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The Promise and Peril of Knowledge Translation For Food Allergy Prevention

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Conflicts of Interest:

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DM: DM has provided consultation for Alladapt and consultation speaker services for Bausch Health, ALK-Abello, Medexus, Miravo, and is an investigator for DBV, ALK-Abello, Astra-Zeneca, Dermavant and serves on the editorial board of the Journal of Food Allergy

EC: has received research support from DBV Technologies; has been a member of advisory boards for Pfizer, Miravo, Medexus, Leo Pharma, Kaleo, DBV, AllerGenis, Sanofi Genzyme, Bausch Health, Avir Pharma, AstraZeneca, ALK; is co-lead of CPS/CSACI Food Allergy Prevention Position Statements; is on the Executive of the CSACI (Canadian Society of Allergy and Clinical Immunology); and is on the Executive of the CPS (Canadian Paediatric Society) Allergy Section.

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Keywords

AAAAI; ACAAI; Cost-Effective Care; Knowledge Translation; NIAID; Food Allergy Prevention

Across recent decades, prevention efforts have evolved considerably from dietary avoidance for both mother and infant to a paradigm that actively encourages early infant introduction of potentially allergenic foods.(1) Contemporary management has been informed by controlled trials and meta-analyses of studies supporting early introduction of peanut, egg, and other potentially allergenic foods. Early introduction is promoted as safe and effective around the world.(1)

The 2015 LEAP study demonstrated significant risk reduction against the development peanut allergy through early peanut introduction, and rapid initial international consensus was reached regarding the importance of implementing early introduction among 10 global allergy, dermatology and pediatric societies.(2) This interim consensus did not require screening prior to introduction, but suggested allergist evaluation as an option for those with greater risk of peanut allergy. In 2017, North American-specific guidance led by the National Institute of Allergy and Infectious Diseases (NIAID) opted to strongly encourage screening allergy tests and supervised early introduction for “high-risk” infants with severe eczema, egg allergy, or both, prior to early peanut introduction.(3) The verbatim wording suggested clinicians “strongly consider evaluation by sIgE measurement and/or SPT and, if necessary, an OFC ”, advocating serologic testing primarily for infants without allergist access.(3) The NIAID document is an outlier, given no other international guidance recommends screening or medicalized introduction for any risk group.

The necessity of screening remains questionable. While LEAP demonstrated that early introduction was effective in at-risk infants without pre-existing peanut allergy, it did not test the hypothesis that screening infants for pre-existing peanut allergy improves prevention outcomes. Since the NIAID document publication, screening has proven challenging to implement and sustain, with unintended consequences, including: a) overall poor cost-effectiveness of medicalized introduction (Table 1), b) overdiagnosis from poor access for follow-up procedures, use of surrogate diagnostic markers, and incomplete implementation of screening algorithms, and c) screening creep in testing for non-peanut allergens and in non-risk populations.(1, 4) In 2021, consensus prevention guidance by the AAAAI, ACAAI, and CSACI addressed these limitations by clarifying that screening prior to early allergenic solid food introduction is not required but may be a preference-sensitive option, aligning North American guidance with every other international early introduction policy.(1)

Knowledge Translation (KT) is a critical, valuable component to implementing clinical guidance, and can result in improved population health outcomes. Effective KT must be contemporary with evolving evidence, a particularly challenging issue in food allergy prevention, given the pace of emerging new knowledge. Recently, a multi-stakeholder effort from www.FoodAllergyPrevention.Org (FAPO) created KT tools to help enhance food allergy prevention uptake (https://foodallergyprevention.org). This difficult work is much appreciated because creating practical and engaging KT tools is highly valuable to both patients and clinicians. Yet, FAPO’s tools struggle to reflect current best practices in its first

published iteration. Specifically, the FAPO tools miss an opportunity to incorporate shared decision making (SDM) regarding a screen-first approach, given that there is remaining clinical equipoise on the utility of peanut allergy screening prior to introduction.

Instead, the FAPO algorithm heavily reflects the 2017 NIAID Addendum Guideline, directing high-risk infants to first obtain a peanut-specific IgE prior to peanut introduction. This approach not only risks delayed early introduction for children most likely to benefit from the intervention by creating a barrier to early introduction (which may also fuel fear and hesitation), but also risks overdiagnosis due to poor test specificity, differential test interpretation, and failure to offer confirmatory infant oral food challenges due to limited access in the real-world. Overdiagnosis is not benign, and poses considerable burden, including unwarranted fear, unnecessary dietary restrictions, impaired quality of life, potential need for lifelong treatment, and excess healthcare costs.(1, 4) In fact, the approach FAPO promotes could accrue costs exceeding $911,211,774 from a societal standpoint and result in 8,981 additional peanut allergy cases of peanut allergy, while failing to identify 22% of cases in the US population alone.(1)

Advocacy partnerships help advance food allergy patient care, and well-developed KT tools help translate evidence to practice. However, if these materials are out-of-date or out of step with current evidence effective KT cannot occur. Relative to prevailing international approaches (including recent US and Canadian consensus), the FAPO algorithm adds complexity through screening. Pre-emptive food allergy screening is not a historical norm (nor advocated for in any international food allergy guidance), and the safety of non-medicalized infant peanut feeding has stood the test of time in other parts of the world where infants have consumed peanut and other allergenic foods for decades. While screening has intuitive appeal, screening programs are nonetheless interventions, subject to the same burden of proof required of pharmacologic or non-pharmacologic interventions. Screening programs must only be implemented after clear evidence of an accurate test, and demonstration that benefits of screening outweigh the risks. To date, the necessity peanut allergy screening for early introduction is unproven, in particular with use of low specificity sIgE testing.

Why a questionably accurate screening paradigm would be forwarded may be rooted in specific cultural attitudes toward screening. As a counter example, Australasian guidance simply recommends “when your baby is around 6 months, but not before 4 months, start to introduce foods including peanut (such as smooth peanut butter/paste) and well-cooked egg”, without mention of a screening option (www.preventallergies.org.au). Without any screening, Australian data have shown fewer than 1% have a severe index reaction from early peanut introduction.(5) These recommendations are similarly reflected in guidance from Israel and in Europe, and the framing of the guidance emphasizes the safety of the process, not the potential harms for some population.

All early introduction strategies pose some risk, including index reactions occurring with or without medical supervision, and overdiagnosis resulting from using cut-off values from testing without clinical reactivity. Ultimately, the setting and approach of early introduction must consider family preferences and goals foremost, and not clinician preferences alone.

The FAPO materials miss the opportunity to highlight the safety of universal peanut introduction – even in at-risk populations – and may instill fear by virtue of requiring medical attention to a specific group. There are no data from other countries suggesting that simple home introduction is unsafe for infants to accomplish without screening and medicalized interventions.

Screening need not be required before allowing babies to eat foods containing peanut butter, and with family partnerships evidence-informed decisions can be made to provide each patient the right care, in the right context, every time. While we applaud the effort by FAPO, we highlight the opportunity for improvement while we each "stand by the good and make it better when we can." Together we can better encourage infants to eat safely, early, and often to decrease food allergy risk for decades to come.

Abbreviations:

AAAAI	American Academy of Allergy, Asthma, and Immunology
ACAAI	American College of Allergy, Asthma, and Immunology
CSACI	Canadian Society of Allergy and Clinical Immunology
NIAID	National Institute of Allergy and Infectious Diseases
OFC	Oral Food Challenge
SPT	skin prick test
sIgE	serum specific IgE

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Table 1.

Cost Effectiveness of Strategies for Early Introduction of Peanut and Egg

Infant Risk Scenario	Cost Per Patient At Risk	QALY Per Patient At Risk	Allergic Reactions Per Patient At Risk	Incremental Societal Cost to Screen
For Peanut Allergy (Personal History of Early Onset Eczema and/or Egg Allergy)				
No Screening, Early Introduction	$6,557	19.63	0.4	--
Skin Test Screening Before Early Introduction	$7,576	19.62	0.35	$654,115,322
Specific IgE Screening Before Early Introduction	$7,977	19.6	0.38	$911,211,774
Delayed Introduction	$11,708	19.46	0.72	
For Peanut Allergy (Sibling History Of Peanut Allergy)				
No Screening Before Introduction	$3,278	19.72	0.2	--
Skin Test Screening with Challenge Before Introduction	$3,984	19.72	0.2	Dominated
For Egg Allergy (Early Onset Eczema)				
No Screening, Early Cooked Introduction	$2,235	19.78	0.03	--
Skin Test Screening Before Early Cooked Introduction	$9,100	19.59	0.12	$2,009,351,175
Specific IgE Screening Before Early Cooked Introduction	$18,957	19.28	0.26	$4,894,445,790
Delayed Cooked Introduction	$10,615	19.53	0.13	

*Model simulations over 20-year time horizons

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