

POSITION PAPER

EAACI Food Allergy and Anaphylaxis Guidelines. Food allergy health-related quality of life measures

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Abstract

Instruments have been developed and validated for the measurement of health-related quality of life in patients with food allergy. This guideline has been prepared by the *European Academy of Allergy and Clinical Immunology's (EAACI) Guidelines for Food Allergy and Anaphylaxis Group*. It draws on a systematic review of the literature on quality of life instruments for food allergy and the Appraisal of Guidelines for Research & Evaluation (AGREE II) guideline development process. Guidance is provided on the use of such instruments in research, and the current limitations of their use in clinical practice are described. Gaps in current knowledge as well as areas of future interest are also discussed. This document is relevant to healthcare workers dealing with food-allergic patients, scientists engaging in food allergy research and policy makers involved in regulatory aspects concerning food allergy and safety.

In recent decades, food allergy has emerged as a significant medical problem throughout Europe (1). As the medical morbidity and mortality associated with food allergy is limited to symptoms resulting from incidental ingestions of allergenic foods, conventional, symptom-based outcome measures fail to reflect the ongoing burden of this condition to patients' well-being. Although health-related quality of

life (HRQL) (Box 1) is an important outcome measure for many diseases, it is of particular importance for food allergy because there are no alternatives of sufficient sensitivity for use in most clinical situations. The relevance of HRQL measurement in allergy research, clinical practice and regulatory processes has been emphasized previously (2).

Scope and purpose of the guideline

A number of studies have been undertaken in the last decade which broadly address the issue of quality of life in patients suffering from food allergy (3–9). Many of these studies have employed questionnaires designed to illuminate some aspect of the experience of patients with food allergy using both qualitative and quantitative approaches. This guideline focuses on instruments designed to measure HRQL in a quantitative and disease-specific fashion and, in particular, draws upon a systematic review of existing instruments, one of seven interlinked evidence syntheses undertaken to provide a state-of-the-art synopsis of the current evidence base in this area (10). That review included a comprehensive search and quality assessment of instruments with special attention to the method of validation used. This guideline examines the possible applications of these instruments and provides advice to clinicians and investigators on their proper use and interpretation of results. Current limitations will also be considered and gaps and areas of future interest identified.

Methods

This guideline was produced using relevant principles detailed in the Appraisal of Guidelines for Research & Evaluation (AGREE II) approach (11). This is in essence a structured approach to guideline production that is designed to ensure appropriate representation of the full range of stakeholders, a careful search for and critical appraisal of the relevant literature, a systematic approach to the formulation and presentation of recommendations, and steps to ensure that the risk of bias is minimized at each step of the process. We provide below an overview of the approach used.

Clarifying the scope and purpose of the guideline

In January 2012, the scope of the intended guidelines was agreed upon, including the target allergy conditions and population, the end-user group and allowing for adequate academic, professional and lay presentation during guidelines development.

Ensuring appropriate stakeholder involvement

Participants represented a range of European countries, and academic and clinical backgrounds (including medical secondary care, primary care and nursing), and patient groups.

Abbreviations

AGREE II, Appraisal of Guidelines for Research & Evaluation; BoT, burden of treatment; CBT, cognitive behavioural therapy; DALY, disability-adjusted life years; EAACI, European Academy of Allergy and Clinical Immunology; FAIM, Food Allergy Independent Measure; FAQL-PB, Food Allergy Quality of Life – Parental Burden; FAQLQ-AF, Food Allergy Quality of Life Questionnaire – Adult Form; FAQLQ-CF, Food Allergy Quality of Life Questionnaire – Child Form; FAQLQ-PF, Food Allergy Quality of Life Questionnaire – Parental Form; FAQLQ-TF, Food Allergy Quality of Life Questionnaire – Teenager Form; FAQL-teen, Food Allergy Quality of Life Assessment Tool for Adolescents; HRQL, health-related quality of life; HRQLQ, Health-Related Quality of Life Questionnaire; IgE, immunoglobulin E; IM, independent measure; MCID, minimal clinically important difference; NNT, numbers needed to treat; OAS, oral allergy syndrome; PFA-QL, Paediatric Food Allergy Quality Of Life Questionnaire; QALY, quality-adjusted life years.

The Food Allergy HRQL Taskforce continued to work together over the ensuing 18 months through email discussions, teleconferences and face-to-face meetings.

Systematic review of the evidence

The initial full range of questions that were considered important were rationalized through several rounds of iteration to agree to a single key over-arching question – namely, ‘Which disease-specific, validated instruments can be employed to enable assessment of the impact of, and investigations and interventions for, food allergy on HRQL?’ The answer to this was then pursued through a formal systematic review of the evidence (S. Salvilla, S. Panesar, A. E. J. Dubois & A. Sheikh, submitted).

Formulating recommendations

The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) (12) approach is a transparent, evidence-based approach to formulating recommendations for interventions and diagnostic tests. However, the GRADE approach is less suitable for use in the context of recommendations on the use of which quality of life instruments to select or how to use or interpret these. Therefore, following identification, critical appraisal and synthesis of relevant data, members of the Taskforce developed draft consensus recommendations on suitable validated instruments for use in the context of IgE-mediated food allergy, and the use of these instruments and interpretation of data for (i) clinical and (ii) research purposes.

Peer review

A draft of this guideline was externally peer-reviewed by experts from a range of organizations, countries and professional backgrounds. In addition, this guideline was posted on the EAACI website for public review for 2 weeks in June 2013. All feedback was considered by the Food Allergy HRQL Taskforce and, where appropriate, final revisions were made in the light of the feedback received. We will be pleased to continue to receive feedback on this guideline, which should be addressed to the corresponding author.

Identification of evidence gaps

The process of developing this guideline has identified a number of evidence gaps and we plan in the future to prioritize

the questions that the Food Allergy HRQL Taskforce believes should be most urgently addressed through formal consensus building techniques. We plan furthermore to draft outline research briefs that funders can use to commission research on these questions.

Editorial independence and managing conflict of interests

The production of this guideline was funded and supported by EAACI. The funders did not have any influence on the guideline production process, on its contents or on the decision to publish. Conflict of interest statements were completed by all members of the Taskforce and these were taken into account by the Food Allergy HRQL Taskforce chair as recommendations were formulated.

Review of guideline

The guidelines will be reviewed in 2017 and updated accordingly. However, important advances will be incorporated prior to this date if required.

Results

The development of instruments used to measure HRQL should follow a specific methodology to ensure their validity, reproducibility, responsiveness (or sensitivity) and interpretability (3) (Box 1). All of these properties were examined in the systematic review (S. Salvilla, S. Panesar, A. E. J. Dubois & A. Sheikh, submitted). Particular emphasis was given to establishment of validity, which is of fundamental importance to proper instrument development.

Sixteen studies were quality-appraised in the systematic review (S. Salvilla, S. Panesar, A. E. J. Dubois & A. Sheikh, submitted), and seven disease-specific HRQL instruments were identified as fulfilling the criteria described above (4–8, 13–15). These included instruments for children, adolescents, adults and parent or caregiver and were either self-reported or proxy-reported (see Table 1).

The Food Allergy Quality of Life Questionnaire (FAQLQ-CF, -TF, -AF and -PF) instruments have undergone the most thorough validation process, including assessment of their psychometric properties. These FAQLQs are available free of charge, and several are available in multiple languages (www.faqlq.com).

Choosing an instrument

If HRQL instruments are to yield useful information in patients with food allergy, it is important to choose a tool that is appropriate for the setting, diagnosis and age of the patient (3, 16). Food allergy-specific HRQL questionnaires (Table 1) have been developed and validated for patients with IgE-mediated allergies [excluding oral allergy syndrome (OAS)] and are therefore not suitable for non-IgE-mediated food allergies. The food allergy-specific HRQL instruments have been designed to detect clinically important differences and changes in the disease-specific quality of life of patients

with food allergy. As they are specific for IgE-mediated food allergy, they do not allow for comparison with other disorders.

Box 1: Key terms

Health-related quality of life (HRQL): the impact of an illness and its therapy upon a patient, as perceived by the patient.

Validity is the degree to which an instrument measures what it is intended to measure. There are different types of validity of which construct validity is most important in HRQL measurement. *Construct validity* ensures that only that part of quality of life is being measured which is related to or driven by the disease in question. It is established by correlating measurements with one or more independent measures (IM) of the disease which provide an estimation of the extent and severity of patients' food allergy. An exact correlation is not expected as the HRQL instrument will not be measuring the same dimensions as the IM.

Reliability includes reproducibility and internal consistency. *Reproducibility* ensures that measurements taken under identical conditions are equivalent, and may be assessed by test–retest analysis. It is generally assessed by asking patients to complete the HRQL instrument twice, a few weeks apart, during a period when there is no change expected in their HRQL (e.g. when they have not experienced any food-allergic reactions or received any relevant interventions). *Internal consistency* ensures that the items of a questionnaire are related to each other and the total questionnaire, and is usually assessed by Cronbach's alpha.

Responsiveness ensures that differences or changes of potential importance are not missed, and is examined by measuring differences or changes in groups where these are expected. It is often assessed in patients whose HRQL is expected to change (e.g. those who have experienced food-allergic reactions or relevant interventions). *Interpretability* ensures that the relevance or clinical significance of measurements is apparent. This is ascertained by calculating the minimal clinically important difference (MCID), or the smallest change in HRQL score associated with a significant change in a global rating reported by patients.

The choice of food allergy-specific HRQL instrument should primarily be determined by the age of the patients, as highlighted in Table 1. In young children (i.e. those ≤8 years), a parent proxy questionnaire (which can be used up to the age of 12 years) is required (7, 8), whereas patient-administered instruments are appropriate for older children (>8 years) (4), adolescents (5, 14, 15) and adults (6), as they can express their own social/emotional and physical well-being. Language may also impact on the choice of instrument, not only because of differences between languages, but also because of cultural differences in various areas where

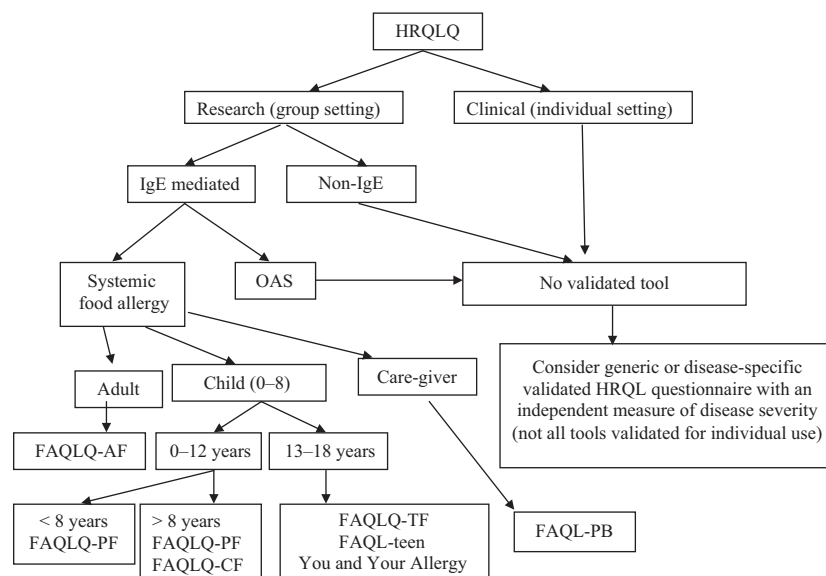
Table 1 Summary of food allergy-specific health-related quality of life instruments

Abbreviation (where stated)	Key reference	Full name	Target population (age range in years)	Respondent
FAQLQ-CF	4	Food Allergy Quality of Life Questionnaire – Child Form	Children (8–12)	Children (8–12)
FAQLQ-TF	5	Food Allergy Quality of Life Questionnaire – Teenager Form	Adolescents (13–17)	Adolescents (13–17)
FAQL-teen	14	Food Allergy Quality of Life Assessment Tool for Adolescents	Adolescents (13–19)	Adolescents (13–19)
You and Your Food Allergy	15	You and Your Food Allergy	Adolescents (13–18)	Adolescents (13–18)
FAQLQ-AF	6	Food Allergy Quality of Life Questionnaire – Adult Form	Adults (≥ 18)	Adults (≥ 18)
FAQL-PB	13	Food Allergy Quality of Life – Parental Burden	Parents	Parents
FAQLQ-PF	7	Food Allergy Quality of Life Questionnaire – Parent Form	Children (0–12)	Parents

the same language is spoken. The FAQLQ-AF has now been validated in several European countries and is available in English (17, N. J. Goossens, B. M. J. Flokstra-de Blok, G. N. van der Meulen, M. H. Arnlin, R. Asero, L. Barreales, P. Burney, I. Cerecedo, M. Clausen, M. Fernández-Rivas, L. Frewer, B. de la Hoz Caballer, S. A. Jansson, M. Jedrzejczak-Czechowicz, A. C. Knulst, M. L. Kowalski, N. G. Papadopoulos, A. Purohit, E. Rokicka, P. Starosta, S. Vazquez-Cortés, E. J. Duiverman & A. E. J. Dubois, submitted), French, Spanish, Italian, Polish, Greek, Dutch and Icelandic (N. J. Goossens, B. M. J. Flokstra-de Blok, G. N. van der Meulen, M. H. Arnlin, R. Asero, L. Barreales, P. Burney, I. Cerecedo, M. Clausen, M. Fernández-Rivas, L. Frewer, B. de la Hoz Caballer, S. A. Jansson, M. Jedrzejczak-Czechowicz, A. C. Knulst, M. L. Kowalski, N. G. Papadopoulos, A. Purohit, E. Rokicka, P. Starosta, S. Vazquez-Cortés, E. J. Duiverman & A. E. J. Dubois, submitted). The FAQLQ-PF has been validated in French, Spanish, German, Dutch, Danish and Mandarin, although only the data on the first have been published in a full-length paper to date (18). Also, the FAQLQ-CF has also been translated and validated into a

number of European languages (N. J. Goossens, B. M. J. Flokstra-de Blok, G. N. van der Meulen, E. Rokicka, P. Starosta, M. Jedrzejczak-Czechowicz, M. L. Kowalski, B. de la Hoz Caballer, I. Cerecedo, L. Barreales, S. Vazquez-Cortés, A. DunnGalvin, J. O'B. Hourihane, A. C. Knulst, T. Le, P. Burney, M. Fernández-Rivas, L. Frewer, B. J. Kollen, E. J. Duiverman & A. E. J. Dubois, submitted). The FAQL-teen, FAQL-PB and You and Your Food Allergy questionnaire are only available in the language of development (English). Figure 1 provides an algorithm guiding the appropriate use of food allergy-specific HRQLs and key factors to take into account are listed in Box 2. After the search period of the current review (1990–September 2012), another disease-specific instrument has been validated in the UK for children with food allergy and their parents: the Paediatric Food Allergy Quality of Life Questionnaire (PFA-QL) (19). In addition, the FAQLQ-CF, -TF and -AF were shown to be longitudinally valid and responsive (20).

Currently, there are no tools that can be used to gain insight on the contribution of the parent–child relationship on the HRQL of a food-allergic child. There is some evi-

**Figure 1** Choosing an appropriate Food Allergy HRQL.

Box 2: Summary box of factors to take into account when choosing a HRQLQ for food allergy

- 1 Type of food allergy (IgE mediated or not, OAS).
- 2 Research or clinical application.
- 3 Inclusion or exclusion of effects of comorbidities.
- 4 Patient age.
- 5 Language and cultural availability/appropriateness.
- 6 Preferred respondent: parent/caregiver as proxy, or child.
- 7 Target population/individual: parent/caregiver or child.

dence that comparison of patient-reported HRQL to parent (proxy)-reported HRQL using the FAQLQs can offer some insights in this area (21, 22). In addition, an optional section in the FAQLQ-PF evaluates the amount of stress felt by mother, father and family as a result of food allergy. Self-reported level of stress has been found to correlate significantly with parent-rated HRQL for the child (23). A parent (proxy)-reported instrument is currently being developed for adolescents with food allergy and may increase our knowledge of the role that adolescent–parent relationships play in teenagers with food allergy. Finally, the dynamics of a family with a food-allergic child may also be informed by assessing the parental burden using the FAQL-PB (13).

Currently, the FAQLQs have only been used in the research setting to provide quantitative information on the HRQL of patients with IgE-mediated food allergy, to assess the effect of interventions and determine outcomes (3). If they are to be used in clinic, the question arises to whether they are a valid measure of HRQL at the level of individual patients and suitable to guide clinical practice. Methods to assess individual validity and patient acceptability of HRQL have been used in other diseases (24, 25). In essence, to be useful in clinical practice, reproducibility of the HRQLQ is required to be high and sensitive enough to detect the effects of differences in allergy management. In addition, the HRQLQ should be simple, easy to score and interpret and the information the instrument provides must be shown to affect patient management (26). Although the instruments described in this guideline have characteristics suggesting that they may be capable of providing valid HRQL assessments at the level of individual patients, more studies are required in this area. One recent study (A. DunnGalvin & J. Hourihane, submitted) evaluated the effectiveness of a developmentally appropriate cognitive behavioural therapy (CBT) intervention specifically developed to improve HRQL for children and teenagers with IgE-mediated food allergy. The FAQLQ-PF, -CF and -TF were used and the results showed that the measures were sensitive enough to detect improvement in HRQL in individual patients relative to a control group.

For patients with food allergy outside the remit of current validated food allergy-specific HRQLQ (e.g. those with non-IgE-mediated food allergy or OAS) validated, generic HRQL questionnaires may be considered. However, these have not been designed to detect HRQL issues specific to

food allergy and so are unlikely to be sensitive to small but potentially important differences or changes in food allergy HRQL. Moreover, generic HRQL questionnaires will be affected by any existing comorbid disorders. Another possibility is to use a food allergy-specific HRQLQ and administer an appropriate independent measure of disease severity simultaneously in order to check the validity of this questionnaire in another population (e.g. non-IgE-mediated food allergy or OAS).

Using an instrument

Ideally, HRQL instruments should be used in the setting (language, culture and age group) in which it was developed. In practice, instruments must often negotiate differences between the setting of their development and their ultimate application. It is thus often advisable to include an independent measure such as the Food Allergy Independent Measure (FAIM) (27) in the study in the new setting. Such a measure should be available in the same language and may help to differentiate between negative study outcomes due to the lack of changes in HRQL from those due to the loss of validity of the HRQL measure in the new setting.

HRQL measurements are imminently suited to determine whether interventions offer a benefit increment to patients which they find meaningful. In order to demonstrate this, the minimal clinically important difference (MCID) for the instrument used must be determined. The MCID is the smallest increment of difference or change in HRQL score which patients find clinically meaningful. Currently, none of the food allergy instruments have provided a MCID. This is thus an unmet need in this area, as it will allow interventions to be assessed quantitatively by permitting calculation of numbers needed to treat (NNT) resulting from the intervention studied.

Pharmaco-economic research is mostly used to identify, measure and compare the costs, risks and benefits of programs, services or therapies and determine which alternative produces the best health outcome for the resources invested. Validated HRQL instruments for food allergy can be of value because they are able to measure the benefits of healthcare interventions from a patient perspective and ascertain whether the benefit of a particular intervention justifies the resources required. Such measurements may be expressed as quality-adjusted life years (QALYs) that capture both the HRQL lost or gained and the time to which this change pertains. Such information is essential to cost-utility analysis, which is important to policy makers.

Aside from the FAIM or similar independent measure and a global assessment, many other psychometric tools may be used concomitantly to gain insight into the patient experience of disease and treatment. Of these, the burden of treatment (BoT) measurement deserves special mention, as it allows the evaluation of disease and treatment by asking patients to weigh these entities in their overall assessment of the benefits of a particular intervention. Together with HRQL, this can offer a comprehensive evaluation of the net benefits of an intervention.

The use of food allergy HRQL questionnaires to measure effect of interventions on HRQL of food-allergic patients is increasing. Outcomes of these studies are described in the EAACI guideline on diagnosis and treatment of food allergy (A. Muraro, T. Werfel, G. Roberts, K. Beyer, C. Bindslev-Jensen, V. Cardona, A. Dubois, G. duToit, P. Eigenmann, M. Fernandez Rivas, S. Halken, L. Hickstein, A. Høst, E. Knol, G. Lack, M. J. Marchisotto, B. Niggemann, B. I. Nwaru, N. G. Papadopoulos, L. K. Poulsen, A. F. Santos, I. Skypala, A. Schoepfer, R. Van Ree, C. Venter, M. Worm, B. Vlieg-Boerstra, S. Panesar, D. de Silva, K. Soares-Weiser, A. Sheikh, B. K. Ballmer-Weber, C. Nilsson, C. A. Akdis & K. Hoffmann-Sommergruber on behalf of EAACI Food Allergy and Anaphylaxis Guidelines Group, submitted).

Gaps in the evidence and recommendations

The healthcare system has traditionally focused on treating disease at point of failure, such as life-saving surgery or intensive medical therapy. In the case of food allergy, this occurs with accidental reactions and/or anaphylaxis. With healthcare professionals and governments now placing more of an emphasis on prevention, a different patient management model is required to assess cost-effectiveness within the continuum of care. Clinically, standardized HRQL measures can enhance screening patients for burdens associated with even asymptomatic periods of food allergy and can be used to monitor changes. Therefore, the development of high-quality food allergy-specific HRQL instruments is a welcome advance in helping to assess the impact of IgE-mediated food allergy on patients' quality of life. That said, it is important to note that there remain a number of important research gaps in order to have a comprehensive set of tools for use in the everyday management of patients with food allergy across Europe. These are summarized below.

First, the MCID of existing instruments needs to be determined. This is essential to allow for the calculation of NNT for clinical care and pharmaco-economic analysis.

Second, there are at present no tools for assessing HRQL in those with non-IgE-mediated food allergy or in those with OAS. Given that these manifestations of food allergy can have a substantial impact on the quality of life of patients and carers, there is a pressing need to develop appropriate instruments.

Third, the tools available for assessing HRQL in those with IgE-mediated food allergy are still only available in a fraction of the languages spoken across Europe. Given that food allergy affects people throughout Europe, formal validation work needs to be undertaken to make these instruments available across the full spectrum of relevant languages.

Fourth, how best to develop an efficient and integrated method of assessment and monitoring of HRQL in patients with co-existent allergic problems has been a matter of recent debate. In order to retain the advantages of a disease-specific instrument, the use of information and communications technology may be an option. Unlike a paper questionnaire, electronic questionnaires can be developed that consist of a

subgroup of questions from a much larger collection to provide personalized instruments that, for example, cater for type of allergy, multiple allergy, distance from medical centre or comorbid condition. Where appropriate, section(s) on coping, anxiety, risk, reactions and management style could also be included. In addition, as electronic questionnaires could facilitate implementation in routine care contexts, it is important that these tools are validated for use across a range of platforms – for example, completion on patient portals, mobile phones, tablets and personal computers. Given the increasing move to electronic health records across Europe (28), electronic data capture will also facilitate seamless transfer into patient records. A further advantage of an electronic system would be the ease with which a detailed database could be generated for health status of individual patients on a longitudinal basis. This would allow healthcare providers to target additional input to individual patients or families experiencing impaired HRQL due to particular circumstances.

Fifth, it should be noted that the available instruments have primarily been developed for use in research contexts. Using instruments in routine clinical contexts is potentially very valuable and is hence on the policy agendas of some European countries, but this does require the MCID of the instruments to be established in order to assess the impact of interventions/care provision on individual patients.

Sixth, how best to assess HRQL in the many patients with co-existent allergic problems is another related clinically important consideration. The main options are either to use an accompanying generic instrument (e.g. the EQ-5D) or to add in additional disease-specific instruments for each comorbidity. Whilst the latter approach may be feasible in those with one comorbidity (e.g. atopic eczema/dermatitis), it is likely to prove much more challenging in those with multiple comorbidities (e.g. atopic eczema/dermatitis, allergic rhinitis and asthma).

Finally, efforts to link quality of life gains and optimal resource allocation has proved challenging in many areas of health care. However, how HRQL can aid policy decisions in allocating healthcare resources is an important issue for policy makers. Decisions are often taken based on the outcomes of an evaluation expressed as incremental costs per QALY gained, or disability-adjusted life years (DALY). Measuring HRQL in economic or monetary terms has not been attempted to date in the area of food allergy. Because QALYs need to be measured against some threshold (usually the monetary or consumption value of QALY gains), disease-specific, meaningful estimates of the value of QALY gains in food allergy need to be developed. Disease-specific HRQL measures can be a key tool in such a development. Therefore, there is a need to identify relevant thresholds for costs per QALY and how these might vary across Europe in order to help inform policy considerations. In this respect, it is important that individual, family and societal perspectives are considered.

Based on the systematic review of HRQL instruments for IgE-mediated food allergy, and the identification of needs and gaps in clinical practice and research, we make the

following recommendations. These can be divided into general recommendations (Box 3), recommendations for clinicians (Box 4) and recommendations for research (Box 5).

Box 3: General recommendations

- 1 Only validated instruments as identified by this systematic review should be used to measure HRQL in food-allergic subjects.
- 2 An independent measure (e.g. FAIM) should be used simultaneously as a correlating measure.
- 3 An established approach should be used when the validated questionnaires are translated into other languages, for example back translation and validation in the local language – there may be important linguistic or cultural issues that invalidate the tool in other countries.
- 4 To date, the FAQLQ (AF, TF, CF and PF) and FAQL-PB and -teen instruments and the You and Your Food Allergy instrument are the only tools sufficiently well validated to be used in research contexts. The appropriate questionnaire will depend on the age of the patient.
- 5 Alterations to questions in the instrument are strongly discouraged, as these may compromise validity. If alterations are made, the instrument requires revalidation.
- 6 The instruments recommended in this review are specific to IgE-mediated food allergy and are not suited for use in patients with non-IgE-mediated disease or oral allergy syndrome. Furthermore, for patients where measurement of HRQL due to comorbid conditions is desirable, appropriate disease-specific and/or a generic instrument may be required.

Box 4: Recommendations for clinicians

- 1 To date, the use of food allergy-specific HRQL tools in clinical practice has been little documented. Clinicians should be aware of this and be cautious when using HRQL measurements to guide management decisions.
- 2 There is currently also no information on the use of HRQL measurements as a form of bench-marking in food allergy.

Box 5: Recommendations for research

- 1 Research is needed on optimum methods of administration (e.g. paper, online, phone), procedures (e.g. frequency) and interpretation (e.g. MCID).
- 2 Research is needed on which HRQL measures (if any) are valid at the level of individual patients to guide clinical practice.
- 3 Research is needed on the efficacy of disease-specific HRQL instruments in the evaluation of medical and technological advances, patient satisfaction and quality of care and health and regulatory policy.

- 4 The inclusion of HRQL in models to explain different pathways in the development, expression and impact of chronic diseases.
- 5 Norms for age, gender and country/culture need to be developed.
- 6 Research is needed on the relationship between responses to both proxy and self-report HRQL measures.
- 7 Research is needed on optimum methods (clinical and statistical) for evaluating HRQL in patients with comorbid conditions.
- 8 Further work is needed to see how QALYs for food allergy can be developed to help inform policy.

Where next with HRQL instruments?

Some questions remain that impact on the future potential value of HRQL measures in allergy. Firstly, what are the correlates of HRQL in food allergy (e.g. anxiety, health beliefs, risk perception, information processing, coping behaviours) and how do they impact on the likelihood of adverse reactions and management? Which of these variables are causally related to HRQL status, and which variables are the effect of HRQL status? Lastly, as HRQL depends on subjective perception of the burden of food allergy, what are the underlying neuropsychological mechanisms (e.g. stress/immune interactions)? These questions have particular relevance for the interpretation and usefulness of HRQL measures in clinical practice. As our knowledge base grows, clarity will evolve about how HRQL relates to other variables. Studies must be theory driven, well designed, multisite and build on previous work. It is important that we design studies that help to clarify the physiological mechanisms that underlie the psycho-social predictor and outcome variables in our models. For example, models should allow for bidirectional and causal pathways linking health to HRQL (including all significant variables and their weights). If the flow is bidirectional for some of the components, this has profound implications in terms of interpretation and application of HRQL results. The mechanisms responsible for any associations should be evaluated. Such models may be seen as a blueprint for exploration as well as a summary of available evidence.

Because the developmental process plays an important role in shaping and determining physical and psychological health and HRQL, an attempt to delineate a developmental pathway is also vital. Life transitions provide a naturalistic research opportunity to investigate adaptability to a diagnosis of food allergy and the link to health outcomes and HRQL. The pathway should take account of sensitive transition points when the interaction of biopsychosocial factors may create an increased vulnerability in terms of health and well-being (9, 29).

In addition to providing a meaningful way to assess the end results of healthcare services, including clinical and therapeutic interventions, and policy, HRQL measures can allow healthcare professionals to pinpoint the time when both parents and children may need further support on issues such as diet, auto-

injectors, risk management, managing anxiety and changing developmental and practical challenges. It can also help us to identify unintended impacts of potential management options. The use of HRQL measures cross-culturally and across countries can delineate similarities, differences and dynamic factors. Taken together, such findings, combined with research on variables related to HRQL, can provide a broader view than has hitherto often been the case on the impact of food allergy.

Expert Panel

We are grateful to the expert panel for providing expert feedback; Prof. Rebecca C. Knibb (Aston University, Birmingham), Prof. Matt Masiello (Windber Research Institute and Windber Medical Center, PA), Prof. Ilaria Baiardini (University of Genoa, Genoa), Prof. Roy Gerth Van Wijk (Department of Allergology, Rotterdam), Prof. Sabine Schnadt (Deutscher Allergie- und Asthmabund, Mönchengladbach).

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Author contributions

Antonella Muraro, Chair of the EAACI Food Allergy and Anaphylaxis Guidelines Initiative, has steered and coordinated the publication. Anthony Dubois facilitated the guidelines group and edited the guidelines document. Bertine Flokstra-de Blok facilitated the identification of research questions for the systematic review and processed the feedback of the experts.

Anthony Dubois, Audrey DunnGalvin, Rosan Meyer, Nicolette de Jong, Aziz Sheikh, Allison Worth and Bertine Flokstra-de Blok drafted specific sections. Sarah Salvilla and Sukhmeet Panesar undertook the supporting systematic review under the supervision of Aziz Sheikh. All authors participated in the discussion of the sections, recommendations, gaps and approved the final version.

Conflicts of interest

Antonella Muraro has provided scientific advice for Meda. Anthony Dubois has provided scientific advice for ALK-Abello and received funding from ALK-Abello to support his research activities. Audrey DunnGalvin has received funding from Novartis for her research. Jonathan O'B. Hourihane has received speaker fees from Mead Johnson, Nutricia, MSD, Pfizer, ALK-Abello and Stallergenes; Thermo Fisher has provided consumables for his research activities. Nicolette W de Jong has no conflict of interests. Rosan Meyer has provided scientific advice for Danone, Nestle and Mead Johnson. Graham Roberts has provided scientific advice for Danone and ALK-Abello; Thermo Fisher and ALK-Abello have provided consumables for his research activities. Aziz Sheikh has provided scientific advice to ALK-Abello, Meda, Lincoln Medical, Thermo Fisher, Pfizer and Stallergenes; he is on the Anaphylaxis Campaign UK's Scientific Committee, World Allergy Organization's Anaphylaxis Special Committee, UK Resuscitation Council's Anaphylaxis Committee and the BSACI's Standard of Care Committee and has received funding for coordinating guideline production and generating the systematic reviews from EAACI. Sarah Salvilla and Sukhmeet Panesar have no conflict of interest. Allison Worth has received funding from ALK-Abello, Meda and Thermo Fisher to attend meetings and provide professional education. Bertine Flokstra-de Blok has no conflict of interest.

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