# Selections from international journals

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### WAO consensus on DEfinition of Food Allergy SEverity (DEFASE)

Stefania Arasi, Ulugbek Nurmatov, Audrey Dunn-Galvin, Graham Roberts, Paul J Turner, Sayantani B Shinder, Ruchi Gupta, Philippe Eigenmann, Anna Nowak-Wegrzyn, Ignacio J Ansotegui, Montserrat Fernandez Rivas, Stavros Petrou, Luciana K Tanno, Marta Vazquez-Ortiz, Brian Vickery, Gary Wong, Montserrat Alvaro-Lozano, Miqdad Asaria, Philippe Begin, Martin Bozzola, Robert Boyle, Helen Brough, Victoria Cardona, R Sharon Chinthrajah, Antonella Cianferoni, Antoine Deschildre, David Fleischer, Flavio Gazzani, Jennifer Gerdts, Marilena Giannetti, Matthew Greenhawt, Maria Antonieta Guzman, Elham Hossny, Paula Kauppi, Carla Jones, Francesco Lucidi, Olga Patricia Monge Ortega, Daniel Munblit, Antonella Muraro, Giovanni Pajno, Marcia Podesta, Pablo Rodriguez Del Rio, Maria Said, Alexandra Santos, Marcus Shaker, Hania Szajewska, Carina Venter, Cristopher Warren, Tonya Winders, Motohiro Ebisawa, Alessandro Fiocchi.

Background: While several scoring systems for the severity of anaphylactic reactions have been developed, there is a lack of consensus on definition and categorisation of severity of food allergy disease as a whole. Aim: To develop an international consensus on the severity of food allergy (DEfinition of Food Allergy Severity, DEFASE) scoring system, to be used globally. Methods phase 1: We conducted a mixed-method systematic review (SR) of 11 databases for published and unpublished literature on severity of food allergy management and set up a panel of international experts. Phase 2: Based on our findings in Phase 1, we drafted statements for a two-round modified electronic Delphi (e-Delphi) survey. A purposefully selected multidisciplinary international expert panel on food allergy (n = 60) was identified and sent a structured questionnaire, including a set of statements on different domains of food allergy severity related to symptoms, health-related quality of life, and economic impact. Participants were asked to score their agreement on each statement on a 5-point Likert scale ranging from "strongly agree" to "strongly disagree". Median scores and percentage agreements were calculated. Consensus was defined a priori as being achieved if 70% or more of panel members rated a statement as "strongly agree" to "agree" after the second round. Based on feedback, 2 additional online voting rounds were conducted. Results: We received responses from 92% of Delphi panel members in round 1 and 85% in round 2. Consensus was achieved on the overall score and in all of the 5 specific key domains as essential components of the DEFASE score. Conclusions: The DEFASE score is the first comprehensive grading of food allergy severity that considers not only the severity of a single reaction, but the whole disease spectrum. An international consensus has been achieved regarding a scoring system for food allergy disease. It offers an evaluation grid, which may help to rate the severity of food allergy. Phase 3 will involve validating the scoring system in research settings, and implementing it in clinical practice.

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# Allergen immunotherapy for atopic dermatitis: Systematic review and meta-analysis of benefits and harms

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Introduction: Atopic dermatitis (AD, eczema) is driven by a combination of skin barrier defects, immune dysregulation, and extrinsic stimuli such as allergens, irritants, and microbes. The role of environmental allergens (aeroallergens) in triggering AD remains unclear. Objective: We systematically synthesized evidence regarding the benefits and harms of allergen immunotherapy (AIT) for AD. Methods: As part of the 2022 American Academy of Allergy, Asthma & Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters AD Guideline update, we searched the MEDLINE, EMBASE, CENTRAL, CINAHL, LILACS, Global Resource for Eczema Trials, and Web of Science databases from inception to December 2021 for randomized controlled trials comparing subcutaneous immunotherapy (SCIT), sublingual immunotherapy (SLIT), and/or no AIT (placebo or standard care) for guideline panel-defined patient-important outcomes: AD severity, itch, AD-related quality of life (QoL), flares, and adverse events. Raters independently screened, extracted data, and assessed risk of bias in duplicate. We synthesized intervention effects using frequentist and Bayesian randomeffects models. The GRADE approach determined the quality of evidence. Results: Twenty-three randomized controlled trials including 1957 adult and pediatric patients sensitized primarily to house dust mite showed that add-on SCIT and SLIT have similar relative and absolute effects and likely result in important improvements in AD severity, defined as a 50% reduction in SCORing Atopic Dermatitis (risk ratio [95% confidence interval] 1.53 [1.31-1.78]; 26% vs 40%, absolute difference 14%) and QoL, defined as an improvement in Dermatology Life Quality Index by 4 points or more (risk ratio [95% confidence interval] 1.44 [1.03-2.01]; 39% vs 56%, absolute difference 17%; both outcomes moderate certainty). Both routes of AIT increased adverse events (risk ratio [95% confidence interval] 1.61 [1.44-1.79]; 66% with SCIT vs 41% with placebo; 13% with SLIT vs 8% with placebo; high certainty). AIT's effect on sleep disturbance and eczema flares was very uncertain. Subgroup and sensitivity analyses were consistent with the main findings. Conclusions: SCIT and SLIT to aeroallergens, particularly house dust mite, can similarly and importantly improve AD severity and QoL. SCIT increases adverse effects more than SLIT. These findings support a multidisciplinary and shared decision-making approach to optimally managing AD.

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#### Utility of biomarkers in the diagnosis and monitoring of asthmatic children

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Asthma imposes a heavy morbidity burden during childhood; it affects over 10% of children in Europe and North America and it is estimated to exceed 400 million people worldwide by the year 2025. In clinical practice, diagnosis of asthma in children is mostly based on clinical criteria; nevertheless, assessment of both physiological and pathological processes through biomarkers, support asthma diagnosis, aid monitoring, and further lead to better treatment outcomes and reduced morbidity. Recently, identification and validation of biomarkers in pediatric asthma has emerged as a top priority across leading experts, researchers, and clinicians. Moreover, the implementation of non-invasive biomarkers for the assessment and monitoring of paediatric patients with asthma, has been prioritized; however, only a proportion of them are currently included in the clinical practise. Although, the use of non-invasive biomarkers is highly supported in recent asthma guidelines for documenting diagnosis and supporting monitoring of asthmatic patients, data on the Pediatric population are limited. In the present report, the Pediatric Asthma Committee of the World Allergy Organization (WAO), aims to summarize and discuss available data for the implementation of non-invasive biomarkers in the diagnosis and monitoring in children with asthma. Information on the most studied biomarkers, including spirometry, oscillometry, markers of allergic sensitization, fractional exhaled nitric oxide, and the most recent exhaled breath markers and "omic" approaches, will be reviewed. Practical limitations and considerations based on both experts' opinion and critical review of the literature, on the utility of all "well-known" and newly introduced non-invasive biomarkers will be presented. A critical commentary on biomarkers' use in diagnosing and monitoring asthma during the COVID-19 pandemic, cost and availability of biomarkers in different settings and in developing countries, the differences on the biomarkers use between Primary Practitioners, Pediatricians, and Specialists and their role on the longitudinal aspect of asthma is provided.

### Clin Exp Allergy. 2023; 53(3):327-336.

# Oral immunotherapy using boiled peanuts for treating peanut allergy: An open-label, singlearm trial

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Background: Peanut allergy affects 1%-3% of children in Western countries. Boiling peanuts has been demonstrated to result in a hypoallergenic product that may provide a safer way of inducing desensitization in peanut-allergic patients by first inducing tolerance to boiled peanut. We aimed to assess the efficacy and safety of oral immunotherapy (OIT) using sequential doses of boiled peanuts followed by roasted peanuts for treating peanut allergy in children. Methods: In this open-label, phase 2, single-arm clinical trial, children aged 6-18 years with a positive history of peanut allergy and positive peanut skin prick test  $\geq 8$  mm and/or peanut-specific IgE  $\geq 15$  kU/L at screening underwent OIT involving sequential up-dosing with 12-hour boiled peanut for 12 weeks, 2-hour boiled peanut for 20 weeks and roasted peanut for 20 weeks, to a target maintenance dose of 12 roasted peanuts daily. Primary outcome: proportion of children passing open-label oral food challenge involving cumulative administration of 12 roasted peanuts (12 g peanuts; approximately 3000 mg peanut protein) 6-8 weeks after reaching the target maintenance dose. Secondary outcomes included treatment-related adverse events and use of medications for treating allergy symptoms. Results: Between 1 July 2017 and 22 June 2018, 70 participants were enrolled and commenced OIT. Desensitization was successfully induced in 56 of 70 (80%) participants. Withdrawal due to treatment-related adverse events was infrequent (n = 3). Treatment-related adverse events were reported in 43 (61%) participants, corresponding to a rate of 6.58 per 1000 OIT doses. Medication use associated with treatment-related adverse events was infrequent, with rescue epinephrine use reported by three (4%) participants (0.05 per 1000 doses). Conclusion: Oral immunotherapy using boiled followed by roasted peanuts represents a pragmatic approach that appears effective in inducing desensitization and is associated with a favourable safety profile.