

## Food Allergy Management Practices Utilizing Individual Patient Thresholds: A Work Group Report of the AAAAI Adverse Reactions to Foods Committee



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The paradigm for food allergy management has been strict avoidance of the food allergen. There is literature supporting a “high-threshold” phenotype, those who tolerate a small-to-modest amount of allergen but react to larger amounts. There is no consensus for best practice for these “high-threshold” individuals. We sought to understand management practices of “high-threshold” reactors using a survey that was distributed to a random sample of fellows and members of the American

Academy of Allergy, Asthma, and Immunology. There were 89 respondents from the United States and Canada (11% response rate), with 64 (72%) answering all questions. Participants worked in private (52%) and academic practice (38%) and saw a median of 30 food allergic patients monthly. Eighty-one percent of respondents reported management strategies other than strict avoidance. When threshold was known, strategies ranged from allowing ingestion up to a specified amount (57%), proactively

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**Abbreviations used**

AAAAI- American Academy of Allergy, Asthma and Immunology  
OFC- Oral food challenge

advising ingestion to a certain amount (56%), or oral immunotherapy (47%). Participants were more likely to choose a permissive approach for a mild reaction in a high-threshold milk-allergic patient compared with a peanut-allergic patient (83% vs 71%,  $p = .01$ ). Important factors that influenced the approach included severity of reaction (52%), comfort with family/patient using emergency medications (42%), and family/patient preferences (41%). These survey results suggest that food allergy management recommendations are no longer binary in nature, with clinicians solely recommending avoidance for those who are allergic and ingestion for those who may not be. © 2023 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2023;11:1083-6)

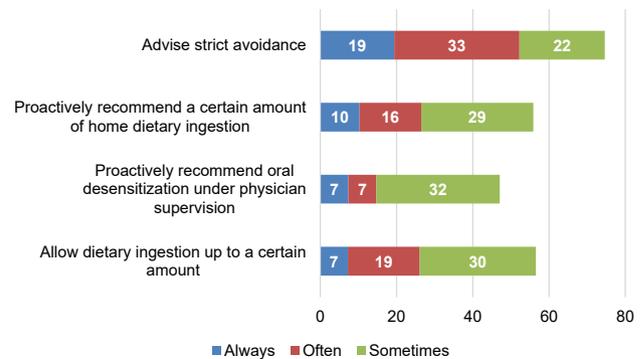
**Keywords:** Food allergy; High threshold; Strict avoidance; Oral food challenge; Oral immunotherapy; Allergen

Historically, the standard of care for food-allergic patients has been to recommend strict allergen avoidance.<sup>1</sup> However, patients with food allergy have a threshold quantity up to which they can tolerate allergen ingestion without reacting.<sup>2</sup> A study describing population-based eliciting doses for 14 allergenic foods suggested that 50% of the food-allergic population could consume a somewhat sizeable, nontrace portion of many of these foods without having a reaction.<sup>2,3</sup> For patients with a high threshold of reactivity (low-dose tolerant, but reactive to higher doses), there may be management options other than strict avoidance, but little is known about allergists' current practice for these patients.

The purpose of this study was to survey the practicing clinician about their approach to food-allergic patients who have or may have a "high" threshold of reactivity, recognizing that there is no accepted definition of a specific high or low reactivity threshold. An ad hoc survey was designed by the workgroup that included questions about general management approaches, case scenarios, and influencing factors when making food avoidance recommendations. Decisions on item wording and inclusion were determined by consensus within the workgroup.

The study was reviewed by the Mount Sinai Institutional Review Board and received exemption under the Common Rule. The survey was reviewed and approved by the Practice, Diagnostics and Therapeutics Committee and distributed via email by the AAAAI to a random sample of 818 United States and Canadian American Academy of Allergy, Asthma and Immunology (AAAAI) members in the category of Fellows and Members (inclusive of physicians and nonphysician providers) from March 18, 2022, to April 13, 2022, with 3 reminders given during that time frame. Comparisons of approaches were analyzed using Wilcoxon signed-rank test. A result was considered statistically significant at the  $P$  less than .05 level. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

There were 89 respondents (response rate 11%), of whom 64 answered all questions (72%). Respondent characteristics can be found in Table E1 in this article's Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org).



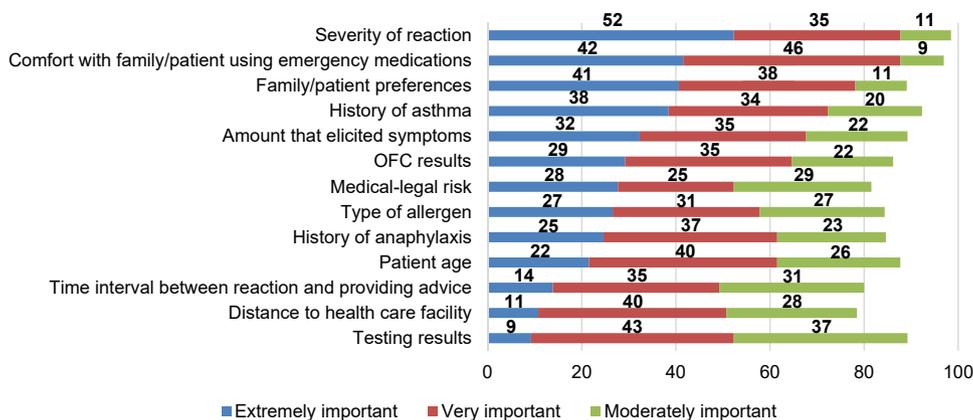
**FIGURE 1.** Percentage of survey participants who responded "always," "often," or "sometimes" to various management strategies for food-allergic patients who are high-threshold reactors as proven by OFC.

Briefly, respondents were from the United States or Canada, with 52% (33 of 64) reporting working in private practice, with a median of 19 years in practice, seeing a median of 30 patients with food allergies per month, and performing a median of 5 oral food challenges (OFCs) per month. In addition, 58% (37 of 64) of respondents reported offering oral immunotherapy in some form, with an additional 20% (13 of 64) planning to start "in the near future."

Without specifying a quantity of food to define a threshold or amount for any survey item or vignette scenario, the survey queried about general management approaches for a patient who is "proven by OFC to tolerate small to modest amounts of a food allergen, but a larger amount causes a reaction" using a scale of always, often, sometimes, rarely, and never (see Figure 1). Overall, 81% (54 of 67) reported approaches other than "always" advising strict avoidance. Regarding other management strategies, 57% (39 of 69) at least sometimes reported they advise dietary intake up to a specified amount, 56% (38 of 68) reported at least sometimes proactively advising ingestion to a specified amount, and 47% (32 of 68) at least sometimes recommended oral desensitization under physician supervision.

Respondents indicated that the 3 top factors (from the choices provided) that were "extremely important" to them when making management decisions regarding whether to recommend or not recommend strict avoidance in patients who can tolerate smaller amounts but react to higher amounts of food allergen. Respondents indicated that severity of reaction (52%, 34 of 65), comfort with family/patient using emergency medications (42%, 27 of 65), and family/patient preferences (41%, 26 of 64) were the most important considerations (see Figure 2). The 3 factors of relatively least importance were test results (9%, 6 of 65), distance to a health care facility (11%, 7 of 65), and the time interval between the reaction and providing advice (14%, 9 of 65).

Survey case scenarios devised by workgroup ad hoc consensus were used to assess management decisions representing common scenarios that occur in practice for food-allergic, high-threshold reactors. Responses are shown in Figure E1 in this article's



**FIGURE 2.** Percentage of survey participants who responded “extremely important,” “very important,” or “moderately important” to different factors that may be considered when developing management strategies for food-allergic patients who are high-threshold reactors.

Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org). For an identical reaction threshold to milk (Figure E1 Q3, Q4), respondents were less willing to permit ingestion up to a threshold (less permissive) for a vignette intended to describe a more severe reaction (anaphylaxis) compared with a milder one (83% [57 of 69] vs 54% [37 of 69];  $P < .0001$ ). In comparing food triggers, respondents were more likely to choose permissive approaches for a mild reaction at a large dose threshold for a milk-allergic patient (Figure E1, Q3) compared with a peanut-allergic patient (83% [57 of 69] vs 71% [48 of 68];  $P = .01$ ) (Figure E1, Q5). Regarding mild reactions to peanut and milk during a food challenge, many respondents (49% [34 of 69] for peanut; 40% [27 of 68] for milk) chose to advise consumption of that food at an amount below the amount at which the reaction occurred. In a case scenario regarding a milk-allergic patient who had a mild reaction to a high-threshold dose, slightly more than half of the respondents (55%, 37 of 67) indicated that they would offer an OFC to baked milk (Figure E1, Q9). In a case scenario regarding peanut allergy prevention (Figure E1, Q6), the vignette described an infant ingesting 3 Bamba peanut sticks without a reaction, who then was given the recommended (and larger) portion of 21 sticks at home and subsequently developed facial hives and a few abdominal hives treated with antihistamine. In this scenario, 69% (47 of 68) advised consumption below the amount triggering a reaction.

Responses for approaches to consumption of various forms of sesame varied. For sesame-allergic patients who tolerated seeds (Figure E1, Q7), the 2 most popular choices (of the options provided) were to advise continued ingestion of seeds up to a threshold previously tolerated (37%, 25 of 67) or advise consumption of both seeds and oil (39%, 26 of 67). For a patient who had never ingested sesame seeds or oil previously and had a mild reaction to a teaspoon of concentrated sesame (tahini) (Figure E1, Q8), respondents indicated they advise strict sesame avoidance (39%, 26 of 67) of all forms, or offer an OFC to sesame seeds or oil (46%, 31 of 67).

Our results of this exploratory study indicate that most respondents consider management strategies other than strict avoidance for high-threshold food-allergic patients. Their responses indicate a willingness to advise patients to actively ingest

subthreshold doses of the allergenic food. However, this was dependent on some key contextual factors, such as the severity of the previous reaction and the specific allergen involved. As reflected in Figures 1 and E1, there was a wide range of responses to the specific case scenarios, which may reflect a lack of clarity and preference in how a clinician may advise a patient, which may be a result of lack of evidence-based guidance for treatment decisions.

These findings add to a growing number of studies examining the benefits of food allergy management based on clinical thresholds. Along with potential benefits to quality of life, some studies indicate that a strategy based on threshold can be more economically viable. For example, a study noted that when considering the risks of accidental exposures, reaction treatments, and family costs of food allergy in the setting of potentially fatal reactions, avoidance of products with advisory labeling for peanut-allergic patients was not cost-effective.<sup>4</sup> It was more cost-effective to offer a single, supervised low-dose challenge to 1.5 mg of peanut protein to exclude peanut-allergic children nonreactive to foods with precautionary allergen labeling.<sup>4</sup> Regarding a potential therapeutic approach with peanut, a study of 10 peanut-allergic children who had a mild reaction to a high dose of peanut in an OFC reported that they were able to achieve sustained unresponsiveness after being advised to regularly consume 1 peanut at home.<sup>5</sup> Such management strategies suggest a therapeutic benefit, although best practices in this area remain unclear, and such approaches are under study (eg, NCT 03907397).

This exploratory survey study has limitations. The primary limitation is a low response rate, which is consistent with other AAAAI workgroup surveys.<sup>6,7</sup> This may result in additional limitations such as responder bias (ie, those with an interest in food allergy may be more likely to participate and complete all items), and the possibility that the participants may have interpreted the still-emerging and largely undefined concepts differently. With exploratory and potentially niche concepts, these are accepted limitations in survey research, and this report does not intend to generalize these findings as representative of the AAAAI membership as a whole. This study was designed as a starting point to assess current practices and attitudes regarding high-threshold reactors and avoidance practices. Further work and

follow-up study are planned to help determine what may constitute practice variation and differences in attitudes regarding the evolution of thought if “strict” avoidance in food allergy is necessary, to help contribute to a knowledge base that can be used to establish best practices in this area.

There is a changing landscape in food allergy where multiple management paths can exist. These results within this sample are a potential sign that food allergy management is no longer exclusively about strict avoidance, and that more permissive and individualized practices may be evolving. Future studies need to evaluate the outcomes and preferences of permissive approaches, to help form an evidence base to establish guidance for tailored food allergy management strategies using individual threshold reactivity, where patients, families, and their allergists can engage in shared decision making to find a mutually acceptable approach.<sup>8</sup>

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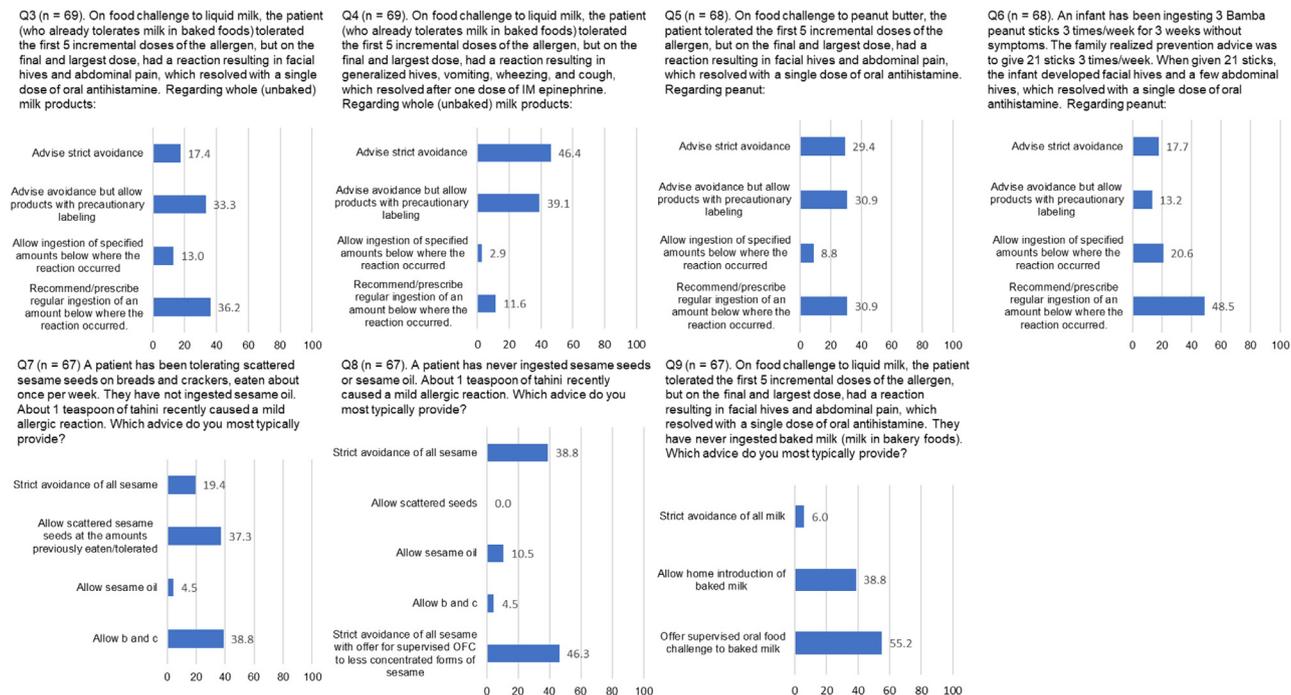


FIGURE E1. Percentage of survey participants who responded to each multiple-choice option for various clinical scenarios.

TABLE E1. Survey respondent and practice characteristics

Respondent and practice characteristics	Value
Country of practice	
United States	56 (87.5)
Canada	8 (12.5)
Type of practice	
Private	33 (51.6)
Academic	24 (37.5)
Other	7 (10.9)
Years in practice, median (range)	19 (2-51)
Food allergy patients per month, median (range)	30 (1-150)
OFC per month, median (range)	5 (0-65)
OFC per month for children younger than 5 y, median (range)	3 (1-90)
Percent of patients counseled to avoid PAL, median (range)	50 (0-100)
Oral immunotherapy	
Offered, to multiple foods	17 (26.6)
Offered, but only FDA-approved product	20 (31.3)
Not offered, but plans to start	13 (20.3)
Not offered with no plans to start	14 (21.9)

FDA, Food and Drug Administration; PAL, precautionary allergen labeling. Values are n (%) unless otherwise indicated.