

Rostrum

International Peanut Allergy Prevention, 6 Years After the Learning Early About Peanut Study

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Six years ago, the Learning Early About Peanut (LEAP) trial findings helped fundamentally shift the paradigm of peanut allergy prevention. Although the results of LEAP are well accepted, policy-makers, caregivers, and clinicians struggle with how best to implement and apply the study's key findings in clinical practice. Differences in guidelines highlight issues related to peanut allergy prevention implementation, including caregiver acceptability, cost, fidelity, feasibility, appropriateness, and adoption. The goals of this rostrum are to review how the LEAP study has informed international peanut allergy prevention policy, as well as to review the strengths and ongoing controversies in peanut allergy prevention implementation. © 2021 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2021;■:■-■)

Key words: LEAP study; Early introduction; Peanut allergy prevention; Eczema; Screening; Allergy testing; Cost-effectiveness; Implementation; Preference-sensitive care; Shared decision-making

INTRODUCTION

Six years ago, the Learning Early About Peanut (LEAP) trial findings helped fundamentally shift the paradigm of peanut allergy prevention.¹ The LEAP study was the first randomized controlled trial to demonstrate that food allergy could be prevented with early versus delayed introduction in high-risk infants (owing to severe eczema and/or egg allergy), showing benefit

from deliberate, active early introduction in a carefully screened population.

Before LEAP, observational studies had noted a lack of protective effect with delayed ingestion of peanut (and other allergens) in large samples of general and high-risk infant populations.² However, although 2008, 2013, and 2014 guidelines denoted no benefit from delayed introduction, none specifically recommended deliberate early introduction, because no published prospective trials established efficacy of such a concept. Since LEAP, a concerted effort has been made to “inform the decision-making process for health care providers regarding ... benefits of early peanut introduction.”³ It has been suggested that the LEAP study will result in “a very real possibility that new generations of infants born in countries with high food allergy prevalence ... will have less food allergy than the generation before.”⁴ Although it may be too early to note such an effect, multiple international guidelines published over the past few years have adopted support of this early introduction message and have evolved to recommend early ingestion of peanut (and egg in some countries) more actively as a means of food allergy prevention.⁵⁻⁹

Although the results of LEAP with respect to the benefits of early peanut introduction (compared with delayed peanut introduction) are well-accepted, policy-makers, caregivers, and clinicians struggle with how best to implement and apply the study's key findings in clinical practice.¹⁰ There are uncertainties regarding the degree to which changes in prevention policy have translated into changes in infant feeding patterns. The goals of this article are to review how the LEAP study has informed international peanut allergy prevention policy and to review the

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for the *Annals of Allergy, Asthma, and Immunology*, and is member of the Joint Taskforce on Allergy Practice Parameters. He has received honorarium for lectures from ImSci and MedLearningGroup. D.P. Mack is a member of the Board of Directors for the Canadian Society of Allergy and Clinical Immunology and serves on the Editorial Board of the *Journal of Food Allergy*. He has provided consultation and speaker services for Pfizer, Aimmune, Merck, Covis, and Padiapharm and has been part of an advisory board for Pfizer and Bausch Health. Received for publication October 6, 2020; revised May 26, 2021; accepted for publication July 2, 2021.

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Abbreviations used

ASCIA- Australasian Society of Clinical Immunology and Allergy

BSACI- British Society of Allergy and Clinical Immunology

EAT- Enquiring About Tolerance study

LEAP- Learning Early About Peanut

NIAID- National Institute of Allergy and Infectious Diseases

strengths and ongoing controversies in peanut allergy prevention implementation.

GUIDELINE RECOMMENDATIONS FOR PEANUT ALLERGY PREVENTION

Immediately after the LEAP study results, 10 international medical professional organizations created an interim consensus communication to translate the LEAP findings into policy, noting level 1 evidence that peanut-containing products should be introduced into the diets of high-risk infants at 4 to 11 months of age in countries where peanut allergy is prevalent, and supported consideration for preemptive evaluation before peanut introduction in infants at high risk based on LEAP screening criteria.³ This consensus communication was followed by more formal guidelines by the Australasian Society of Clinical Immunology and Allergy (ASCIA), the British Society of Allergy and Clinical Immunology (BSACI), and in the United States, the National Institute of Allergy and Infectious Diseases (NIAID) 2017 addendum guidelines.⁹ The NIAID addendum guidelines recommend introducing peanut into the diet of high-risk infants (with severe eczema and/or egg allergy) as early as age 4 to 6 months, and strongly recommend the step of preemptively screening for evidence of peanut sensitization by skin testing before ingestion in select populations, with in-office introduction for infants with positive skin tests, and restricting introduction if the test result wheal size is 8 mm or greater.⁹ In infants of lesser or no risk, no screening was recommended, and peanut introduction was recommended to begin at around 6 months in lower-risk infants, or in accordance with the values and preferences of the family. This guidance was endorsed by the three major North American allergy societies, the American Academy of Pediatrics, and several other medical societies.

However, other countries have adopted divergent approaches to the NIAID guidelines (Figure 1). The ASCIA recommends early introduction of all foods in the first year of life ("around 6 months, but not before 4 months") for all infants regardless of risk factors, without skin test screening or restriction.⁵ The United Kingdom through the BSACI adopted similar guidelines to ASCIA, limited to peanut and hen's egg introduction along the same time line without screening, although that wording denotes that some families "may wish" to have infants assessed before early introduction, reflecting a statement of preferences and values.⁶ Although Canada initially supported the NIAID guidelines, the Canadian Pediatric Society subsequently adopted guidelines closely mirroring ASCIA guidelines.⁷ Similarly, recently published guidance approved by the three major North American allergy societies emphasized early introduction without requiring screening, as did the updated European Academy of Allergy and Clinical Immunology 2021 guidelines.¹¹ The EAACI guideline emphasizes early peanut introduction in populations with a high prevalence of peanut allergy.

The differences between guidelines and guidances highlight larger issues related to food allergy prevention policy development and implementation. As noted in a recent review of peanut allergy prevention, whereas "there is now high-quality evidence that peanut allergy may be prevented by consumption of peanut protein in infancy ... the translation of this evidence into clinical practice is garnering significant debate."¹² Effective interventions are only as good as the extent to which they are adopted by clinicians who choose to deliver the intervention and how well they complete that task, by eligible populations willing and able to receive the intervention, and by public health approaches to sustain the intervention. The remainder of this article focuses on implementation outcomes such as acceptability, cost, fidelity, appropriateness, and adoption (Table 1) as they pertain to the knowns and unknowns of implementing peanut allergy prevention within the context of differing international policy.

ACCEPTABILITY

Acceptability is the sense among stakeholders that an intervention is agreeable.¹³ Although early peanut introduction has been shown to be effective, the data thus far are mixed regarding acceptability of early peanut introduction on the part of caregivers.

Greenhawt et al¹⁴ reported results of a nationally representative US survey of expectant caregivers and caregivers of infants aged less than 12 months (at the time of the launch of the NIAID guidelines), noting poor willingness for early allergenic solid food ingestion and little concern for infant development of food allergy.¹⁴ Among the primarily female sample of 2000 caregivers, or expectant caregivers, only 31% were willing to introduce peanut before or at age 6 months, whereas 40% were willing to introduce it after age 11 months. The Enquiring About Tolerance (EAT) study, a randomized controlled trial of early (3 months) versus standard (6 months) introduction of six common allergens including peanut into the diets of general population infants demonstrated very low adherence with the study protocol (only 42.8% compliance overall).¹⁵ In contrast, the population-based cross-sectional study HealthNuts in Australia found that compared with participants recruited in 2007 to 2009, those recruited in 2009 to 2011 (with a change in Australian guidance) were more likely to introduce solids at age 4 months (adjusted multinomial odds ratio = 1.21; 95% confidence interval [CI], 1.02-1.45) and less likely to introduce peanut after 12 months (adjusted multinomial odds ratio = 0.70; 95% CI, 0.49-0.98).¹⁶ Both the EAT study and HealthNuts examined factors associated with poor caregiver acceptability of early introduction, including lower socioeconomic status,¹⁶ family history of atopy,¹⁶ parent-reported food symptoms, and feeding difficulties.¹⁷

Available data suggest that even when effective, allergen ingestion early in life may be difficult to implement among certain subsets of caregivers.^{14,15} Qualitative data are lacking to explore barriers and facilitators to early introduction, and further studies are necessary, although a theme that has emerged is concern regarding a severe reaction in infancy.¹² A nationwide US survey of allergists and immunologists noted that both parental (47.6%) and clinician (21.8%) concern for allergic reactions in infancy poses a barrier to implementing early peanut ingestion.¹⁸ Similarly, fears about the process of early introduction were mentioned in a survey of New York pediatricians and parents.¹⁹ However, parents identified that written materials and

NIAID (USA)	Australia and New Zealand	Canada	United Kingdom
• Addendum 1: infants with severe eczema, egg allergy or both should have introduction of age-appropriate peanut-containing food as early as 4 to 6 months of age to reduce the risk of peanut allergy. ... The expert panel recommends that evaluation with peanut-specific IgE (peanut sIgE) measurement, SPTs, or both be strongly considered before introduction of peanut to determine if peanut should be introduced and, if so, the preferred method of introduction. • Addendum 2: infants with mild to moderate eczema should have introduction of age-appropriate peanut-containing food around 6 months of age, in accordance with family preferences and cultural practices, to reduce the risk of peanut allergy. • Addendum 3: infants without eczema or any food allergy have age-appropriate peanut-containing foods freely introduced in the diet, together with other solid foods, and in accordance with family preferences and cultural practices.	• When your infant is ready, at around 6 months, but not before 4 months, start to introduce a variety of solid foods, starting with iron-rich foods, while continuing breast-feeding. • All infants should be given allergenic solid foods including peanut butter, cooked egg, dairy, and wheat products in the first year of life. This includes infants at high risk of allergy. • Hydrolyzed (partially or extensively) infant formula is not recommended for the prevention of allergic disease. • No specific screening, testing, evaluation recommendations prior to introduction	• Infants considered to be at high risk for allergic disease have either a personal history of atopy or a first-degree relative with atopy. • For high-risk infants, and based on developmental readiness, consider introducing common allergenic solids at around 6 months of age, but not before an infant is 4 months of age. • For infants at no or low risk for food allergy, introducing complementary foods at about 6 months is recommended. • Breastfeeding should be protected, promoted and supported for up to 2 years and beyond. • Allergenic foods should be introduced one at a time, to gauge reaction, without unnecessary delay between each new food. • If an infant appears to be tolerating a common allergenic food, advise parents to offer it a few times a week to maintain tolerance. If an adverse reaction is observed, advise parents to consult with a primary care provider about next steps.	• Exclusive breastfeeding for around the first six months of life. • Foods containing peanut and hen's egg need not be differentiated from other complementary foods and should be introduced in an age-appropriate form from around six months of age, alongside continued breastfeeding, at a time and in a manner to suit both the family and individual child. • The deliberate exclusion of peanut or hen's egg beyond six to twelve months of age may increase the risk of allergy • Once introduced, and where tolerated, these foods should be part of the infant's usual diet, to suit both the individual child and family. • Families of infants with a history of early-onset eczema or suspected food allergy may wish to seek medical advice before introducing these foods.

FIGURE 1. Comparison of formally endorsed guidance regarding early allergenic solid food introduction in the United States, Australia and New Zealand, Canada, and the United Kingdom. *NIAID*, National Institute of Allergy and Infectious Diseases; *SPT*, skin prick test.

physician advice would help overcome this barrier. Evidence to date suggests that a risk for a severe reaction in infancy upon first ingestion of peanut is exceptionally low, even among infants considered at risk.²⁰ Knowledge translation about true risk may improve acceptability of early ingestion moving forward.

COST

Cost is defined as the economic impact of implementing recommendations.¹³ To date, two studies have been conducted in the United States after publication of the NIAID policy.^{21,22} Cost-effectiveness data have shown that a non-screening strategy is preferred to screening or delayed introduction in terms of total societal costs, quality-adjusted life-years, and number of peanut allergy cases prevented.^{21,22} With screening, both a low ambient peanut allergy prevalence and the poor specificity of skin prick test (SPT) as a screening test create a setup for case misclassification, costing about \$650,000,000 more versus not screening over a 20-year model horizon.²¹ Ironically, more automobile fatalities are expected to occur resulting from travel for pre-introduction screening appointments than anaphylaxis fatalities from first peanut introduction at home in unscreened infants, an important perspective to maintain in determining acceptable risk trade-offs.^{21,22} Additional cost-effectiveness analysis of the NIAID policy has revealed that unless infants at very high risk for peanut allergy have parents with a very high health disutility equivalent to being willing to trade 76 to 148 days of life in a year for supervised first peanut consumption (and avoiding at-home introduction), the NIAID policy is not cost-effective.²² Although LEAP used peanut SPT screening cutoffs to restrict enrolling infants presumptively considered already allergic, pre-emptive SPT was not a study variable and LEAP did not actually demonstrate that enrollment screening criteria were necessary or

effective at preventing peanut allergy, but rather that the early introduction of peanuts in this screened population was effective. This is a subtle but meaningful difference based on this a priori decision, which was not formally evaluated in either LEAP or EAT, but which has had a significant influence on policy in multiple countries. Some clinicians and researchers may harbor concern regarding the safety of applying early introduction without prescreening. Indeed, high certainty evidence to inform this practice is lacking. However, observational data from Australia and Israel have shown the safety and benefit of early ingestion of cow's milk, egg, and peanut on a population level without screening as a preventative strategy, and this has proceeded despite a lack of high certainty evidence.^{2,23,24}

FIDELITY

Fidelity refers to the degree with which early peanut introduction is implemented: whether early peanut introduction is delivered as intended.¹³ This remains to be studied in depth, although data suggest that some recommendations such as pre-emptive screening may have unintended consequences hindering the true goal of policy change: to reduce the burden of peanut allergy.^{21,22,25}

The screening recommendation attempts to prevent index peanut reactions in children presumed to have preexisting, undiagnosed peanut allergy. However, allergy tests are inconsistent screening instruments and are poorly specific compared with peanut ingestion at establishing a diagnosis, and the NIAID recommendations accept some trade-off in overdiagnosis to prevent (or delay) potentially severe reactions in highly sensitized infants.²⁵ Paradoxically, this population is precisely the group that the LEAP study suggests would benefit most from early peanut introduction, if not yet truly allergic.²⁶ Allen and

TABLE 1. Implementation outcomes and definitions

Implementation outcome	Definition
Acceptability	Sense among stakeholders that an intervention is agreeable
Cost	Cost impact of implementing an intervention
Fidelity	Degree to which the intervention is implemented as intended
Feasibility	Degree to which an intervention can be carried out in a particular setting
Appropriateness	Fit or relevance of an intervention among a particular group or setting
Adoption	Intention or employment of an intervention (uptake)

Based on Proctor et al.¹³

Koplin²⁷ stated that “although the quality of design and excellence in study execution is unquestioned, the particular difficulty this study raises is how to generalize results from a trial of high-risk infants, which screened infants for the presence of peanut allergy prior to peanut introduction, to the general population.” They raised concern that with current resources, screening infants with eczema risks delay in service and may inadvertently cause peanut allergy if the window is missed for screening and/or oral food challenges.²⁷ Allen and Koplin further noted that “those at highest risk delay introduction of allergenic foods, thus the window of opportunity for intervention with early peanut introduction might be missed.”²⁷ A final fidelity concern is the risk for a “screening creep,” in which “parental pressures and perhaps physician over-cautiousness”²⁸ result in extension of testing to foods other than peanut or infants with lesser risk, neither of which is supported by any guideline. One new study suggests that Ara h 2 could be a superior screening test to skin testing and may further reduce false-positive results, although this contradicts the LEAP team data, which suggested that skin testing was the better screening assessment.²⁹

Furthermore, the urgency of when early food introduction should occur remains uncertain, and there may be limitations to an approach focused on achieving this within a narrow time window in early infancy. A wider time frame for allergen introduction, as recommended by ASCIA and BSACI (within the first year of life, closely approximating the 4- to 11-month window of the LEAP study itself), may maintain fidelity with the intended prevention outcome while providing a less medicalized approach. A secondary analysis of the LEAP study dataset suggested that whereas the overall probability for peanut tolerance was high through the study frame, when comparing the subset that was introduced to peanut at 4 and 5 months versus 6 to 11 months, the probability of tolerance was higher and the CI was narrower in the later age bracket, although controversy exists regarding how these data are best interpreted.³⁰ These findings could relate to issues of sample size by age strata, but evidence does not clearly or conclusively indicate that introduction before 6 months is critical compared with introduction before 12 months of life, although earlier introduction would certainly be encouraged if feasible. However, for some families, the more gradual introduction time of 4 to 11 months may provide needed time to address familial hesitancy, acclimate caregivers to early introduction, and be comfortable with the child being ready, and it would deemphasize the concept of a narrow window closing.

FEASIBILITY

Feasibility is defined as the degree to which an intervention can be carried out in a particular setting.¹³ To date, only one study has examined the feasibility of preemptive screening at a populational level, performed retrospectively in the HealthNuts cohort, applying the high-risk screening criteria before peanut introduction.³¹ Among the Health Nuts cohort of 5,276 infants, the researchers mentioned that having to screen all infants with early-onset eczema and/or egg allergy required testing up to 16% of the population, missed 23% of peanut allergy cases, and required 29% of infants screened to require clinical follow-up because of positive testing. The authors concluded that “a population program aiming to identify and screen all infants at risk of peanut allergy would pose major logistic challenges that need to be carefully considered.” A recent cost-effectiveness analysis regarding optimizing the NIAID guidelines cited the same number of missed cases from screening in a simulation.²¹ Further feasibility studies are needed regarding prevention approaches.

APPROPRIATENESS

Appropriateness is the fit or relevance of an intervention, such as early peanut ingestion, among a particular target group, such as those at high risk.¹³ Prior international guidance was conflicting regarding whether only high-risk or any infant should have early peanut introduction (although it is clear that introduction should not be delayed in any infant). It was argued that risk factors suggested to date, such as those with atopy or an immediate family history of atopy, are insufficient or unnecessary for the development of peanut allergy.³² Early peanut introduction is effective (although less so) in standard-risk populations as well, and the earliest study to suggest an association between early peanut ingestion and a reduction of peanut allergy was among general population infants.² Although these data have been limited to selected populations, the low prevalence of peanut allergy in some populations may be multifactorial, in which early introduction likely had the most prominent role. Further research among broader populations is a reasonable consideration, although how to design such research may be challenging because it would be ethically difficult to perform a placebo-controlled trial or randomize a group to delayed introduction given evidence that this strategy could be harmful. No study to date has shown early peanut ingestion to be detrimental to infants, irrespective of risk (although few studies have explored this topic), and the issue is more about quantifying the benefit that may be seen in all populations where such policy exists. Limiting early peanut ingestion to high-risk infants is a highly selective policy that will produce smaller benefit than a universal promotive approach (early peanut ingestion irrespective of risk), less poised to miss anyone if risk factors are too narrowly defined.^{32,33}

ADOPTION

Adoption refers to the intention or employment of an intervention such as early peanut introduction, otherwise known as uptake.¹³ Changes in national policy have to be translated and applied to a societal perspective. There are major differences to date in the adoption of early introduction guidance between the United States and other countries such as Australia and New Zealand. A 2017 survey of pediatricians in the United States showed that only 11% of pediatricians were compliant with

TABLE II. Arguments for and against screening infants before peanut introduction

For	Against
Screening is recommended by the 2017 Addendum guidelines for the prevention of peanut allergy in the US Report of the National Institute of Allergy and Infectious Diseases—sponsored expert panel.	Screening is inconsistent with all other international guidelines regarding early allergen introduction. No data indicate that screening is necessary for safe and effective early allergen introduction.
Screening may prevent or delay index reactions in some infants who are already peanut-allergic before introduction.	Testing used to screen infants has poor specificity and it risks misclassifying some tolerant infants as allergic. Life-threatening reactions upon first ingestion of peanut in infancy are rare. Paradoxically, screening can result in allergic reactions in infants owing to delay in introduction.
Screening may encourage some hesitant parents to allow introduction.	False-positive testing may lead to significant delays in introduction, which may result in a missed window of opportunity to establish tolerance.
Some clinicians are more comfortable with a screening approach because of previous practice.	False-negative testing will miss peanut-allergic individuals, and reactions may occur despite negative testing.
Screening prioritizes some infants who need to be seen promptly by the clinician.	Limited testing and oral food challenges create disparities in access.
	Rapid clinic introduction of larger amounts of peanut (vs slow, gradual home introduction) may make a severe reaction more likely.
	There are significant costs and more limited benefits associated with screening when considered in the context of introduction over a lifetime.
	There are long-term increases in rates of peanut allergy owing to delays in peanut introduction and false-positive tests.
	Screening criteria miss a significant proportion of infants who develop peanut allergy.
	Partial implementation of guidelines leads to testing for sensitization but without confirmation of allergy in many infants.
	Screening creep leads to additional harm by testing infants who do not meet screening criteria.

NIAID guidelines on early peanut introduction.³⁴ A 2018 survey of 1781 US pediatricians found that of those who had knowledge of NIAID guidelines, only 28.9% (95% CI, 26.8% to 31.1%) reported full adoption of them, whereas 64.3% (95% CI, 62.0% to 66.6%) reported partial implementation.³⁵ A 2018 US survey of 53 family medicine, pediatrics, and internal medicine pediatric residents found that whereas 73% reported being familiar with current early introduction guidelines, about 73% chose answers that represented the 2000 American Academy of Pediatrics recommendation to delay allergen introduction including peanut.³⁶ The recent survey of pediatricians revealed that only 28.9% were fully implementing guidelines (compared with only 64.5% of board certified allergists), and a recent case series from a large academic food allergy referral center documented poor compliance with guidelines.^{18,35,37} A survey of Canadian pediatricians, family physicians, and allergists found that although most allergists (58.6%) were recommending introduction of peanut at 4 to 6 months for high-risk infants, the majority of non-allergists were recommending introduction at 6 months to a year.³⁸ In contrast, data from the EarlyNuts cohort noted that by 2018, 88.6% of all Australian infants had introduced peanut by age 1, a greater than threefold increase from 10 years before, in just 2 years since the new guidelines.³⁹

The reasons for the discrepancy in adoption require further study and likely require targeted interventions to help improve adoption to early peanut introduction. It will be interesting to see the quasi-study ongoing in Canada, studying the difference in their adoption rate as they move from the NIAID guidelines toward the Canadian Pediatric Society ones. It has been said that adoption of early peanut introduction guidelines takes a village.⁴⁰ Factors that may be limiting adoption include practice variables

(such as the volume of food-allergic children seen),³⁴ lack of education regarding new guidelines, ongoing follow-up by an allergist, and perceived need for further training.^{18,35,36} Pre-emptive screening as recommended by the NIAID guideline has also presented some barriers to adoption in the United States and Canada, including its impact on clinician time and space, and a lack of comfort performing oral food challenges in infants.^{35,41} A recent survey of Canadian allergists reported that only 42.1% of allergists routinely perform infant oral food challenges (OFCs), and only 11.1% could perform an OFC on the same day as testing.⁴¹ A US survey of 670 practicing allergists showed poor willingness to offer OFCs for early peanut introduction and worsening of perceived barriers associated with OFCs over time.⁴² In the setting of medicalized infant food introduction, comprehensive resource reallocation is needed to improve timely patient and family access to allergy evaluation and OFCs for young infants.^{14,41} If policy expects that allergists are available, willing, and comfortable to provide infant OFCs for peanut, attitudes must change, skills must evolve, and resources must be allocated; or, perhaps the policy needs to adapt to what allergists are willing and able to do.⁴¹

CONTRASTING VIEWPOINTS

Adoption and implementation of early peanut introduction to prevent peanut allergy have been influenced by some who advocate for doing so in a manner closely aligned and replicating the LEAP trial approach. Specifically, some have advocated for screening in certain populations, for skin test cutoffs requiring further evaluation with in-office introduction or exclusion from the intervention (eg, when the skin test wheal size is above a level at which peanut is

strongly recommended not to be introduced owing to the belief that this degree of sensitization infers too high a likelihood of preexisting peanut allergy), for minimum dosing of 6 g peanut protein weekly, as well as for a concerted effort in high-risk infants (eg, eczema and/or egg allergy) to introduce peanut between age 4 and 6 months and not delay past this age. However, few international guidelines have stipulated minimum quantity and frequency of peanut ingestion (given the lack of randomized, controlled dose ranging studies), although some have advocated maintaining the 6-g/wk LEAP regimen as a reasonable target in the absence of any other data, and only the NIAID has recommended the screening approach.^{9,11} The obvious practical challenge of a high, fixed dose occurs when extrapolation to other allergenic foods results in a dietary monopoly of allergenic foods to the exclusion of other complementary foods. Similarly, most guidelines agree on the target age of 4 to 6 months to start peanut introduction, although no guideline specifically cautions that introduction after 6 months runs the risk of poorer outcomes as long as the introduction is accomplished in the first year of life. Although data from real-world experiences to date do not support a robust risk for anaphylaxis upon initial peanut ingestion,³⁹ this is not well-studied, and it is possible that unreported cases have occurred or that future cases may occur. Food allergy fatality at any age remains statistically rare,^{43,44} but some allergists are concerned that this is a risk waiting to happen in this age group, in particular with home introduction of an allergen such as peanut. Two studies suggested that there is a higher probability for an initial reaction in infants with a skin test wheal greater than 4 mm, which was part of the rationale for the LEAP study screening criteria, although this has not been consistently shown even within the same population at different time points.⁴⁵⁻⁴⁷ For these reasons, some experts have advocated using screening as a safeguard against these potential outcomes, and practically, some allergists may feel more comfortable with such an approach.

However, medicine rarely has firmly black-and-white areas of correctness and incorrectness. Decisions are largely contextual based on where in the world one practices, the population in question, the resources available to execute particular decisions in these settings, and the values and preferences of individual families and patients. Thus, although multiple societies share a strong recommendation to introduce peanut early (based on robust data), no such strong recommendation exists regarding how best to implement this. Implementation is preference-sensitive and dependent on the values and ideals of the individual making the decision, because there are no randomized, controlled studies regarding optimal implementation of key facets such as dose and frequency, the necessity and value of screening, and the optimal age between 4 and 11 months for introduction. Interestingly, all approaches but the NIAID guidelines offer a truly preference-sensitive care paradigm. Although the international experience of peanut introduction argues for a less medicalized approach (particularly in Australia),³⁹ some argue that it is still too early in the implementation phase to determine whether more rigid and conservative approaches are responsible for lower rates of early peanut introduction in the United States.³⁵ Still, more fluid and flexible approaches to peanut introduction that emphasize patient-centered decision-making may lead to better clinical outcomes.⁴⁸ Table II details some key considerations both for and against screening prior to early peanut introduction.

CONCLUSION

The past 6 years have witnessed remarkable change regarding food allergy prevention, from the publication of landmark clinical trials to multiple countries translating this into policy. However, work is still needed to support full dissemination and implementation of the policy, including establishing critical outcomes frameworks to help with the knowledge translation process. More research into caregiver and clinician acceptability and tolerability of interventions is needed to inform future policy. An intervention's effectiveness entirely depends on the degree to which it is adopted by health care providers, received and accepted by families, and sustained as a best practice.

Although the LEAP study was a large impetus to policy change, pragmatic data related to the implementation outcomes of such change, including acceptability and feasibility of new guidance, were unavailable to inform how to translate these findings into populational policy. Randomized studies provide a high degree of internal validity and minimize confounding, but they provide little data about the external validity of such approaches or any practical information about population implementation. Learning Early About Peanut is no different in that respect. A medical guideline has no impact on a population when it cannot or will not be implemented by the critical stakeholders involved, and evidence to support population-based screening practice is at best of very low certainty. Variables such as acceptability, tolerability, sustainability, equity, and feasibility must be considered when drafting policy. Because early peanut introduction is a time-sensitive intervention to prevent peanut allergy (eg, within the 4- to 11-month-of-life window noted in the LEAP study), prescriptive policy may present a barrier to timely and effective implementation. Difficulties in achieving timely peanut introduction may result from screening implementation barriers that inadvertently cause more harm than benefit. A patient-sensitive care paradigm focused on shared decision-making might vastly improve implementation, as has recently been advocated by the American Academy of Allergy, Asthma and Immunology, American College of Allergy, Asthma and Immunology, and Canadian Society of Allergy and Clinical Immunology.⁴⁸

Evolving policy explicitly acknowledges both certainty of evidence and strength of recommendations that distinguish between the necessity of screening evaluation versus simple food introduction.⁴⁸ A more fluid approach adopted by countries outside the United States that share similar nonmedicalized food introduction policies, and which was recently endorsed by the US and Canadian allergy societies, offers a realistic step forward to allow both more progressive and conservative management paths for early introduction without excluding either approach.⁴⁸

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