

CME Review

The epidemiology of food allergy in adults



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Key Messages

- Data from random digit dial and other population-based surveys indicate a high burden of food allergy in North America among adults and a growing burden among adults from other parts of the globe.
- Shellfish seems to be the most common trigger of immunoglobulin E (IgE)-mediated food allergy among adults, followed by peanut and cow's milk.
- Adult-onset allergy also seems to be increasingly common, especially to shellfish.
- Not all adult food allergy is IgE-mediated. For example, food protein-induced enterocolitis syndrome is a non-IgE-mediated allergy that has been estimated to affect a growing number of adults in the United States and Europe. Eosinophilic esophagitis is another condition that has a non-IgE-mediated component, yet is commonly comorbid among adults with IgE-mediated food allergy.
- Alpha-gal syndrome affects a growing number of adults in the Southern and Midwestern regions of North America, where the lone star tick resides. This syndrome arises when individuals are sensitized to a glycoprotein commonly found in red meat after being bitten by a tick. Other tick species are also proven vectors and are responsible for alpha-gal syndrome in other global regions, including Europe, Australia, Brazil, Central America, West Africa, and South Africa.

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ABSTRACT

The prevalence and awareness of food allergy (FA) among US adults is arguably at a historical high, both with respect to primary immunoglobulin E-mediated food hypersensitivity and other food-triggered conditions that operate through a variety of immunologic mechanisms (eg, pollen-FA syndrome, alpha-gal syndrome, food protein-induced enterocolitis syndrome, eosinophilic esophagitis). Worryingly, not only are many adults retaining childhood-onset food allergies as they age into adulthood, it seems that many adults are experiencing adult-onset allergies to previously tolerated foods, with correspondingly adverse physical, and psychological health impacts. Consequently, this review aims to summarize what is currently known about the epidemiology and population-level burden of FA among adult populations in North America and around the globe. This article also provides insights into the natural history of these conditions and what we need to know as we look to the future to support effective care and prevent FA.

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Participants will be able to demonstrate increased knowledge of the clinical treatment of allergy/asthma/immunology and how new information can be applied to their own practices.

Learning Objectives

At the conclusion of this activity, participants should be able to:

- Summarize the current literature regarding the prevalence and public health burden of IgE-mediated FA on adult populations.
- Discuss the extent to which other non-IgE-mediated FAs affect adult populations in the United States, Canada, and elsewhere.

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Physicians involved in providing patient care in the field of allergy/asthma/immunology.

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Introduction

Because of its rising prevalence and increasing health care utilization, food allergy (FA) has become a condition of growing concern for patients, physicians, and policymakers around the world. Food allergy (FA) has been reported to affect people of all socioeconomic and demographic backgrounds, including patients of all ages.^{1,2} Most epidemiologic work to date has focused on estimating the burden of disease among pediatric populations; however, increasing attention is now being paid to affected adults—both those who retain their childhood allergies into adulthood and those who develop novel, adult-onset allergies to previously tolerated foods.³ The need to better understand the distribution of FA among adult populations is increasingly urgent because effective allergy prevention and treatment modalities are emerging, which overwhelmingly target pediatric populations.

Awareness of FA among US adults is arguably at a historical high, both with respect to primary immunoglobulin E (IgE)-mediated food hypersensitivity⁴ and other food-triggered conditions that operate through a variety of immunologic mechanisms (eg, pollen-FA syndrome, food protein-induced enterocolitis syndrome, eosinophilic esophagitis [EoE]). Consequently, this review aims to summarize what is currently known regarding the epidemiology and population-level burden of FA among adult populations and what we need to know as we look to the future to support effective care and prevent FAs.

North American Food Allergy Epidemiology Among Adult Populations

“Random Digit Dial” Prevalence Surveys Assessing Specific Food Allergy Prevalence

In the North American context, there have been numerous surveys conducted over the past 25 years that have assessed the prevalence of IgE-mediated FA among US adults. Sicherer et al.^{5,6} in 1999⁵ and 2002,⁶ reported the prevalence of peanut allergy (PA) to be 0.7% and 0.6% among US adults aged 18 and above, whereas tree nut allergy was estimated to affect 0.7% and 0.5% of US adults, respectively. The 2002 survey reported that around half of respondents with peanut or tree nut allergy reported allergies to additional (unspecified) foods, suggesting that more than 1 FA (or multi-FA) is common among US adults with FA. In 2004, this group conducted a seafood allergy prevalence survey,⁷ in which 0.5% of US adults reported allergy to at least 1 finned fish and 2.5% reported allergy to at least 1 shellfish—identifying shellfish as an allergen of major concern in adults. Women were more affected than men by both shellfish (2.6% vs 1.5%) and finned fish (0.6% vs 0.2%) allergies. These findings stand in stark contrast to the available pediatric data, which found a preponderance of boys were allergic to shellfish relative to girls. Among both children and adults, individuals of non-Hispanic Black race were more likely to be allergic to finned fish (1.1% [0.6%–1.7%] vs 0.3% [0.2%–0.4%]) or shellfish (3.1% [2.3%–4.1%] vs 1.8% [1.5%–2.0%]), than those of non-Hispanic White race. In a 2008 follow-up survey of PA and tree nut allergy prevalence, Sicherer et al.⁸ incorporated an assessment of sesame allergy prevalence. This survey found similar rates of PA and tree nut allergy to those reported in 1997 and 2002 among US adults, and estimated the prevalence of sesame allergy to be 0.1%.

Food and Drug Administration Food Safety Surveys

Over a similar time period, repeated cross-sectional data⁹ from the US Food and Drug Administration (FDA) food safety surveys—administered in 2001, 2006, and 2010—suggested that the prevalence of self-reported allergy to any food—not just peanut, tree nut,

and shellfish—increased substantially among US adults during that time, rising from 9.1% in 2001 to 14.9% in 2010, whereas the number self-reporting physician-diagnosed FA also increased, rising from 5.3% to 7.6% over this same time frame. These data were collected from random digit dial landline telephone surveys conducted by the FDA every 3 to 5 years, which included a version of the following question: “Do you currently have any food allergy or suspect that you have a food allergy?” Individuals responding affirmatively to this question were then asked about reaction symptoms, and whether the allergy was physician-diagnosed.

In the 2010 food safety survey⁹ among adults reporting physician-diagnosed FAs, only 2% reported being diagnosed by means of an oral food challenge, whereas 6% reported receiving a physician diagnosis after a combination of clinical history, physical examination, and skin prick test and specific IgE (sIgE) testing. Only 15% of adults with physician-diagnosed FA reported being prescribed epinephrine—the one and only first-line treatment for food-induced anaphylaxis. Participants with self-reported FA and physician-diagnosed FA, 45% and 41.6%, respectively, reported experiencing an allergic reaction within the past 12 months; and 26% and 24%, respectively, reported experiencing their last allergic reaction in the past 1 to 5 years, whereas 29% and 34%, respectively, reported having gone 5-plus years without experiencing a food-allergic reaction. Among adults with physician-diagnosed FA, 15% reported having an allergic reaction treated in a hospital, with three-quarters of adults with reported FAs reporting reactions to at least 1 of the major food allergens defined by the Food Allergen Labeling and Consumer Protection Act¹⁰ at the time (ie, cow’s milk, dairy, eggs, finned fish, shellfish, tree nuts, peanuts, wheat, gluten, soy).

Centers for Disease Control and Prevention’s National Health and Nutrition Examination Surveys

The National Health and Nutrition Examination Surveys (NHANES) 2005 to 2006 serologic data,¹¹ collected from 8000 participants, estimated sensitization rates to cow’s milk, egg, peanut, and shrimp to be approximately 15% of US adults, with significant racial, and socioeconomic differences in food-allergic sensitization. Self-reported non-Hispanic Black adults and those reporting lower annual incomes were most likely to report any sensitization (>0.35 kU/L), and higher levels of sensitization indicative of likely FA to these 4 specific foods. However, overall rates of possible and likely allergy to these foods on the basis of serologic data were generally low—though substantially higher among participants with comorbid asthma and allergic rhinitis.

Between 2007 and 2010, the NHANES assessed the prevalence of self-reported FA to wheat, cow’s milk, eggs, finned fish, shellfish, corn, peanuts, other nuts, soy products, and other foods. Because NHANES also assesses dietary consumption patterns in the previous 30 days along with reported FA status, secondary analyses by McGowan et al.¹² were able to identify the subset of FA cases who also reported no consumption of specific allergens (ie, cow’s milk, shellfish, finned fish) in the previous 30 days for which dietary intake data were available. By excluding cases with reported consumption of the specific allergen, the authors argued they were able to derive a more precise estimate of FA prevalence. This analysis of more than 20,000 individuals estimated adult self-reported FA prevalence at 9.7%, which was only slightly attenuated after excluding those adults who consumed cow’s milk, shellfish, or finned fish in the past 30 days. Among reported FAs, those to cow’s milk (2.6%; 95% confidence interval [CI], 2.2–3.1), shellfish (2.0%; 95% CI, 1.8–2.4), peanut (0.9%; 95% CI, 0.6–1.2), and tree nuts (0.8%; 95% CI, 0.6–1.0) were most common, followed by egg (0.5%; 95% CI, 0.4–0.7), wheat (0.5%; 95% CI, 0.4–0.7), and finned fish (0.45%; 95% CI, 0.34–0.57). This study also found FA rates to be highest among women, individuals with higher

educational attainment, those reporting non-Hispanic Black race, and individuals with comorbid atopy (eg, asthma, and allergic rhinitis). Notably, among adults reporting an asthma attack in the past year, nearly a quarter (23.1%; 95% CI, 19.1–28.3) reported at least 1 current FA.

United States Population-based Surveys by the Gupta Research Team

From 2015 to 2016, Gupta et al.¹³ leveraged the nationally-representative AmeriSpeak panel—a market research panel recruited by means of probability-based sampling methods—to estimate the prevalence and burden of FA among US adults aged 18 years and older. A 51% survey completion rate was observed, and complex survey-weighting was used to adjust for nonresponse among the 40,443 total survey respondents. After applying stringent symptom report –based criteria to rule out suspected cases of food intolerance or pollen-food allergy syndromes (PFAS), the authors estimated the current FA prevalence to be 10.8% (95% CI, 10.4–11.1%), with an additional 8.2% reporting reaction symptomatology that was not convincingly IgE-mediated. Approximately half of these convincing FA cases were physician-confirmed, for an estimated 5.1% (95% CI, 4.9–5.4%) of US adults. Among all adults surveyed, the most common convincing allergies were shellfish (2.9%), cow's milk (1.9%), peanut (1.8%), and tree nuts (1.2%). The estimated rates of specific allergies are reported in Figure 1. This study also estimated that more than half of US adults report multi-FA, half reported a history of at least 1 severe food-allergic reaction (characterized by multiple organ system involvements), and roughly 1 in 3 had experienced at least 1 FA-related emergency department visit in their lifetime. Despite this relatively high rate of severe reactions, only 24% reported a current epinephrine autoinjector (EAI) prescription, suggesting suboptimal FA management. Predictors of FA status again included female sex, race other than White, ethnicity, comorbid atopy, higher levels of educational attainment, and younger age.

Canadian Food Allergy Prevalence From Surveying Canadians to Assess the Prevalence of Food Allergy and Attitudes Toward Food Labeling and Risk, SPAACE, and SPAACE to SPAACE

The Surveying Canadians to Assess the Prevalence of Food Allergy and Attitudes Toward Food Labeling and Risk (SCAALAR) study¹⁴ leveraged a national cross-sectional telephone interview to estimate the prevalence of FA among Canadian adults in 10 provinces. The SCAALAR survey was conducted from 2008 to 2009, using a comparable random digit dial telephone methodology to that used in previous work by Sicherer et al.^{2,5–7} A 35% survey completion rate was

observed among the 3613 respondents who provided data for 7469 individual Canadians. Food allergy was defined as perceived (on the basis of self-report), probable (on the basis of convincing history or self-report of physician diagnosis), or confirmed (on the basis of history and evidence of confirmatory tests). Among all respondents, 8.3% of adults reported at least 1 allergy to any food, which was attenuated to 6.6% after adjusting for survey nonresponse and conservatively excluding any adult who only reported allergy to cow's milk, egg, wheat, or soy. The most typically reported FAs were shellfish (1.9%; 95% CI, 1.6–2.2), cow's milk (1.9%; 95% CI, 1.6–2.2), fruits (1.6%; 95% CI, 1.3–1.9), vegetables (1.3%; 95% CI, 1.0–1.6), tree nuts (1.1%; 95% CI, 0.8–1.3), peanut (0.8%; 95% CI, 0.6–1.0) and egg (0.7%; 95% CI, 0.5–0.9). When cases that were undiagnosed or did not meet stringent symptom report criteria were excluded, these estimates were only slightly attenuated. The FAs were more typically reported by respondents with higher degrees of educational attainment (OR, 1.24; 95% CI, 1.03–1.51) and those who were born in Canada (OR, 1.47; 95% CI, 1.10–1.92). However, when compared with the general Canadian population, SCAALAR survey respondents were more educated, had higher income, and were more likely to be born in Canada.

To better understand the prevalence of FA among vulnerable populations in Canada—defined as individuals of low education or income, those who immigrated less than 10 years ago, and First-Nation individuals—the SCAALAR study investigators initiated the Surveying Prevalence of FA in All Canadian Environments (SPAACE) study,¹⁵ which aimed to estimate FA prevalence in these populations and to identify demographic characteristics predictive of FA. To accomplish this, the authors deliberately oversampled 100 Canadian census tracts with a high representation of individuals meeting their definition of vulnerable populations and surveyed them by means of telephone between September 2010 and 2011. Among the 14,113 households that were reached, 1351 households were ineligible to participate because of a language barrier or unavailability of an adult or individual residing in the household. A 45% response rate was observed among the remaining eligible households, resulting in estimates for 15,022 individuals. On the basis of these data, the researchers found that FA was less typically reported among adults (and children) who lived in households with lower educational attainment, and among immigrant populations—who were more likely to be food-allergic the longer they had resided in Canada. The researchers also estimated FA prevalence to be comparable among Canadians of First-Nation identity. As in previous work, the authors relied on FA case definitions on the basis of self-report of a convincing history or self-report of a physician diagnosis.

To improve and update estimates of Canadian population-level adult FA prevalence, the SCAALAR and SPAACE study investigators

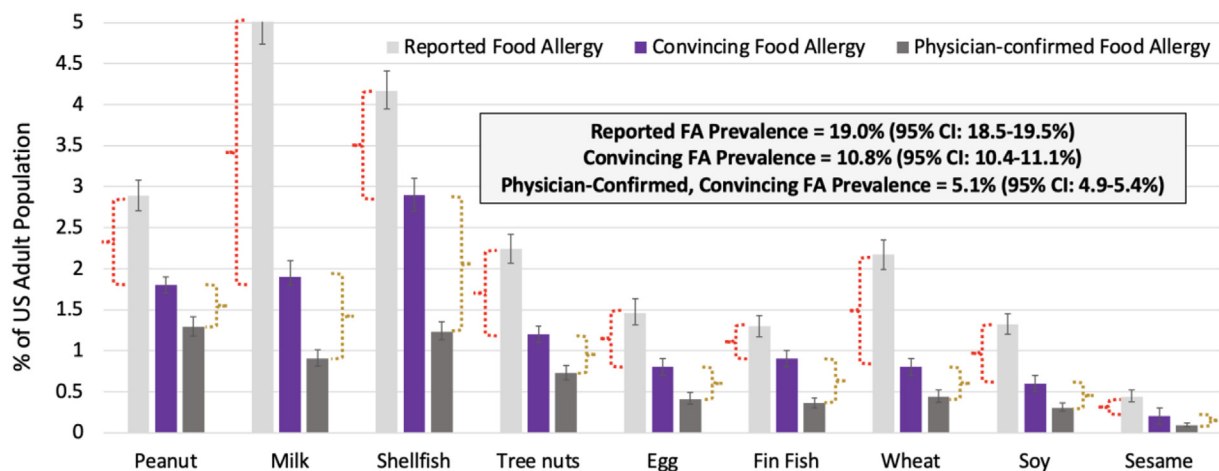


Figure 1. Estimated overreporting and clinical underrepresentation of IgE-mediated food allergy among US adults. CI, confidence interval; FA, food allergy; IgE, immunoglobulin E.

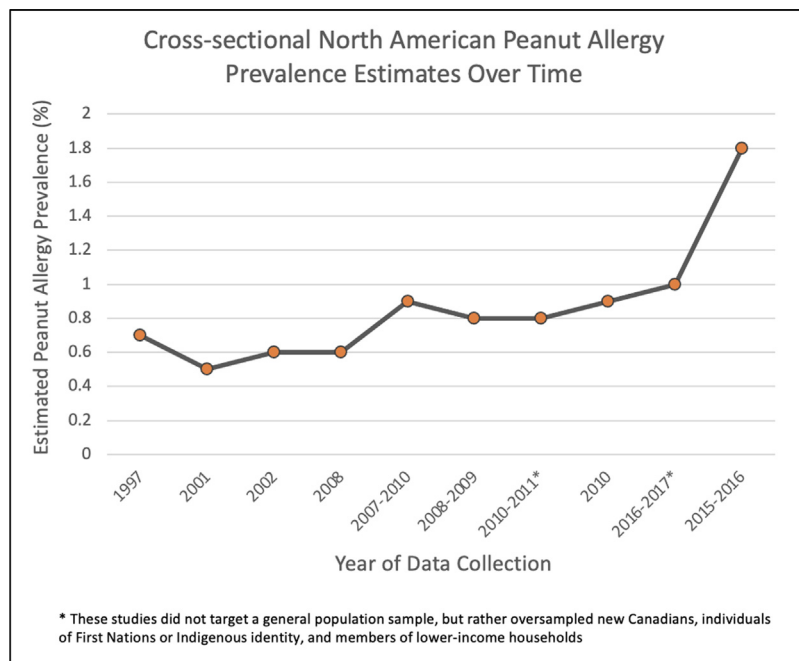


Figure 2. Rising pediatric peanut allergy prevalence estimates from North American population-based studies.

launched a follow-up study to Surveying Prevalence of FA in All Canadian Environments called SPAACE to SPAACE¹⁶ in 2016. This survey was completed by 15,322 individuals. Researchers made special efforts to sample new Canadians (ie, those who immigrated within the past 10 years), individuals of First-Nation identity, and lower-income households. Once again, estimates were derived for reported and convincing IgE-mediated FA, with specific attention paid to peanut, tree nut, shellfish, fish, cow's milk, egg, wheat, sesame, and soy. The SPAACE to SPAACE study estimated that the prevalence of FA stayed stable relative to the SCAALAR data collected 8 years before (with 7.1% and 9.3% of adults reporting at least 1 FA at each wave, which attenuated to 5.9% and 6.1%, respectively after application of more stringent case definitions.) *Figure 2* situates these Canadian prevalence estimates—for peanut allergy in particular—in the context of the aforementioned epidemiologic studies of pediatric food allergy prevalence in the US, indicating a growing burden over recent decades.

Key Questions and Next Steps

When considering the findings from each of these North American FA prevalence surveys together, the reliable discrepancy between “perceived” (ie, self-reported) and “convincing” or “probable” FA as defined by symptom-report and dietary intake highlights important knowledge gaps for future work. It is imperative that we better understand to what extent the observed differences in reported or perceived vs convincing or probable vs physician-confirmed FA cases reflect the clinical underrepresentation of adults living with true IgE-mediated FA. It is also essential that we better understand to what extent these adults with survey-reported FA who meet symptom-based criteria for FA are truly at risk of anaphylaxis or severe outcomes owing to primary sensitization to trigger foods, or whether their reported allergic reaction history is attributable to PFAS or oral allergy syndrome (OAS) or other differential diagnoses. Refining and validating current epidemiologic survey-based FA case definitions to identify true FA cases accurately and reliably is not only vital for improving the quality of epidemiologic prevalence estimates but could also provide a pathway through which adults with self-diagnosed or perceived FA can be responsibly triaged and clinically evaluated.

Pollen-Food Allergy Syndrome and Oral Allergy Syndrome

Pollen-FA syndrome (PFAS), including the mild form of OAS,¹⁷ is another form of IgE-mediated food-induced allergic reactions that impact adult populations. It stands in contrast to “traditional” IgE-mediated immunologic reactions to food proteins insofar as they involve reactions resulting from respiratory allergy to pollens and subsequent cross-binding between pollens and homologous epitopes present in plant-derived food proteins. The symptomatology of PFAS may take various forms ranging in severity, whereas OAS symptoms are restricted to oropharyngeal reactions and allergens and are typically denatured by heat and stomach acids resulting in a lower risk of reactions involving multiple organ systems or resulting in potentially life-threatening anaphylaxis. For these reasons, recommended management of OAS generally does not include the prescription of epinephrine, recommendation of continuous EAI carriage, or associated patient education that are fundamental to patient management of “traditional” FAs. Unfortunately, PFAS epidemiology is limited, and its prevalence and distribution remain unclear, particularly in the general US population, although its prevalence in adults with allergic rhinitis seems to be high. A 2018 national survey¹⁸ of Korean adult patients with allergic rhinitis reported a PFAS prevalence of 43%. Recent data from Turkey,¹⁹ Italy,²⁰ and Croatia²¹ suggest that 20% to 30% of children with allergic rhinitis have PFAS, with higher PFAS rates observed in those children who experienced allergic rhinitis for a longer period. Unfortunately, no corresponding adult data are available. Common PFAS triggers include legumes, seeds, soy, barley, rice, and wheat. Additional work is needed to better characterize the distribution and determinants of PFAS to achieve a more comprehensive understanding of its etiology and public health burden.

Other Select Epidemiologic Data From Around the Globe

Europe

As part of the EuroPrevall (the prevalence, cost and basis of food allergy across Europe) study,^{22,23} screening questionnaires were administered to a random sample of adults in 8 major European metropolitan regions—Athens, Greece; Reykjavik, Iceland; Utrecht, The

Netherlands; Lodz, Poland; Madrid, Spain; and Zurich, Switzerland. Respondents who reported reaction symptoms to 24 “priority” allergens (hen’s egg, cow’s milk, fish, shrimp, peanut, hazelnut, walnut, peach, apple, kiwi, melon, banana, tomato, celery, carrot, corn, lentils, soy, wheat, buckwheat, sesame seed, mustard seed, sunflower seed, and poppy seed) were invited for clinical follow-up, which included sIgE testing, and detailed clinical history. Individuals with a convincing IgE-mediated history and sensitization ($\text{sIgE} \geq 0.35 \text{ kUA/L}$) to either cow’s milk, egg, fish, shrimp, peanut, hazelnut, apple, peach, or celery were invited for double-blind placebo-controlled oral food challenges (DBPCFC). This process allowed the authors to estimate the prevalence of self-reported allergy to any food, self-reported allergy to at least 1 of the 24 priority foods, and probable FA to at least 1 priority food (which required food-specific sensitization). The prevalence of challenge-confirmed allergy could not be reliably estimated owing to a very high rate of refusal to undergo challenge testing. Oral food challenge testing provided evidence of FA in approximately three-quarters of participants with probable FA who underwent DBPCFC.

The authors observed tremendous between-country variability in FA prevalence, with rates of self-reported allergy to any food ranging from 1.7% in Vilnius to 37.3% in Zurich; rates of self-reported allergy to at least 1 priority food ranging from 0.5% in Vilnius to 16.7% in Zurich; and rates of probable allergy to at least 1 priority food ranging from 0.3% in Athens to 5.6% in Zurich.^{22,23} The most common foods causing probable allergy across all 6 urban centers were hazelnut, peach, apple, carrot, walnut, melon, shrimp, sunflower seed, and banana. These data suggest that both FA prevalence and causative foods are remarkably heterogeneous across these European regions and are likely related to pollen exposure, given the predominance of plant-based allergies.

Middle East

Although generally sparse, emerging data from outside Europe and North America also indicate a substantial burden of FA among adult populations. For example, a recent cross-sectional study²⁴ of 5497 Saudi Arabian young adults enrolled at a large national university between 2008 and 2018 estimated the prevalence of clinically-diagnosed FA to be 9.6% with an additional 8.1% reporting a perceived but clinically undiagnosed FA. Of these young adults, approximately 1 in 5 reported an adult-onset FA.

Only a quarter of respondents reported having a prescription for an EAI because of limited domestic availability—highlighting data from earlier studies^{25,26} that found that EAI prescriptions were only available in 26 of 44 World Allergy Organization member countries. Only approximately 5% of all respondents with clinically-diagnosed FA reported always carrying an EAI—a similar rate as previously observed in comparably-aged student populations living in the United States.²⁷

In a 2015 to 2016 survey-based study of Kuwaiti students attending Kuwait University,²⁸ 12% reported perceived FA, with 5.4% meeting the criteria for physician-confirmed FA. This study observed a high (86%) response rate among the 1000 students surveyed. Cow’s milk, egg, peanut, tree nut, and shellfish allergies were the most reported allergies that met study criteria for IgE-mediated allergy (ie, report of physician diagnosis by means of 1 or more confirmatory tests). Half of the participants reported multi-FA and 71% reported a history of food-induced anaphylaxis. Conversely, reported rates of EAI prescription were very low.

Whereas the above studies only engaged college students, another more recent study,²⁹ which surveyed a national sample of 4709 Saudi adults in June 2020, observed a 75% response rate with respondents well-distributed by sex, age, and education level. The study reported that the weighted national prevalence of Saudi adults

reporting at least 1 current FA was 19.7%, with 20% reporting multi-FA. Interestingly, there was no difference in FA prevalence by sex or age although respondents with asthma were at increased risk. Common allergens were peanut (3.0%), shellfish (3.7%), cow’s milk (2.6%), and finned fish (2.5%), whereas tree nuts (1.7%), soy (0.9%), and wheat (0.8%) were the next most common specific allergens, although 8.8% of the sample reported other allergies.

Asia

The EuroPrevall INCO study³⁰ provided the first estimates of food sensitization and probable FA prevalence in a large sample of South Indian adults recruited from the general population of the state of Karnataka. The authors sampled and screened 11,791 adults aged 20 to 54 years, resulting in 588 participants in a case-control study (236 cases and 352 controls). These individuals completed a detailed questionnaire and provided samples for sIgE estimation to 24 common foods. More than 1 in 4 respondents were sensitized at greater than 0.35 kU/L to at least 1 of the 24 foods. In contrast, the rates of probable FA to any of these foods were very low, with only 1.2% meeting the criteria—mostly to cow’s milk (0.5%) and apple (0.5%), with cases of probable egg (0.05%), banana (0.05%), sesame (0.02%), wheat (0.02%), and tomato (0.02%) allergy also identified. The highest levels of sensitization were observed for shrimp (15.5%), sesame (14.0%), buckwheat (12.4%), wheat (11.9%), corn (10.8%), tomato (9.8%), banana (9.3%), and soy (9.2%). The levels of food-allergic sensitization observed in this Indian sample are higher than those observed in the large multisite European cohort study (EuroPrevall),²² despite extremely low rates of probable FA. It is notable that, relative to European, and US samples, these Indian study participants had elevated total IgE with nearly half exceeding 300 IU/mL.

Africa

Unfortunately, few epidemiologic studies of FA have been conducted in Africa,³¹ and most used allergic sensitization as a surrogate marker for allergy or were conducted in high-risk pediatric populations. A single South African study,³² which used oral food challenge—proven FA as an outcome in an unselected population, found marked urban-rural differences³³ with the prevalence of FA 2.5% in children aged 1 to 3 years in Cape Town, but only 0.5% in the rural Eastern Cape. No comparable work has sampled African adults, although such studies would provide a valuable contribution to the epidemiologic literature. Among African studies to characterize FA among adults, 1 study³⁴ used DBPCFC to confirm reported cases of seafood allergy among adults living in the Western Cape. This study of 105 participants with suspected fish allergy recruited by means of local press identified prawns, crayfish, abalone, and black mussels to be the most common clinically confirmed seafood allergens, whereas hake, yellowtail, salmon, and mackerel were the most common triggers of allergy to bony fish in this cohort.

A 2004 cross-sectional survey³⁵ of 509 adult volunteers (age range 18–60 years) from a university in Mozambique estimated the lifetime prevalence of self-reported FA at 19%, with the most common allergen-eliciting foods as seafood (55%), meat (13%), and fruit and vegetables (13%). Another cross-sectional survey³⁶ of randomly selected households in the Dar es Salaam region of Tanzania, conducted in 2008, estimated that 17% of adult respondents reported at least 1 self-perceived FA. However, no further information was provided regarding the specific eliciting allergens or allergic symptomatology.

A 2009 cross-sectional study³⁷ in Kinshasa in the Democratic Republic of Congo tested patients with allergic rhinitis in an outpatient ear-nose-throat clinic with skin prick testing to aeroallergens and foods (crab, soybean, and wheat flour). Of these individuals

(among whom 87% were adults), 5% were sensitized to 1 of the 3 foods, with 3% sensitized to crab.

Higher rates of seafood sensitization were observed in a Zimbabwean study³⁸ of 50 urban-dwelling patients with allergy who were randomly selected from a larger cohort (N = 650) and tested for sensitization to 20 foods. Of these foods, sensitization to apple (24 %), tomato (24 %), crab (22 %), soy (22 %), and peanut (20 %) were the most common. Notably, 60% of individuals were sensitized to dust mites, which was identified as a possible mechanism through which sensitization to crab may have occurred by means of cross-binding with tropomyosin.

On the northern side of the African continent, a 2009 Moroccan study³⁹ of 180 adults and 20 children screened by means of sIgE to food and aeroallergens identified no cases of sensitization (and, therefore, allergy) to cow's milk, egg, soy, wheat, peanut, or fish among the adult participants, despite the fact that half of the adult participants were sensitized to at least 1 aeroallergen.

Better Understanding the Natural History of Food Allergy in Adults

Recent data⁴⁰ suggest that allergies that develop during childhood may be more likely to persist into adulthood than was previously assumed—leading to a greater burden of adult FA. At the same time, adult-onset allergies, especially to shellfish, seem increasingly common. In a chart review of Chicago-area patients with clinically confirmed FAs, 15% were adult-onset. In a subsequent national, US population-based cross-sectional survey³ of 40,443 adults, 21% of adults with FA developed all their current FAs during adulthood. However, a remarkable 48% of adults with FA reported at least 1 adult-onset FA. The specific FA with the highest rates of adult-onset both in terms of the absolute number of cases and proportion of cases that are adult- vs childhood-onset is shellfish.

Survey data suggest that the estimated 14 million US adults with solely childhood-onset FA are more likely to report a severe reaction history and greater psychosocial impact from the FA compared with the approximately 6 million adults with only adult-onset FA. In addition, adults with childhood-onset FA reported higher rates of health care utilization, with more than half having a physician-confirmed FA diagnosis, compared with only approximately 30% of adults with adult-onset FA.³

Whereas extant epidemiologic data remain of limited use in helping us understand how and why some adults develop allergies to previously tolerated foods, a recent case series⁴¹ of 22 Israeli patients presenting with FA to previously tolerated foods does permit some insights. First, FAs to previously tolerated foods primarily appear after an elimination diet in atopic patients. Specifically, in this case series, patients avoided the trigger food for a median of 45 weeks, and in 70% of patients, the avoidance period was greater than 4 weeks. In 72% of patients, the avoidance was deliberate, and among these patients, most avoidance was initiated because of physician recommendation. It was also notable that anaphylactic reactions were common in this group of patients, with more than half experiencing at least 1 anaphylactic episode and 1 in 3 experiencing multiple such episodes.

Sex Differences

Numerous studies and systematic reviews^{42,43} have identified sex differences in the prevalence of IgE-FA, which mirror those observed for other atopic conditions (eg, allergic rhinitis, asthma, and atopic dermatitis).⁴⁴ For example, the Mirabel cohort study⁴⁵ observed a male-female sex ratio of 1.50 in children with FA, which flipped to 0.67 among young adults. More recent data from a large electronic health records allergy module⁴⁶ found a comparable sex ratio of 0.69 for adverse food reactions among a mostly adult population.

Age Differences

Whereas longitudinal data⁴⁷ are sparse among older adults, findings from cross-sectional surveys^{13,47} suggest that FA prevalence and indicators of FA-related health care utilization (eg, emergency department visits)¹³ are lowest among the older adult populations. This is consistent with a cohort effect whereby changes in environmental exposures that have occurred gradually across recent decades have increased FA risk at the population level. Consistent with this theory, findings from the Isle of Wight birth cohort⁴⁰ that began in 1989, which followed approximately 1500 live births through age 18 years, estimated that the reported prevalence of FA did not differ substantially across assessments made at age 1, 2, 4, 10, and 18 years (ranging between 8.0% and 9.1%). Although these estimates were attenuated when restricting FA cases to those that were clinically confirmed, particularly at the 10-year assessment, rates of FA were only slightly more prevalent at age 1 (5.3%) and 2 (4.4%) years than at the 18-year (4.1%) follow-up. This suggests that FA is not only a major concern during infancy, as currently understood,⁴⁸ but that many children develop new-onset FAs later in childhood and retain FAs from infancy into adolescence and beyond.

Non-Immunoglobulin E-mediated food allergies

Emerging data also suggest that the burden of non-IgE-mediated FAs is increasing among adult populations.^{49–53} For example, food protein-induced enterocolitis syndrome (FPIES)^{54,55} is a non-IgE-mediated FA (non-IgE FA)^{56,57} with onset during early infancy that is typically triggered by cow's milk or soy formula in late infancy during the introduction of oats and rice and other foods. Whereas it is often outgrown in the first 3 to 5 years of life, infantile FPIES⁵⁸ can persist into older childhood and adulthood. In contrast, the adult-onset phenotype of FPIES is typically triggered by seafood.^{50,51,59} Whereas the natural history of adult-onset FPIES remains poorly understood, data indicate that it is persistent though no clear prognostic factors have been able to determine if or when clinical reactivity will resolve.

In a recent case series of 42 patients with adult-onset FPIES,⁶⁰ the mean age of onset was 40 years, with a mean time from ingestion to symptom onset of 2.8 hours (SD = 1.7 hours). Most reactions were characterized by diarrhea (93%) and abdominal cramps (71%), with nausea (69%) and repetitive vomiting (59%) also common. Most cases were treated with intravenous fluids, antiemetics, and analgesics. As in IgE-mediated FA, women were overrepresented relative to men (83% vs 17%), despite a slight male predominance in pediatric cases. High rates of comorbid IgE-mediated disease were estimated in this cohort, which is consistent with 2 Spanish^{51,60} (72% and 48% of adult FPIES cases, respectively) and 1 Australian⁶¹ (52% of adult FPIES cases) case series, and a large US population-based survey⁶² in which 43% had comorbid IgE-mediated FA. However, this may not be universal, as a recent small Canadian case series⁶³ documented comorbid atopy in only 16% of adult patients with suspected FPIES.

Other emerging data from a Northeastern US academic medical center suggest that the most common triggers of acute FPIES among adult patients are cow's milk, shellfish, wheat, hen's egg, and soy. In contrast, the most common triggers of chronic FPIES among adult patients are wheat, cow's milk, hen's egg, soy, and oat.⁶⁴ A US population-based survey conducted from 2015 to 2016⁶² estimated the lifetime FPIES prevalence in US adults at 0.21% of the general population.

To date, no published studies have evaluated FPIES-related health care utilization and economic impact. However, it is well documented^{65–67} that among adult patients with FPIES, diagnosis is often delayed, after multiple office and emergency department visits and extensive diagnostic testing, including sepsis work up, abdominal ultrasound, radiographic studies, electrocardiograms, electroencephalograms, metabolic studies, and genetic testing. Severe, acute,

and chronic FPIES may require intravenous rehydration and, in extreme cases, life support. The delayed and missed diagnosis of FPIES can be attributed to a delayed onset after food ingestion, lack of typical IgE-mediated allergic symptoms, and lack of accurate laboratory diagnostic tests. As such, improved awareness of FPIES among clinicians treating adults with suspected FA is critical. The advancement of clinical FPIES diagnostics and more widespread utilization of oral food challenges for disease confirmation would be helpful in improving epidemiologic surveillance of this emerging FA.⁵⁶

Eosinophilic Esophagitis

Eosinophilic esophagitis (EoE) is characterized by eosinophilic inflammation in the esophagus. In adults, it typically presents with food impaction or dysphagia and can cause esophageal remodeling and stricture formation.⁶⁸ The highest disease burden is in Western industrialized countries, with recent survey data⁶⁹ indicating that 0.18% of US adults have been diagnosed with EoE at some point in their lifetime. Whereas evidence suggests that EoE can be induced by oral immunotherapy (OIT), affecting an estimated 3% of treated patients, most patients with EoE have not undergone OIT.

Alpha-Gal

Alpha-gal syndrome is a unique clinical entity in many ways.⁷⁰ The origin of sensitization is being bitten by hard-bodied tick species resulting in the localized geographic distribution of the allergy. The food allergen is a glycoprotein found in red meat. The food-related reactions are typically IgE-mediated in their manifestations but occur after a substantial delay. There is considerable intraindividual variation in the dose of food that may cause the reaction with reactions occurring with large amounts on some occasions and small amounts on others. Alpha-gal allergy occurs predominantly in adults rather than children. In addition to reactions on ingestion of mammalian meats, meat products, and medications with mammalian meat constituents, alpha-gal sensitization also results in xenotransplantation reactions (organ rejection) and immediate-type allergy to parenterally administered medications containing alpha-gal epitopes such as cetuximab⁷¹ and gelatin.⁷²

In North America, the major culprit tick species is *Amblyomma americanum*,⁷³ which is predominantly geographically localized to the East Coast and Midwest, particularly North Carolina, Virginia, Tennessee, Arkansas, and Missouri. The lone star tick, however, is expanding its habitat northwards and westwards partially in response to climate change,⁷⁴ and cases now occur outside of the East Coast and Midwest, possibly because of a broader distribution of the tick in North America than previously understood rather than predominantly through patient travel to affected areas.

Outside of North America, major focused areas of high prevalence include Australia, Central Europe, Japan, and South Africa. The culprit tick species in these locations are *Ixodes holocyclus* (Australia),⁷⁵ *Ixodes ricinus* (Europe),⁷⁶ *Haemaphysalis longicornis* and *Amblyomma testudinarium* (Japan),^{77,78} *Ixodes cajennense* (Central America)⁷⁹ and possibly *Amblyomma sculptum* (Brazil),⁸⁰ *Amblyomma variegatum* (Ivory Coast)⁸⁰ and *Amblyomma hebraeum* (South Africa).⁸¹ Other ticks might also be vectors and it is possible that other organisms may cause sensitization to alpha-gal⁸² and elicit alpha-gal syndrome.⁸³

Alpha-gal syndrome is an acquired allergy with onset generally occurring after infancy. Affected individuals are not affected by atopy any more than the general population.⁸⁴ Because of the insect vector, people who spend more time outdoors are more affected. This results in a higher prevalence in adults such as forest workers,^{79,85,86} hunters,⁷³ and recreational hikers⁸⁷ in North America and Europe, in which the animal vectors for the tick are usually wild animals such as deer. In the African cohorts, however, very close everyday contact

between tick-infested domesticated animal livestock results in a high proportion of affected individuals being children.⁸¹ In both groups, there may be a history of the tick bite with the syndrome occurring shortly thereafter. However, even when the eliciting trigger is not identified, it is typical for patients to have a history of tolerating mammalian meat for many years before the onset of the syndrome.

The clinical manifestations of alpha-gal syndrome are noteworthy. In stark contrast to other IgE-mediated FA, the reaction to alpha-gal—containing foods and medications occurs after a delay, likely because of a delay in absorption of the antigen.⁸⁸ Few studies have performed oral food challenges thus affording an accurate measure of the time between exposure and onset of symptoms. In North America, a delay of 3 to 6 hours after ingestion of mammalian meat was initially reported,^{89,90} whereas in South Africa a more rapid onset of symptoms (median: 100 minutes) was described.⁹¹

Symptoms include typical IgE-mediated reactions such as urticaria, angioedema, and anaphylaxis^{84,92}; however, reactions may also manifest with abdominal pain in addition to skin reactions, and, in some cohorts, as isolated abdominal pain without any other manifestations.⁹¹ The onset of symptoms does not seem to vary between participants with isolated abdominal symptoms and those with skin symptoms, and there are no clear differences in clinical or laboratory parameters between the 2 groups.⁹¹

However, there is a large interindividual variation in the dose required to cause an alpha-gal reaction.⁷⁰ Although most patients react only to ingestion of meat, particularly alpha-gal rich “organ meats” or offal,⁹³ some react to very low dose exposures and even to medications and sweets containing small amounts of gelatin.⁷² In addition, there is large intraindividual variation in the dose required for a reaction and the severity of a resultant reaction, which may be because of the large role that cofactors play⁹⁴ in absorption and reaction to the antigen.⁹⁵

Patients with alpha-gal sensitization are also at risk of nonfood reactions, including immediate-type reactions to parenterally administered medications. Most notably, the original description of alpha-gal reactions identified the concomitant syndrome of anaphylaxis to cetuximab, a chimeric antibody to the epidermal growth factor receptor containing the alpha-gal antigen⁷¹ on the mouse-derived antigen-binding portion of the antibody. Reactions to cetuximab (and gelatin and other alpha-gal-containing parenteral medications) are, thus, also highly localized to the geographic areas in which alpha-gal syndrome typically occurs.^{96,97}

Food-Dependent Exercise-Induced Anaphylaxis

Food-dependent exercise-induced anaphylaxis (FDEIA) is a rare condition with a reported prevalence of 0.048%.⁹⁸ It is the best-studied model of cofactor anaphylaxis in adults.⁹⁹ Ingesting the causative allergen without exertion or exertion in the absence of the causative allergen does not lead to clinical symptoms. Anaphylaxis occurs when exercise occurs within 4 to 6 hours after ingestion of the causative food. Anaphylaxis typically occurs within 30 to 60 minutes after starting moderate-intensity exercise, although episodes can vary, and do not always have the same intensity.¹⁰⁰ The most common triggers are wheat with components of omega-5 gliadin, cereals, apples, cow's milk, tree nuts, beef, pork, peanuts, egg, chickpea, and chicken. The proposed pathogenesis of FDEIA include increased gastric permeability, increased activity of tissue transglutaminase in the gut mucosa, redistribution of blood flow and mast cell heterogeneity, increase in plasma osmolality inducing basophil histamine release, exercise-induced acidosis, and mast cell degranulation.¹⁰¹ A food exercise challenge is essential in the diagnosis if the allergenic trigger is uncertain. The variability of the testing makes it difficult to accurately assess a positive challenge. False-negative challenges can occur in 30% of cases because of difficulty reproducing the environmental

factors triggering the episodes.¹⁰² There are no standard treatment protocols for FDEIA, but challenges should include a negative exercise challenge and a negative challenge to the food in the absence of exercise. All FDEIA challenges should be done by experienced staff in an experienced center with available resuscitation equipment and epinephrine available. Patient education includes recognition of early symptoms and administration of epinephrine if symptoms progress to anaphylaxis. Preventive management includes avoidance of the allergen and other cofactors 4 to 6 hours before exercise.^{100,102}

Other Allergies to “Adult” Substances

Cannabis

As both recreational and medicinal cannabis become increasingly accessible to adults in edible formats,¹⁰³ allergies to these compounds may become an increasingly relevant public health concern especially given the known allergenicity of inhaled and topical forms of cannabis.¹⁰⁴ Cannabis allergens include profilin (Can s 2), nonspecific lipid transfer protein (Can s 3), oxygen-evolving enhancer protein 2 (Can s 4), and pathogenesis-related protein 10 homolog (Can s 5). There are no population-based epidemiologic studies of the prevalence of allergy to orally-consumed forms of cannabis—which include tinctures, beverages, and a wide variety of prepared foods—and therefore, the extent to which it is a true FA remains unknown. However, it has been suggested that cannabis sativa acts as a primary sensitizing allergen,¹⁰⁵ given that many patients with cannabis allergy are sensitized to Can s 3¹⁰⁶—a nonspecific lipid transfer protein found in cannabis—and have severe allergies to plant foods.^{107–109} Data also indicate that cross-binding between nonspecific lipid transfer proteins in patients sensitized to Can s 3 may result in clinical allergy symptoms to an array of fruits, vegetables, cereals, wine, beer, Hevea latex, and tobacco.^{108,110–112}

Alcoholic Beverages

A rare allergy among adults is to alcoholic beverages. Case studies¹¹³ implicate sensitization to nonspecific lipid transfer proteins from cereals in causing reactions to beer but not to other alcoholic beverages. In the United States, the Food Allergen Label and Protection Act does not apply to alcoholic products and, therefore, unlabeled allergens may be present (eg, nuts like almonds, fruits, seeds, spices such as coriander; wheat, and other grains) albeit likely in denatured, less-allergenic forms particularly if added before distillation.¹¹⁴ Allergic reactions to alcohol itself have also been reported,¹¹⁵ but the prevalence of alcohol allergy is unknown. However, alcohol is a well-known allergic cofactor that reportedly is implicated in an estimated 1.5% to 2% of anaphylaxis cases.⁹⁹ Whereas its mechanism of action in this context is not completely understood, it is believed that alcohol increases intestinal permeability and thereby can lead to increased antigen uptake, and therefore, allergic symptomatology.¹¹⁶

Advancing Adult Food Allergy Epidemiology

Improving Access to Quality Allergy Care

As infants and children with FA age into adulthood and adults develop new-onset FAs, it is clear that the burden of FA among the adult population is growing. This is happening, as noted throughout this review, in concert with an increasing prevalence of other allergic conditions, including allergic asthma, PFAS, and other environmental allergies, wherein cross-reactivity with foods is implicated and requires careful clinical evaluation. Despite the increased number of individuals who require allergy evaluation, the number of board-certified allergists in the United States has not grown commensurately.^{117,118} The relative dearth of allergists is one of the

numerous factors that has contributed to the large, estimated proportion of US adults who are currently living with undiagnosed FA, which in turn is neither clinically documented nor available for secondary analysis by researchers aiming to characterize the burden and natural history of FA in adults.

Establishing Standardized Survey-based Food Allergy Surveillance Systems to Estimate Burden of Disease

Rigorous estimation of FA prevalence is not incorporated into key North American population-based health surveys (eg, NHANES, National Health Interview Survey [NHIS]), and its execution currently relies on inconsistently funded efforts like those reported above. This is a major barrier to understanding the current and future burden of both IgE and non-IgE-mediated FAs. The growing need for a more systematic assessment of FA prevalence was recently codified into law when the US federal government passed the Food Allergy Safety, Treatment, Education and Research Act of 2021, the first section (317U) of which directs the Centers for Disease Control and Prevention to “expand and intensify the collection of information on the prevalence of food allergies for specific allergens in the US, such as through the NHANES.”¹¹⁹

Until 2019, the CDC’s NHIS¹²⁰ only asked questions regarding FA status among children in the sampled households. The survey was subsequently redesigned in 2019 to incorporate a limited assessment of adult FA status on a triennial basis beginning in 2021. Specifically, all sampled adults are now asked the following “rotating core” questions (exact text from the NHIS survey follows):

“The next question is about food allergies. People with food allergies have reactions such as hives, vomiting, trouble breathing, or throat tightening that occur within 2 hours of eating a specific food.”

“Do you have an allergy to one or more foods? (Read if necessary: Food allergies are different from food intolerances, such as lactose and gluten intolerance, and other digestive disorders, including irritable bowel syndrome.)”

“Have you ever been told by a doctor or other health professional that you had an allergy to one or more foods? Food allergies are different from food intolerances, such as lactose and gluten intolerance, and other digestive disorders, including irritable bowel syndrome.”

Beginning in 2019, the NHIS sample is expected to yield completed interviews from 30,000 adults and 9000 children. Although limited, these standardized, repeated assessments will be of some public health use moving forward. As feasible, we recommend that other state and federal disease surveillance surveys consider incorporating similar assessments of perceived and physician-diagnosed FA (preferably incorporating a more detailed assessment of triggers, symptomatology, and onset-timing, leading to a fuller understanding of the population-level burden of FA). Ideally, such work will augment population-based sIgE seroprevalence data, such as that incorporated into the 2005 to 2006 NHANES allergy component.¹²¹

Expansion and Harmonization of Clinical Food-Induced Anaphylaxis Registries

In 2018, the Australian State of Victoria established the first standardized governmental anaphylaxis registry,¹²² which includes both pediatric and adult patients. By mandating reporting of all anaphylaxis cases identified by the public and private emergency departments using a structured case report form, these data can provide

valuable insights into current trends of food-induced anaphylaxis. The requirement to report all cases of food-induced anaphylaxis caused by exposure to packaged foods within 24 hours also provides an opportunity to promptly address labeling errors and prevent accidental allergen exposures. Evaluations of the effectiveness of this new mandate are ongoing and—if effective—may provide a template that can be broadly adopted.

Furthermore, the expansion of ongoing national and international collaborative efforts holds promise for building the necessary infrastructure to collect standardized epidemiologic data on adult FA. These efforts include the US-based Food Allergy Research and Education (FARE) Clinical Network of Centers of Distinction,¹²³ and the Anaphylaxis Centers of Reference and Excellence organized by The Global Allergy and Asthma European Network (ie, GA²LEN ANACARE).¹²⁴

Conclusion

Whereas most US and international epidemiologic studies of FA have focused on pediatric populations, it is increasingly clear that FA affects large numbers of adults around the world. Not only does FA persist into adulthood among patients diagnosed during childhood, but an increasing number of adults are developing new-onset allergies later in life.

More systematic regional, national, and international FA surveillance efforts are warranted to better understand and ameliorate the growing burden of allergic disease. At the same time, therapeutic advances in the treatment of FA, which recently led to the first FDA-approved peanut allergen OIT for children aged 4 to 17 years,¹²⁵ have generally not been as effective in treating older patients compared with young children. Therefore, there remains a substantial need for safe, effective, accessible, FDA-approved food allergen immunotherapies that can reduce the burden of FA among affected adults, including those living with multiple food allergies. Because disease management also seems suboptimal among adults with FA, further efforts are needed to facilitate prompt, accurate diagnosis of suspected adult FA cases and support individuals in the day-to-day management of their allergic disease. In so doing, these efforts are not only likely to improve FA outcomes and reduce the psychosocial burden of disease,¹²⁶ but by reducing the number of adults with suspected yet clinically unconfirmed allergies these efforts will also facilitate efforts to advance the epidemiology of adult FA.

References

- Warren CM, Jiang J, Gupta RS. Epidemiology and burden of food allergy. *Curr Allergy Asthma Rep*. 2020;20(2):6.
- Sampath V, Abrams EM, Adlou B, Akdis C, Brough HA, Chan S, et al. Food allergy across the globe. *J Allergy Clin Immunol*. 2021;148(6):1347–1364.
- Hultquist H, Dyer A, Jiang J, Gupta R, Warren C. Phenotypic characterization of childhood- and adult-onset food allergy among adults in the United States. *J Allergy Clin Immunol*. 2022;149(2):AB227.
- Anvari S, Miller J, Yeh CY, Davis CM. IgE-mediated food allergy. *Clin Rev Allergy Immunol*. 2019;57(2):244–260.
- Sicherer SH, Munoz-Furlong A, Burks AW, Sampson HA. Prevalence of peanut and tree nut allergy in the US determined by a random digit dial telephone survey. *J Allergy Clin Immunol*. 1999;103(4):559–562.
- Sicherer SH, Munoz-Furlong A, Sampson HA. Prevalence of peanut and tree nut allergy in the United States determined by means of a random digit dial telephone survey: a 5-year follow-up study. *J Allergy Clin Immunol*. 2003;112(6):1203–1207.
- Sicherer SH, Munoz-Furlong A, Sampson HA. Prevalence of seafood allergy in the United States determined by a random telephone survey. *J Allergy Clin Immunol*. 2004;114(1):159–165.
- Sicherer SH, Munoz-Furlong A, Godbold JH, Sampson HA. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. *J Allergy Clin Immunol*. 2010;125(6):1322–1326.
- Verrill L, Bruns R, Luccioli S. Prevalence of self reported food allergy in US adults: 2001, 2006, and 2010 [e-pub ahead of print]. *Allergy Asthma Proc*. doi:10.2500/aap.2013.36.3895, accessed June 23, 2022.
- Public Law. Title II—Food allergen labeling and consumer protection Act. 2004. Available at: <https://www.fda.gov/media/77570/download>. Accessed March 23, 2022.
- Salo PM, Arbes Jr SJ, Jaramillo R, Calatroni A, Weir CH, Sever ML, et al. Prevalence of allergic sensitization in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2005–2006. *J Allergy Clin Immunol*. 2014;134(2):350–359.
- McGowan EC, Keet CA. Prevalence of self-reported food allergy in the National Health and Nutrition Examination Survey (NHANES) 2007–2010. *J Allergy Clin Immunol*. 2013;132(5):1216–1219.e5.
- Gupta RS, Warren CM, Smith BM, Jiang J, Blumenstock JA, Davis MM, et al. Prevalence and severity of food allergies among US adults. *JAMA Netw Open*. 2019;2(1):e185630.
- Soller L, Ben-Shoshan M, Harrington DW, Fragapane J, Joseph L, Pierre YS, et al. Overall prevalence of self-reported food allergy in Canada. *J Allergy Clin Immunol*. 2012;130(4):986–988.
- Soller L, Ben-Shoshan M, Harrington DW, Knoll M, Fragapane J, Joseph L, et al. Prevalence and predictors of food allergy in Canada: a focus on vulnerable populations. *J Allergy Clin Immunol Pract*. 2015;3(1):42–49.
- Clarke AE, Elliott SJ, St Pierre Y, Soller L, La Vieille S, Ben-Shoshan M. Temporal trends in prevalence of food allergy in Canada. *J Allergy Clin Immunol Pract*. 2020;8(4):1428–1430.e5.
- Werfel T, Asero R, Ballmer-Weber BK, Beyer K, Enrique E, Knulst AC, et al. Position paper of the EAACI: food allergy due to immunological cross-reactions with common inhalant allergens. *Allergy*. 2015;70(9):1079–1090.
- Kim MA, Kim DK, Yang HJ, Yoo Y, Ahn Y, Park HS, et al. Pollen-food allergy syndrome in Korean pollinosis patients: a nationwide survey. *Allergy Asthma Immunol Res*. 2018;10(6):648–661.
- Ozdemir SK, Ozguvarsigmalu S. Pollen food allergy syndrome in Turkey: clinical characteristics and evaluation of its association with skin test reactivity to pollens. *Asian Pac J Allergy Immunol*. 2018;36(2):77–81.
- Dondi A, Tripodi S, Panetta V, Asero R, Businco AD, Bianchi A, et al. Pollen-induced allergic rhinitis in 1360 Italian children: comorbidities and determinants of severity. *Pediatr Allergy Immunol*. 2013;24(8):742–751.
- Ivkovic-Jurekovic I. Oral allergy syndrome in children. *Int Dent J*. 2015;65(3):164–168.
- Lyons SA, Burney PGJ, Ballmer-Weber BK, Fernandez-Rivas M, Barreales L, Clausen M, et al. Food allergy in adults: substantial variation in prevalence and causative foods across Europe. *J Allergy Clin Immunol Pract*. 2019;7(6):1920–1928.e11.
- Burney PG, Potts J, Kummeling I, Mills EN, Clausen M, Dubakiene R, et al. The prevalence and distribution of food sensitization in European adults. *Allergy*. 2014;69(3):365–371.
- Hassan A, Alsaifati A, Al Shammari M, Alaitan H, Al-Johani W, AlShamlan N, et al. Food allergy among university students: uncharted territory. *Allergy Asthma Clin Immunol*. 2020;16(1):1–6.
- Simons FE. Lack of worldwide availability of epinephrine autoinjectors for outpatients at risk of anaphylaxis. *Ann Allergy Asthma Immunol*. 2005;94(5):534–538.
- Simons FE, World Allergy Organization. Epinephrine auto-injectors: first-aid treatment still out of reach for many at risk of anaphylaxis in the community. *Ann Allergy Asthma Immunol*. 2009;102(5):403–409.
- Greenhawt MJ, Singer AM, Baptist AP. Food allergy and food allergy attitudes among college students. *J Allergy Clin Immunol*. 2009;124(2):323–327.
- Ali F. A survey of self-reported food allergy and food-related anaphylaxis among young adult students at Kuwait University, Kuwait. *Med Princ Pract*. 2017;26(3):229–234.
- Althumiri NA, Basyouni MH, AlMousa N, AlJuwaysim MF, BinDhim NF, Alqahtani SA. Prevalence of self-reported food allergies and their association with other health conditions among adults in Saudi Arabia. *Int J Environ Res Public Health*. 2021;18(1):347.
- Mahesh PA, Wong GW, Ogorodova L, Potts J, Leung TF, Fedorova O, et al. Prevalence of food sensitization and probable food allergy among adults in India: the EuroPrevall INCO study. *Allergy*. 2016;71(7):1010–1019.
- Hossny E, Ebisawa M, El-Gamal Y, Arasi S, Dahdah L, El-Owaidy R, et al. Challenges of managing food allergy in the developing world. *World Allergy Organ J*. 2019;12(11):100089.
- Basera W, Botha M, Gray CL, Lunjani N, Watkins AS, Venter C, et al. The South African Food Sensitisation and Food Allergy population-based study of IgE-mediated food allergy: validity, safety, and acceptability. *Ann Allergy Asthma Immunol*. 2015;115(2):113–119.
- Botha M, Basera W, Facey-Thomas HE, Gaunt B, Gray CL, Ramjith J, et al. Rural and urban food allergy prevalence from the South African Food Allergy (SAFFA) study. *J Allergy Clin Immunol*. 2019;143(2):662–668.e2.
- Zinn C, Lopata A, Visser M, Potter PC. The spectrum of allergy to South African bony fish (Teleostei). Evaluation by double-blind, placebo-controlled challenge. *S Afr Med J*. 1997;87(2):146–152.
- Lunet N, Falcao H, Sousa M, Bay N, Barros H. Self-reported food and drug allergy in Maputo, Mozambique. *Public Health*. 2005;119(7):587–589.
- Justin-Temu M, Risha P, Aba O, Massawe A. Incidence, knowledge and health seeking behaviour for perceived allergies at household level: a case study in Ilala district Dar es Salaam Tanzania. *East Afr J Public Health*. 2008;5(2):90–93.
- Nyembue TD, Ntumba W, Omadajala LA, Muyunga C, Hellings PW, Jorissen M. Sensitization rate and clinical profile of Congolese patients with rhinitis. *Allergy Rhinol (Providence)*. 2012;3(1):e16–e24.
- Westritschnig K, Sibanda E, Thomas W, Auer H, Aspöck H, Pittner G, et al. Analysis of the sensitization profile towards allergens in central Africa. *Clin Exp Allergy*. 2003;33(1):22–27.

39. Bouhsain S, Kamouni Y, Dami A, Zrara A, Mechtani S, Ouziff Z, et al. Biological profile of type I allergies at Mohamed V Hospital (Rabat- Morocco). *Ann Biol Clin (Paris)*. 2008;66(6):643–646.
40. Venkataraman D, Erlewyn-Lajeunesse M, Kurukulaatchy RJ, et al. Prevalence and longitudinal trends of food allergy during childhood and adolescence: results of the Isle of Wight Birth Cohort study. *Clin Exp Allergy*. 2018;48(4):394–402.
41. Nachshon L, Goldberg MR, Elizur A, Appel MY, Levy MB, Katz Y. Food allergy to previously tolerated foods: course and patient characteristics. *Ann Allergy Asthma Immunol*. 2018;121(1). 77–81.e1.
42. Pali-Scholl I, Jensen-Jarolim E. Gender aspects in food allergy. *Curr Opin Allergy Clin Immunol*. 2019;19(3):249–255.
43. Kelly C, Gangur V. Sex disparity in food allergy: evidence from the PubMed database. *J Allergy (Cairo)*. 2009;2009: 159845.
44. Ridolo E, Incorvaia C, Martignago I, Caminati M, Canonica GW, Senna G. Sex in respiratory and skin allergies. *Clin Rev Allergy Immunol*. 2019;56(3):322–332.
45. De Martinis M, Sirufo MM, Suppa M, Di Silvestre D, Ginaldi L. Sex and gender aspects for patient stratification in allergy prevention and treatment. *Int J Mol Sci*. 2020;21(4):1535.
46. Acker WW, Plasek JM, Blumenthal KG, Lai KH, Topaz M, Seger DL, et al. Prevalence of food allergies and intolerances documented in electronic health records. *J Allergy Clin Immunol*. 2017;140(6). 1587–1591.e1.
47. Sicherer SH, Warren CM, Dant C, Gupta RS, Nadeau KC. Food allergy from infancy through adulthood. *J Allergy Clin Immunol Pract*. 2020;8(6):1854–1864.
48. Sampson HA. Food allergy. *JAMA*. 1997;278(22):1888–1894.
49. Du YJ, Nowak-Węgrzyn A, Vadas P. PFIES in adults. *Ann Allergy Asthma Immunol*. 2018;121(6):736–738.
50. Tan JA, Smith WB. Non-IgE-mediated gastrointestinal food hypersensitivity syndrome in adults. *J Allergy Clin Immunol Pract*. 2014;2(3). 355–357.e1.
51. Gonzalez-Delgado P, Caparros E, Moreno MV, Cueva B, Fernandez J. Food protein-induced enterocolitis-like syndrome in a population of adolescents and adults caused by seafood. *J Allergy Clin Immunol Pract*. 2019;7(2):670–672.
52. Zubrinich C, Hew M, O'Hehir R. Egg provoked food protein-induced enterocolitis-like syndrome in an adult. *Clin Case Rep*. 2016;4(9):899–901.
53. Gonzalez-Delgado P, Ruano-Zaragoza M, Gutierrez A, Lopez F, Fernandez J. Chronic adult food protein-induced enterocolitis syndrome. *Ann Allergy Asthma Immunol*. 2020;125(6):716–717.
54. Gonzalez-Delgado P, Muriel J, Jimenez T, Cameo JI, Palazon-Bru A, Fernandez J. Food protein-induced enterocolitis syndrome in adulthood: clinical characteristics, prognosis, and risk factors. *J Allergy Clin Immunol Pract*. 2022;10(9):2397–2403.
55. Anvari S, Ruffner MA. Adult food protein-induced enterocolitis syndrome. *Front Allergy*. 2022;3: 889879.
56. Nowak-Węgrzyn A, Berin MC, Mehr S. Food protein-induced enterocolitis syndrome. *J Allergy Clin Immunol Pract*. 2020;8(1):24–35.
57. Nowak-Węgrzyn A, Chehade M, Groetch ME, Spergel JM, Wood RA, Allen K, et al. International consensus guidelines for the diagnosis and management of food protein-induced enterocolitis syndrome: executive summary-Workgroup Report of the Adverse Reactions to Foods Committee, American Academy of Allergy, Asthma & Immunology. *J Allergy Clin Immunol*. 2017;139(4). 1111–1126.e4.
58. Caubet JC, Ford LS, Sickles L, Järvinen KM, Sicherer SH, Sampson HA, et al. Clinical features and resolution of food protein-induced enterocolitis syndrome: 10-year experience. *J Allergy Clin Immunol*. 2014;134(2):382–389.
59. Gleich GJ, Sebastian K, Firszt R, Wagner LA. Shrimp allergy: gastrointestinal symptoms commonly occur in the absence of IgE sensitization. *J Allergy Clin Immunol Pract*. 2016;4(2):316–318.
60. Crespo J, Perez-Pallase ME, Skrabski F, Zambrano G, Rojas-Pérez-Ezquerro P, Noguera-Mellado B, et al. The Natural Course of Adult-Onset Food Protein-Induced Enterocolitis Syndrome. *J Allergy Clin Immunol Pract*. 2022;10(11):2986–2992.
61. Frith K, Campbell D, Joshi P, Smart J, Peake J, Smith P, et al. The first 12 months of PFIES surveillance in Australia. *Int Med J*. 2013;43(54):11.
62. Nowak-Węgrzyn A, Warren CM, Brown-Whitehorn T, Cianferoni A, Schultz-Matney F, Gupta RS. Food protein-induced enterocolitis syndrome in the US population-based study. *J Allergy Clin Immunol*. 2019;144(4):1128–1130.
63. Li DH, Wong-Pack A, Macikunas AL, Kim H. Adults with possible food protein-induced enterocolitis syndrome with crustacean ingestion. *Allergy Asthma Clin Immunol*. 2020;16(1):99.
64. Crespo J, Skrabski F, Perez-Pallase ME, De Castro-Martinez FJ, Zubeldia JM, Infante S. Relevant features of adult-onset food protein-induced enterocolitis syndrome. *J Allergy Clin Immunol Pract*. 2021;9(4). 1759–1760.e1.
65. Nowak-Węgrzyn A, Jarocka-Cyrt A, Castro AM. Food protein-induced enterocolitis syndrome. *J Investig Allergol Clin Immunol*. 2017;27(1):1–18.
66. Feuille E, Menon NR, Huang F, Greenhawt M, Nowak-Węgrzyn A. Knowledge of food protein-induced enterocolitis syndrome among general pediatricians. *Ann Allergy Asthma Immunol*. 2017;119(3). 291–292.e3.
67. Baker MG, Nowak-Węgrzyn A. Food protein-induced enterocolitis syndrome: epidemiology and comorbidities. *Curr Opin Allergy Clin Immunol*. 2020;20(2):168–174.
68. Dellon ES, Hirano I. Epidemiology and natural history of eosinophilic esophagitis. *Gastroenterology*. 2018;154(2). 319–332.e3.
69. Cianferoni A, Warren CM, Brown-Whitehorn T, Schultz-Matney F, Nowak-Węgrzyn A, Gupta RS. Eosinophilic esophagitis and allergic comorbidities in a US-population-based study. *Allergy*. 2020;75(6):1466–1469.
70. Levin M, Apostolovic D, Biedermann T, Commins SP, Iweala OI, Platts-Mills TA, et al. Galactose alpha-1,3-galactose phenotypes: lessons from various patient populations. *Ann Allergy Asthma Immunol*. 2019;122(6):598–602.
71. Chung CH, Mirakhor B, Chan E, Le QT, Berlin J, Morse M, et al. Cetuximab-induced anaphylaxis and IgE specific for galactose-alpha-1,3-galactose. *N Engl J Med*. 2008;358(11):1109–1117.
72. Mullins RJ, James H, Platts-Mills TA, Commins S. Relationship between red meat allergy and sensitization to gelatin and galactose-alpha-1,3-galactose. *J Allergy Clin Immunol*. 2012;129(5). 1334–1342.e1.
73. Commins SP, James HR, Kelly LA, Pochan SL, Workman LJ, Perzanowski MS, et al. The relevance of tick bites to the production of IgE antibodies to the mammalian oligosaccharide galactose- α -1,3-galactose. *J Allergy Clin Immunol*. 2011;127(5). 1286–1293.e6.
74. Raghavan RK, Peterson AT, Cobos ME, Ganta R, Foley D. Current and future distribution of the Lone Star tick, *Amblyomma americanum* (L.) (acari: Ixodidae) in North America. *PLoS One*. 2019;14(1): e0209082.
75. Van Nunen S, O'Connor KS, Fernando SL, Clarke LR, Boyle RX. The association between Ixodes holocyclus tick bite reactions and red meat allergy. *Int Med J*. 2007;37(suppl 5):A132.
76. Hamsten C, Starkhammar M, Tran TA, Johansson M, Bengtsson U, Ahlén G, et al. Identification of galactose-alpha-1,3-galactose in the gastrointestinal tract of the tick Ixodes ricinus; possible relationship with red meat allergy. *Allergy*. 2013;68(4):549–552.
77. Chinuki Y, Ishiwata K, Yamaji K, Takahashi H, Morita E. Haemaphysalis longicornis tick bites are a possible cause of red meat allergy in Japan. *Allergy*. 2016;71(3):421–425.
78. Hashizume H, Fujiyama T, Umayahara T, Kageyama R, Walls AF, Satoh T. Repeated Amblyomma testudinarium tick bites are associated with increased galactose- α -1,3-galactose carbohydrate IgE antibody levels: a retrospective cohort study in a single institution. *J Am Acad Dermatol*. 2018;78(6). 1135–1141.e3.
79. Wickner PG, Commins SP. The first 4 Central American cases of delayed meat allergy with galactose-alpha-1,3-galactose positivity clustered among field biologists in Panama. *J Allergy Clin Immunol*. 2014;133(2):AB212.
80. van Nunen SA. Tick-induced allergies: mammalian meat allergy and tick anaphylaxis. *Med J Aust*. 2018;208(7):316–321.
81. Mabelane T, Basera W, Botha M, Thomas HF, Ramjith J, Levin ME. Predictive values of alpha-gal IgE levels and alpha-gal IgE: total IgE ratio and oral food challenge-proven meat allergy in a population with a high prevalence of reported red meat allergy. *Pediatr Allergy Immunol*. 2018;29(8):841–849.
82. Arkesteal K, Sibanda E, Thors C, Troye-Blomberg M, Mdluluzi T, Valenta R, et al. Impaired allergy diagnostics among parasite-infected patients caused by IgE antibodies to the carbohydrate epitope galactose- α 1,3-galactose. *J Allergy Clin Immunol*. 2011;127(4):1024–1028.
83. Murangi T, Prakash P, Moreira BP, Basera W, Botha M, Cunningham S, et al. Ascaris lumbricoides and ticks associated with sensitization to galactose α 1,3-galactose and elicitation of the alpha-gal syndrome. *J Allergy Clin Immunol*. 2022;149(2). 698–707.e3.
84. Wilson JM, Schuyler AJ, Workman L, Gupta M, James HR, Posthumus J, et al. Investigation into the alpha-gal syndrome: characteristics of 261 children and adults reporting red meat allergy. *J Allergy Clin Immunol Pract*. 2019;7(7). 2348–2358.e4.
85. Fischer J, Lupberger E, Hebsaker J, Blumenstock G, Aichinger E, Yazdi AS, et al. Prevalence of type I sensitization to alpha-gal in forest service employees and hunters. *Allergy*. 2017;72(10):1540–1547.
86. Venturini M, Lobera T, Sebastian A, Portillo A, Oteo JA. IgE to alpha-gal in foresters and forest workers from La Rioja, north of Spain. *J Investig Allergol Clin Immunol*. 2018;28(2):106–112.
87. Hamsten C, Tran TAT, Starkhammar M, Brauner A, Commins SP, Platts-Mills TA, et al. Red meat allergy in Sweden: association with tick sensitization and B-negative blood groups. *J Allergy Clin Immunol*. 2013;132(6):1431–1434.
88. Eller E, Stahl Skov P, Baumann K, Hilger C, Ollert M, Bindslev-Jensen C. Delayed reaction in alpha-gal allergy is reflected in serum levels after ingestion of pork kidney, and absorption is dependent on food processing. *Clin Exp Allergy*. 2022;52(1):197–200.
89. Commins SP, Jerath MR, Cox K, Erickson LD, Platts-Mills T. Delayed anaphylaxis to alpha-gal, an oligosaccharide in mammalian meat. *Allergol Int*. 2016;65(1):16–20.
90. Commins SP, Satinover SM, Hosen J, Mozena J, Borish L, Lewis BD, et al. Delayed anaphylaxis, angioedema, or urticaria after consumption of red meat in patients with IgE antibodies specific for galactose-alpha-1,3-galactose. *J Allergy Clin Immunol*. 2009;123(2):426–433.
91. Mabelane T, Botha M, Thomas HF, Levin M. Alpha gal allergy in rural black African subjects associated with a high prevalence of abdominal manifestations and a more rapid onset of symptoms. *J Allergy Clin Immunol*. 2018;141(2):AB200.
92. Apostolovic D, Tran TA, Starkhammar M, Sanchez-Vidaurre S, Hamsten C, Van Hage M. The red meat allergy syndrome in Sweden. *Allergo J Int*. 2016;25(2):49–54.
93. Fischer J, Yazdi AS, Biedermann T. Clinical spectrum of alpha-Gal syndrome: from immediate-type to delayed immediate-type reactions to mammalian innards and meat. *Allergo J Int*. 2016;25:55–62.
94. Fischer J, Hebsaker J, Caponetto P, Platts-Mills TA, Biedermann T. Galactose-alpha-1,3-galactose sensitization is a prerequisite for pork-kidney allergy and cofactor-related mammalian meat anaphylaxis. *J Allergy Clin Immunol*. 2014;134(3). 755–759.e1.
95. Skypala LJ. Food-induced anaphylaxis: role of hidden allergens and cofactors. *Front Immunol*. 2019;10:673.
96. O'Neil BH, Allen R, Spiegel DR, Stinchcombe TE, Moore DT, Berlin JD, et al. High incidence of cetuximab-related infusion reactions in Tennessee and North Carolina and the association with atopic history. *J Clin Oncol*. 2007;25(24):3644–3648.

97. Yamaguchi K, Watanabe T, Satoh T, Ishiguro M, Izawa M, Inoshiri S, et al. Severe infusion reactions to cetuximab occur within 1 h in patients with metastatic colorectal cancer: results of a nationwide, multicenter, prospective registry study of 2126 patients in Japan. *Jpn J Clin Oncol*. 2014;44(6):541–546.
98. Aihara Y, Takahashi Y, Kotoyori T, Mitsuda T, Ito R, Aihara M, et al. Frequency of food-dependent, exercise-induced anaphylaxis in Japanese junior-high-school students. *J Allergy Clin Immunol*. 2001;108(6):1035–1039.
99. Wolbing F, Fischer J, Koberle M, Kaesler S, Biedermann T. About the role and underlying mechanisms of cofactors in anaphylaxis. *Allergy*. 2013;68(9):1085–1092.
100. Pravettoni V, Incorvaia C. Diagnosis of exercise-induced anaphylaxis: current insights. *J Asthma Allergy*. 2016;9:191–198.
101. Ansley L, Bonini M, Delgado L, Del Giacco S, Du Toit G, Khaitov M, et al. Pathophysiological mechanisms of exercise-induced anaphylaxis: an EAACI position statement. *Allergy*. 2015;70(10):1212–1221.
102. Del Giacco S. Exercise-induced anaphylaxis: an update. *Breathe*. 2012;8:298–306.
103. Warren CM, Zaslavsky J. Should cannabis be a higher priority for allergists?: A history and look down the pipe. *Ann Allergy Asthma Immunol*. 2022;129(4):393–394.
104. Jackson B, Cleto E, Jeimy S. An emerging allergen: Cannabis sativa allergy in a climate of recent legalization. *Allergy Asthma Clin Immunol*. 2020;16:53.
105. Decuyper II, Van Gasse AL, Faber MA, Elst J, Mertens C, Rihs HP, et al. Exploring the diagnosis and profile of cannabis allergy. *J Allergy Clin Immunol Pract*. 2019;7(3):983–989.e5.
106. Rihs HP, Armentia A, Sander I, Bruning T, Raulf M, Varga R. IgE-binding properties of a recombinant lipid transfer protein from Cannabis sativa. *Ann Allergy Asthma Immunol*. 2014;113(2):233–234.
107. Metz-Favre C, Pauli G, Bessot JC, De Blay F. Molecular allergology in practice: an unusual case of LTP allergy. *Eur Ann Allergy Clin Immunol*. 2011;43(6):193–195.
108. Drouet M, Hoppe A, Moreau AS, Bonneau JC, Leclerc JM, Le Sellin J. Cannabis and crossed allergy with food. *Rev Pneumol Clin*. 2017;73(6):290–293.
109. Ebo DG, Swerts S, Sabato V, Hagendorens MM, Bridts CH, Jorens PG, et al. New food allergies in a European non-Mediterranean region: is Cannabis sativa to blame? *Int Arch Allergy Immunol*. 2013;161(3):220–228.
110. Faber MA, Sabato V, Bridts CH, Nayak A, Beezhold DH, Ebo DG. Clinical relevance of the Hevea brasiliensis lipid transfer protein Hev b 12. *J Allergy Clin Immunol*. 2015;135(6):1645–1648.
111. Faber M, Van Gasse A, Sabato V, Hagendorens MM, Bridts CH, De Clerck LS, et al. Marijuana allergy: beyond the joint. *J Invest Allergol Clin Immunol*. 2015;25(1):70–72.
112. Skypala IJ, Jeimy S, Brucker H, Nayak AP, Decuyper II, Bernstein JA, et al. Cannabis-related allergies: an international overview and consensus recommendations. *Allergy*. 2022;77(7):2038–2052.
113. Pita JS, Sousa N, Bartolome B, Loureiro C, Bom AT. Beer: an uncommon cause of anaphylaxis. *BMJ Case Rep*. 2019;12(1):e227723.
114. American Academy of Allergy Asthma & Immunology. Amaretto contents and allergy. Available at: [https://www.aaaai.org/allergist-resources/ask-the-expert/answers/old-ask-the-experts/amaretto-\(1\)](https://www.aaaai.org/allergist-resources/ask-the-expert/answers/old-ask-the-experts/amaretto-(1)). Accessed April 2, 2022.
115. Australian Society of Clinical Immunology and Allergy. Alcohol allergy. Information for patients, consumers and carers. 2019. Available at: https://www.allergy.org.au/images/pcc/ASCA_PCC_Alcohol_allergy_2019.pdf. Accessed April 2, 2022.
116. Shin M. Food allergies and food-induced anaphylaxis: role of cofactors. *Clin Exp Pediatr*. 2021;64(8):393–399.
117. American College of Allergy Asthma & Immunology. Allergist Report: America Faces an Allergy/Asthma Crisis. Available at: <https://college.aaaai.org/sites/default/files/AllergistReport.pdf>. Accessed April 3, 2022.
118. Malick A, Meadows JA. Allergy and Immunology Physician Workforce: where do we stand today? *Ann Allergy Asthma Immunol*. 2021;127(5):522–523.
119. Congress US. Food allergy safety, treatment, education, and research (FASTER) Act of 2021. 2021. Available at: <https://www.congress.gov/bill/117th-congress/senate-bill/578>. Accessed April 12, 2022.
120. National Center for Health Statistics. National health interview survey. Available at: https://www.cdc.gov/nchs/nhis/index.htm?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fncchs%2Fnhis.htm. Accessed April 2, 2022.
121. Centers for Disease Control and Prevention. National health and nutrition examination survey 2013. Available at: https://wwwn.cdc.gov/nchs/nhanes/2005-2006/AL_IJE_D.htm. Accessed March 28, 2022.
122. Victoria State Department (AUS). Anaphylaxis notifications. 2021.. Available at: <https://www.health.vic.gov.au/public-health/anaphylaxis-notifications>. Accessed June 22, 2022.
123. Food Allergy Research and Education. Clinical Network Centers of Distinction. Available at: <https://www.foodallergy.org/resources/fare-clinical-network-centers-distinction#:~:text=FARE%20Clinical%20Network%20Centers%20of%20Distinction%202D%20FoodAllergy.org&text=Join%20over%2014%2C000%20individuals%20and,changing%20improvements%20in%20patient%20care>. Accessed March 22, 2022.
124. Global Allergy and Asthma European Network. Anaphylaxis Centres of Reference and Excellence. Available at: <https://ga2len-anacare.eu/>. Accessed December 21, 2022.
125. US Food and Drug Administration. FDA approves first drug for treatment of peanut allergy for children. 2020. Available at: <https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-treatment-peanut-allergy-children>. Accessed March 27, 2022.
126. Franxman TJ, Howe L, Teich E, Greenhawt MJ. Oral food challenge and food allergy quality of life in caregivers of children with food allergy. *J Allergy Clin Immunol Pract*. 2015;3(1):50–56.