**Varying approaches to management of IgE-mediated food allergy in children around the world**

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**ABSTRACT**

Food allergy is a chronic disease that affects individuals of all ages, and is a significant public health problem globally. This narrative overview examines clinical management strategies for IgE-mediated food allergy in children around the world, to understand variations in practice. Information was drawn from clinical practice guidelines, recent research, the websites of professional and governmental bodies with expertise in food allergy, and clinical experts from a broad cross-section of geographical regions. The structure and delivery of clinical services, allergen avoidance and food labelling, and resources to support the management of allergic reactions in the community are discussed in detail. Adoption of emerging food immunotherapies is also explored. Wide variations in clinical management of food allergy were apparent across the different countries. Common themes were continuing issues with access to specialist care, and recognition of the need to balance risk reduction with dietary and social restrictions to avoid unnecessary detrimental impacts on the quality of life of food allergy sufferers. Findings highlight the need for standardized presentation of practice and priorities, and may assist clinicians and researchers when engaging with government and funding agencies to address gaps.

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**Introduction**

Food allergy is a common chronic disorder affecting infants, children, adolescents and adults.1,2 Studies suggest that prevalence has increased in recent decades across the globe, not limited to westernised countries.3 Intense research effort has been directed to identifying disease modifying treatments, however, to date a curative solution remains elusive. While management continues to centre on allergen avoidance together with education of patients and carers in the emergency treatment of acute reactions, approaches are increasingly permissive of selective allergen intake within defined parameters (e.g. intake of milk in baked foods for those with milk allergy) and active desensitization with oral immunotherapy (OIT) is available in many countries. Despite recommendations for strict avoidance, accidental reactions occur in around 45% of children with food allergy each year, although most reactions are mild or moderate in severity.4,5 Admissions due to food anaphylaxis are between 4 to 20 per 100,000 population, and fatalities are rare with reported incidence of 0.03-0.3 per million person years in people who have food allergy.6-8 Nevertheless, patients and families affected by food allergy are understandably fearful of an unexpected serious or fatal reaction, leading to high levels of anxiety and psychological distress in many.9,10 The lifestyle restrictions that come with strict allergen avoidance and the unpredictability of reactions due to accidental ingestion can cause significantly reduced quality of life.11

The approach to management of food allergy is expected to vary between countries, in part dictated by disease prevalence in the population, access to diagnostic and specialist care, availability of national or regional guidelines and resources to support clinicians, health service models, and cultural attitudes to food and health. Until recently, management recommendations have mostly focused on mitigating fatality risk through allergen avoidance and early treatment of reactions. Notably though, fatal food anaphylaxis is rare and appears to have remained stable, possibly due to increased food allergen labelling, diagnostic services, epinephrine injector (EI) prescription rates and food allergy awareness.12 Strategies to address the day-to-day burden of living with food allergy are equally relevant, yet have received less attention to date.11,13 It is unclear to what extent these parallel issues have been recognised and prioritised by clinicians in various settings. Furthermore, recent developments in food immunotherapy have led to controversy and debate.14-16 The literature surrounding optimal management of food allergy is rapidly changing. This overview aims to present the approaches to **management** of **IgE mediated food allergy in children** across the globe, highlighting commonalities and differences in clinical practice and research priorities. Gaps in knowledge and evidence are discussed.

**Allergy service structure and management pathways**

Formal diagnosis of food allergy (via history together with skin prick testing (SPT), allergen-specific IgE (sIgE), or oral food challenge (OFC)) is commonly provided by Paediatricians or specialist allergy physicians (Allergists) in all countries included in this review. The number of Allergists per 100,000 population in Germany (6.5) is highest of all included countries (Figure 1, Supplementary Table 1), though the proportion of these who specialise in food allergy is low. In Germany, allergy is a sub-specialty with clinicians drawn from paediatrics, dermatology, pneumology, ear-nose-throat or internal medicine. In comparison, there is <1 Allergist per 100,000 population in Canada, Singapore, Brazil and Australia, and <1 per million population in South Africa. Australia’s high prevalence of allergic disease alongside limited access to Allergists has resulted in long waiting times for specialist assessment in both the public and private health sectors.17 Significant global heterogeneity in the training and availability of allergy specialists has been documented previously.18-20

Responsibility for ongoing (long-term) medical management of food allergy is more varied across countries, and is often provided by a variety of specialist and/or generalist clinicians depending on availability of resources (Supplementary Table 2). In public-funded healthcare systems (e.g. Australia, UK, Canada, Italy and Hong Kong), referral to an Allergist is usually via the General Practitioner (GP) or Paediatrician. In some countries, self-referral to an Allergist is possible, particularly in the private setting (e.g. US, Singapore, Japan, Brazil). While patients can self-refer to an Allergist in Germany, referral to those specialised in food allergy within a tertiary care hospital must be via a GP or Pediatrician, and only a small number of food allergic patients will see a food allergy specialist during their lifetime. Where demand for Allergist services exceeds availability, such as in Australia and the UK, ongoing care may be provided by a GP or Paediatrician in conjunction with semi-regular or limited Allergist reassessment.17,20 Paediatricians are also involved in ongoing management of food allergies in Singapore, South Africa and Brazil, while in the US, Canada, Hong Kong and Japan, regular reviews are generally completed by the Allergist.

The value of multidisciplinary clinical services in providing holistic care for food allergy is well recognised, and increasingly addressed in many countries (Supplementary Table 2).21-25 This is most evident in countries with universal publicly-funded healthcare, such as the UK, Japan, Singapore, Australia and Germany, where specialist nurses and dieticians trained in food allergy management are increasingly integrated into clinical services at tertiary centres, while access to other professions (e.g. mental health services, speech pathology) is available on a needs basis via referral.20,26 In Australia, access to dietetic and psychology services with specific expertise in food allergy is commonly offered through public-funded services and available in the private sector. In Germany, privately funded anaphylaxis-teaching groups (structured educational programmes for patients at risk for anaphylaxis) conducted by a dietician, psychologist and Allergist are commonly available. Limited access to allied health services in other countries and settings is generally due to under-supply of food allergy specialist-trained clinicians, and a lack of awareness of food allergy practice within those disciplines.20,27,28 Specialized training programs for dieticians are at various stages of development in the US and Canada.29 Nutritional counselling, particularly for individuals with multiple food allergies, is recommended in clinical practice guidelines in Japan, Australia, the UK, Italy, Germany and US.22-24,30-32 In Brazil and South Africa, multidisciplinary care and specialist food allergy training for nurses and allied health clinicians are rarely available.

The importance of regular review for reassessment of food allergy status and management is universally acknowledged. The time interval between visits for reassessment of food allergy status (by SPT, sIgE testing and/or OFC), patient education, renewal of emergency action plans and epinephrine (adrenaline) prescription is variable (see Table 1). Yearly review schedules are common in the UK, Australia, US, Canada and Germany, with shorter review intervals reported for Hong Kong, Japan and South Africa. Factors impacting on the review interval include availability of Allergist services, age of child (more frequent in pre-school aged children), type and number of food allergies (more frequent in egg / milk allergy due to increased likelihood of resolution) or evidence of risk factors (e.g. poorly controlled asthma, risk taking behaviours, frequent accidental reactions, severe reactions).20,32-37

sIgE testing to whole or component allergens is available in all countries examined, though not yet widely used in many (Table 1). Access is limited due to cost in some places, and public-funding of this service is very restricted globally. Diagnostic food challenge services are similarly widely available, though tend to be utilized as clinically indicated rather than offered routinely (according to a standardized review schedule).23,38-40 OFCs are typically open challenges in clinical settings, with single blind and double-blind placebo-controlled food challenges predominantly performed in research settings. Barriers to performing OFCs include funding constraints, limited availability of facilities and staff with appropriate experience, hospital proximity and patient fear of reaction.41,42 There is concern that guideline-driven diagnosis of food allergy without concomitant formal diagnostic testing (SPT, sIgE, OFC) may promote overdiagnosis, which is a significant issue for cow’s milk allergy in infants and may be a broader issue for other IgE-mediated food allergies in some countries.43-45

Transition from paediatric to adult clinical services has been identified as a key milestone in the management of food allergy.46 Variable approaches to this transition are observed, with some countries (e.g. UK, Germany, Australia) offering separate specialist services (and even institutions) for children and adults.20,26 In countries where joint accreditation in adults and paediatrics is common (Canada, US, Japan), patients can often continue with the same clinician into adulthood, facilitating improved continuity of care. Of note, there are very limited specialist allergy services for adults in Hong Kong, meaning only those with multiple food allergies receive specialist review beyond childhood.

**Food labelling**

Food labelling regulations identifying specific allergens are in place in all countries surveyed for this review (Supplementary Table 3). Most countries follow the *Codex Alimentarius* international food standards, guidelines and codes of practice, which have covered the labelling of ingredients commonly causing food hypersensitivities since 1991.47 *Codex* exists to ensure that food products meet minimum standards for safety and quality, and are in accordance with their specifications. Many countries also have national legislation in place to regulate food labelling. While there is some variation in the allergens that must be identified across countries, the most commonly regulated ingredients are milk, egg, wheat or gluten, soy, peanut, tree nuts, fish, shellfish, sulphites and sesame. Compliance with compulsory ingredient labelling is enforced via periodic inspection, sampling, surveys and investigation of adverse incidents and self-reported allergic reactions. While ELISA testing is commonly used to detect allergens, the US FDA has recently developed the xMAP food allergen detection assay that can simultaneously detect 16 allergens in a single analysis, with a design that allows for expansion to target additional food allergens.48 While this technology is not yet in routine use it is expected to enhance the effectiveness and efficiency of testing and therefore improve compliance.49,50 At the time of this review, there is wide variation in the level of regulation and compliance globally (Supplementary Table 3).

In contrast to the wide adoption of legislation covering the listing of allergens as ingredients, only Japan has implemented legislation regarding precautionary allergen labelling (PAL) to warn of possible cross contamination and non-specific “may contain” statements are prohibited.51,52 In other countries, it has been left to the food industry to self-regulate on this matter. Consequently, PAL are not standardized and are included at the discretion of food manufacturers, creating confusion for consumers.53-55 Despite the lack of enforcement, PAL is widely used in some countries (e.g. US, Canada, Australia), with a Canadian study identifying overuse and inconsistency of “may contain” statements as a key contributor to dietary restriction for food allergic children.53,56 To address inconsistencies, an ad hoc FAO/WHO Expert Consultation on Food Allergen Risk Assessment is being conducted by the Codex Committee on Food Labelling, with the goal of promoting an internationally harmonized risk assessment framework (including guidance values and reference doses) to aid companies in making transparent, risk-based decisions on the use of PAL.57 In the UK, The Food Standards Agency (FSA) is also currently seeking views on potential approaches to PAL for prepacked and non-prepacked foods.58

The Voluntary Incidental Trace Allergen Labelling (VITAL) Program is an initiative of the Allergen Bureau, the peak industry body representing food industry allergen management. VITAL establishes a standardized allergen risk assessment process for food industry that aims to provide consistent labelling for foods, based upon assessment of likely sources of allergen cross contact from raw materials and the processing environment, evaluation of the amount present and review of approaches to reduce allergen contamination from all contributing sources. VITAL also provides for ongoing monitoring and verification of the risk assessment process to ensure any changes to the level of risk are acted upon without delay.59 This provides reassurance for both food manufacturers and consumers, with guidelines based on robust science and a clear risk assessment framework. While compliance is not mandatory in any country, VITAL was introduced in Australia and New Zealand in 2007 and has since been implemented in Singapore.60 With improved sensitivity of proteomic tests enabling identification of low allergen levels, PAL can be avoided in cases where evaluations in mass spectrometry can establish that the amount of contaminating allergen in a given pre-packaged food is below the threshold of possible reactivity. Recently, a cut-off of 5 parts per million content has been proposed for this purpose. Although there may be some reservations about applying a specific limit, patients would certainly benefit from a substantial reduction in PAL.61-63

**Allergen avoidance**

To balance the risk of reactions against unnecessary dietary restriction, specialists across the globe have increasingly recognized the importance of providing individualized and pragmatic clinical advice on avoidance practices. Strict avoidance of foods that include allergen as a listed ingredient is recommended in guidelines for food allergic patients (e.g. Australia, US, South Africa),30,39,64-66 however, advice around avoiding foods with PAL is more individualized according to perceived risk and shared decision making with the patient. In Australia and Singapore, there is an emphasis on patient education to improve understanding of food labelling and high risk situations, and advice to avoid foods with PAL is largely directed at patients with history of anaphylaxis to low level allergen exposure.67,68 In the US, existing clinical practice guidelines remain strict regarding allergen avoidance including foods with precautionary labelling,30,69 though some Allergists, Paediatricians and families may take a more relaxed approach based on high eliciting dose during OFC or low severity of prior reactions.70-72

Permissive consumption strategies vary greatly according to country, the specific allergen in question and whether or not the allergy is IgE-mediated (Table 2). Although the risks associated with a reaction are greater for IgE mediated allergy, there is impetus to reduce restrictions for common foods like milk and egg leading clinicians in many countries to seek ways to safely broaden diets even in cases of IgE mediated allergy.73 Ladder diets (where progressively less cooked or processed forms of the allergen are consumed where tolerated), which have been widely applied for the management of non-IgE mediated egg and milk allergy, are now increasingly adopted in the management of mild to moderate IgE-mediated egg or milk allergy.39,69,74 For example, an academic allergy centre in the US has developed a staggered exposure strategy for children with milk allergy, with sequential oral food challenges to assess for ability to safely consume baked milk products, followed by heated cheese, and then whole milk with periods of regular consumption in between.70,75,76 A similar process has been suggested for both egg and milk allergy in Italy and Canada, with the importance of careful patient selection emphasized,74,77 and staged ‘ladders’ are recommended by BSACI.39,78-80 While there is no national level guidance on appropriate strategies for the introduction of egg or milk in the US, a recent American Academy of Allergy Asthma and Immunology workgroup report discussed utilisation of OFC to baked milk or baked egg in clinical practice to identify patients who tolerate baked forms of these allergens.40 The German guideline also emphasizes that testing for “partial tolerance” (ie. to baked milk or egg) allows dietary expansion and the potential to develop tolerance if the culprit food is regularly consumed in a baked form.32 In Japan, guidelines recommend OFC-guided stepwise consumption for egg, milk and wheat allergy, which has allowed two-thirds of OFC positive patients to consume low or medium doses of causative foods.81,82 This approach, with intake of the allergen in amounts below an individual’s OFC reaction threshold is becoming more common in some countries (Italy, Japan).

In the case of nut, fish and shellfish allergies, there has been a recent shift toward selective avoidance of the trigger food rather than broad recommendations to avoid all foods within a food group (e.g. avoidance of peanut, while allowing intake of tolerated tree nuts in peanut allergic patients, or avoidance of shrimp while allowing intake of other tolerated shellfish) (Table 2). In Hong Kong, individuals with shrimp allergy often disregard the strict elimination advice due to ready availability and community appreciation of an abundance of fresh seafoods. Recognising the species-specific nature of fish and shellfish allergy, research efforts have been directed to identify “precision medicine” strategies that facilitate the identification of patients with species-specific allergy via component testing and OFCs.83-85

**Resources to support the management of accidental allergic reactions in the community**

Emergency action plans are now routinely utilized globally, though standardized national plans and adoption are variable across countries (Table 3). In Australia, standardized Australasian Society of Clinical Immunology and Allergy (ASCIA) action plans are mandated in National clinical practice guidelines, and State legislation in Victoria requires that a current (updated annually) ASCIA action plan is provided to schools, day cares and children’s services.64,86,87,88 Standardized action plans are also available and recommended in anaphylaxis clinical practice guidelines in South Africa, Canada, UK, Singapore, Brazil and Japan (Table 3).23,89-92

Compliance with routine provision of action plans to food allergic patients is variable across countries and tends to depend on whether provision of an action plan is mandated in practice guidelines or other regulatory frameworks. Where standardized plans are mandatory, adoption is thought to be excellent. Other countries report variability according to medical speciality, with high levels of provision by Allergists, and lower utilization by GPs (Hong Kong, Brazil). Quality data on the utilization of action plans is only available from the UK; elsewhere, evidence is limited and relies on the opinion of the authors.20

Regrettably, even in areas with high levels of action plan provision, adherence by patients is poor, particularly in relation to carrying and using an EI according to instructions. A 2021 meta-analysis found that pre-hospital epinephrine was implemented in only 1 in 5 children and 1 in 14 adults with an anaphylactic reaction.93 Reasons given for failure to carry a prescribed EI included inconvenience or a belief that it was not needed.93 A Canadian study of anaphylaxis in individuals with a prescribed EI found the device was used prior to ED arrival in only 41% of reactions, although use of an EI outside hospital was more likely in teenagers and those with severe reactions.94 Self-administration of an EI occurred in less than 20% of food anaphylaxis cases reported to the European Anaphylaxis Registry (including Germany) between 2007 and 2018.95 Measuring compliance and correct usage of EIs is difficult because of wide variability in the definition of anaphylaxis, indications for use, education given to patient / carer and other situational dependencies that may influence a decision to administer epinephrine. There is also very limited scientific evidence that intramuscular epinephrine is an effective treatment for either terminating allergic reactions or preventing fatalilties.96

Although emergency allergic reaction action plans across most countries advise patients to call an ambulance or go to the nearest urgent care centre immediately after administering an EI (or equivalent)30,64,97 , the clinical utility and cost-effectiveness of this as a blanket approach for all instances of epinephrine use is uncertain.98 Consequently, some Allergists in the US and Canada are starting to consider the option of home observation for lower-risk patients if there is response to epinephrine, rather than immediate hospital attendance.99,100

EIs are not widely available in some countries and prescribing recommendations vary accordingly (Table 4). Alternatives, such as a pre-filled syringe or syringe self-administration kit, are prescribed in some settings. Selective versus universal prescription of EIs is guided by national guidelines.64,91,101-104 Where selective prescribing is practiced, this is advocated for individuals with a history of prior severe reaction, comorbid asthma, allergy to triggers that are known to be more likely to cause systemic reactions (e.g. nuts), exercise induced or idiopathic anaphylaxis, and mast cell disorders.97,101,103,105 For countries with universal prescription for all patients with IgE–mediated food allergy (e.g. US, Canada), broad provision of EIs is justified by the lack of accurate predictors for future severe reactions.69 Quality of life considerations are important in prescribing decisions because of the low probability that an EI will save the life of an individual patient, and the inconvenience of carrying an EI.96 Additionally, the reassurance gained by parents from having epinephrine on hand should be balanced against potential unintended consequences (e.g. inappropriate use creating more anxiety and emergency healthcare activity, restrictions around school trips, not being allowed to join the armed forces, negative impact on quality of life etc.).106

Guidelines or regulations for the management of food allergy in schools and childcare centres are established in Australia, Canada, the US, Singapore and Japan (Table 5). To promote consistency of evidence based practice, international practice guidelines for the prevention and management of allergic reactions in schools and childcare centres were recently developed by an international expert working group (published 2021).107 At the time of this review, however, the scope of regulations and recommendations continues to vary between countries and enforcement is variable (Table 5). Mandatory staff training in the management of allergic reactions is enforced in Australia, Canada, Singapore and Japan.108,109 Practice is varied in European countries; an EAACI task force suggested that school policies should reflect anaphylaxis guidelines, but more research is needed to understand how guidelines and legislation in schools are best implemented.22

All international practice guidelines recommend against site-wide allergen bans in schools and childcare centres, instead advising that alternative developmentally appropriate strategies be implemented to manage risk on a case-by-case basis.107,110 Nevertheless, the decision to impose bans is often at the discretion of the individual school or childcare, and practice may not always align these recommendations (Table 5). In Canada, a case brought before the Human Rights Tribunal did not support the mandate of bans on allergen containing foods in recreational settings.111

**Treatments for food allergy**

Two commonly measured outcomes from a food allergy treatment are desensitization and remission of allergy (also referred to as sustained unresponsiveness).112 Desensitization refers to a transient increase in reaction threshold that is only maintained through continuous regular treatment or allergen exposure.113 Remission, on the other hand, refers to an absence of clinical reactivity even when treatment has been discontinued for a period of time (e.g. weeks or months), allowing discontinuation of treatment and incorporation of the allergen as part of the usual diet, noting that some ingestion is thought to be important for maintaining the remission state.114,115 There is no consensus on the most important outcomes to measure in trials of food allergy treatments. While all food immunotherapy trials have included challenge-confirmed endpoints such as desensitization and/or remission, few have assessed for patient important measures such as allergic reactions (to either continuing treatment or accidental exposure) and patient quality of life. Two European projects are trying to address this gap.116

Over the past decade, various immunotherapies have been evaluated in multiple clinical trials with the hope of developing a treatment that can modify long-term outcomes and/or the natural history of food allergy.16,117 Numerous immunotherapies are in various stages of development (preclinical, phase-1, phase-2, and phase-3 clinical trials),118 and the Viaskin Peanut patch (epicutanous peanut immunotherapy; EPIT) is currently undergoing regulatory approval in various jurisdictions. Additionally, OIT using readily available food products is also offered in some countries.119 However, to date, only one food immunotherapy (Palforzia, a peanut OIT) has been approved for use in the US, UK, and Europe, and none have been approved for use elsewhere.120-122 Even in countries where approval has been granted, uptake of Palforzia in routine clinical practice has been less than expected. A small single-centre US study (n=237) found that less than 10% of eligible candidates decided to pursue treatment with the two most common reasons to decline therapy being “concern over adverse effects,” and “concern over the degree of commitment”.123 In the UK, although Palforzia had a positive cost-effectiveness assessment by National Institute of Health and Care Excellence (NICE) and is publicly-funded,120 there are significant concerns about the benefits versus risks of this treatment and the capability of clinical services to deliver OIT safely.124,125 In Europe, while Palforzia was approved by the European Medicines Agency in December 2020,122 it is only available on the market in German-speaking countries to date. Here also there are some reported logistical problems around timely delivery of the medication since pharmacies are required to deliver Palforzia to the physician’s office instead of dispensing directly to the patient.

OIT using commercially available foodstuffs (e.g. defatted peanut flour, egg white protein powder) is now available on a privately funded basis in most developed countries, and publicly funded OIT is increasingly offered in some countries, for example Japan, Singapore, Italy and Canada (Quebec only); however protocols, acceptability and cost vary widely (Table 6). Formal clinical guidelines recommending food OIT exist in Canada and the EU, 73,126,127 and the World Allergy Organization (WAO) recommends the use of OIT in milk allergy for individuals meeting specific eligibility criteria and preferences.128 In Australia and South Africa, position statements on OIT for food allergy recommend that OIT should not be offered in routine clinical practice (outside of a clinical trial setting) as current evidence does not support safety and benefit over standard care.129,130 In Canada, approximately 52% and 7% of Allergist respondents in a nationwide survey were offering OIT and SLIT respectively, primarily to peanut, though the high cost of OIT raised concerns around equitable access to care.131 Respondents reported that remuneration and practical expenses pose a barrier to offering or expanding OIT in clinical practice131; a reasonable OIT fee that recognizes the significant clinical investment and expertise, patient support and education, is considered crucial to ensure safe, sustainable and comprehensive care. In the US, there has been conflicting literature on the adoption of OIT, with reports of slow uptake but also publications suggesting increasing “real world” use.132-134 Prior to approval of Palforzia, 14% of US allergists, in a survey with a 10% response rate, were reported to offer OIT.132 In Canada, Italy and Singapore, the use of OIT for a variety of foods has been well established in some centres for many years.119,135,136 Similarly in Japan, OIT is offered widely in both inpatient and outpatient hospital settings.23,137 OIT using unregistered food products is also offered by a small number of Allergists in Hong Kong, South Africa and Brazil (Table 6). Accessing OIT through private services can be a costly option for patients.

Use of biological therapies, such as omalizumab, alongside food immunotherapy has been explored as an option to increase safety and effectiveness.138,139 However, a 2021 systematic review concluded that there are currently too few studies in food allergy to draw meaningful conclusions about the use of biological therapies alone or as an adjunct to immunotherapy.117 Nevertheless, WAO suggests the use of Omalizumab during the initial stages of oral immunotherapy in IgE-mediated cow’s milk allergy.128 Omalizumab is sometimes prescribed off-label in conjunction with OIT in certain countries (e.g. Canada, Italy, Japan and Hong Kong) (Table 6). Omalizumab is approved for several allergic conditions (e.g. chronic urticaria or severe asthma) and may assist with reducing food allergy associated symptoms in these patients.138,140 Minimal data exists on the use of Omalizumab for the treatment of food allergy-related symptoms in routine clinical practice.117,141,142

**Innovation, evidence gaps and future research**

The relative importance of alternative technologies, management strategies and policies for food allergy varies between countries due to differences in epidemiology, education, socioeconomic wellbeing and cultural preferences of the population (Box 1). In Western societies, egg, milk, peanut and tree nut allergies tend to be given priority, while in many Asian countries seafood allergies demand greater attention. In the US, Europe and Australia, significant resources have been dedicated to research and development of immunotherapies.16,117,143-146 However, to date, clinical trials have focused on providing desensitization in highly sensitive patients; whereas research into treatments that induce remission, which can address the needs of patients who are less sensitive (for example, comprising almost half of peanut allergic patients147) remains limited. The development of a drug that is effective in achieving remission is a high priority, given the recent evidence that this clinical outcome significantly improves quality of life compared with desensitization.145,148 In other countries, establishment of specialized training programs and clinical services for the safe provision of OFCs has dramatically changed the way in which food allergy is managed, reducing dietary restriction and facilitating safe re-introduction of foods in low risk individuals.37,149,150

Consistent with the wide variations in clinical management of food allergy across the globe, evidence gaps and research priorities identified by authors were diverse (Box 2). In countries where commercial immunotherapy products have not yet been approved for use and allergen avoidance remains the mainstay of clinical management (e.g. Australia),23,129 identification of effective food allergy treatments is a priority, with emphasis on the need for late-stage clinical trials and real-world outcomes data.17,133,134 In places where reintroduction through OFC threshold determination or immunotherapy is becoming more common (Germany, Italy, US, Canada, UK, Japan), questions regarding the impact of allergen consumption or avoidance on transient and persistent immune mechanisms are highlighted. Where multidisciplinary food allergy clinical services are segregated by patient age (e.g. Australia, Germany and the UK), establishment of a framework to safely transition patients from paediatric to adult services is a vital gap in care. In Singapore and Hong Kong where seafood is a prevalent dietary inclusion, development of a safe and effective treatment for shellfish allergy is a priority.83,151 In some countries, evidence-based treatments and models of care are poorly implemented for economic, policy, educational or cultural reasons; hence, clinician training and implementation of evidence-based management, patient education, action plans, and food labelling regulations are priorities.37 Worryingly, EIs are still unavailable or have limited availability in some countries, due to cost and licencing restrictions.

**Conclusions**

This overview is not intended to be an exhaustive or systematic review of the literature, but rather aims to illustrate variation in management approaches and guidelines, as well as research priorities, in a number of geographically dispersed countries. Food allergy management in countries not included in this report may vary substantially and, even within the countries examined here, there is variability and debate beyond the scope of what can reasonably be discussed in a single paper. Instead, this manuscript aims to highlight the commonality and divergence in paediatric food allergy management approaches around the world.

Across the globe, the long-term management of IgE-mediated food allergy continues to rely on allergen avoidance, whether in conjunction with desensitization therapies or as a standalone management approach, to mitigate the risk of allergic reactions due to accidental ingestion. Models for delivery of care vary between countries, largely related to availability of resources. There is increasing recognition that current risk mitigation approaches come at a cost to patient quality of life and it is necessary to strike a balance between the competing considerations of risk reduction and excessive lifestyle restriction. While reactions from accidental ingestion are rare, dietary and social limitations together with emotional impacts have a significant long-term impact on quality of life. If strict dietary restriction, including complete avoidance of foods bearing PAL declarations, are implemented stringently without careful consideration of whether such precautions are individually justified, negative implications for patient wellbeing may exceed benefit. Growing recognition of this paradox is driving a global movement away from overly restrictive avoidance advice towards an individualized approach where clinical decision making is tailored to the patient’s preferences around risk management and lifestyle restriction. Until a remission treatment becomes available, and while allergen avoidance with or without desensitisation remains at the centre of food allergy management, multidisciplinary allergy services will continue to play a vital role in supporting dietary avoidance and maximising the psychosocial wellbeing of individuals with food allergy.

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**Author contribution statement**

MLKT conceived the topic and developed the scope of the review. ML and MLKT coordinated the information collection and literature review, and reviewed the compiled information for completeness and accuracy. ML drafted the manuscript. All other authors contributed information relevant to their countries of residence, and reviewed the draft manuscript for accuracy.

**Figure 1. Availability of Allergy specialists per 100,000 population for countries included in the review**

**Legend:** **\*For these countries, data is presented for number of Paediatric Allergists per 100,000 population <18-years.**

**Table 1: Routine management pathways for food allergy: frequency of review**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Country** | **General review interval (including action plan update and patient education)** | **Reassess for possible tolerance (skin prick testing, sIgE)** | **Component testing (molecular diagnosis)** | **Oral food challenges** |
| Australia | Ideally yearly. | 1-2 years, depending on the allergen. Egg and milk yearly but others less frequently (nuts, fish, seafood). | Available but at a cost. Ara h2 more commonly used, particularly in Victoria due to local research.152 Others available (ovomucoid, casein) but rarely used. | 1-2 year interval (or longer) depending on the allergen and test results (ie. if SPT results decreasing).38 |
| US | Approximately yearly. | No specific recommendation but roughly yearly with more often younger than older.30,69 | Yes, some are FDA cleared. Peanut diagnosis has Ara h 2 in a practice parameter.153 | As appropriate.40,41 |
| Canada | Yearly. | Yearly. Some provinces do not cover cost of IgE testing, so SPT is performed first or singularly. | Available and increasingly used but not publicly funded in all provinces. | Yes. Barriers to access with many provinces not having OFC billing codes, limited compensation or restricted access (frequency / setting).42 |
| UK | Yearly. Sometimes two-yearly for isolated nut allergy.20 | Regular repeat testing in preschool years (annually), less often once at school (~3-yearly). | Component resolved diagnostics commonly offered.20 | Available at over 90% of services,20 usually open challenges. DBPCFC offered at 50% of tertiary centres. Frequency varies greatly by service, clinician and patient. |
| Italy | EAACI suggest should be re-evaluated regularly but review interval not specified.22 | No fixed schedule, as clinically indicated. | Available but inconsistently used. | OFC recommended to avoid unnecessary dietary restrictions (e.g. 6-12 months milk / egg, 2 years peanut or tree nuts in absence of an accidental reaction).22 |
| Germany | Approximately yearly.97 | Timeframe not specified in guideline.32 Usually milk and egg allergy SPT/IgE test yearly; for nuts and sesame at time of school systems change**.** | Available. | Depends on allergen and age of child.32 Every 6-12 months in young children with egg / milk allergy. For other foods as indicated; a reduction of sensitization may guide this decision.32 OFC are performed in both inpatient and outpatient public hospital settings but are only adequately reimbursed as an inpatient procedure. |
| Singapore | Widely variable. Action plans usually reviewed annually at the start of the school year. | Widely variable. sIgE testing is not routine with each visit. | Available. | As indicated. Conducted in both clinic setting and self-administered at home for low risk cases. |
| Hong Kong | 6-12 monthly | 9-12 months for patients aged <4 years, 24-36 months for >4 years. SPT used more widely due to out-of-pocket cost for sIgE. | Mostly in some private labs or for research. | Open challenges in both inpatient and outpatient public hospital settings. Offered when signs of tolerance developed. |
| Japan | 3-monthly. Action plans reviewed annually. | Once per year (school aged), twice a year (infants). | Routine practice. Covered by nationwide insurance (Ovomucoid, Casein, o-5 Gliadin, Ara h 2, Jug r 1, Ana o 3, Gly m 4). | Covered by nationwide insurance and offered by more than 400 paediatric training facilities.25 Stepwise OFC and consumption recommended for egg, milk and wheat.23 |
| South Africa | 6-monthly | Repeated every 6-24 months depending on allergen.66 | Only at tertiary teaching hospitals. | Open challenges.39,66 |
| Brazil | 6-12 monthly | Widely variable. sIgE testing: mostly annually. SPT: mostly performed in private system and a few public centres - repeated as needed, generally every year. | Milk and egg available both in the public and private setting (routinely used). For other foods, only in private labs and mostly requested by Allergists. ImmunoCAP ISAC available only in private system. | Performed mainly in public tertiary academic centres (mostly open but also DBPCFC) and by a very few private Allergists on day-care (great majority open); frequency varies according to indication. Fully funded for cow’s milk allergy in children up to 24-months. |

Abbreviations: DBPCFC: Double-blind placebo-controlled food challenge; FDA: Food and Drug Administration (United States); sIgE: specific immunoglobulin-E; SPT: skin prick testing; OFC: oral food challenges.

**Table 2 – Advice given to patients and families regarding allergen avoidance and permissive consumption**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Country** | **Egg** | **Milk** | **Peanut / tree nuts** | **Fish / seafood** |
| Australia | Not standardised - some Allergists allow baked egg ingestion at home if initial reaction to egg is mild, some will only allow after passing a formal baked egg OFC.31 | Majority of allergists allow baked milk after passing formal OFC. Milk ladder only used for non-IgE mediated allergy.154 | Variable. General approach is to permit consumption of nuts that the patient is not allergic to. | Very variable. Recent move towards trying to individualize by fish or seafood species, avoiding only those to which the individual is allergic. Many patients continue to avoid all fish or seafood however. |
| US | Variable, no strict parameter. Baked egg options are increasingly common practice.155,156 | Variable, no strict parameter. Multiple different strategies. Milk ladder is used for some.70,75,76 | Variable, no strict parameter. | Variable, no strict parameter. |
| Canada | Variable. In general, most allergists will support baked egg ingestion and may provide OFCs for this. Joint practice statement has been recently released by CSACI / BSACI.74,157 | Variable. In general, most allergists will support baked egg ingestion and may provide OFCs for this. Joint practice statement has been recently released by CSACI / BSACI.74,157 | Highly variable. Generally try to introduce nuts that not allergic to. Panel testing discouraged, do not test for nuts that have not been eaten and reacted to. | Recent work to promote a clear distinction between finned fish and shellfish in product labelling.158 |
| UK | Very variable, depends on the clinician. Guidelines recommend baked egg introduction from a year of age in low risk patients.80 87% of Allergists use the egg ladder.20 | Various protocols used. BSACI guideline is quite pragmatic and permits introduction at home. However, most GPs and many secondary/tertiary care services use the MAP/iMAP guidance which is more conservative. All services use the milk ladder.20,78,79 | Common to now encourage consumption of other nuts the patient is not allergic to. Ignore precautionary labelling for nuts in most cases.159 | Varies. Many services test and advise specific fish introduction, especially tuna or shellfish, depending on family wishes. |
| Italy | Complete avoidance; periodical repetition of OFCs. Baked egg OFCs generally precede raw egg OFCs. | Complete avoidance; periodical repetition of OFCs. Baked milk OFCs generally precede raw milk OFCs. | Elimination diet should be based on a formal allergy diagnosis identifying  the food allergen(s) responsible for the patient’s symptoms/reactions.22 | Elimination diet should be based on a formal allergy diagnosis identifying  the food allergen(s) responsible of the patient’s symptoms/reactions.22 |
| Germany | If patient is raw egg allergic the patient should avoid raw egg.32 Otherwise varies, with guidelines recommending assessment of tolerance to baked egg.32 | Guidelines recommending assessment of tolerance to baked milk.32 | Varies. Food-specialized Allergists recommend nut allergic individuals continue eating other nuts they are already tolerating. Other clinicians may advise avoiding all nuts. | Varies. Food-specialized Allergists will give an individualized recommendation based on OFCs. Other clinicians may advise avoiding all forms of fish. Crustaceans and molluscs considered separate from fish. |
| Singapore | Avoidance is standard. Baked egg challenges to determine tolerance to baked eggs common. No specific guidelines. | Baked milk OFCs practiced. The milk ladder is used as a guide. | Varies. Although clinicians advise avoiding only the nuts allergic to, parent reluctance to undergo OFCs with positive sensitization hampers introduction. Parents usually avoid all nuts. | Crustacean shellfish allergy is common. Generally, avoidance is advised. Molluscs may be tolerated by some with shellfish allergy. Advice on fish allergy varies. |
| Hong Kong | Commencement of home-based egg ladder in patients with mild allergy often advised by Allergists. Individuals can start baked egg intake at home after passing the baked egg OFC in the hospital setting. | Baked milk not as commonly recommended as baked egg. Milk ladder is less commonly adopted and compliance is often poor. | For patients with a specific tree nut allergy, Allergists tend to advise avoidance of all tree nuts due to potential cross contamination. | Individualized seafood intake recommendations are favoured. OFC and component testing utilised to identify those with selective allergies to particular seafoods, permitting consumption of other species.83,84,151 |
| Japan | Advice given regarding consumption of baked egg. Partial intake below stepwise OFC threshold advised.23,82 | Partial intake below threshold (by stepwise OFC) is advised.23,81 | OFC used to diagnose specifically, no blanket avoidance of nuts.23 | Individualized by fish or shellfish species or category (eg white vs red flesh fish, molluscs vs crustaceans) - OFC to diagnose.23 Dashi (derived from fish peptide) and canned tuna may be introduced. |
| South Africa | If baked egg tolerated, continue ingesting. If baked egg never ingested, then OFC to baked egg.39 | If baked milk tolerated, continue ingesting. If baked milk never ingested, then OFC to baked milk. Milk ladder used for mild non-IgE mediated food allergy.39 | Do not avoid nut types tolerated previously. If peanut allergy, SPT or sIgE for tree nuts and sesame. If negative: ingest, if raised: OFC, if very raised: avoid.39 | Molluscs considered separate allergy to crustacea. Avoid all fish unless history suggestive of mono-species allergy. |
| Brazil | Not standardized. GP and Paediatricians often prescribe strict avoidance. Allergist may allow baked egg if already consumed without symptoms or perform OFC (if available). | Same as for egg. Milk-ladder may be used for home introduction (in non-IgE mediated food allergy only) if OFC is not possible. | Not standardized. GP and Paediatricians and some Allergists tend to recommend avoiding all nuts if sIgE/SPT are positive. | Variable. Crustaceans and molluscs considered separate from fish. Tendency to recommend avoiding all fish species. |

Abbreviations: BSACI: British Society of Allergy and Clinical Immunology; CSACI: Canadian Society of Allergy and Clinical Immunology; GP: General Practitioner; OFC: Oral food challenge; sIgE: specific immunoglobulin-E; SPT: skin prick testing.

**Table 3 – Emergency action plans**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Country | Regulation and standardization | Applicability | Compliance with action plan provision | Compliance with instructions given in action plans by patients |
| Australia | ASCIA mandated, standardized written documentation used nationwide.86 | Separate plans for allergic and anaphylaxis. | No data but compliance thought to be very good. All schools and childcare centres require the standardized plan on enrolment. | Carrying of an EIs in social and sporting settings is poor, particularly in teenagers. Compliance with action plans within school settings is high.160 |
| US | Not standardized, but guideline recommended.30 Multiple organizations have developed their own.161 | Depends on clinician and location. | Limited recent data available. Older studies demonstrate poor compliance with documentation for EIs in schools.162,163 Rate of provision of action plans unclear.164,165 | Unclear. One study suggested that severe reactions often undertreated n community.166 |
| Canada | Standardized. Ideally should be provided to all patients with food allergy.90 | All patients with diagnosed food allergy. | No data but compliance thought to be very good. | Poor. Less than half of patients with anaphylaxis receive epinephrine prior to arrival at the ED.94,167 |
| UK | Standardized by BSACI.89 Should be given to all patients with food allergy.91 | Different plans for those with / without autoinjector. | Almost universal.20 | No data. |
| Italy | Guideline recommended – EAACI suggest an example of an individualised action plan adapted from BSACI.168 | All food allergic individuals.22 | Compliance with guidelines very good in specialist allergy centres, less so outside of this setting.169 | Poor. A European Anaphylaxis Registry study of anaphylactic reactions found that almost one in two peanut allergic children (44%) already prescribed an EI did not use or carry the device.95 |
| Germany | Standardized and guideline recommended.97 | Only patients at risk for anaphylaxis. Individual guidance and education recommended for others.32 | Compliance unclear but thought to be low outside specialized food allergy centres. No reference data available. | Use of EIs is the community is very low.170 |
| Singapore | Standardized.171 | All incorporated as one. | Good. No reference data available. | Mostly good except for hesitancy to use EI. No reference data available. |
| Hong Kong | Not mandated or standardized. Some institutions have developed their own.172 | All patients with food allergy but depends on clinician. | Generally good for Allergists but poor for GPs. | Pre-hospital management of anaphylaxis is poor and the use of EIs is low (10% administered epinephrine prior to hospital arrival).173 |
| Japan | Standardized and mandated as per guidelines.23 | Same plan for all allergic patients. | No data but compliance thought to be excellent. All schools and childcare centres require the standardized plan on enrolment. | Compliance with action plans within nursery and school settings is high. |
| South Africa | Recommended but not mandatory.66 Standardized plan available.174 | Same plan for all allergic patients. | Low. Application of preventative measures, action plans and alerts, and prescription of EIs needs improvement. Rate of recurrent reactions is high.175 | Low. Use of EIs in the community is rare.175 |
| Brazil | Recommended by ASBAI.176 | Individualized. There are models of plans provided by ASBAI and by Anafilaxia Brasil.177 | Varies though compliance by Allergists likely good. Compliance with food allergy guidelines by Paediatricians is low.178 | No data. |

Abbreviations: ASBAI: Brazilian Association of Allergy and Immunology; ASCIA: Australian Society of Clinical Immunology and Allergy; BSACI: British Society of Allergy and Clinical Immunology; EAACI: European Academy of Allergy and Clinical Immunology; ED: Emergency Department; EI: Epinephrine injector; WAO: World Allergy Organization.

**Table 4 – Provision of Epinephrine injectors**

|  |  |  |  |
| --- | --- | --- | --- |
| **Country** | **Guidelines and regulations** | **Routine vs. selective prescribing** | **Brands available** |
| Australia | Yes - ASCIA guidelines.102 | Selective. History of anaphylaxis, food allergy (excluding oral allergy syndrome) and co-existing unstable or persistent asthma, underlying mast cell disorders. Additional risk factors should be considered.102 | Anapen and EpiPen. |
| US | Yes, multiple.30,69,105 | Guidelines vary, generally selective. | AuviQ, EpiPen and a prefilled syringe brand (not autoinjector). Generics also available. |
| Canada | Yes – CSACI position statement.90,104 | Routine for patients with an IgE-mediated allergy. | Allerject (called Auvi-Q in the US), Emerade and EpiPen |
| UK | Yes – BSACI Guidelines.91 | Selective – history of severe reaction only.91 | JEXT, Emerade and EpiPen. |
| Italy | Yes – EAACI guidelines.168 | Selective with absolute and relative criteria specified (including undergoing OIT treatment).168 | EpiPen and JEXT |
| Germany | Yes, German anaphylaxis guidelines.97 | Selective. History of anaphylaxis, a high future risk of anaphylaxis or life-threatening reactions, those who react to very small amounts of allergen. | Currently four (it sometimes varies from 2-4) |
| Singapore | Yes - Ministry of Health.68 | Selective. Physician determined. History of anaphylaxis consistent indication. | Epipen only. Access (importation) is an issue, out of pocket cost for autoinjectors (not subsidized). |
| Hong Kong | Public sector management guideline on childhood anaphylaxis.103 EAACI guideline also used.22 | Selective. All patients with a history of anaphylaxis or serious reaction, or coexistent food allergy and persistent asthma.103 | Public sector - Jext only; Private sector – EpiPen and Jext. |
| Japan | Yes – Japanese Guidelines 2020.23 | Past history of anaphylaxis including results of OFC, and high-risk patients. 23 | Epipen only |
| South Africa | Yes – SAFAWG Guidelines.101 | Selective. Absolute criteria: prior severe reaction, food allergy with asthma, exercise induced anaphylaxis, idiopathic anaphylaxis, mast cell disorders. Relative indications: peanut allergy over 5, teenagers, remote from care, trace amount reactions.101 | Epipen only. |
| Brazil | Yes – ASBAI Guideline, but not specific to FA.177 | Selective. Mostly prescribed by Allergists in case of severe reaction to any food. Often considered by specialists in case of peanut/nut allergy. 177 | None. Patients are advised to import themselves. Some public services give ampule and syringe to those who cannot afford autoinjectors. |

Acronyms: ASBAI: Brazilian Association of Allergy and Immunology; ASCIA: Australian Society of Clinical Immunology and Allergy; BSACI: British Society of Allergy and Clinical Immunology; CPG: Clinical Practice Guideline; CSACI: Canadian Society of Allergy and Clinical Immunology; EAACI: European Academy of Allergy and Clinical Immunology; OFC: Oral food challenge; SAFAWG: South African Food Allergy Working Group.**Table 5 – Food allergy management policies in childcare centres and schools**

|  |  |  |  |
| --- | --- | --- | --- |
| **Country** | **Guidelines or legislation** | **Allergen bans utilized** | **Mandatory staff training\*** |
| Australia | Yes.88,87 | Depends on school but not recommended.88 | Yes.87 |
| US | Yes, and additional legislation in development. Not well enforced.167,179 | Generally not recommended but some restrictions encouraged.107,179,180 | No, optional. |
| Canada | Yes.181,182 | Not recommended.107 | Yes, but different between jurisdictions. |
| UK | No current national guidance or legislation. A model policy has been drawn up with the BSACI for schools.183 | Nearly all schools and preschool nurseries, and some other settings such as university halls of residence, have nut free policies. | Not mandatory but recommended.183 |
| Italy | School policies should reflect the EAACI guidelines.184 | EAACI has published resources for schools discouraging blanket bans.185 Level of implementation unclear and subject to policy of school. | Guideline recommended.184 |
| Germany | No. | Not recommended, however some schools offer this.110 | Available but not mandatory. Often parents will train teachers on a needs basis. |
| Singapore | Individualized by school. Overseen by Ministry of Education and Health Promotion Board Singapore. | Depends on school. Often at international schools. | Yes. |
| Hong Kong | No. | In some international schools only. | No, in most schools staff will call parents or ambulance if a reaction occurs. |
| Japan | Yes, legislation and guidelines.186 | Not recommended. | Yes. |
| South Africa | In Western Cape Province only. | No. | No. |
| Brazil | Legislation guarantees special menus for children with any feeding issue, including FA.187 | In some international schools only. | No, optional. |

\*Covering topics such as reaction management, first aid, epinephrine administration, risk reduction.

Abbreviations: BSACI: British Society of Allergy and Clinical Immunology; EAACI: European Academy of Allergy and Clinical Immunology; FA: food allergy.

**Table 6 - Oral immunotherapy treatment and adjunctive therapies**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Country** | **Guidelines available** | **Palforzia – approval, funding and uptake** | **OIT using commercially available foodstuffs – availability, accessibility and cost** | **Other treatments available** |
| Australia | Yes. OIT not recommended.129 | Not approved. | No data available. | No. |
| US | Various review and opinion papers have been published.188,189 | Approved. Funded by insurance but has been refused on occasion requiring appeal. Uptake less than expected.123 | Available in a limited number of settings. Mostly appears to be offered by allergists. Insurance may pay for OFC, office visits or in some cases “desensitization” but there are no official billing codes. Some charge cash and costs vary widely. There are some industries emerging.132-134 | Some physicians use off-label Omalizumab. |
| Canada | Yes.126 | Not approved. | OIT offered by significant proportion of Allergists, small number offering SLIT too.131 This is an uninsured service. Costs can range from CA$2000-8000 for single food OIT and up to CA$10000 for multifood OIT (privately), lower in public services. No billing code for OIT currently except in Quebec, and the way this treatment is offered varies greatly.190 | Yes, Omalizumab is commonly used in conjunction with OIT. |
| UK | No. BSACI is currently developing guideline for Palforzia implementation. | Approved.120 Within the NHS this is government funded. Academic centres not planning extensive use Palforzia, uptake likely in private practice. Private treatment costs ~£20,000 per child. Limited data available. | Peanut OIT offered by small number of private allergists, less costly than Palforzia. Milk and egg OIT offered by a limited number of NHS centres (locally developed protocols), with some others offering it as part of research programmes. | Only used in research setting for food allergy. However, used to treat other conditions that frequently coexist with food allergy. |
| Italy | Yes - EAACI Guidelines available.73,127 | Approved by European Medicines Agency.122 Price currently being negotiated with the agencies of the individual states. Only available on the market in German-speaking countries to date. | A 2022 study found over 7 food allergy immunotherapy centres (primarily in publicly funded hospitals) had treated over 3000 patients in Italy using unregistered food products.119 | Biologicals (such as omalizumab) may enhance the safety of food immunotherapy,127 though currently only used in the research setting for food allergy.138 |
| Germany | Yes - EAACI Guidelines available.127 | Approved and funded by governmental and private insurances (with official billing code) but uptake slow. | Not approved or publicly funded but no data available. | No other approved drugs for food allergy. Some physicians may prescribe off-label omalizumab on an individual basis. |
| Singapore | No. | Not approved. | Yes, commercial defatted peanut powder and tree nut powders are used. Provided at one public and one private institution by allergists. Program costs approx. S$10,000.136 | Omazilumab is not used for food allergy therapy. |
| Hong Kong | No | Not approved as a registered product. Prescription has to be through a named-patient basis (used for a patient under the doctor's direct responsibility). Uptake low. Cost not supported by insurance or the government. | Yes, unregistered peanut and tree nut extracts, and baked milk and egg are used in OIT by small number of Allergists, predominantly private sector, easily accessible if cost is not a concern. Cost is US$1500-2500 per month.191 | Omalizumab used with OIT in some cases.191 Prescription of biologics is not supported by insurance or government funding. |
| Japan | Yes.23 | Not approved. | Common in research setting at tertiary hospitals.137 Cost only for examination and OFC. Partial intake of causative food below OFC threshold is encouraged for low risk cases.23 | Some physicians use off-label Omalizumab. |
| South Africa | No | Not available. | Yes, very small number of Allergists. Privately funded only. No data available. | Not used. |
| Brazil | No | Not approved. | Very few in research setting or offered by private specialists at cost to patient.192,193 | Omalizumab used off-label in some cases. |

Abbreviations: OFC: oral food challenge; OIT: oral immunotherapy. BSACI: British Society of Allergy and Clinical Immunology; CPG: Clinical Practice Guideline; CSACI: Canadian Society of Allergy and Clinical Immunology; EAACI: European Academy of Allergy and Clinical Immunology

**Box 1: Milestone discoveries in food allergy management over the past-5 years**

|  |
| --- |
| Novel treatments   * Multiple food immunotherapy approaches (oral, sublingual, epicutaneous) in development for various common allergens (peanut, multi-nut, egg, milk, shrimp). * Multiple biologics and other agents are under investigation as allergen non-specific therapies, or as adjuncts to allergen-specific immunotherapies.   Clinical management and guidelines   * Increased use of component resolved diagnostics in diagnosis of food allergies. * Enhanced guidance and training for epinephrine injector prescription and usage. * Reduced dependence on Panel Testing for different food allergies. * Increasing permissiveness of ingestion for people with high threshold/low severity, with shift from total to selective avoidance for some of classes of food (e.g. fish/shellfish, peanuts and tree nuts). * Precision-based management of allergy via oral food challenge and component-resolved diagnostics. * Recognition of overdiagnosis and excessive treatment of food allergy as an emerging clinical issue, especially for cow’s milk allergy.   Health services and policy   * Rapid expansion of services for specialized diagnosis and management of food allergy, especially in children. * Establishment of specialized oral immunotherapy centres. * Establishment of food challenge services. * Establishment of food allergy specific non-profit organizations for patient support, education and philanthropy. * Centralised and standardized training of teachers and educators in the management of food allergy. |

**Box 2: Priority evidence gaps and future research**

|  |
| --- |
| Avoidance and prevention of reactions   * Balancing risk of reaction with lifestyle restrictions and regulatory burden imposed on the wider population. * Anaphylaxis registers to facilitate risk-factor identification and effective prevention of fatal anaphylaxis. * Improved treatments for the acute management of allergic reactions.   Treatment   * Development of a food immunotherapy that can safely induce remission and allow free consumption of allergens. * Real world experience of peanut OIT treatment and long-term outcomes. * Development of effective OIT for allergens other than peanut. * Development of a treatment to reduce the risk of fatal anaphylaxis in individuals with severe food allergy. * Identification of factors driving transient and persistent immune mechanisms; influence of consumption or avoidance on long-term tolerance in individuals with high eliciting doses.   Clinical services management   * Increasing access to food allergy specialty training for clinicians from all relevant professions (medicine, nursing, allied health). * Proper and safe transition of food allergic children to adult care. * Consensus on the most effective strategy for avoiding and managing allergic reactions in schools and childcare centres. * Introduction of strategies to measure and reduce the psychosocial burden of food allergy. * Strategies that can reduce unnecessary avoidance of foods (e.g. standardized food challenge protocols, baked foods, nutritional education). |

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