

Editorial

Adult peanut allergy: What we know and what we need to learn

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FROM PREVALENCE TO PRACTICE

The prevalence of food allergy (FA), including peanut allergy (PA), has been on the rise around the globe. Although the prevalence of FA is greater in childhood, FA can develop at any age, and this is true for PA. Regardless of the age of onset, PA can lead to significant morbidity, impaired quality of life, and higher health care costs. The increase in PA over time is likely due to a combination of rising prevalence in children with spontaneous resolution in only 20%,¹ along with the possibility of adult-onset PA. Although epidemiological data cannot explain causal relationships, it can assist in diagnosis, prognosis, and the general management of FA, which changes with the age and life conditions of the food-allergic individual. For example, in the early 2000s, the LEAP study team found that the risk of developing PA was 10 times higher among Jewish children in the United Kingdom as compared with Israeli children with similar ancestry and presumably similar genetic background.² This was attributed to early consumption of peanut in infancy by Israeli children and became the foundation of the landmark Learning Early About Peanut Allergy or LEAP study, which has shaped our understanding of not only PA, but FA in general, and our current guidelines for primary prevention.

DETERMINATION OF PREVALENCE DEPENDS ON STUDY PARAMETERS

Accurately determining the prevalence of FA is difficult and depends on numerous factors, including the definition of allergy, the characteristics of the study population, the foods included,

geographic location, dietary and environmental exposure, economic status, and more. Estimation of FA prevalence in adults is even more difficult to determine due to factors such as development of natural tolerance, cross-reactivity, including pollen-food syndrome, and adults frequently self-diagnosing and pursuing dietary elimination in the absence of a formal diagnosis by an allergist. This is further complicated by the overuse of IgE food panels in primary care and by direct-to-consumer food allergy and “sensitivity” testing, leading to overdiagnosis of FA in both medical and home settings. To date, there have been few studies evaluating the prevalence of FA in adults, with there being heterogeneity in design and varied results, some of which are presented in [Table I](#).

Given the many unanswered questions regarding adult PA, Warren et al³ published a large study in the journal determining the prevalence and characteristics of PA in US adults (included in [Table I](#)). They demonstrate the prevalence of adult PA to be significantly higher than previously reported, with differences in PA based on adult versus childhood age of onset, and that 17.5% of adults with convincing PA developed PA in adulthood.³ Key findings include that despite similar demographic characteristics and symptoms among childhood and adult onset of PA, those with adult-onset PA are less likely to carry an epinephrine autoinjector and are more likely to treat reactions with antihistamines. There are also higher levels of adult females with childhood-onset PA, indicating that females may be less likely to outgrow childhood PA. Adults with PA were more likely to be female, nonwhite, and have more self-reported comorbid atopic conditions than adults without PA.

In the case of children, factors such as timing and exposure through the skin or inhalation before known ingestion have been shown to contribute to development of PA, whereas early oral ingestion has been shown to be preventative. Exposures via skin,⁴ respiratory mucosa (pollen-food syndrome), and gut, in addition to sex,³ vitamin D deficiency,⁵ comorbid conditions,⁶ and occupational and environmental⁷ exposures, have been implicated in the development of FA in adults.

Although the report by Warren et al³ offers valuable insight into adult PA, the authors acknowledge the limitations of a survey-based design and self-reported FA diagnosis in the absence of diagnostic testing. Although it is impractical to complete appropriate skin prick testing, specific IgE levels, and/or a physician-supervised oral food challenge in such a large cohort, the absence of this essential diagnostic information necessitates that the results be interpreted with caution, because it may lead to overestimating the true prevalence of PA in US adults. Woods et al⁸ demonstrated minimal agreement between self-reported FA and the presence of sensitization based on skin prick test, with only 1.5% of adults likely to have a “true FA” based on these criteria.⁸ Similarly, Fleischer et al⁹ showed that in individuals aged 1 to 19 years, 84% were able to tolerate a food despite there being a

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TABLE I. Adult FA studies

Study country and when surveyed	Adult PA prevalence	Adult FA prevalence	Overall FA prevalence	Data collection and comments	References
Canada 2008-2009	0.78%	8.34%	8.07%	Cross-sectional telephone survey of the general population; SCAALR study of 9667 individuals from 10 Canadian provinces, including 7469 adults. Different prevalence estimates were made: adult FA prevalence dropped to 6.58% and total to 6.67% if milk, egg, wheat, and/or soy allergy in adults were excluded	Soller L, Ben-Shoshan M, Harrington DW, Fragapane J, Joseph L, St Pierre Y, et al. Overall prevalence of self-reported food allergy in Canada. <i>J Allergy Clin Immunol</i> 2012;130:986-8.
Canada 2010-2011	0.4%-1.1%	NA	6.4%-8.9%	The SPAACE study, using 2006 Canadian Census data, was a random telephone survey of 5734 households (15,022 participants), which targeted vulnerable Canadians (ie, those of low income, New Canadians, and of self-reported Aboriginal identity)	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. <i>J Allergy Clin Immunol Pract</i> 2015;3:42-9.
EU 2005-2009 ● Athens ● Reykjavik ● Utrecht ● Lodz ● Madrid ● Zurich	0%-0.45%	0.3% 1.4% 2.1% 2.8% 3.3% 5.6%	2%-37% for 24 foods 1%-19% for any food	A multicenter cross-sectional study (2005-2009) of the general population, with a combination of self-reported FA and matching IgE-sensitization and of confirmed FA (diagnosed by double-blind placebo-controlled food challenge) in adults across Europe, using the EuroPrevall 2009 data (adults aged 20-54 y), 81.6% of which had PFS	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. <i>J Allergy Clin Immunol Pract</i> 2019;7:1920-8.
Israel 2016	0.14%	0.67%	NA	A study of 12,592 Israeli adults (aged 17-18 y) that included OFCs confirmed a prevalence of 0.67%, with tree nuts 0.28% > milk 0.16% > peanut > fish > sesame > egg 0.015% as most common adult food allergens. All recruits were from 1 urban area recruitment center of the Israel Defense Forces over a period of 6 mo	Nachshon L, Schwartz N, Elizur A, Schon Y, Cheryomukhin M, Katz Y, et al. The prevalence of food allergy in young Israeli adults. <i>J Allergy Clin Immunol Pract</i> 2019;7:2782-9.
India 2009-2015	0.0	1.2%	NA	Random screening of 11,791 adults aged 20-54 y in South India. Case-control study of 236 cases and 352 controls. Part of EuroPrevall-INCO. FA defined as +sIgE and self-reported adverse symptoms. Cow's milk (0.5%) and apple (0.5%) accounted for most	Mahesh PA, Wong GWK, 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. <i>Allergy</i> 2016;71:1010-9.
Kuwait 2017	1.6%	5.4%	NA	A total of 974 paper questionnaires were distributed to Kuwait University students (mean age, 20.7 y), 865 returned. Probable FA in 47 who reported being diagnosed by a physician who used 1 or more confirmatory tests. 14% were onset age 16-19 y, but all PA was earlier onset	Ali F. A survey of self-reported food allergy and food-related anaphylaxis among young adult students at Kuwait University. <i>Med Princ Pract</i> 2017;26:229-34.
Saudi Arabia 2020	3%	19.7%	NA	A nationwide (13 regions) cross-sectional survey conducted via phone interviews in June 2020; 4709 (75.48%) participants completed the interview. Most common self-reported FAs were egg 3.7% > shellfish > peanut 3%. No questions were asked to ascertain for IgE-mediated symptoms or physician diagnosis of food allergy	Althumiri NA, Basyouni MH, Al Mousa N, Al Juwaysim MF, BinDhim NF, Alqahtani SA. Prevalence of self-reported food allergies and their association with other health conditions among adults in Saudi Arabia. <i>Int J Environ Res Public Health</i> 2021;18:347.

(Continued)

TABLE I. (Continued)

Study country and when surveyed	Adult PA prevalence	Adult FA prevalence	Overall FA prevalence	Data collection and comments	References
Saudi Arabia 2008-2018	NR	9.6% (19.2% adult-onset)	NA	An online survey-based cross-sectional study of 5497 students surveyed regarding presence and age of onset of FA. Of the 526 students who had a positive screening history, 174 students had clinically diagnosed FA, of which 19.2% had adult onset of FA and 38% did not have epinephrine at the time of their most recent reaction	Hassan A, Alsaihati A, Al Shammari M, Alaithan H, Al-Johani W, Al Shamlan N, et al. AACI Food allergy among university students: uncharted territory. <i>Allergy Asthma Clin Immunol</i> 2020;16:1-6.
US 2002	0.6%	1.3% any nut	NA	A nationwide, cross-sectional, random telephone survey using a standardized questionnaire that included 4855 households, a census of 13,493 individuals. A male dominance in children with peanut/tree nut allergy and a female dominance in adults with a 1.4% peanut-tree nut or both overall	Sicherer SH, Munoz-Furlong A, Sampson HA. Prevalence of peanut and tree nut allergy in the US determined by means of a random digit dial telephone survey. <i>J Allergy Clin Immunol</i> 2003;112:1203-7.
US 2005-2006	1.3%	0.9%-1.2%	2.5% for 4 foods 0.6% in >60-y-olds	A total of 8203 participants in the National Health and Nutrition Examination Survey 2005-2006 had food-specific serum IgE measured to peanut, cow's milk, egg white, and shrimp. Estimated clinical FA in order was 2.5% (peanut + milk + shrimp + egg). In order: peanut 1.3% > shrimp > milk > egg 0.23%	Liu AH, Jaramillo R, Sicherer SH, Wood RA, Bock SA, Burkset AW, et al. National prevalence and risk factors for food allergy and relationship to asthma: results from the National Health and Nutrition Examination Survey 2005-2006. <i>J Allergy Clin Immunol</i> 2010;126:798-806.
US 2007-2010	0.9%	9.7%	9%	Self-reported FA from a US population-based door-to-door survey conducted between 2007 and 2010. Self-reported FA was compared with the subjects who reported consumption of milk, shellfish, fish and peanut	McGowan EC, Keet CA. Prevalence of self-reported food allergy in the Health and Nutrition Examination Survey (NHANES) 2007-2010. <i>J Allergy Clin Immunol</i> 2013;132:1216-9.
US 2015	NA (9% adult-onset)	NA (15% adult-onset)	NA	Not a population study, but a retrospective chart review of 1111 adults with FA physician diagnosis in Chicago; 171 cases were adult-onset. They excluded PFS. Patient eligibility required a positive SPT result. FAs in order: shellfish 54%, tree nuts > finfish > soy > peanut 9%	Kamdar Peterson S, Lau CH, Saltoun CA, Gupta RS, Bryce PJ. Prevalence and characteristics of adult-onset food allergy. <i>J Allergy Clin Immunol Pract</i> 2015;3:114-5.
US 2015-2016	1.8%	10.8% (48% adult-onset)	NA	A nationally representative, cross-sectional FA survey via telephone and web in 2015 and 2016, resulting in complex-survey weighted data for 40,443 adults. Reported higher-than-anticipated numbers of adults with convincing adult-onset FA to "childhood" allergens. FA order: shellfish 2.9% > milk > peanut > tree nut > fin fish 0.9%. Reported 39% with 1 ED visit/life and 9% 1 ED visit/that year. Nearly 19% of adults believed they had FA, but only 10.8% were "convincing"	Gupta RS, Warren CM, Smith BM, Jiang J, Blumenstock JA, Davis MM, et al. Prevalence and severity of food allergies among US adults. <i>JAMA</i> 2019;2:e185630.
US 2015-2016	1.8% (17.5% adult-onset)	10.8%	NA	Same database as above; 2.9% reported PA, but only 1.8% were convincing	Warren et al ³

ED, Emergency department; *EuroPrevall-INCO*, EuroPrevall International Cooperation; NA, not applicable; *OFC*, oral food challenge; *PFS*, pollen-food syndrome; *SCAAALAR*, Surveying Canadians to Assess the prevalence of food Allergies and Attitudes towards food Labelling and Risk; *sIgE*, specific IgE; *SPAACE*, Surveying Prevalence of Food Allergy in All Canadian Environments; *SPT*, skin prick test.

Adult onset: where data are available, adult onset for FA is indicated in the table.

reported history of food reaction, including 76% of those with reactions involving the skin, 18% with respiratory reactions, and even 5% of patients with anaphylaxis. In 2020, Solymosi et al¹⁰ conducted a prospective evaluation of FA in adults and found only 1% to have a physician-diagnosed FA, despite many individuals reporting symptoms of acute urticaria on exposure to a culprit food.

We commend the authors for using stringent symptoms (see Fig E1 in this article's Online Repository at www.jacionline.org), which led to a convincing history of FA, but note that many of these symptoms are subjective (difficulty swallowing, throat tightening, chest tightening, trouble breathing, rapid heartbeat, etc), and routinely encountered in clinical practice even in the absence of IgE-mediated allergic reactions. In addition, the results in Table V in Warren et al suggest that a significant percentage of adults who report adult-onset PA also report adult onset of allergy to other foods, such as cow's milk (17.3%), egg (10.1%), wheat (13.7%), and soy (17.7%). These results mirror previous studies citing self-reported allergies but are contrary to the typically accepted natural history of FA, where these specific food allergies are almost exclusively diagnosed in early childhood, with most resolving by adolescence. However, we can hypothesize that these adults, because they report significantly higher environmental allergies, might have had IgE-facilitated antigen presentation to plant-derived food proteins that initially were recognized because of pollen-food cross-reactivity, but now have IgE directed to other epitopes and a progression beyond oral allergy syndrome. The high prevalence of tree nut, wheat, and soy allergy could be supported by this hypothesis, but the high level of milk and egg allergy is not. The prevalence of adult FA, including PA, can have important impacts on both the individual and community, and as clinicians, we must therefore take all measures to make an accurate diagnosis of PA regardless of age.

PREVALENCE IN DIVERSE POPULATIONS

Although survey-based studies have limitations, they have advantages as well. Large survey-based results are more likely to assess characteristics, such as socioeconomic determinants and prevalence of FA in underrepresented populations, as apparent in the study by Warren et al in which Asians, blacks, and Hispanics were significantly overrepresented in the group with PA compared with adults without current PA.³ Such surveys do not have to

contend with recruitment-associated challenges such as cost, time, convenience, and location-dependent demographics involved with a physician-based diagnosis, particularly in adults. Indeed, this may be an acceptable or desirable method to specifically target studies to the less-reachable populations, as described in the self-reported food allergy survey of vulnerable populations in Canada (Table I).

PREVALENCE IN THE ADULT POPULATION IS AN UNMET NEED

Despite limitations, the study by Warren et al is an important epidemiological study with novel insights into PA in US adults, an area of unmet need. The study stresses the need for future research into numerous aspects of adult FA, including prevalence, demographic characteristics, impact on quality of life, and appropriate treatment options, along with the differences between adult and childhood-onset FA.

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