

lifelong.⁵⁻⁷ Outcomes of allergic reactions to cow milk, egg, tree nut, seed, or any other number of allergens are likely to be nested within the estimates for peanut, making this a good “representative” item for the purposes of modeling.²⁻⁴ To enhance the generalizability of this model, very broad ranges of all variables were used in sensitivity analyses, which acts as a failsafe to ensure that any single point estimate/input is explored robustly to verify if a small or large shift in the value would change the analysis.²⁻⁴ Thus, based on the fact that the costs and outcomes for peanut allergy tend to incorporate outcomes likely experienced for other allergens, combined with very broad sensitivity around these inputs to deliberately ensure that the investigation is not narrow, peanut is an appropriate choice.²⁻⁴ No model can be perfect, but we feel that ours represents a highly plausible reality and has accounted for considerable uncertainty.²⁻⁴

The authors suggest that gastrointestinal symptoms are potentially pivotal in establishing anaphylaxis diagnosis, which is supported by both the National Institute of Allergy and Infectious Diseases and World Allergy Organization anaphylaxis criteria.^{5,7} However, this argument has no bearing on our model and findings regarding when a single- versus 2-device prescription would be most cost-effective.^{1,2} We applaud the authors on their advocacy for anaphylaxis education. Appropriate trigger avoidance, preparedness, and rapid treatment of anaphylaxis are cornerstones in prevention and management of severe allergic reactions.⁵⁻⁷ Education is not antagonistic to value-based care, and such a rigorous provision of education by the prescribing allergist is already nested within our model.²⁻⁷ We agree that the role of the allergist-immunologist is to provide individualized care in a patient-preference sensitive context. There certainly exist settings where providing multiple epinephrine devices for a patient at risk for anaphylaxis (but who has never experienced anaphylaxis) is appropriate.² Our message is that identification of low-value practices can be used as a navigation signal to invite shared decision-making into the clinical conversation to facilitate the right care to each patient in every setting.

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Aimmune Therapeutics, DBV Technologies, Nutricia, Kaleo Pharmaceutical, Nestle, and Monsanto; is a member of the scientific advisory council for the National Peanut Board; has received honorarium for lectures from Thermo Fisher, Before Brands, multiple state allergy societies, the American College of Allergy, Asthma & Immunology, and the European Academy of Allergy and Clinical Immunology; is an associate editor for the *Annals of Allergy, Asthma, and Immunology*; and is a member of the Joint Taskforce on Allergy Practice Parameters.

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REFERENCES

1. Cazes N, Briquet A. Food allergy: one more book rather than one less pen. *J Allergy Clin Immunol Pract* 2022;10:1670.
2. Shaker M, Turner PJ, Greenhawt M. A cost-effectiveness analysis of epinephrine autoinjector risk stratification for patients with food allergy-one epinephrine autoinjector or two? *J Allergy Clin Immunol Pract* 2021;9:2440-51.e3.
3. Shaker M, Greenhawt M. A primer on cost-effectiveness in the allergy clinic. *Ann Allergy Asthma Immunol* 2019;123:120-8.e1.
4. Shaker M, Greenhawt M. Providing cost-effective care for food allergy. *Ann Allergy Asthma Immunol* 2019;123:240-8.e1.
5. Shaker MS, Wallace DV, Golden DBK, Oppenheimer J, Bernstein JA, Campbell RL, et al. Anaphylaxis—a 2020 practice parameter update, systematic review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) analysis. *J Allergy Clin Immunol* 2020;145:1082-123.
6. Shaker M, Chalil JM, Tran O, Vlahiotis A, Shah H, King T, et al. Commercial claims costs related to health care resource use associated with a diagnosis of peanut allergy. *Ann Allergy Asthma Immunol* 2020;124:357, 65.e1.
7. Cardona V, Ansoategui JJ, Ebisawa M, El-Gamal Y, Fernandez Rivas M, Fineman S, et al. World allergy organization anaphylaxis guidance 2020. *World Allergy Organ J* 2020;13:100472.

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Experience monitoring adverse events in a commercial early allergen introduction product



To the Editor:

We thank Cox et al¹ for their report of 12 infants who developed food allergies despite use of a range of commercial early allergen introduction products. Allergic reactions occurred either on first introduction of the product, or at a later stage when exposed to the natural food and/or the commercial product. We acknowledge the value of these data to help better understand the growing category of early introduction products.

Commercially prepared multiallergen introduction products contain intact proteins from multiple food groups.² It is therefore expected that some infants with pre-existing, but not yet manifest, food allergies may react to a product at the time of first introduction. Food-allergic reactions that occur at a later stage despite using a multiallergen product for some time are more difficult to assess. We agree with the authors that there is a need to study the efficacy of individual allergen introduction products, acknowledging the varying allergen composition and protein integrity in this category.

Because of the rising incidence of food allergies, many parents have become hesitant to introduce food allergens into the diet of their young infants that may contribute to an increased risk of food allergies.³ To guide parents in this context, the child's pediatrician should have a conversation about the potential risks and

benefits of early allergen feeding, including the role of allergen introduction products.⁴ Data show that most food-allergic reactions in infants manifest as gastrointestinal or dermatologic symptoms, consistent with the report by Cox et al.⁵

As referenced by the authors, the acceptability and tolerability of our multiallergen introduction product has been demonstrated in a low-risk population and use in a population at higher risk (ie, eczema and/or family history of allergies) remains of interest.⁶ We therefore initiated the “Infancy to Toddlerhood: Early Nutrition & Tolerance” (INTENT) Study (<https://clinicaltrials.gov/ct2/show/NCT04803981>). The INTENT Study aims to recruit over 1500 infants aged 4 to 6 months, including approximately 30% of participants with eczema. Infants are randomized 1:1 to daily use of SpoonfulONE or a control intervention. Primary and secondary outcomes are parent-reported tolerance to 5 common food allergens at 18 and 12 months’ follow-up, respectively. Clinical and demographic details will be prospectively collected. Parents and caregivers are asked to complete regular diaries on feeding and diet diversity, as well as any adverse reactions and product compliance. The INTENT study will help to better define the benefits and potential risks associated with SpoonfulONE, both for infants at normal and increased risk of food allergy.

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REFERENCES

1. Cox AL, Shah A, Groetch M, Sicherer SH. Allergic reactions in infants using commercial early allergen introduction products. *J Allergy Clin Immunol Pract* 2021;9:3517-35120.e1.
2. Weihe O, Cornyn C, Shewchuk G. Concerns about the approach of measuring allergens in early introduction foods for prevention of food allergy. *J Allergy Clin Immunol Pract* 2021;9:2944-5.
3. Gupta R, Jiang J, Iyer A, Hultquist H, Cohn R, Ibrahim K, et al. Pediatric clinicians’ knowledge of infant peanut introduction guidelines following iREACH training modules. *J Allergy Clin Immunol* 2022;149:AB38.
4. Schroer B, Groetch M, Mack DP, Venter C. Practical challenges and considerations for early introduction of potential food allergens for prevention of food allergy. *J Allergy Clin Immunol Pract* 2021;9:44-56.e1.
5. Samady W, Trainor J, Smith B, Gupta R. Food-induced anaphylaxis in infants and children. *Ann Allergy Asthma Immunol* 2018;121:360-5.
6. Holl JL, Bilaver LA, Finn DJ, Savio K. A randomized trial of the acceptability of a daily multi-allergen food supplement for infants. *Pediatr Allergy Immunol* 2020;31:418-20.

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