Developing National and International Guidelines

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KEYWORDS

• Guidelines • Food allergy • Methodology • Evidence-based medicine

KEY POINTS

- Allergic diseases are considered an important public health problem, and the development of guidelines aims to help health care professionals in an accurate diagnosis and management of such diseases in order to match patient's requirements and provide more standardized procedures.
- The management of food allergy may differ among countries.
- Standardization processes are needed to guarantee the quality of the critical analysis of the evidences and the methodology in the implementation of the guidelines.
- World Allergy Organization applied the standardized Grading of Recommendations Assessment, Development and Evaluation methodology for the first time in the field of food allergy.
- As we consider a cost-effective approach to health care, the quality of evidence and tradeoffs between strategies will emerge to provide care tailored to fit each patient and family.

INTRODUCTION

Allergic diseases are considered an emerging public health problem worldwide, mainly because of the increasing prevalence and the risk of severe and even life-threatening reactions with high impact on quality of life and social costs. Globally established scientific allergy societies are investing their efforts into the development of evidence-based guidelines to help health care professionals for an accurate diagnosis and appropriate management. Guidelines may potentially smooth out the variations existing between the different centers in the different countries of the world.

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EPIDEMIOLOGY

The epidemiology of food allergy (FA) paints a contrasting picture across countries worldwide. International studies found that the overall prevalence of oral challenge-proven FA in children younger than 5 years was only 1% in Thailand but as high as 5.3% in Korean infants and 10% in Australian preschoolers.[1–3]

Although milk and eggs are the most common allergens in early childhood in the United Kingdom, United States, Australia, and many parts of Europe and Asia, distinct differences in prevalence are observed even between countries located within the same continent. The EuroPrevall birth cohort, which recruited infants from 9 European centers with different climatic and cultural backgrounds, found that the incidence of challenge-proven cow's milk allergy was lower in southwestern European countries, such as Greece (0%) and Italy (0.3%), but was highest in the United Kingdom (1.24%).[4] The prevalence of egg allergy was also variable—the highest incidence was reported in the United Kingdom (2.18%) and the lowest in Greece (0.07%).[5]

Differences in Food Allergy Around the World

There are differences in the presence of factors that influence FA development and management in the various regions of the world, including the following[6]:

1. *Genetics:* peanut allergy heritability has been demonstrated in western populations in absence of studies in nonwhite populations; associations between filaggrin null mutations and FA risk vary between different populations.
2. *Atopic dermatitis (AD):* AD phenotypes and skin immune responses differ between Asians and Caucasians.
3. *Aeroallergen cross-reactivity:* variable patterns of cross-sensitization between aeroallergens components and food allergens exist in different geographic regions; cross-sensitization with different aeroallergen components confer differential severity of FA symptoms.
4. *Dietary patterns:* food preparation methods may alter food allergenicity.
5. *Meteorologic influences:* climatic factors (eg, latitude, season of birth, vitamin D status, ethnicity-related vitamin D binding protein polymorphisms) confer differential FA risk.

From this perspective, different national guidelines have been created that consider the FA epidemiology of different geographic area with variable local algorithms for diagnosis and specific prevention objectives.

On the other side, it is necessary to encourage standardization processes that have the sole objective of guaranteeing the quality of the critical analysis of the evidences and of the methodology in the implementation of the guidelines.

APPROPRIATE AND UNIVERSAL METHODOLOGY IN DEVELOPING GUIDELINES

Whatever the pathology and the geographic context to which the guidelines are addressed, there are aspects that need to be respected.

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) collaboration compiled a comprehensive checklist of items linked to relevant resources and tools that guideline developers could consider, without the expectation that every guideline would address each item.[7] The items are summarized in **Fig. 1**.

A fundamental role is played by a Coordinating Committee (CC), which has the following main tasks:

a. Oversight of the development of the Guidelines;

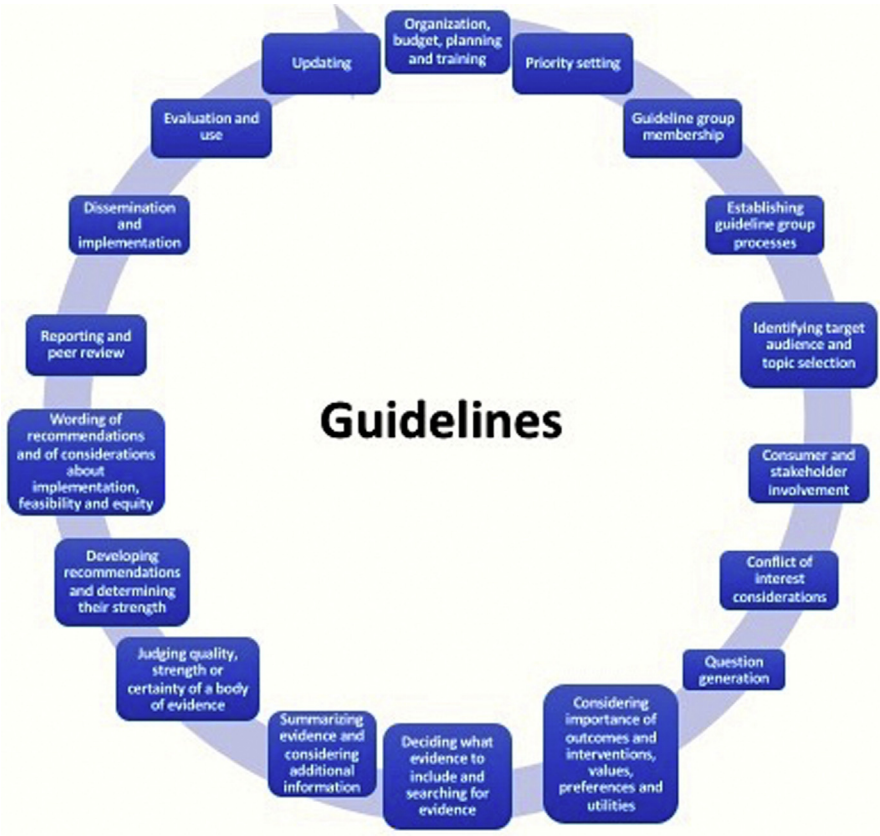

Fig. 1. The items that guideline developers should consider for Grading of Recommendations Assessment, Development and Evaluation (GRADE) collaboration.

b. Review of the Guidelines draft for accuracy, practicality, clarity, and broad utility of the recommendations in clinical practice;
c. Review of the final draft of the Guidelines;
d. Dissemination of the Guidelines.

Along these lines, each guideline is promoted by a CC, who convene an Expert Panel (EP): specialists from a variety of relevant clinical, scientific, and public health areas, with the essential participation of patient representatives.

Every member should be vetted for financial Conflict of Interest (COI) and approved by the CC.

The charge to the EP is to use an independent up-to-date systematic literature review providing a quantitative (when applicable) and/or qualitative synthesis of the scientific evidence, in conjunction with consensus expert opinion and EP-identified supplementary documents, to develop Guidelines that provide a comprehensive approach based on the current state of the science.

A well-recognized Evidence-Based Medicine (EBM) group prepares an independent, systematic literature review and evidence report on the state of the science in FA. The CC and the EP develop an extensive set of key questions, which are further refined in discussions with the EBM group. Literature searches are performed on

the most important database (eg, PubMed, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effects, and Cochrane Central Register of Controlled Trials). Inclusion and exclusion criteria are strictly defined in terms of populations, study design, year, and language of publication. After identification of potentially eligible studies, duplicate publications are removed and titles and abstracts of identified studies are checked against the inclusion/exclusion criteria independently by 2 reviewers. Afterward, full-text papers are retrieved if their titles and/or abstracts seemed to meet the eligibility criteria or if the decision could not be made based on the titles and/or abstracts alone. Assessment of the full texts of each retrieved paper is undertaken independently by 2 reviewers using the same criteria. Furthermore, for each key question, in addition to assessing the quality of each of the included studies, the EBM group assesses the quality of the body of evidence. The main tool for this purpose is currently recognized in the GRADE approach, which was developed in 2004.[8] GRADE provides a comprehensive and transparent methodology to develop recommendations for the diagnosis, treatment, and management of patients. In assessing the body of evidence, GRADE considers study design and other factors, such as the precision, consistency, and directness of the data. Using this approach, GRADE then provides a grade for the quality of the body of evidence.

Based on the available scientific literature, the EBM group assesses the overall quality of evidence according to the following criteria[9,10]:

High—further research is very unlikely to have an impact on the quality of the body of evidence, and therefore, the confidence in the recommendation is high and unlikely to change.

Moderate—further research is likely to have an impact on the quality of the body of evidence and may change the recommendation.

Low—further research is very likely to have an important impact on the body of evidence and is likely to change the recommendation.

The EP prepares a draft version of the Guidelines based on EBM group's evidence report and supplementary documents that are identified by the EP but not included in the report.

The EP uses this additional information only to clarify and refine conclusions drawn from sources in the systematic literature review. All the EP members discuss the first written draft version of the Guidelines and their recommendations. Then, the EP incorporates any panel-wide changes to the recommendations within the draft Guidelines. These revised recommendations are then subjected to an initial panel-wide vote to identify whether there is any panel disagreement. Controversial recommendations are discussed to achieve group consensus.

Following discussion and revision as necessary, a second vote is held. All recommendations that received 90% or higher agreement are included in the draft Guidelines for public review and comment.

FROM NATIONAL ALLERGY SOCIETY POSITION PAPERS TO STANDARDIZED INTERNATIONAL GUIDELINES

The DRACMA Experience

Up to 2008, clinical practice parameters for the treatment of cow's milk allergy (CMA) consisted mainly of national allergy society position papers reflecting local views and needs. These were aimed at different treatment strategies and were not always evidence based. For these reasons, it was decided that clinical practice guidelines issued on behalf of WAO would apply the GRADE methodology for the first time in the field of FA.

WAO tried to apply this standardized approach to the management of CMA and developed the Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) guidelines.[11]

Before DRACMA, oral food challenge (OFC) was not part of the diagnostic workup and was indicated only after an elimination period of a few months or on a specialist's advice in more severe cases; this exposed whole populations to overdiagnosis of CMA and excessive use of elimination diets.[12]

DRACMA guidelines strongly recommended OFC for diagnosing CMA to avoid the risk of anaphylactic reactions at home in false-negative sensitization tests, unnecessary treatment for false-positive cases, and inappropriate resource utilization. On the other side, they also indicated that challenge may not be necessary in many cases. Assessing the clinical history, physicians can determine the diagnostic likelihoods estimating the pretest probability of CMA. As examples, the pretest probability will be low in cases of AD or gastroesophageal reflux disease, average in cases of immediate reactions, or high in cases of anaphylaxis. In the latter, physicians reach a highly probable diagnosis using simpler diagnostic tests such as skin prick tests and/or specific immunoglobulin E (IgE) determination.[13]

OFCs remain necessary in all cases of high uncertainty. The search for replacement tests has been very active in the past years. Specific IgE cutoff points, skin prick tests diameters, and/or atopy patch test have been proposed as replacement tests. In DRACMA, the limits of these diagnostic practices are clearly indicated, and their possible use is reevaluated.

The other area in which DRACMA guidelines heavily influenced clinical practice is CMA treatment. Outcomes and their ranking were not arbitrarily chosen but selected from the literature by the expert panel. This method allows the pediatrician to tailor treatment of CMA to changing conditions while observing the recommendations.

The guidelines can affect the market but the reverse should not happen

CC and EP have an enormous responsibility in the realization of guidelines free from conflicts of interest and that reflect a scientific methodology free from any influence.

However, there are factors linked to the geographic context that require the recommendations to be adapted to the population to which the guidelines are addressed.

In the context of CMA, as the cost of the same formula differs substantially from country to country, the implementation of the recommendations may differ. Among DRACMA recommendation, for example, extensively hydrolyzed formula (eHF) is preferred to amino acid formula (AAF), if there is no risk of anaphylaxis. The reason for this approach is mainly the high cost of AAF formula, together with the low palatability of the latter. Based on these considerations, at least an Italian company decided in 2012 to decrease the cost of their AAF by 30%, so that it dropped from 2.4 to 2 times that of eHF. Although the prescription of a specific formula ideally includes economic modeling, the factors in the equation generated in the mind of every single pediatrician is multifold and include the seriousness of the condition, the assessable economic capacity of the family, the psychological readiness of the family to meet with failure of the dietary therapy, and the probability of the refusal of the child due to the low palatability of the formula itself.[14]

The EAACI Guidelines on Food Allergy

The *European Academy of Allergy and Clinical Immunology* (EAACI) plays a crucial role as well in the development of international evidence-based guidelines for different stakeholders in the field of FA. In 2014,[15] the EAACI Food Allergy and Anaphylaxis Group provided evidence-based recommendations for the diagnosis and

management of FA based on previous EAACI position papers on adverse reaction to foods and 3 recent systematic reviews on the epidemiology, diagnosis, and management of FA.[16–18] The document offered the current understanding of the manifestations of FA, the role of diagnostic tests, and the effective management of patients with FA of all ages. The acute management of non–life-threatening reactions has been covered in these guidelines,[15] whereas a guidance on the emergency management of anaphylaxis was published in the EAACI Anaphylaxis Guidelines. Evidence level and grade have been provided for each recommendation.[15] An update of the abovementioned EAACI guidelines is ongoing and highly anticipated due mainly to the novelties in the field of FA diagnosis. Recently the updated systematic review on anaphylaxis[19] has been published, and respective guidelines based on GRADE approach are expected soon.

In 2014, EAACI recommended approaches to prevent the development of immediate-onset/IgE-mediated FA in infants and young children.[20] The EAACI Food Allergy Prevention Guideline Task Force has revised the 2014 EAACI guidelines. The guideline has been developed using the AGREE II framework and the GRADE approach. An international Task Force with representatives from 11 countries and different disciplinary and clinical backgrounds systematically reviewed research and considered expert opinion. Recommendations were created by weighing benefits and harms, considering the certainty of evidence and examining values, preferences, and resource implications. The guideline was peer-reviewed by external experts, and feedback was incorporated from public consultation. Key changes from the 2014 guideline include suggesting the following: (1) supporting breast feeding and avoiding supplementation with routine cow's milk formula in the first week of life (low certainty of evidence) and (2) the introduction of peanut and well-cooked egg as part of complementary feeding (moderate certainty of evidence).

Other Relevant International Guidelines

In 2006, an FA practice parameter was published by a task force established by the American College of Allergy, Asthma and Immunology; the American Academy of Allergy, Asthma, and Immunology; and the Joint Council of Allergy, Asthma and Immunology. The document, *"Food Allergy: A Practice Parameter*," has been an outstanding resource for the allergy and immunology clinical community, but may not have had broad impact outside of this community, and did not use GRADE methodology.[21]

In 2010, because of concerns about different settings for FA diagnosis and the need to distinguish FA and food intolerance, *the National Institute of Allergy and Infectious Diseases (NIAID)*, part of the National Institutes of Health, working with more than 30 professional organizations, federal agencies, and patient advocacy groups, led the development of clinical guidelines for the diagnosis and management of FA in United States.[22]

Based on a comprehensive review and objective evaluation of the scientific and clinical literature on FA, the Guidelines were developed by and designed for allergists/immunologists, clinical researchers, and practitioners in the areas of pediatrics, family medicine, internal medicine, dermatology, gastroenterology, emergency medicine, pulmonary and critical care medicine, and others. The Guidelines included both IgE-mediated and some non–IgE-mediated reactions to food.

The evidences were evaluated through the GRADE approach. US Guidelines were specifically aimed at all health care professionals who cared for adult and pediatric patients with FA and related comorbidities.

Although these guidelines explored the diagnosis and management of FA, the absence of the theme of prevention emerged. The NIAID therefore decided to fill that gap in 2017.[23]

The evidences of a landmark clinical trial and other emerging data suggested that peanut allergy could be prevented through introduction of peanut-containing foods beginning in infancy.

Prompted by these findings, the NIAID facilitated development of addendum guidelines to specifically address the prevention of peanut allergy.

The addendum provided 3 separate guidelines for infants at various risk levels for the development of peanut allergy and is intended for use by a wide variety of health care providers. Topics addressed include the definition of risk categories, appropriate use of testing, and the timing and approaches for introduction of peanut-containing foods in the health care provider's office or at home. The addendum guidelines provided the background, rationale, and strength of evidence for each recommendation.

Other organizations developed, or are currently developing, guidelines for FA. Clinical practice guidelines on FA in children and young people have been developed for use in the National Health Service in England, Wales, and Northern Ireland by the *National Institute for Health and Clinical Excellence* (NICE). These guidelines are intended for use predominantly in primary care and community settings. The model used for development of the NICE guidelines is overall similar to that used to generate some of the EAACI and US Guidelines.[24]

IMPLEMENTATION

The production of clinical practice guidelines alone is not sufficient, and there is a need for implementation strategies for their introduction into daily practice.

The relevance of guidelines is widespread recognized as pivotal. Overall, their dissemination is interpreted as articulating a "standard of care," a standard that has political, sociologic, and even legal ramifications when compared with day-to-day practice. Notwithstanding, guidelines are not always translated to policy or practice.[25] Their limited use contributes to omission of nonbeneficial treatments, preventable harm, suboptimal patient outcomes or experiences, or waste of resources.[26]

The implementation science aims to identify barriers and choose and tailor implementation strategies to optimize their clinical impact.[27,28] Implementation approaches and strategies have been categorized and include characteristics of the recommended practice and patient, provider, institutional, and system-level factors.[29]

There is evidence that many guidelines are implemented using educational approaches, such as workshops, directed at health professionals or patients. Educational approaches are often combined with other more complex interventions such as organizational, financial, or regulatory strategies, which require large-scale change and/or considerable funding.[30] However, the use of single versus multiple implementation approaches and strategies remains controversial, and the choice of the most effective tools should be defined case by case.[31]

CONTROVERSIES

In FA, health-economic models are limited by how health state utilities are derived and generalized. When faced with low-benefit/high-cost care propositions, the role for understanding patient-preference sensitive decision-making, and how this may change over the course of specific diseases, must be clarified. In some population segments such care has higher relative value. This complicates the quest for the "best" practice, which depends on the patient. Today the practicing allergist is part of a complex health care system in a dynamic world. Understanding the broader ramifications of clinical decision-making and appreciating how risks, benefits, and costs become manifest over short- and long-term horizons is key. Providing optimal care incorporates patient

preferences at every stage, and these preferences may shift discrete individual values and cost-effectiveness of some interventions. As we consider a cost-effective approach to health care, the quality of evidence and tradeoffs between strategies will emerge to provide care tailored to fit each patient and family.[32]

DISCUSSION

To optimize the clinical management of FA, it is therefore necessary to analyze the state of the art at the national and local level.

From this analysis, the management aspects that need real improvement and implementation can emerge. The questions that need to be answered will therefore arise from these aspects. In this context, the patients' point of view would also be pivotal.

The burden of the disease, the local logistical difficulties, costs, and quality of life are in fact elements that could be affected by the guidelines produced.

The scientific methodological approach described will therefore be the impartial tool that will allow experts to express the best of their knowledge and experience.

Schünemann HJ, describing the work of the GRADE working group based in the field of allergy and asthma, stated that "decisions are like double-edged swords: they always come with benefits and downsides. That is, any decision in life bears desirable and undesirable consequences, even if the latter only involves the time it takes to make or think about the decision, which can be considered the harm of decision making. Therefore, it is impossible to adhere to the Hippocratic Oath's concept of "primum non nocere," which is frequently interpreted as "never do harm." The guiding principle for health care decision making should be to ensure that there is, in summary, more benefit than harm—in other words, "to do no net harm" ("primum non nocere"). Practice guidelines support decision making and, consequently, would require the explicit consideration of both desirable and undesirable consequences, and assigning due considerations depending on the magnitude and importance of the consequences.".[33]

FUTURE DIRECTIONS

The current challenge is to integrate omics into the implementation of guidelines for FA.

Precision medicine aims to empower clinicians to predict the most appropriate course of action for patients with complex diseases.

With a progressive interpretation of the clinical, molecular, and genomic factors at play in diseases, more effective and personalized medical treatments are anticipated for many disorders. Understanding patient's metabolomics and genetic make-up in conjunction with clinical data will significantly lead to determining predisposition, diagnostic, prognostic, and predictive biomarkers and paths, ultimately providing optimal and personalized care for diverse and targeted chronic and acute diseases. In clinical settings, we need to timely model clinical and multiomics data to find statistical patterns across millions of features to identify underlying biological pathways, modifiable risk factors, and actionable information that support early detection and prevention of complex disorders and development of new therapies for better patient care.[34]

SUMMARY

In conclusion, the national and international guidelines for FA should start from an interpretation of the real local and universal needs of patients.

However, the action of the panels of experts should be organized according to a rigorous scientific methodology, capable of bringing out high-quality evidence and therefore universally recognized and applicable conclusions in different clinical contexts.

Guideline statements should be free from conflicts of interest and tested by clinicians in the context of validation workshops. The -omics sciences promise to transform allergy into precision medicine capable of delivering the best for the specific patient.

For now, it is worthwhile to identify what is best for most patients.

CLINICS CARE POINTS

- FA management may differ in various regions of the world based on socioeconomic conditions.
- To standardize FA guidelines, the most effective approach seems to be the "Grading of Recommendations Assessment, Development and Evaluation" (GRADE).
- Guideline statements should be tested by clinicians in the context of validation workshops.

DISCLOSURE

The authors have nothing to disclose.

REFERENCES

1. Lao-araya M, Trakultivakorn M. Prevalence of food allergy among preschool children in northern Thailand. Pediatr Int 2012;54(2):238–43.
2. Kim J, Chang E, Han Y, et al. The incidence and risk factors of immediate type food allergy during the first year of life in Korean infants: a birth cohort study. Pediatr Allergy Immunol 2011;22(7):715–9.
3. Peters RL, Koplin JJ, Gurrin LC, et al. The prevalence of food allergy and other allergic diseases in early childhood in a population-based study: HealthNuts age 4-year follow-up. J Allergy Clin Immunol 2017;140(1):145–53.e8.
4. Schoemaker AA, Sprikkelman AB, Grimshaw KE, et al. Incidence and natural history of challenge-proven cow's milk allergy in European children–EuroPrevall birth cohort. Allergy 2015;70(8):963–72.
5. Xepapadaki P, Fiocchi A, Grabenhenrich L, et al. Incidence and natural history of hen's egg allergy in the first 2 years of life-the EuroPrevall birth cohort study. Allergy 2016;71(3):350–7.
6. Tham EH, Leung DYM. How different parts of the world provide new insights into food allergy. Allergy Asthma Immunol Res 2018;10(4):290–9.
7. Schünemann HJ, Wiercioch W, Etxeandia I, et al. Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. CMAJ 2014;186(3):E123–42.
8. GRADE working group. 2000-present. Internet. Available at: http://www.gradeworkinggroup.org/. Accessed January 9, 2021.
9. Brozek JL, Akl EA, Jaeschke R, et al, GRADE Working Group. Grading quality of evidence and strength of recommendations in clinical practice guidelines: Part 2 of 3. The GRADE approach to grading quality of evidence about diagnostic tests and strategies. Allergy 2009;64(8):1109–16.

10. Schünemann HJ, Oxman AD, Brozek J, et al, GRADE Working Group. Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. BMJ 2008;336(7653):1106–10. Erratum in: BMJ. 2008;336(7654).
11. Fiocchi A, Brozek J, Schünemann H, et al. World Allergy Organization (WAO) Special Committee on Food Allergy. World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) Guidelines. Pediatr Allergy Immunol 2010;21(Suppl 21):1–125.
12. Fierro V, La Marra F, Fiocchi A. Interpreting the Results of Guideline Implementation: A Long and Winding Road. J Pediatr Gastroenterol Nutr 2016;62:665–6.
13. Fiocchi A, Schunemann H, Terracciano L, et al. DRACMA one year after: Which changes have occurred in diagnosis and treatment of CMA in Italy? Ital J Pediatr 2011;37:53.
14. Vandenplas Y, Alarcon P, Fleischer D, et al. Should partial hydrolysates be used as starter infant formula? a working group consensus. J Pediatr Gastroenterol Nutr 2016;62(1):22–35.
15. Muraro A, Werfel T, Hoffmann-Sommergruber K, et al. EAACI Food Allergy and Anaphylaxis Guidelines Group. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. Allergy 2014;69(8):1008–25.
16. Nwaru BI, Hickstein L, Panesar SS, et al. EAACI Food Allergy and Anaphylaxis Guidelines Group. The epidemiology of food allergy in Europe: a systematic review and meta-analysis. Allergy 2014;69(1):62–75.
17. Soares-Weiser K, Takwoingi Y, Panesar SS, et al. EAACI Food Allergy and Anaphylaxis Guidelines Group. The diagnosis of food allergy: a systematic review and meta-analysis. Allergy 2014;69(1):76–86.
18. de Silva D, Geromi M, Panesar SS, et al. EAACI Food Allergy and Anaphylaxis Guidelines Group. Acute and long-term management of food allergy: systematic review. Allergy 2014;69(2):159–67.
19. de Silva D, Singh C, Muraro A, et al. European Academy of Allergy and Clinical Immunology Food Allergy and Anaphylaxis Guidelines Group. Diagnosing, managing and preventing anaphylaxis: Systematic review. Allergy 2020. https://doi.org/10.1111/all.14580.
20. Muraro A, Halken S, Arshad SH, et al. EAACI Food Allergy and Anaphylaxis Guidelines Group. EAACI food allergy and anaphylaxis guidelines. Primary prevention of food allergy. Allergy 2014;69(5):590–601.
21. American College of Allergy, Asthma, & Immunology. Food allergy: a practice parameter. Ann Allergy Asthma Immunol 2006;96(3 Suppl 2):S1–68.
22. NIAID-Sponsored Expert Panel, Boyce JA, Assa'ad A, Burks AW, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol 2010;126(6 Suppl):S1–58.
23. Togias A, Cooper SF, Acebal ML, et al. Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases-sponsored expert panel. J Allergy Clin Immunol 2017;139(1):29–44.
24. Walsh J, O'Flynn N. Diagnosis and assessment of food allergy in children and young people in primary care and community settings: NICE clinical guideline. Br J Gen Pract 2011;61(588):473–5.
25. Gagliardi AR, Alhabib S, members of Guidelines International Network Implementation Working Group. Trends in guideline implementation: a scoping systematic review. Implement Sci 2015;10:54.

26. Pronovost PJ. Enhancing physicians' use of clinical guidelines. JAMA 2013; 310(23):2501–2.
27. Francke AL, Smit MC, de Veer AJ, et al. Factors influencing the implementation of clinical guidelines for health care professionals: a systematic meta-review. BMC Med Inform Decis Mak 2008;8:38.
28. Flottorp SA, Oxman AD, Krause J, et al. A checklist for identifying determinants of practice: a systematic review and synthesis of frameworks and taxonomies of factors that prevent or enable improvements in healthcare professional practice. Implement Sci 2013;8:35.
29. Mazza D, Bairstow P, Buchan H, et al. Refining a taxonomy for guideline implementation: results of an exercise in abstract classification. Implement Sci 2013; 8:32.
30. Gagliardi AR. "More bang for the buck": exploring optimal approaches for guideline implementation through interviews with international developers. BMC Health Serv Res 2012;12:404.
31. Kajermo KN, Boström AM, Thompson DS, et al. The BARRIERS scale – the barriers to research utilization scale: A systematic review. Implement Sci 2010;5:32.
32. Shaker M, Greenhawt M. Providing cost-effective care for food allergy. Ann Allergy Asthma Immunol 2019;123(3):240–8.e1.
33. Schünemann HJ. Guidelines 2.0: do no net harm-the future of practice guideline development in asthma and other diseases. Curr Allergy Asthma Rep 2011;11(3): 261–8.
34. Ahmed Z. Practicing precision medicine with intelligently integrative clinical and multi-omics data analysis. Hum Genomics 2020;14(1):35.