surrogate completion reduces stress for the target group (e.g. in very elderly or sick persons), but the surrogate’s perception of HRQL may differ from the patient group’s perception. Parents may complete HRQL questionnaires by proxy in young children. Older children can make judgements about their own health
state and may complete HRQL questionnaires by themselves. Obvious discrepancy between the judgements of children and parents about quality of life is often cited as a problem, but children differ from adults in their understanding of health and have their own views about quality of life. In addition, children’s view about quality of life changes with age 30.

**Development of disease-specific HRQL instruments**

The fundamental characteristics of a good instrument are reliability, validity and responsiveness 31. A measure is regarded as reliable if the same result is obtained when the same unchanged subject is measured again. Validity is a measure of the instrument’s ability to actually measure what it is intended to measure. Responsiveness relates to the ability of the questionnaire to detect small but potentially important changes in HRQL over time, which is important for use in clinical settings.

The development of a disease-specific measure may involve a number of steps: item generation, item reduction, cross-sectional validation and longitudinal validation. Translation and cross-cultural validation are necessary for application of the instrument in different languages and in different cultural settings. Each of these steps will now be described in more detail.

**Item generation**

Item generation is a process by which all potential items for a new measure are assembled. Sources for possible items are patients or parents, experts and the literature. Items can be generated through interviews and focus groups. Patients or parents are asked to think of quality of life items related to their own or their child's disease. Experts may be asked which HRQL items their patients cite in the clinical setting. Individual interviews and focus group sessions can be used. Focus groups involve a small number (usually less than ten) of people who discuss a certain subject (in this case HRQL) freely, under the guidance of an experienced facilitator 32.

Items are generated and organised into domains or groups of related items, such as emotions, social functioning, or activities of daily living. The number of items that may be generated is in principal unlimited, but item generation is complete when no important new items are named or identified. It is important to ensure that the spectrum of patients contributing items (i.e. with regard to the limits of the age group and difference of severity of disease) is complete, or as complete as possible. The end product of this first step, called the extended instrument, is a relatively long list of HRQL items worded as problems.

**Item reduction**

This aims to eliminate redundant or personal items and to reduce the questionnaire to a manageable and feasible number of items. The extended instrument is presented to other patients or parents to indicate which items are troublesome for themselves or their children. The answer to this question is a simple ‘yes’ or ‘no’, followed by a grading of importance for the ‘yes’ answers on a five-point response scale with
responses varying from ‘almost unimportant’ to ‘extremely important’. Alternate wordings may be tested.

Each candidate item is then scored for overall importance, which is the product of the frequency with which an item is identified as being important by patients and the mean impact of that importance using the five-point scale \(^{33,34}\). This allows for a selection of items for a prototype instrument. The number of items selected depends on the need to cover all areas of HRQL and the need to produce a manageable instrument. In general, HRQL instruments become unmanageable if they take more than 20 minutes to complete \(^{35}\). The prototype HRQL instrument is now suitable for validation.

It is important that the questionnaire is appropriately formatted. Each question should be easy to understand, free of medical jargon and inconsistencies, clear with respect to the time frame to which they refer, and encompass only one item. Also, the response options should be clear, brief and consistent. In paediatric questionnaires these formatting details are even more important. Moreover, it is extremely important that the reading level of the questionnaire is age-appropriate. Pilot testing the questionnaire will assess whether the format, wording, and feasibility are appropriate \(^{32}\).

**Cross-sectional validation**

Validation may occur by comparing the HRQL questionnaire with an independent measure. This measure is independent of HRQL and is often a disease-specific parameter that reflects the severity of disease (e.g., \(FEV_1\) in asthma). However, in patients with food allergy such a disease-specific parameter is not available, because symptoms caused by foods only occur following exposure, and such accidental exposures are relatively infrequent. Therefore, the perceived risk of the chance of and consequences of accidental exposure is the driving force of quality of life and this perceived expectation of outcome may be used as the independent measure. A specific instrument that is capable of capturing this expectation may be developed: the Expectation of Outcome measure \(^{36}\).

The Expectation of Outcome measure asks patients or parents what they expect the outcome to be of their disease in the future. For example, in patients with food allergy a possible question that could be considered for the Outcome Expectation measure is: What chance do you think you have/your child has of accidentally ingesting the food to which you are allergic? Answers to these questions are expressed on a seven-point scale with responses varying from ‘a negligible chance’ to ‘a very great chance’. The correlation between the Expectation of Outcome measure and the answers to the individual questions of the HRQL questionnaire are calculated. This method allows for selection of a small number of items having the best correlation for use in the final instrument. Consistency of the questionnaire can be further confirmed by calculating the correlation between an individual item and the other items of the questionnaire (i.e. Cronbach’s alpha). The end product of this third step is a cross-sectionally validated HRQL instrument.
Longitudinal validation
In order to investigate if a cross-sectionally validated instrument will be capable of measuring within patient differences over time, the instrument must be longitudinally validated. This can be done in patients in whom HRQL is expected to change because of diagnostic and/or therapeutic interventions. With regard to food allergy, one can think of studies involving improved diagnosis, counseling, and expert dietary intervention. Food allergic patients in these studies would be expected to have an improvement in their HRQL if they would be included in the active intervention group. Patients would receive the HRQL instrument and the Expectation of Outcome measure at the beginning of the study. After the intervention, patients would need to be followed for a period of time during which they could become accustomed to their new health state. This usually requires several months. After this period, the HRQL instrument and the Expectation of Outcome measure could be re-administered. Changes in the average score for the total instrument are then correlated to changes in the Expectation of Outcome measure, comparing values before and after the intervention described. Good correlation between the Expectation of Outcome measure and the HRQL scores validate the instrument longitudinally and simultaneously demonstrate the impact on HRQL of the intervention used. The final product is the definitive HRQL instrument and the impact of the intervention on HRQL can be reported.

Translation and cross-cultural validation
In order to use the HRQL instrument in different languages and cultural settings, translation of the questionnaire to the language of the patient population studied is required to reliably compare data across populations. Forward and backward translation may be used in order to check content comparability. However, translation alone, without consideration of cultural differences, may not be sufficient. Cross-sectional validation in the new language and cultural setting allows for the assessment of the performance of individual items in that language and culture. Good cross-sectional correlation coefficients indicate validity for that particular language setting. Low correlation coefficients may be encountered if the translation is inaccurate or if the item does not appear to be a problem in the new cultural context. If cultural comparisons are made before the item reduction phase, it may be possible to identify items that are applying to only certain cultural settings or countries. Following successful cross-sectional validation in the new language and cultural setting, a final instrument can be generated by incorporating it into a longitudinal study in the new language as indicated above.


Introduction

Current knowledge regarding food allergy and quality of life

Studies on quality of life and food allergy

There are only a few studies that have measured the HRQL in patients with a food allergy. Of the published five studies, three used general questionnaires to measure quality of life and two used disease-specific questionnaires. In three of these five studies the parents or caregivers completed the questionnaires.

Primeau et al. \(^{40}\) compared the quality of life and family relations of children and adults with a peanut allergy to that of children and adults with a rheumatological disease. To quantify the impairment in quality of life, they used a vertical visual analogue scale (VAS) adapted from the European Quality of Life questionnaire (EQ-5D) \(^{41}\). The impact of the peanut allergy or rheumatological disease on the family was measured by the Impact on Family Questionnaire (IFQ) \(^{42}\). This questionnaire contains four dimensions of family life: familial-social, personal strain, financial burden, and mastery. They found that the parents of peanut-allergic children reported that their children had significantly more disruption in their daily activities as compared to the parents of children with a rheumatological disease. Furthermore, the parents of peanut-allergic children reported more impairment in the familial-social dimension of the IFQ. According to the authors this parental perception of considerable disruption of daily and social activities of the peanut-allergic child may be due to the perceived risk of death of their child. The loss of parental mastery when someone else cares for the child makes some parents even refuse to allow their child to go, for example, to birthday parties or school excursions.

Sicherer et al. \(^{43}\) studied the impact of childhood food allergy on quality of life. The parental perceptions of physical and psychological functioning of the food-allergic child were measured with the Child Health Questionnaire (CHQ-PF50) \(^{44}\). This questionnaire contains twelve scales of general health: 1) physical functioning, 2) role social / emotional, behavioural, 3) role social / physical, 4) bodily pain, 5) general behaviour, 6) mental health, 7) self-esteem, 8) general health, 9) parental impact-emotional, 10) parental impact-time, 11) family activities, and 12) family cohesion. They showed that the parents of children with food allergy scored significantly lower on the scales of general health perception, emotional impact on the parent and limitation on family activities as compared to established norms.

Marklund et al. \(^{45}\) studied the HRQL among adolescents with allergy-like conditions, with emphasis on food hypersensitivity. They investigated the magnitude of self-reported allergy-like conditions and used the Medical Outcome Trust Short Form 36 Health Survey (SF-36) to measure HRQL \(^{46}\). The SF-36 consists of 36 items divided into eight scales: 1) physical functioning, 2) role functioning-physical, 3) bodily pain, 4) general health, 5) vitality, 6) social functioning, 7) role functioning-emotional, and 8) mental health. The adolescents with allergy-
like conditions reported significantly lower HRQL on seven of the eight SF-36 scales (not on physical functioning), compared with adolescents without allergy-like conditions. This finding was regardless of whether the condition had been doctor-diagnosed or not. Nineteen percent of the respondents reported food hypersensitivity. Females with food hypersensitivity scored significantly lower on bodily pain, general health, and social functioning than females with other allergy-like conditions. Males with food hypersensitivity did not show this HRQL impairment.

In contrast to the above-mentioned studies, Avery et al. 47 used a disease-specific questionnaire that was self-completed by the children. Avery et al. compared the quality of life in children with a peanut allergy to that of children with insulin-dependent diabetes mellitus. To measure quality of life, they used two disease-specific quality of life questionnaires. One was designed by themselves and the other was adapted from the Vespid Allergy Quality of Life Questionnaire 36. However, they do not describe how they designed or adapted these questionnaires. Moreover, these two questionnaires were not tested for reliability and validity. Therefore, caution is needed by the interpretation of these results. The results of this study were that children with a peanut allergy reported a poorer quality of life than children with insulin-dependent diabetes mellitus. Children with peanut allergy reported more fear of an adverse reaction and more anxiety about eating and only peanut allergic children reported fear of death.

Recently Cohen et al. 48 developed a disease-specific questionnaire to measure quality of life in families with a child with food allergy: the Food Allergy Quality of Life – Parental Burden (FAQL-PB) questionnaire. This questionnaire is completed by the parents and measures the parental burden associated with having a child with food allergy. They used the principles of item generation, item reduction and cross-sectional validation previously established in the development of other disease-specific HRQL questionnaires 49-51. They reported strong internal and cross-sectional validation. However, the instrument was not longitudinally validated.

**Is quality of life affected by food allergy, how much and by what?**

The few studies that have measured the HRQL in patients with a food allergy all showed that the HRQL is negatively affected in these patients. There may be some variables that influence the magnitude of the impact of food allergy on HRQL.

First, the food to which one is allergic. Primeau et al. and Avery et al. investigated solely peanut-allergic patients while the other studies included patients with different food allergies although peanut and tree nut were most frequently reported. From these latest studies, only Sicherer et al. compared the HRQL of patients with peanut allergy to those with other food allergies, but found no differences. The other studies have not investigated the differences between different food allergies. Hence, it is not known if for example milk allergy has a greater negative impact on quality of life than, for example, peanut allergy. However, it is a fact that some foods are easier to avoid than others and may make living with a food allergy easier.
Second, the severity of the allergy, because it is reasonable that the lives of patients who have experienced an anaphylactic reaction are more disrupted than patients who have only experienced dermal reactions. Only Cohen et al. studied this and found that parents who reported an anaphylactic reaction in the past scored significantly lower on the FAQL-PB questionnaire than parents not reporting anaphylaxis.

Third, the number of foods to which one is allergic. This topic was investigated in two of the above mentioned studies. Sicherer et al. found that seven of the twelve CHQ-PF50 scales were significantly lower in families with multiple food allergies as compared to families with one or two food allergies. Also Cohen et al. found a significantly lower total score on the FAQL-PB questionnaire in families whose children had three or more food allergies compared to those with two or fewer food allergies. Moreover, the mean score of thirteen of the seventeen individual questions of the FAQL-PB questionnaire differed significantly in these two populations.

Fourth, many allergic patients have co-morbid conditions (e.g. atopic dermatitis, allergic rhinitis, or asthma) and this may have an additional negative impact on quality of life. Sicherer et al. showed that only the CHQ-PF50 scale general health was significantly impacted by co-morbid conditions. In agreement with this, Marklund et al. showed that adolescents with food hypersensitivity who also reported allergic diseases, scored significantly lower on the SF-36 scales bodily pain and general health compared to adolescents who only reported food hypersensitivity. However, co-morbid conditions will affect outcome using generic HRQL instruments, but it should not affect outcome of disease-specific HRQL instruments.

Fifth, gender may play a role in the impact of food allergy on quality of life. Most of the above-mentioned studies did not take this topic into account. Only Marklund et al. gave special attention to gender differences and, as previously stated, they found that females with food hypersensitivity scored significantly lower on the SF-36 scales bodily pain, general health, and social functioning than females with other allergy-like conditions. Males with food hypersensitivity did not show this HRQL-deterioration. Unfortunately, Marklund et al. did not make a comparison between females and males within the food hypersensitivity condition. However, in patients allergic to yellow jacket venom HRQL was significantly more impaired in women than in men.

Finally, it is interesting that Marklund et al. found that adolescents with allergy-like conditions had similar scores on the SF-36 whether they had verified allergy or not. Apparently, the perception of having a food allergy with the consequences of food avoidance is associated with deterioration in HRQL comparable to a verified food allergy. This underlines the importance of a correct diagnosis in order to abandon self-perceived but unproven food allergies and to prevent needless deterioration of HRQL.
Future priorities for research

As described above, there are only a few studies that have investigated the quality of life in patients with food allergy. This is remarkable because food allergy appears to have a significant negative impact on the quality of life. It is important to develop good food allergy specific HRQL questionnaires in order to identify the specific disabilities and problems of food allergic patients. Such questionnaires can provide additional information to the measurements of usual outcomes namely, insight into the burden and consequences of food allergy. It can also be used to study the relationship between management strategies and the improvement in HRQL.

Currently, there is only one HRQL questionnaire specific for food allergy available. This has only recently been published and represents a significant milestone in this field. However, this FAQL-PB questionnaire developed by Cohen et al. has some significant limitations. First, it was developed to measure HRQL in children. Therefore, it cannot be used in adults with food allergy. Second, the questionnaire is completed by parents and measures the parental burden associated with having a child with food allergy. Therefore, it provides no information about the impact of having a food allergy on quality of life perceived by the child. Third, the instrument is used for children across all age groups (range two months to seventeen years). No distinction is made between the problems associated with having a newborn, schoolchild, or teenager with food allergy, in which the problems are presumably different. Fourth, the questionnaire is not longitudinally validated. This means that the capability of this questionnaire to measure within patients differences over time is not documented. And finally, the questionnaire was developed and validated in the United States of America and may therefore not suitable for Europe. Moreover, it should be noted that the term food allergy covers a spectrum of disorders and perceived disorders. Over time it might be necessary to examine the impact on quality of life of specific food allergies, such as milk or peanut, whose impacts on quality of life may differ significantly.

In the scope of a large European multicenter research project funded by the European Union known as EuroPrevall, several new food allergic-specific HRQL instruments will be developed. In order to overcome the limitations of the FAQL-PB, questionnaires will be developed that will be completed by the parents and questionnaires that will be completed by the child. It may be interesting to compare the outcomes of the questionnaires completed by the parents to the outcomes of the questionnaires completed by children themselves. Moreover, different questionnaires for different age groups of childhood and also a specific questionnaire for adults with food allergy will be developed. A questionnaire specific for adults with oral allergy may be developed when it turns out that these patients experience other quality of life items than patients with a systemically reaction.

The new HRQL questionnaires will be cross-sectionally and longitudinally validated by the method described above. The longitudinal study will investigate if these questionnaires are capable of measuring within-patient differences over time.
It will also aim to show the impact of quality of life following the intervention (diagnosis by double-blind placebo-controlled food challenges). HRQL may be negatively influenced in patients with self-perceived food allergy. A good diagnosis may give certainty to the patient and HRQL may improve, even when the diagnosis is verified and even more if the diagnosis is rejected. This hypothesis has never been investigated and will be one of the topics of this study.

The new questionnaires will be subsequently translated into different languages followed by cross-sectional and longitudinal validation in the new language in different European countries. By doing so, reliable and valid disease-specific HRQL questionnaires will be provided for patients with food allergy that can be used in different age groups and in different European countries. These instruments will be usable to measure changes in quality of life in food allergic patients from any cause, including spontaneous fluctuation or following interventions. Next to this, other possibilities for future research are comparison of HRQL measured by disease-specific instruments and generic instruments or to combine the measurement of HRQL with economic calculations.

Aims and outline of this thesis

The main aim of this thesis was to develop and validate disease-specific health-related quality of life (HRQL) questionnaires for children (8-12 years), adolescents (13-17 years) and adults (18 years and older) with food allergy (chapters 3, 4 and 5). Additional aims were to investigate the reliability of these three questionnaires (chapter 6) and to investigate HRQL outcomes measured with these disease-specific questionnaires as compared to other generic questionnaires (chapter 7). Finally, this thesis aims to give an overview of current knowledge in the field of food allergy and HRQL at the beginning of the EuroPrevall project (chapter 2) and towards the end of the project (chapter 8).

Chapter 2

Chapter 2 contains a EuroPrevall state of the art paper describing a framework for measuring the social impact of food allergy across Europe. It describes the current knowledge on food allergy and HRQL at the beginning of the EuroPrevall project and how HRQL could be measured in food allergy. Finally, relevance and practical implementation of HRQL questionnaires are discussed.

Chapter 3

In chapter 3, we describe the development and validation of the Food Allergy Quality of Life Questionnaire - Child Form (FAQLQ-CF) in the Dutch language. This questionnaire was specially developed for food allergic children aged 8 to 12 years and the questionnaire is completed by the children themselves.
Chapter 4
Chapter 4 describes the development and validation of the Food Allergy Quality of Life Questionnaire - Teenager Form (FAQLQ-TF) in the Dutch language. This questionnaire was specially developed for food allergic adolescents aged 13 to 17 years and the questionnaire is completed by the adolescents themselves.

Chapter 5
In chapter 5 we describe the development and validation of the Food Allergy Quality of Life Questionnaire - Adult Form (FAQLQ-AF) in the Dutch language. This questionnaire was specially developed for food allergic adults 18 years and older.

Chapter 6
Chapter 6 contains the results of test-retest reliability of the FAQLQ-CF, -TF, -AF. The questionnaires were completed by the same patients twice with a 10-14 day interval and we investigated the reproducibility of the questionnaires over time when no change in the condition has taken place.

Chapter 7
In chapter 7, a study is presented on HRQL of food allergic patients measured with generic and disease-specific questionnaires. The aim of this study was to compare generic HRQL of food allergic patients with the general population and other diseases. In addition, it compares the HRQL of food allergic patients measured with generic and disease-specific questionnaires.

Chapter 8
In chapter 8, we present a review on how HRQL can be measured in food allergy and we discuss recent findings on how food allergy might impact HRQL.

Chapter 9
In chapter 9, a general summary and discussion are provided and future perspectives are discussed.
Reference list


