

A Brief History of Food Allergy Prevention

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Those Who
Complain Will
Be Given A
Committee
Assignment!

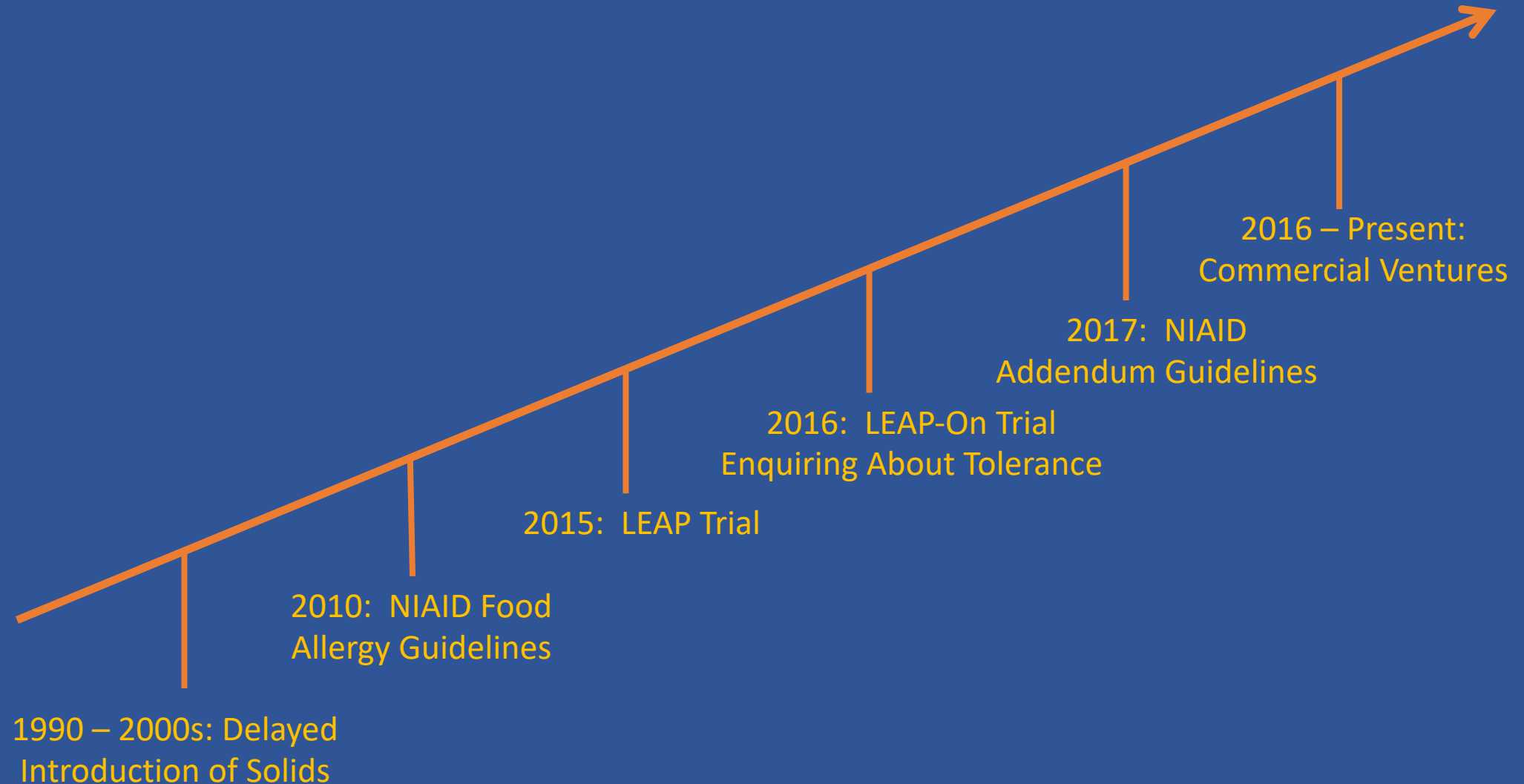
DOC MATTERS POST:



Robert Sugerman
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I would like to thank the makers of SpoonfulONE for the referrals to our practice. We've seen plenty of infants and toddlers with substantial food allergy risk factors who have experienced allergic reactions to this perfect concoction of allergenic proteins.

How Did We Get Here?



1990s – 2000s: Something is Terribly Wrong!

- Allergists and pediatricians are advising parents to delay introduction of solid foods based on conventional wisdom
 - Milk products at 12 months
 - Egg at 18 months
 - Nuts at age 3 years
- Prevalence of peanut allergy rises rapidly during this period
 - 1997: 0.4%
 - 2002: 0.8%
 - 2008: 1.4%

Sicherer, et al
Telephone Surveys

2010 NIAID Guidelines For Diagnosis and Management of Food Allergies in the U.S.

Expert Panel Recommendations Regarding Prevention of Food Allergies in Children: A Major Paradigm Shift !

“Insufficient evidence exists for delaying introduction of solid foods, including potentially allergenic foods, beyond 4 to 6 months of age, even in infants at risk of developing allergic disease.”

2015 LEAP Trial

The NEW ENGLAND JOURNAL *of* MEDICINE

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Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy

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ABSTRACT

2015 LEAP Trial

Background Observations:

- >2-fold rise in prevalence of peanut allergy worldwide during the previous 10 years with delayed introduction of peanut
- 10-fold greater prevalence of peanut allergy in young UK children of Eastern European Jewish descent compared to Israeli children of similar ancestry (“Bamba™ effect”)

2015 LEAP Trial

Study Design

- Randomized, open label, controlled trial
- Infants ages 4-11 months of age with severe eczema, egg allergy, or both
- Stratified into 2 cohorts based on SPT reactivity:
 - No measurable wheal response
 - 1-4 mm wheal response (> 4 mm responders were excluded)
- Both cohorts randomized into 2 groups:
 - Peanut consumption (2 grams PP TIW) until age 60 months
 - Peanut avoidance until age 60 months

2015 LEAP Trial

Study Design

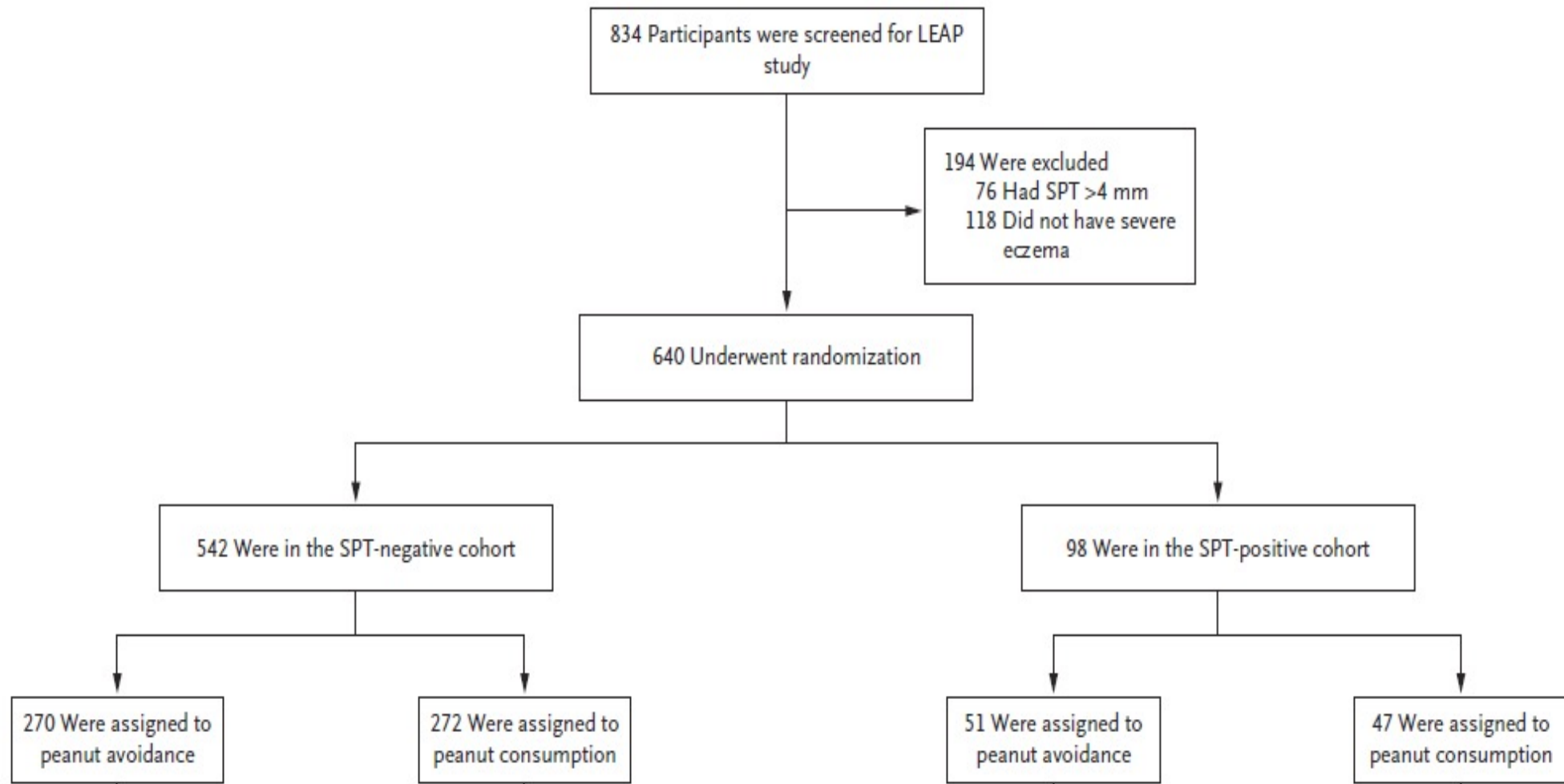
- Clinical assessments at baseline, then 12, 30 and 60 months of age
- Between visit telephone follow-up:
 - Every 1 week until age 12 months
 - Every 2 weeks from ages 12 – 30 months
 - Every 4 weeks from ages 30 – 60 months

2015 LEAP Trial

Primary Outcome Measurement:

- Compare percentages of children with peanut allergy (positive peanut OFC) in peanut consumption group versus peanut avoidance group at age 60 months

2015 LEAP Trial Randomization



2015 LEAP Trial

Results of Intention to Treat Analysis At 60 Months

COHORT	N	PEANUT ALLERGY [(+) OFC]		RISK REDUCTION	P VALUE
		AVOIDANCE	CONSUMPTION		
SPT (-)	530	13.7%	1.9%	86%	<0.001
SPT (+)	98	35%	10.6%	70%	0.004
COMBINED	628	17%	3.2%	81%	<0.001

2015 LEAP Trial Conclusions

- Early, sustained consumption of peanut products is associated with a substantial and significant decrease in the development of peanut allergy in high-risk infants
- Peanut avoidance is associated with a greater frequency of clinical peanut allergy than peanut consumption

2016 LEAP-On Study

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Avoidance on Peanut Allergy after Early Peanut Consumption

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ABSTRACT

2016 LEAP-On Study

Objective:

- Determine the durability of peanut oral tolerance following primary LEAP trial
- Does the prevalence of peanut allergy following 12 months of peanut avoidance remain significantly lower in the primary LEAP trial peanut consumption group versus the peanut avoidance group?

2016 LEAP-On Study

Study Design:

- 556 of 628 (88.5%) LEAP participants successfully recruited
- All participants advised to avoid peanut products strictly for a period of 12 months
- Peanut OFCs performed at age 72 months

2016 LEAP-On Study

Results of Intention to Treat Analysis At 72 Months

COHORT	N	PEANUT ALLERGY [(+) OFC]		RISK REDUCTION	P VALUE
		AVOIDANCE	CONSUMPTION		
2016 LEAP-On	550	18.6%	4.8%	74%	<0.001
2015 Primary LEAP Trial	628	17%	3.2%	81%	<0.001

2016 LEAP-On Study

Conclusion:

- Early introduction and regular consumption of peanut up to age 5 years induced sustained unresponsiveness to peanut following 12 months of dietary avoidance

2016 EAT Trial

Enquiring About Tolerance (EAT) study: Feasibility of an early allergenic food introduction regimen



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Background: The influence of early exposure to allergenic foods on the subsequent development of food allergy remains uncertain. **Objective:** We sought to determine the feasibility of the early introduction of multiple allergenic foods to exclusively breast-fed infants from 3 months of age and the effect on breastfeeding performance.

Methods: We performed a randomized controlled trial. The early introduction group (EIG) continued breastfeeding with sequential introduction of 6 allergenic foods: cow's milk, peanut, hard-boiled hen's egg, sesame, whitefish (cod), and wheat; the standard introduction group followed the UK infant feeding recommendations of exclusive breastfeeding for around 6 months with no introduction of allergenic foods before 6 months of age.

Results: One thousand three hundred three infants were enrolled. By 5 months of age, the median frequency of consumption of all 6 foods was 2 to 3 times per week for every food in the EIG and no consumption for every food in the standard introduction group ($P < .001$ for every comparison). By 6 months of age, nonintroduction of the allergenic foods in the EIG was less than 5% for each of the 6 foods. Achievement of the stringent per-protocol consumption target for the EIG proved more difficult

(42% of evaluable EIG participants). Breastfeeding rates in both groups significantly exceeded UK government data for equivalent mothers ($P < .001$ at 6 and at 9 months of age).

Conclusion: Early introduction, before 6 months of age, of at least some amount of multiple allergenic foods appears achievable and did not affect breastfeeding. This has important implications for the evaluation of food allergy prevention strategies. (J Allergy Clin Immunol 2016;137:1477-86.)

Key words: Food allergy, diet, allergens, infancy, breastfeeding

Discuss this article on the JACI Journal Club blog: www.jaci-online.blogspot.com.

The point prevalence of self-reported food allergy in a recent systematic review was around 6%,¹ and that for particular foods is increasing.² The role of allergen consumption in early infancy and its effect on the development of allergy or tolerance to food proteins remains uncertain.

The World Health Organization Global Strategy for Infant and Young Child Feeding,³ which is endorsed by the United Kingdom (UK) Government,⁴ recommends exclusive breastfeeding for the first 6 months with nutritious complementary foods introduced thereafter and continued breastfeeding up to the age of 2 years or beyond.⁵ The UK Government infant feeding information

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2016 EAT Trial

Objectives:

- Determine feasibility of early introduction of multiple allergenic foods to exclusively breastfed infants from 3 months of age and the effect on breastfeeding performance

2016 EAT Trial

Study Design:

- 1303 exclusively breastfed infants enrolled in a prospective, randomized controlled trial at 13-17 weeks of age without regard to atopic status
 - Early Intervention Group (EIG)
 - Continue breastfeeding and add 6 foods sequentially (4 gm protein) every 1 week: CM yogurt, egg, peanut, sesame, fish, wheat (in any order, but saving wheat for last)
 - Standard Intervention Group (SIG)
 - Exclusive breastfeeding until age 6 months
 - Introduction of solids after age 6 month per parents' discretion

2016 EAT Trial

Study Design:

- Outcomes monitored by online questionnaires
 - Weekly food frequency questionnaire to determine how frequently 6 allergenic foods were being consumed
 - Reporting of atopic symptoms and AEs completed monthly until age 12 months, then every 3 months until age 36 months

2016 EAT Trial

Findings:

- Multiple allergenic foods could be introduced into an infant's diet safely and without compromising breastfeeding
- Compliance with early introduction of allergenic foods was low
 - Cow's milk products: 69%
 - Peanut: 52%
 - Egg: 36%
 - Sesame: 44%
 - Fish: 49%
 - Wheat: 33%

PETIT Trial

Randomized Controlled Trial > Lancet. 2017 Jan 21;389(10066):276-286.

doi: 10.1016/S0140-6736(16)31418-0. Epub 2016 Dec 9.

Two-step egg introduction for prevention of egg allergy in high-risk infants with eczema (PETIT): a randomised, double-blind, placebo-controlled trial

Osamu Natsume¹, Shigenori Kabashima², Junko Nakazato³, Kiwako Yamamoto-Hanada⁴,
Masami Narita⁴, Mai Kondo⁵, Mayako Saito⁴, Ai Kishino⁶, Tetsuya Takimoto⁷, Eisuke Inoue⁷,
Julian Tang⁷, Hiroshi Kido⁸, Gary W K Wong⁹, Kenji Matsumoto¹⁰, Hirohisa Saito¹⁰,
Yukihiro Ohya¹¹, PETIT Study Team

PETIT Trial

- Infants with eczema randomized 1:1 heated egg white vs. placebo: HEW 50 mg/day from ages 6-9 months -> 250 mg/day from ages 9-12 months
- Egg OFCs performed at age 12 months
 - Egg allergy 38% placebo vs. 8% HEW group (79% risk reduction)
 - However, 10% of HEW group required hospitalization for allergic reactions at some point during the 6 months treatment phase

2017 NIAID Addendum Guidelines: Three New Recommendations for Early Introduction of Peanut

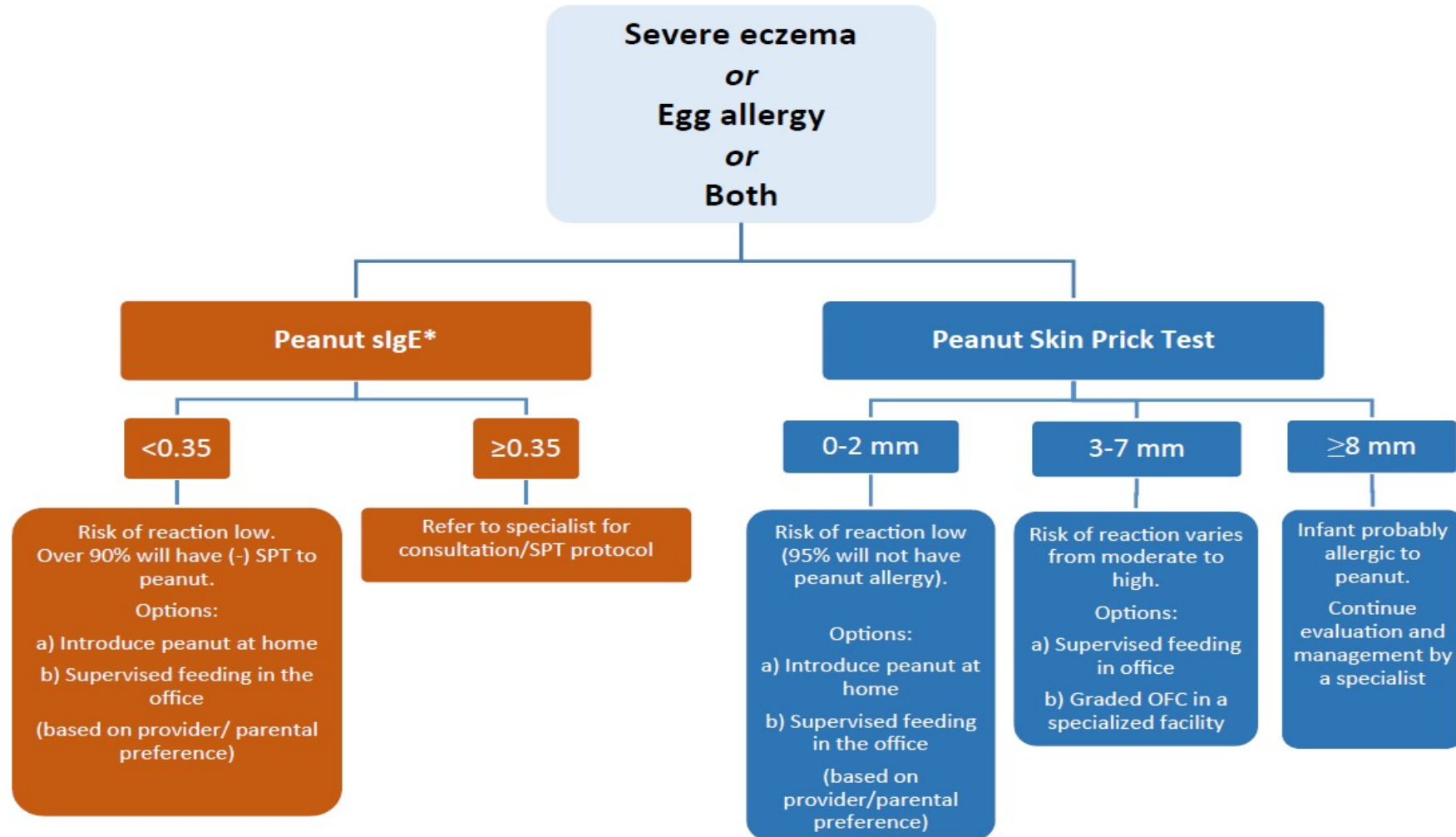
Addendum guidelines based on important new developments:

- Major reduction in peanut allergy seen with early introduction of peanut in infants with severe eczema, egg allergy or both (2015 LEAP Trial)
- Durability of oral tolerance to peanut demonstrated by results of 2016 LEAP-On study
- Need to “operationalize LEAP findings by developing clinical recommendations focusing on peanut allergy prevention”

2017 NIAID Addendum Guidelines: Three New Recommendations for Early Introduction of Peanut

Addendum Guideline	Criteria	Recommendations	Age of Peanut Introduction
1	Severe eczema, egg allergy or both	Evaluate with peanut sIgE and/or SPT -> OFC if necessary. Based on test results, introduce peanut-containing foods	4-6 months
2	Mild to moderate eczema	Introduce peanut-containing foods	Around 6 months
3	No eczema or any food allergy	Introduce peanut-containing foods	Age appropriate and in accordance with family preferences and cultural practices

2017 NIAID Addendum Guidelines: Evaluation of High-Risk Infants



Commercial Products Promoted for Early Introduction of Allergenic Foods

- Hello, Peanut!™
- SpoonfulOne™
- Ready, Set, Food!™
- Inspired Start™

Hello, Peanut!™

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THE BEST SOLUTION FOR EARLY PEANUT INTRODUCTION

An easy, measured system for infant peanut introductions because a baby's first peanut shouldn't be scary



Hello, Peanut!™



Ready, Set, Food!™

Staged Introduction of Powdered Food Proteins

- Stage 1: New food introduced every 4 days
 - Days 1-4: cow's milk 200 mg -> 430 mg protein
 - Days 5-8: add cooked egg white 25 mg -> 125 mg protein
 - Days 9-11: add peanut 100 mg -> 430 mg protein
- Stage 2: Continue maintenance doses for 6 months, or until baby is regularly consuming milk, egg and peanut

Ready, Set, Food!™

Staged Introduction of Powdered Food Proteins

- Stage 3: The whole shebang!
 - Addition of wheat, soy, almond, cashew, walnut & sesame
- 2.5 grams total protein per serving
 - Assuming equal portions of each of the 9 ingredients listed would yield 277 mg protein of each allergenic food per serving

Ready, Set, Food!™

READY. SET. FOOD!

Supplement Facts

Serving Size: 1 Packet (6.7g)

Servings Per Box: 30

Amount Per Serving	% Daily Value for infants up to 12 month of age	
Calories	25	
Total Carbohydrate	3g	3%
Protein	2.5g	
Calcium	16mg	6%
Sodium	10mg	†
Potassium	55mg	8%

† Daily Value not established

INGREDIENTS:

(Stage 3 Packets): Organic wheat flour, organic cashew flour, organic milk powder, organic walnut flour, organic sesame flour, organic peanut flour, organic almond flour, organic soy flour, baked organic egg powder

"Since my daughter has a severe peanut allergy, I know firsthand how life-changing food allergies can be. I'm excited to partner with Ready, Set, Food! to make families like

SpoonfulOne™

- Available in powders, puffs & crackers
- Proprietary blend of 9 allergenic foods: milk, egg, wheat, soy, fish, shrimp, peanut, multiple tree nuts (almond, cashew, pistachio, hazelnut, walnut, pecan) mixed in rice & oat flour
 - Puffs ingredients label lists 1 gram protein per serving -> unlikely more than 80 mg protein for each food

Inspired Start™



FDA Approval of Qualified Health Claim for Peanut Products (2017)

For most infants with severe eczema and/or egg allergy who are already eating solid foods, introducing foods containing ground peanuts between 4 and 10 months of age and continuing consumption may reduce the risk of developing peanut allergy by 5 years of age. FDA has determined, however, that the evidence supporting this claim is limited to one study.

- Assured Bites (Hello, Peanut!™) received an FDA exemption letter in 2017
- Before Brands (SpoonfulONE™) and Prollergy Corporation (Ready, Set, Food!™) both received FDA warning letters dated 10/9/2020

Take Home Messages

- Early introduction of peanut and other allergenic foods reduces the likelihood of developing food allergy in children with risk factors
- Precautions should be taken when introducing allergenic foods to children with risk factors
- Food products sold for the purpose of allergy risk reduction are subject to FDA regulations