

Early introduction without screening is a good deal, if caregivers will buy it

More than 3 years after the LEAP trial,¹ the best way to implement early introduction (EI) of foods to infants at high risk of food allergy (FA) is still a matter of debate. Given the cost of screening and limited healthcare resources, the perfect balance between fair resources allocation and optimal patient care can be elusive.

Currently in *Allergy*, two cost-effectiveness studies comparing different approaches to promote EI of peanut² or egg³ in infants at high risk of FA are published. The authors have considered a variety of clinical scenarios including no testing, testing with a reflex food challenge, as well as delayed introduction due to positive testing, and they have performed extensive sensitivity analyses considering realistic prevalence and cost ranges. Both studies provide compelling evidence that EI at home without prior screening is the most cost-effective approach to prevention.

While economic studies are at the cornerstone in the process to provide efficient care to the population and inform policies, they may suffer from various pitfalls and must be interpreted with caution. In the specific context of food allergy, adherence is possibly the main limit to consider.

The authors' no-screening modeling assumes parents will take the initiative to do EI of egg and peanut, or the primary care provider will advise EI to parents who then comply. High-risk infants, as defined in the model, have a 16% risk of allergic reaction with EI to peanut at home. Real-life adherence would likely be lower than the modeled 100%, and therefore, the cost estimates would move toward the modeling for no-screening and delayed introduction (Figure 1).

As the authors acknowledge, there are factors of parent and provider preference and risk aversion. While some parents may feel reassured by the virtually absent risk of fatal anaphylaxis, the remote possibility of any reaction may prevent caregivers from EI. In the FRATRIES study, which looked at younger siblings of peanut-allergic children, 82% of parents said they would ignore a physician's home EI advice despite the risk being low.⁴ Interestingly, these parents were more willing to introduce peanut under clinical supervision after a positive test than to introduce at home without testing.

To achieve high rates of compliance with EI, tools and programs aimed at medical professionals, support groups, and parents need to continue to be developed. As an example, the EI discussion in primary care can require time and sensitivity and may need to be specifically supported in well-baby visits to be actualized effectively. These support measures and initiatives will incur costs.

The authors have performed similar economic models for EI for peanut and egg. These analyses are based predominantly on two

seminal papers, LEAP¹ for peanut and PETIT⁵ for egg, which have very different methodologies. The LEAP study approached EI in a binary fashion with an age-appropriate full-dose peanut challenge which characterized children as allergic or not. The authors acknowledge that the EI in the PETIT trial could be argued was actually immunotherapy for some children due to the tiny initial dose of heated egg powder daily for 3 months followed by a dosing increase. From a clinical and economic point of view, it is unclear that this highly medicalized approach can be equated to EI of baked egg.

Cost should always be considered in light of the associated benefit. The benefit from preventing or treating FA stems from improved quality of life (QoL) much more than from the number of anaphylactic events or death. In health economic research, cost-effectiveness analyses (CEA), which use natural units as outcomes of effectiveness (eg, number of death averted, improvement in some physiological markers), are distinguished from cost-utility analyses (CUA), which use a universal outcome called the QALY (quality-adjusted life year). QALY is now a gold standard in many health economic guidelines because it allows comparing various interventions for different diseases within a single measure unit.⁶ QALY is the result of various dimensions of health-related QoL combined with the length of life. In other words, QALY can be viewed as a quantification of health-related QoL where 0 corresponds to death and 1-1 year of full health.

Current QALY values used for FA lack precision as they are not validated in the FA population and, as the authors recognize, the minimal important clinical difference is unknown. The utility of the intermediate health state in FA is hard to value. As direct methods (ie, time trade-off and standard gamble)⁷ are time-consuming and hard to conduct, indirect measures (eg, EQ-5D, SD-6D, and HUI) have been developed. To date, all these measures are based on the preferences of the general population. This means that they ask people from the general population to imagine being in various health states and to indicate which state they prefer. The general population may exaggerate or underestimate the utility associated with living in such health states, vs people with the disease.

One justification for using health utility values derived from the general population is that healthcare choices should reflect the perspective of the whole society. However, whose values count most is now subject of debate⁸ and recent recommendations argue to consider both QALY based on the preferences of patients and of the general population.⁹ In the latest guidelines on FA, the European Association of Allergy and Clinical Immunology identified the lack of QALY measures for FA as an important gap in knowledge and a

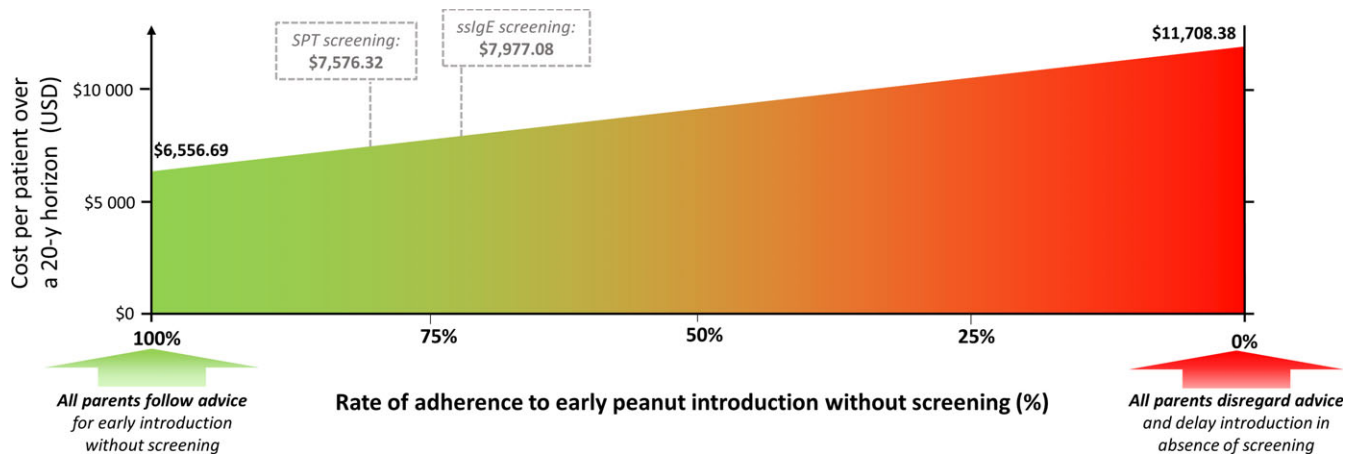


FIGURE 1 Effect of parental adherence on cost-effectiveness. The no-screening, early introduction approach becomes a no-screening delayed introduction approach with non-adherence; hence, the need for clinical judgment, flexibility, educational support, and understanding patient needs and preferences when choosing the best strategy to promote early introduction to infants. Illustrative costs are based on the peanut modeling by Shaker et al² (SPT, skin prick test; ssIgE, serum-specific IgE)

TABLE 1 Future needs to study and promote early introduction strategies

Continue to develop strategies to promote parents' comfort and adherence with home introductions

Perform cost-utility analysis along with cost-effectiveness/consequences analysis

Develop measures of QALY specific for allergic patients to improve sensitivity

Develop preference weights and population norms for allergic people for reuse in data modeling

priority for future research¹⁰ as it limits our capacity to conduct robust cost-utility assessment of interventions and therefore our ability to advocate for resources for our patients.

In conclusion, while all economic analyses in FA have limitations, these analyses present persuasive economic data for EI for peanut and egg with no prior screening, assuming full adherence. Therefore, a continuing focus on understanding patient needs and preferences and learning how to best promote adherence to early introduction in our patients is a high priority (Table 1). And just as was seen for peanut, any future guidelines for egg will stir healthy ongoing debate about how to translate medicalized EI trial procedures into practice.

CONFLICTS OF INTEREST

JU reports acting as investigator on clinical trials DBV Technologies and Aimmune, outside the submitted work. PB reports acting as investigator on clinical trials from DBV technologies, outside the submitted work. TP has nothing to disclose.

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