



Update on Early Introduction of Peanut to Prevent Allergy Development: Challenges with Implementation

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Abstract

Purpose of Review This review summarizes the evidence leading towards the development of new guidelines that recommend early introduction of peanut to prevent the development of peanut allergy. It also reviews the current understanding of challenges faced with implementation of these recommendations on a widespread basis.

Recent Findings Prior recommendations to avoid feeding allergenic foods to infants have been updated and reversed. This paradigm shift in advice has created an opportunity on a population level to try and halt the recent increase in prevalence of peanut allergy. However, challenges with implementation of these new guidelines exist in many areas.

Summary While evidence supports the early introduction of peanut to prevent allergy development, the application and challenges faced with these recommendations are not fully understood. Persistent efforts from pediatricians and allergists, as well as acceptance from parents, will be necessary in order to make a significant impact on the prevalence of peanut allergy.

Keywords Peanut allergy · Early introduction · Prevention · Food allergy · Infant feeding · Quality improvement

Abbreviations

EAT	enquiring about tolerance
IgE	immunoglobulin E
LEAP	learning early about peanut
NIAID	National Institute of Allergy and Infectious Disease
OFC	oral food challenge
PDSA	Plan Do Study Act
QI	quality improvement
SPT	skin prick test
UK	United Kingdom
US	United States

Introduction

Food allergies affect approximately 8% of children in the United States (US) and data from the US Centers for Disease Control and Prevention have demonstrated an

increase in prevalence from 3.4 to 5.1% between 1997 and 2011 [1, 2]. Peanut allergy affects 2–3% of children in Westernized countries and is the leading cause of food-related anaphylaxis [1]. Unlike milk or egg allergy, which often resolves with age, only approximately 20% of peanut allergic individuals develop tolerance, leading to a lifelong need for avoidance [3]. Furthermore, a diagnosis of peanut allergy is associated with significantly decreased quality of life for both patients and their families [4, 5]. Recent evidence and guidelines have demonstrated a pathway towards preventing peanut allergy development through early introduction and maintenance in the diet. Despite the best intentions of researchers, physicians, and professional societies, there are many challenges that may prevent widespread implementation of this advice. This review article will discuss the history surrounding these new recommendations and barriers towards implementation.

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Background

Until recently, clinical practice guidelines recommended delaying the introduction of peanut and other allergenic foods to infants at risk for developing allergy until 3 years of age [6]. In 2008, several observational studies presented evidence

contradicting these guidelines, but no specific active recommendations on the appropriate timing to introduce highly allergenic foods were established [7]. One of the earliest thought provoking studies published by Du Toit et al. during this time found that Ashkenazi Jewish children living in London, England, had a 10-fold higher prevalence of peanut allergy compared with Ashkenazi Jewish children living in Israel [8]. This was a striking observation as the notable primary difference between the two groups was the timing of peanut introduction. Israeli families almost universally introduced peanut in the first year of life whereas English families delayed introduction until children were closer to 2 or 3 years of age. While this observation could not imply causality, it was the basis for the Learning Early About Peanut Allergy (LEAP) randomized controlled trial. The LEAP trial was designed to test the hypothesis that early introduction and frequent ingestion of peanut was associated with a decreased incidence of peanut allergy in infants at risk for developing the disease [9]. In this landmark study, 640 infants with either severe eczema, egg allergy, or both were randomized to either introduce peanut between 4 and 11 months of age or continue strict avoidance until 5 years of age, at which time blinded peanut oral food challenges (OFC) were performed to determine the prevalence of peanut allergy within each group. In order to risk-stratify children at the beginning of the study, participants had skin prick tests (SPT) placed and any child with a peanut wheal diameter of 0–4 mm was included. Remarkably, children who introduced peanut between 4 and 11 months of age had a relative risk reduction in the development of peanut allergy of approximately 80% (3.2% vs. 17.2%, $p < .001$), providing the first level 1 evidence that early introduction of peanut can dramatically reduce the risk of developing peanut allergy.

Although the LEAP trial examined a specific population of children living within the United Kingdom (UK), the large number of children included in the study along with the size of the observed effect led to the publication of a consensus statement by several national and international allergy academies. The initial consensus recommended that infants at high risk for peanut allergy (as defined by the LEAP criteria) should be introduced to peanut early in life [10]. Subsequently, the National Institute of Allergy and Infectious Disease (NIAID) in the US as well as health authorities from several other countries have updated their guidelines for the prevention of peanut allergy, all encouraging early introduction into the diet [11, 12, 13, 14].

Only one other randomized prospective interventional study has subsequently examined the effect of early peanut introduction during infancy. The Enquiring About Tolerance (EAT) study enrolled 1303 exclusively breastfed UK infants to either introduce 6 different highly allergenic foods (including peanut) at 3 months of age or continue to exclusively

breast feed until 6 months of age, at which time foods could be introduced according to parental preference [15]. Although the study did not find a statistically significant difference in the prevalence of peanut allergy at 3 years of age between the early introduction group and the standard introduction group in an intention to treat analysis, there are some important differences between the EAT and LEAP studies to consider. First, while the LEAP study included infants that were at high risk of developing peanut allergy, the EAT study enrolled infants from the general population with no predefined risk criteria. Another important difference between the EAT and LEAP studies is the age of peanut introduction in the delayed introduction groups. In the EAT study, infants in the standard introduction group were able to start introducing peanut at 6 months of age (3 months after the early introduction group), whereas infants randomized to the avoidance group in the LEAP study did not introduce peanut until 5 years of age. A final important difference between the EAT and LEAP studies is that only 42.8% of EAT study participants were able to follow the vigorous introduction protocol of all 6 allergenic foods, compared to 94.5% of participants in the LEAP study [9, 15]. This is particularly important to note as the per protocol analysis performed in the EAT study demonstrated that the prevalence of peanut allergy at age 3 was significantly lower in the early introduction group compared to the standard introduction group (0% vs 2.5%, $p = 0.003$) [15]. Despite limitations related to difficulty adhering to the stringent study protocol, the EAT study demonstrated similar outcomes to LEAP in that those infants who consistently ingested peanut on a regular basis beginning early in infancy demonstrated a decreased risk of peanut allergy compared to those infants who did not have regular ingestion.

While both studies are not without flaws, the LEAP and EAT studies provide high-quality evidence that early peanut introduction and ongoing ingestion can reduce the risk of developing an allergy to peanut. Since the original LEAP study was published, the permanence of this intervention was examined in the LEAP-On study [16]. This study followed LEAP participants (88.5% retention rate) for one additional year during which time they were all told to avoid peanut. At the conclusion of this study, peanut oral food challenges were performed. Importantly, there was no significant increase in the prevalence of peanut allergy even after a year of avoidance, demonstrating the long-term preventative effect of early peanut introduction, as opposed to a prolonged desensitization [17]. It is unlikely that we will see many additional large randomized prospective studies evaluating early introduction of peanut as it will be challenging, and somewhat unethical, to recruit families willing to avoid introducing peanut to their infants given the current evidence demonstrating a dramatic decrease in risk for developing allergy through feeding early in infancy.

Controversy Surrounding Screening Prior to Introduction

Although it is widely agreed upon that early peanut introduction can be beneficial in reducing the risk of developing peanut allergy, there has been some controversy in how best to implement this recommendation. All recently published peanut prevention guidelines include varying statements encouraging the introduction of peanut during infancy; however, there is debate whether or not to screen high-risk infants prior to peanut introduction. For example, the NIAID guidelines (observed within the US and Canada) recommend performing a peanut SPT or specific immunoglobulin E (sIgE) evaluation prior to introducing peanut in infants with severe eczema, egg allergy, or both based on the entry criteria of the LEAP study [11•]. Other countries in Europe and Asia make no specific recommendations in this regard [12, 13]. In Australia, recently published infant feeding guidelines recommend introducing peanut to all infants regardless of risk factors and without screening [14]. For higher risk infants, they suggest feeding approximately 1 teaspoon of peanut butter in a graded dose manner over the course of about an hour either at home or in the office with an emergency action plan provided should a reaction occur. The guidelines acknowledge that it is important to consider the cultural fear that exists given historical recommendations to avoid, but notes that there have been no reported fatalities in countries who have practiced early introduction for many years [14].

The pros and cons for this ongoing debate of whether or not to screen high-risk infants were highlighted in a recent publication by Tang et al. wherein the authors highlight important considerations for a population level [17]. These considerations relate to the impact that testing would have on the allergy workforce, the risks associated with screening (particularly with overuse of testing and misdiagnosis leading to unnecessary avoidance), the benefit of screening compared to not screening, and the safety of introducing peanut without testing. The authors point out that while the main argument for testing is to ensure the safe introduction of peanut, the risk of a severe reaction on the first exposure of peanut appears to be low. Furthermore, based on the LEAP trial, 87% of high-risk infants would pass an OFC and testing would unnecessarily delay introduction in these infants, possibly increasing their risk of developing peanut allergy [17].

If the decision is made to screen prior to peanut introduction, another area of controversy is how to best identify infants early who are at the greatest risk of developing peanut allergy. Although severe eczema and/or egg allergy were used to identify high-risk infants in the LEAP study, the majority of participants in the early introduction group were not allergic based on OFC [9•]. Based on population-based data from

Australia (HealthNuts cohort), eczema alone is a poor predictor of peanut allergy with only 4% of infants with severe eczema at 6 months of age being diagnosed with a peanut allergy at 1 year of age [18]. In this cohort, the presence of egg allergy at 1 year of age was a stronger predictor of peanut allergy; however, only 0.4% of egg allergic infants were diagnosed by 6 months of age making this alone a sub-optimal criteria for the early identification of patients. One proposal to better identify higher risk infants is to have general pediatricians obtain a peanut specific IgE on infants that have severe eczema and/or egg allergy [17]. While this would reduce the number of infants needing further evaluation by approximately 50%, it is important to consider the costs associated with this approach given that 10–15% of infants would require additional laboratory testing [18, 19]. This also increases the risk for inappropriate use of sIgE testing, misdiagnosis, and unnecessary avoidance. Furthermore, it is estimated that approximately 25% of patients diagnosed with peanut allergy by 1 year of age never had a history of severe eczema or an egg allergy and these infants would not be entered into consideration for screening protocols [20].

It will be interesting to observe and learn from real-world experiences of pediatricians and allergists as guidelines are implemented into practice. The first such report originated from Australia and the EarlyNuts cohort, a large population-based, cross-sectional study of 12-month-old infants [21]. Parents of infants in the EarlyNuts cohort were exposed to the new guidelines recommending early peanut introduction in a variety of ways, such as direct interaction with their child's pediatrician and public health campaigns. Infants in the EarlyNuts cohort (recruited from November 2016 to October 2018) had a threefold increase in peanut introduction prior to 12 months of age (88.7%; 95% CI, 86.1–90.9) compared to a cohort of similar infants in the HealthNuts study (28.4%; 95% CI, 27.2–29.7), which took place between 2001 and 2011, during a time when early peanut introduction was not recommended [21]. These results were observed in a region where screening was not utilized prior to introduction. Similar population-based studies in different countries and over various time periods will be necessary to better understand whether parental feeding practices have changed and are sustainable on a large scale. Regional variation in experience of medical professionals, availability of testing, access to allergists, parental preferences, and cultural norms will undoubtedly influence the use of screening tests as well as age of introduction. Regardless of which side of this “to screen or not to screen” debate individual medical providers lean, we will all need to have a clear understanding of the evidence as well as the risks and benefits of testing in order to provide effective communication and practice shared decision-making with parents.

Challenges with Implementation

There are many challenges that will impede widespread implementation of early peanut introduction guidelines (Fig. 1). In addition to buy-in from pediatricians, primary care providers, and allergists, parents will need to be convinced that current guidelines and evidence are the best approach. This will be particularly challenging given the complete reversal in advice for introducing allergenic foods to infants stated in the 2000 American Academy of Pediatrics guidelines, which recommended avoiding peanut and tree nuts until children were at least 3 years of age. Even for those physicians and parents that agree with early introduction, this will take time devoted to education and discussion, clinical resources, effort, and dedication to both implement and then sustain. It takes years, sometimes decades, before any clinical guidelines are adopted into practice on a widespread level. Some of the reasons for potential slow adoption pertaining to peanut introduction will be addressed in this section.

Knowledge Gaps

As with many new changes to medical practice, there has been some resistance on the part of both families and providers to implement the new guidelines. In a survey conducted 3 months after the NIAID guidelines were released (and 26 months after the LEAP data was published), Greenhawt et al found that only 30% of expecting or new parents were willing to introduce peanut to their infant around 6 months of age [20]. The survey conducted was a nationally representative (other than age, gender, and marital status) sample of 1000 expectant caregivers and 1000 new caregivers (mean age 30.1, 99.6% female and 79% married). Interestingly, half of the sample agreed that the timing of food introduction could influence the development of food allergy, but nearly 40% preferred to wait until after 11 months of age to introduce peanut, and more than half preferred allergy testing and OFC after 11 months of age. Another interesting finding was that respondents with a family history of peanut allergy were *not* more likely to favor

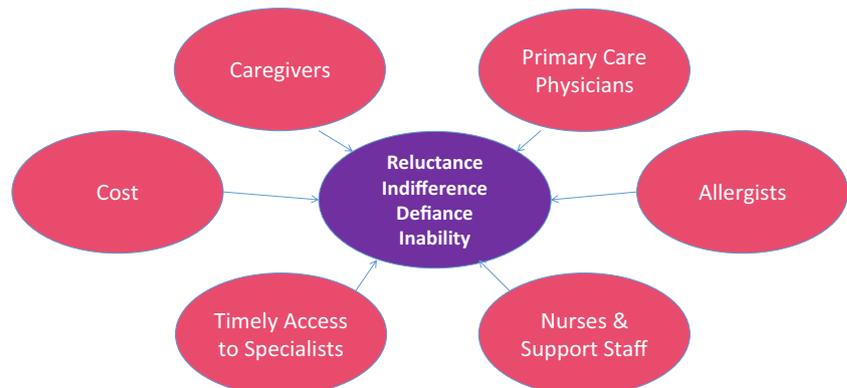
early peanut introduction. It will be interesting to see similar surveys repeated in the future to determine if sentiments change with time.

The misinformation regarding early peanut introduction extends beyond patient families to medical providers. Abrams et al. found that pediatricians and family practitioners were unclear on the risk factors for infants at high risk of developing peanut allergy. They surveyed allergists, pediatricians, and family practitioners on their approach to an infant at risk for developing peanut allergy and a sibling with peanut allergy was most frequently selected as the most important perceived risk factor. In this study, only 24.6%, 3.95%, and 4.22% of allergists, pediatricians, and family practitioners, respectively, recommended preemptive testing for infants with severe eczema prior to peanut introduction [22]. In an abstract presented at the 2018 American Academy of Allergy Asthma and Immunology annual meeting, members of our institution described challenges in obtaining referrals from primary care pediatricians to a designated early peanut introduction clinic, designed to address the need to test and challenge high-risk infants in a timely manner [23].

Resources

There are several difficulties with implementation of the new guidelines beyond addressing the knowledge gaps. An important logistical issue is timely access to an allergist for high-risk infants who require evaluation. There is concern that limiting peanut introduction until after allergy skin testing may delay peanut introduction in the most vulnerable patients. As such, it is essential that high-risk infants have access to allergists that are able to accommodate them in a timely fashion. In areas that lack timely access to allergy care, there needs to be an alternate pathway for peanut introduction as a delay of several months for an allergy evaluation will be problematic given the relatively narrow window of opportunity to introduce peanut into an infant's diet. In some communities, there is legitimate concern if allergists will be able to meet the demand for not only a new influx of patients, but timely access. For instance,

Fig. 1 Barriers to implementation



in the HealthNuts study, an estimated 11% of infants in Australia would have met inclusion criteria of moderate-to-severe eczema or egg allergy by 6 months of age. With an expected 300,000 births each year, this would equate to 33,000 referrals annually for evaluation and allergy testing. In addition, based on the LEAP trial, approximately 4488 infants would require OFCs. Koplin et al. used this data to estimate the feasibility of implementing the LEAP criteria for screening and concluded there would not be enough allergists in Australia to perform the necessary OFC to adequately implement the NIAID guidelines [18].

Another challenging part of implementation is use of in office food challenges or even supervised feedings for many of these infants. While many allergists are comfortable performing supervised feedings in the middle of a regular clinic, an oral food challenge for an infant with an elevated SPT to peanut is more time consuming and often needs to be scheduled on a later date. Some infants may be too young at the time of referral and unwilling or unable to ingest age appropriate peanut products (Table 1). In addition, some providers may be unwilling to introduce due to perceived risk for severe reaction upon initial introduction. Finding time in daily outpatient office flow is challenging as well and many providers may not offer or perform an OFC at the initial visit. However, we previously described the implementation of the NIAID guidelines in clinical practice and found that 40% of infants who were advised to return for an OFC were lost to follow up. When infants were challenged on the same day as SPT, a resolution was more likely to be established [24]. Amigo et al. also described the rate of change of the peanut SPT over time and found that the peanut SPT in high-risk groups increased 2–2.5 mm in a 6-month period [25]. This indicates that delaying introduction due to inability to meet the demand at time of visit in the office setting will completely prevent some families from introducing peanut early, and for others, may change their risk for reaction by missing a critical window of opportunity. Clearly, it is advantageous to perform OFC on the same day or as soon to testing as possible but implementing this into clinical practice requires dedication, ability to change current patient flow, time, and effort.

Table 1 Age appropriate peanut formulations to use for early introduction in the office and at home. Families should always be advised to avoid whole or partial peanuts due to risk of choking until children are at least 5 years old

Peanut product	Amount to equal 2 g	Vehicle for mixing
Thinned smooth peanut butter	2 teaspoons	Water (2–3 teaspoons)
Thinned smooth peanut butter	2 teaspoons	Fruit or vegetable puree (2–3 tablespoons)
Peanut flour or powder	2 teaspoons	Fruit or vegetable puree (2–3 tablespoons)
Bamba or equivalent peanut puff product with similar protein content	21 pieces	Water (4–6 teaspoons)

1 teaspoon = 5 mL; 1 tablespoon = 15 mL

Cost

It is important to note that early peanut introduction, with and without screening, has been shown to be cost saving at the population level [26]. As the merits of universal screening continue to be discussed at the population level, willingness to introduce peanut without screening and access to screening must be considered. For instance, if screening is recommended in a community that does not have access to allergy care or oral food challenges, peanut introduction will be delayed. On the other hand, if universal screening is not recommended in a community with great reluctance to introduce peanut without testing, peanut introduction will also be delayed. As these issues are discussed at the population level, it is important for health care providers to proactively develop strategies to deal with both scenarios in order to increase the number of high-risk infants who introduce and maintain peanut into their diet, beginning in infancy. Although early introduction has shown greatest benefit in the high-risk infants, it is unclear what benefit, if any, it holds in other populations.

Peanut Consumption at Home

Contrary to much of the messaging surrounding early introduction, the frequent and regular long-term ingestion of peanut in the diet appears to be a key measure that promotes tolerance. After negative testing to peanut or a passed peanut OFC, families are instructed to introduce peanut in the diet. However, infants who either passed an OFC to peanut or had mildly elevated skin testing to peanut may return for evaluation after experiencing a reaction to peanut. This can occur when families are reluctant to keep in the diet on a consistent basis or even by delaying introduction for several weeks. Although we do not know if these infants would have developed a peanut allergy if they had they been regularly consuming peanut, we rarely see the development of peanut allergy when peanut is being consumed on a regular basis. Other studies have documented rare reoccurrence or re-development of peanut allergy after passing an OFC to peanut when peanut is not regularly ingested [27]. Although we do not know the exact frequency with which this happens, we anecdotally recognize this in our clinical practice. In the LEAP trial, infants were consuming 2 g of peanut three times

a week (Table 1). It is unclear if this amount or frequency is necessary to maintain tolerance. For many families, this can be challenging, especially if there are other children with peanut allergy in the house or if the infant does not like peanut products. This purposeful, regular consumption is not required indefinitely. Indeed, one of the strengths of the LEAP trial was that infants were able to eventually stop consuming peanut and were able to maintain their tolerance to peanut. As such, it is likely that many infants will receive the same protection from developing peanut allergy by ingesting less amounts or on a less frequent basis. Unfortunately, at this time, we lack evidence to actively recommend any other specific amount or frequency. However, a common sense approach and consistent messaging to families can hopefully help them understand that the overall long-term inclusion in the diet starting at an early age is much more important than worrying about measuring specific amounts or adhering to an exact schedule. Lastly, all parents should be counseled on the signs and symptoms of an allergic reaction and when to call or return for additional evaluation should concerning symptoms develop after feeding peanut (or any food) to their infant.

Lessons Learned from Implementation of Early Peanut Introduction at Our Institution

Early Peanut Introduction Clinic and Logistical Challenges

As a tertiary care referral center serving a wide geographic area, the wait times at our institution for a new allergy evaluation can reach 3–4 months. Shortly after the LEAP data were published, we recognized that this delay in access would prevent timely evaluation of at-risk infants. Many of these patients were being referred around 7–9 months of age for assistance in treating their eczema, and we were subsequently not evaluating them until they were 10–12 months of age. Despite our use of peanut allergy testing and food challenges after the LEAP data were published, we recognized that we may have missed a critical window in some of these infants.

We initiated the Early Peanut Introduction (EPI) Clinic in September 2016 to address this challenge. Through this approach, the EPI clinic would also allow us to challenge children on the same day as initial evaluation. All referrals to the EPI clinic are triaged by a nurse familiar with the guidelines and need for timely access. Patients are advised at the time of scheduling that the visit will focus on peanut introduction and additional allergy related concerns will be addressed at a follow up visit. EPI clinic is held once or twice a month and 10–12 patients are scheduled in the same session, which is staffed by two allergists +/- a nurse practitioner. A protocol was established to offer consistent evaluation and care for all patients given the rotation of ten different providers that staff this

clinic. The evaluation consists of a focused clinical history, followed by SPT. If SPT is less than 2 mm, patients are offered an in clinic supervised feeding or advised to introduce peanut at home, based on family preference. If SPT is 3–8 mm, patients are offered a dose graded OFC at the day of the visit. If SPT is greater than 8 mm, an OFC is still discussed with families, but these are usually scheduled on another day, when less OFC are occurring and different staffing is available for a potentially high-risk challenge. We have found that many families opt to have an OFC even when the SPT is greater than 8 mm (and they understand the chance of passing is less than 5%) and this is approached through shared decision-making and a discussion of the risks and benefits of OFC. All infant peanut OFCs are performed with 2 g of peanut protein, usually in the form of peanut butter. Although the LEAP trial used 4 g for the challenge, the maintenance dose was 2 g. We opted to use the maintenance dose, as this is the amount the patient will be advised to continue to eat and also less time consuming, particularly for infants at low risk for having a reaction.

Despite the availability of the EPI clinic, many eligible infants are scheduled in the regular outpatient allergy clinic—either because they are referred to allergy instead of EPI, they have other allergy related concerns, or they have conflicts with the dates and times of available EPI clinics. When a high-risk patient is seen in a regular allergy clinic, they are triaged based on SPT size. If the SPT is negative, they are advised to introduce peanut at home. If SPT is 1–2 mm, they are often offered a supervised oral feeding in clinic on day of visit or instructed to introduce at home. When SPT is 3 mm or greater, they often need to return for an OFC. We are able to schedule peanut introduction food challenges within 1–2 months, depending on the age of the child and the size of the skin test, giving priority to infants with larger skin tests and older infants. In addition, various peanut products are stored in our clinic area to allow for same day feedings.

After SPT, many infants are able to safely introduce peanut into their diet at home or through an in office food challenge. It is encouraging that when these children do develop symptoms, the reactions are typically mild and often self-resolve or resolve with anti-histamines alone. Epinephrine is required on rare occasions and symptoms resolve rapidly when used. A significant part of our education surrounds a strong recommendation and encouragement for families to immediately begin peanut introduction after testing or challenge.

Quality Improvement Approach

Surprisingly, despite efforts to educate colleagues through Grand Rounds presentations, educational flyers, and personal discussion, we received very few referrals to EPI clinic initially. We adopted a quality improvement (QI) approach to determine the underlying causes and develop efforts to help

increase referrals. An aim statement was created to increase the number of referrals, which helped track data over time and monitor for improvement. In addition, several Plan-Do-Study-Act (PDSA) cycles were utilized and through these efforts, we learned from our primary care colleagues that the 4- and 6-month well child appointments were time consuming and overwhelming given the breadth of critical health information to discuss. In addition, our primary care colleagues reported feeling overwhelmed with triaging patients based upon the new NIAID guidelines. They specifically mentioned an inability to determine “moderate-to-severe” eczema. In response to these meetings, we established an electronic referral for the EPI clinic, distributed flyers with clear messaging and pictures discussing moderate-to-severe atopic dermatitis, and reinforced our willingness to see any patient they deemed worthy of evaluation, thus alleviating the burden of having to properly identify all infants exactly according to guidelines.

Through our QI approach, we were able to increase the percentage of scheduled appointments in the EPI clinic from 0% at baseline to 100% within 1 year and have sustained this for another year. Unfortunately, we still do not see the majority of the at-risk patients in our hospital. Tapke et al. reviewed charts of 4-, 6-, and 9-month well child visits among patients seen in our institution’s primary care network and found that only 20% were discussing peanut introduction in any capacity and only 12% were being referred specifically for peanut introduction [28].

Even with a dedicated approach to create a special clinic designed to allow for timely access and evaluation specifically to implement early peanut introduction guidelines, we continue to encounter challenges and barriers to implementation. However, the QI approach has been very effective in identifying and addressing specific barriers to implementation of the guidelines. Figure 2 shows the initial key driver diagram we

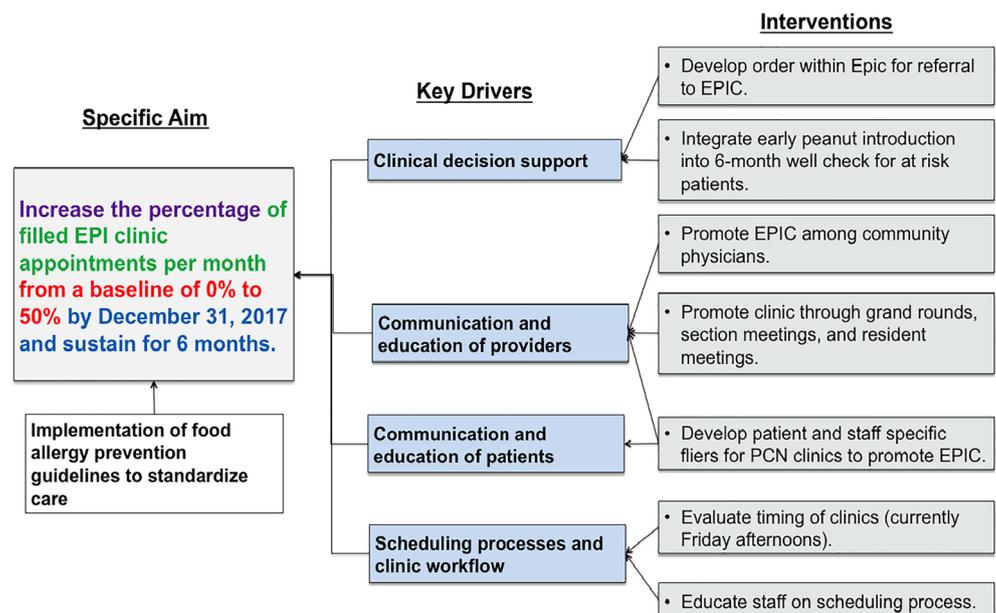
implemented to increase referrals to the EPI clinic. We have used similar methodology to address other barriers, including no show visits after scheduling and timelier access to OFC for eligible infants seen in the general allergy clinic.

Unanswered Questions

There are many unanswered questions related to early peanut introduction, including who needs to be screened for peanut allergy, who should be offered an OFC, how to advise families when children have mild cutaneous reactions near the end of their OFC, the optimal dosing during the OFC, how much peanut is required for maintenance, and how long purposeful maintenance of ingestion is required. Many of these questions will be difficult to study systematically through randomized control trials. However, they are important questions to address moving forward.

More importantly, we really have no understanding of how well these guidelines are being implemented on a population level. We will likely find individual and perhaps regional differences related to access, knowledge, and willingness to adopt new recommendations. In addition, we will need to continue to repeat peanut allergy prevalence studies to try and identify whether any shift happens in the future after more widespread implementation with current and future infants has had time to occur. Of course, all of this hinges on dedicated efforts to not only introduce peanut to infants, but for researchers to study implementation in a systematic fashion and report their findings. The inevitable delay in designing, conducting, and publishing research studies will lead to long lag times between identifying and reporting any barriers, let alone making any changes to address them.

Fig. 2 Key driver diagram outlining the aim and interventions used for a quality improvement approach to increasing referrals to the Early Peanut Introduction Clinic



Perhaps a QI approach to implementation on a population level will be the best approach as this can result in better tracking and faster cycles of change to try and improve results. But this will require largescale organized efforts likely led by professional organizations, ability to collect and track data, willingness on the part of pediatricians and allergists to not only participate but also adopt a QI approach (and ultimately change their practice in some manner), as well as funding and organization. As such, a large nationwide QI project is not likely going to occur in the near future. Registries offer another approach that can at least offer data and tracking, but all of the barriers that apply to QI projects will occur with attempting to implement widespread use of registry data as well.

In reality, ~98% of the general population will never have to worry about developing a peanut allergy. For the vast majority of children, the age of peanut introduction will never matter nor have any influence on their risk for developing peanut allergy. As such, focusing on the high-risk population, particularly infants with severe eczema and other food allergies may have the greatest impact on decreasing the overall prevalence of peanut allergy. This will also allow a more focused approach to implementation and perhaps improve our ability to meet the many challenges described in this article. Regardless of approach, success will ultimately depend upon dedicated physicians and willingness of parents.

Conclusions

We now have strong evidence to support early introduction of age appropriate peanut products to infants beginning around 4–6 months of age and ongoing inclusion in their diet, which can markedly decrease the development of peanut allergy. While the evidence demonstrating this decreased risk is limited to a few studies, multiple studies have shown that this approach is safe. As such, the benefits of early introduction outweigh the risks, particularly on a population level. However, multiple barriers exist that will need to be addressed if these guidelines are going to be adopted and implemented on a wide and meaningful basis. Through consistent dedication, education and ongoing efforts to learn from a variety of barriers, implementation of early peanut introduction will hopefully lead towards a reversal in the trend of increasing prevalence of peanut allergy among children.

Compliance with Ethical Standards

Conflict of Interest Dr. Stukus was a member of the expert panel and coauthor of the 2017 NIAID Addendum guidelines for early introduction of peanut to prevent allergy. This was unpaid and his role does not serve as a conflict of interest. Drs. Mikhail and Prince declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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