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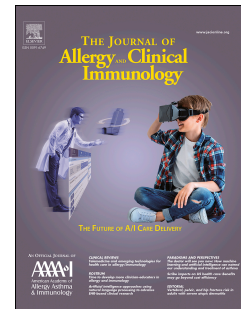
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Adult Peanut Allergy, What We Know and What We Need to Learn

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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, it can develop at any age, and this is particularly true for PA. Regardless of age of onset, PA can lead to significant morbidity, impaired quality of life and higher healthcare costs. The increase of 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. While 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 ten times higher amongst Jewish children in the United Kingdom as compared to 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 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 (PFS), 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 food allergy 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 shown in Table 1.

Given the many unanswered questions regarding adult PA, Warren et al. published a large study in the journal determining the prevalence and characteristics of PA in U.S. adults (included in Table 1)³. 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 demographics and symptoms among childhood and adult-onset of PA, those with adult-onset PA are less likely to carry an epinephrine auto-injector 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, non-white, 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 prior to known ingestion have been shown to contribute to development of PA, whereas early oral ingestion has been shown to be preventative. Exposures via skin⁴, lung (PFS) and gut, in addition to sex³, vitamin D deficiency⁵, comorbid conditions⁶, occupational and environmental⁷ exposures have been implicated in the development of FA in adults.

Although the report by Warren et al. 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. While it is impractical to complete appropriate skin prick testing (SPT), 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, since it may lead to overestimating the true prevalence of PA in US adults. Woods et al demonstrated minimal agreement between self-reported FA and the presence of sensitization based on SPT, with only 1.5% of adults likely to have a “true FA” based on these criteria.⁸ Similarly, Fleischer et al. showed that in individuals 1-19 years of age, 84% were able to tolerate a food despite there being a 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.⁹ In 2020, Solymosi et al. 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 upon exposure to a culprit food.¹⁰

We commend the authors for using stringent symptoms (Figure E1) that 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. Additionally, the results in Table V in Warren et al. suggest 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, since they report significantly higher environmental allergies, might have had IgE-facilitated antigen presentation to plant-derived food proteins that initially were recognized due to 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

While 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 over-represented in the group with PA compared to 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 1).

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 versus childhood-onset FA.

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Table 1. Adult Food Allergy 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 ten Canadian provinces, including 7,469 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 et al, 2012 JACI Overall prevalence of self-reported food allergy in Canada JACI, 130 (4): 986-988 doi: 10.1016/j.jaci.2012.06.029
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 (15022 participants), which targeted vulnerable Canadians (i.e., those of low income, New Canadians, and of self-reported Aboriginal identity).	Soller et al, 2015 JACIP Prevalence and Predictors of Food Allergy in Canada: A Focus on Vulnerable Populations JACIP, 3 (1): 42-49 doi: 10.1016/j.jaip.2014.06.009
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 [DBPCFC]) in adults across Europe, using the EuroPrevall 2009 data (adults aged 20–54), 81.6% of which had PFS.	Lyons et al 2019 JACIP Food allergy in adults: substantial variation in prevalence and causative foods across Europe. J Allergy Clin Immunol Pract 2019;7:1920-8. doi: 10.1016/j.jaip.2019.02.044
Israel 2016	0.14%	0.67%	NA	A study of 12592 Israeli adults (aged 17-18 years) that included OFCs confirmed a prevalence of 0.67%, with tree nuts 0.28%> milk	Nachshon et al 2019 JACIP The prevalence of food allergy in young Israeli adults. J Allergy

				0.16%> peanut>fish>sesame> egg 0.015% as most common adult food allergens. All recruits were from one urban area recruitment center of the Israel Defense Forces (IDF) over a period of 6 months.	Clin Immunol Pract 2019;7:2782-9. doi: 10.1016/j.jaip.2019.05.046
India 2009-2015	0.0	1.2%	NA	Random screening of 11,791 adults ages 20-54 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 et al 2016 Prevalence of food sensitization and probable food allergy among adults in India: the EuroPrevall INCO study. Allergy. 2016 Jul;71(7):1010-9. doi:10.1111/all.12868
Kuwait 2017	1.6%	5.4%	NA	974 paper questionnaires were distributed to Kuwait University students (mean age 20.7), 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, but all PA was earlier onset.	Ali F et al 2017 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 doi: 10.1159/000464361
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 et al 2021 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. doi: 10.3390/ijerph18010347
Saudi Arabia 2008-2018	NR	9.6% (19.2% adult-onset)	NA	An on-line 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	Hassan et al 2020 AACI Food allergy among university students: uncharted territory. Allergy, Asthma Clin Immunol. 2020;16(1):1-6. doi: 10.1186/s13223-020-0415-

				the time of their most recent reaction.	5
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 et al. 2003 JACI Prevalence of peanut and tree nut allergy in the US determined by means of a random digit dial telephone survey. J Allergy Clin Immunol 2003;112:1203-7 doi: 10.1016/s0091-6749(99)70224-1
US 2005-2006	1.3%	0.9-1.2%	2.5% for 4 foods 0.6% in > 60yrs old	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 et al 2010 JACI National prevalence and risk factors for food allergy and relationship to asthma: results from the National Health and Nutrition Examination Survey 2005-2006. J Allergy Clin Immunol 2010;126:798-806. doi: 10.1016/j.jaci.2010.07.026
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 that reported consumption of milk, shellfish, fish and peanut.	McGowan et al 2013, JACI Prevalence of self-reported food allergy in the Health and Nutrition Examination Survey (NHANES) 2007-2010. J Allergy Clin Immunol 2013; 132:1216-9. doi: 10.1016/j.jaci.2013.07.018
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 allergy physician diagnosis in Chicago; 171 cases were adult-onset. They excluded PFS. Patient eligibility required a positive SPT. FAs in order: shellfish 54%, tree nuts>finfish>soy> peanut 9%.	Kamdar et al 2015 JACIP Prevalence and characteristics of adult-onset food allergy. J Allergy Clin Immunol. Pract 2015;3:114-5. doi: 10.1016/j.jaip.2014.07.007.

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 one 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 et al 2019, JAMA Prevalence and Severity of Food Allergies Among US Adults. JAMA. 2019;2:e185630. doi: 10.1001/jamanetworkopen.2018.5630
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 2021 JACIP Prevalence and Characteristics of Peanut Allergy in US Adults. J Allergy Clin Immunol 2021 (this issue) doi: 10.1016/j.jaci.2020.11.046

* SCAALAR: Surveying Canadians to Assess the prevalence of food Allergies and Attitudes towards food Labelling and Risk

SPAACE: Surveying Prevalence of Food Allergy in All Canadian Environments; ^ EuroPrevall-INCO: EuroPrevall International Cooperation

FA: Food Allergy; SPT: Skin Prick Test; sIgE: specific IgE; NA: Not Applicable; adult onset: where data is available, adult onset for FA is indicated in the table.