Food Allergy Overview and its Prevention

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Faculty/Presenter Disclosure

- **Faculty:** Dr. Edmond S. Chan
- **Relationships with commercial interests:**
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  - Expert Panel for NIAID (National Institute of Allergy & Infectious Diseases), Early peanut introduction addendum guidelines
  - CSACI, AAAAI, AGA
  - Research support from CIHR, AllerGen, and BCCH Foundation

Objectives

- 1) Provide an overview of food allergy (prevalence, diagnosis)
- 2) Examine early infant feeding guidelines for food allergy prevention (changes, supporting research, recommendations)

Overview of food allergy

Prevalence of food allergy

- Canada
  - Self-reported

	Children
Estimate 1: Including all adults	
Peanut	1.77 (1.21-2.33)
Tree nut	1.73 (1.16-2.30)
Fish	0.18 (0.00-0.36)
Shellfish	0.55 (0.21-0.88)
Sesame	0.23 (0.03-0.43)
Milk	2.23 (1.51-2.95)
Egg	1.23 (0.69-1.77)
Wheat	0.45 (0.08-0.83)
Soy	0.32 (0.08-0.55)
Fruits	1.14 (0.68-1.60)
Vegetables	0.45 (0.17-0.74)
Other	1.32 (0.80-1.84)
All foods	7.14 (5.92-8.36)
Estimate 2: Excluding some adults	
All foods	7.14 (5.92-8.36)
Estimate 3: Estimate 2 adjusted for nonresponse	
All foods	7.12 (6.07-8.28)

Soller L et al. J Allergy Clin Immunol. 2012 Oct;130(4):986-8

- Australia
  - Most accurate data (oral food challenge proven in 12 month old infants)
    - Peanut 3.0% (95% CI, 2.4-3.8)
    - Raw egg allergy, 8.9% (95% CI, 7.8-10.0)
    - Sesame allergy, 0.8% (95% CI, 0.5-1.1).

Osborne NJ et al. J Allergy Clin Immunol. 2011 Mar;127(3):668-76

What does “food allergy” really mean?

- ADVERSE REACTION to food=any abnormal reaction, due to:

- I) TOXIC
  - Bacterial enterotoxins
  - Other food poisonings

- II) NON-TOXIC
  - 1. **“Food Allergy”** = Immune mediated
  - 2. Food Intolerance = Non-immune

Boyce JA et al. J Allergy Clin Immunol. 2010 Dec;126(6):1105-18

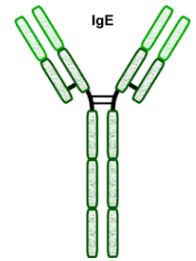
Definitions, cont'd

- 1. "Food Allergy"
  - **IgE mediated** (e.g. anaphylaxis, oral allergy syndrome)
  - Mixed IgE/non-IgE (e.g. eosinophilic esophagitis)
  - Non-IgE (e.g. Food Protein induced enterocolitis, FPIES)

- 2. Food Intolerance
  - Enzyme deficiency (e.g. lactase deficiency)
  - Pharmacologic sensitivity (e.g. caffeine)
  - Psychologic (e.g. food aversion)

Boyce JA et al. J Allergy Clin Immunol. 2010 Dec;126(6):1105-18

When to suspect a food allergy in children



- 1. IgE-mediated:
  - Recent history of **immediate reaction** to food
    - Timing (typically onset <2 hrs, duration<24 hrs), typical symptoms (urticaria, respiratory, cardiovascular, gastrointestinal), type of food
    - Potentially anaphylactic
  - Suspected food **not** eaten regularly

- *2.* Non IgE-mediated:
  - Severe, delayed gastrointestinal symptoms

IgE mediated Food Allergy: Common foods

- Majority of IgE mediated reactions due to these foods:
  - Cow's milk*
  - Egg*
  - Peanut* & Tree nuts
  - Sesame seed
  - Fish & Shellfish
  - (Soy)
  - (Wheat)

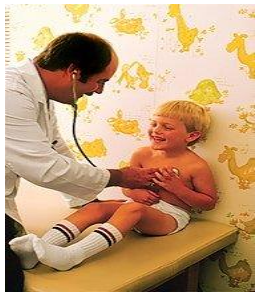
Boyce JA et al. J Allergy Clin Immunol. 2010 Dec;126(6):1105-18

Predictive values for *skin tests and specific IgE blood tests*

- Positive predictive value low unless recent and clear history
  - **"Asymptomatic sensitization" ("false positives") are common**
- Negative predictive value high
- i.e.) negative results more useful than positive ones

Boyce JA et al. J Allergy Clin Immunol. 2010 Dec;126(6):1105-18

Oral Food Challenges (OFC's)



- Gold standard but under-utilized, **for all ages** ("new"=infant)
  - Done if no recent, convincing history
  - For ruling out food allergy when other tests inconclusive
  - For the follow-up of food allergy (outgrowing) after period of avoidance
    - Best offered when ~50% chance tolerating
- *Many patients will not need "emerging therapies" (e.g. Oral Immunotherapy, "OIT")…*all they need is an OFC to determine if they've outgrown their food allergy

Boyce JA et al. J Allergy Clin Immunol. 2010 Dec;126(6):1105-18

What happens during OFC's?

- Signed consent before proceeding useful
- Trained, experienced, certified allergist supervising; management of anaphylaxis
- ~3 hrs duration if no reaction, ~4-8 hrs if reaction:
  - Total cumulative dosing of ~4 to 8 g protein
  - Split into ~5 graded amounts every ~20 minutes
  - Special situations:
    - Subjective symptoms, Asthma control, Food aversion, Infant OFC's (e.g. how to implement early peanut introduction)

Sampson HA et al. J Allergy Clin Immunol. 2012 Dec;130(6):1260-74
Bird JA et al. J Allergy Clin Immunol Pract 2017;5:301-11

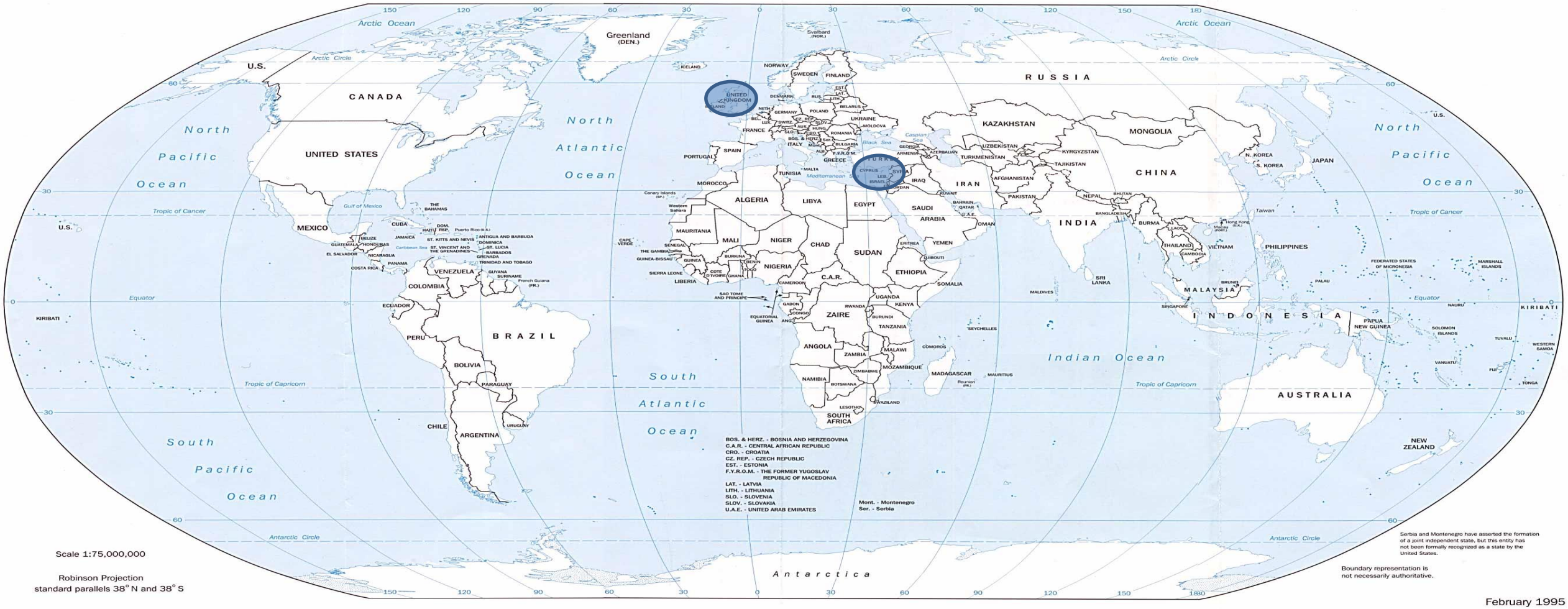
Early infant feeding guidelines

2000 AAP recommendations for "High Risk" infants (first degree relative with an atopic condition)

- Pregnancy: possibly avoid peanuts
- Lactation: avoid peanuts/tree nuts
- Newborns: Delay of…
  - Solids until 6 months
  - Dairy until 12 months
  - Egg until 2 years
  - Peanuts, nuts, fish (+ shellfish) until 3 years

AAP Committee on Nutrition, Pediatrics 2000;106:346-9

10 fold difference in peanut allergy in the UK versus Israel



J Allergy Clin Immunol 2008 Nov; 122: 984-91

2013 CPS/CSACI Position Statement

Recent CPS recommendations* to prevent food allergy include the following:

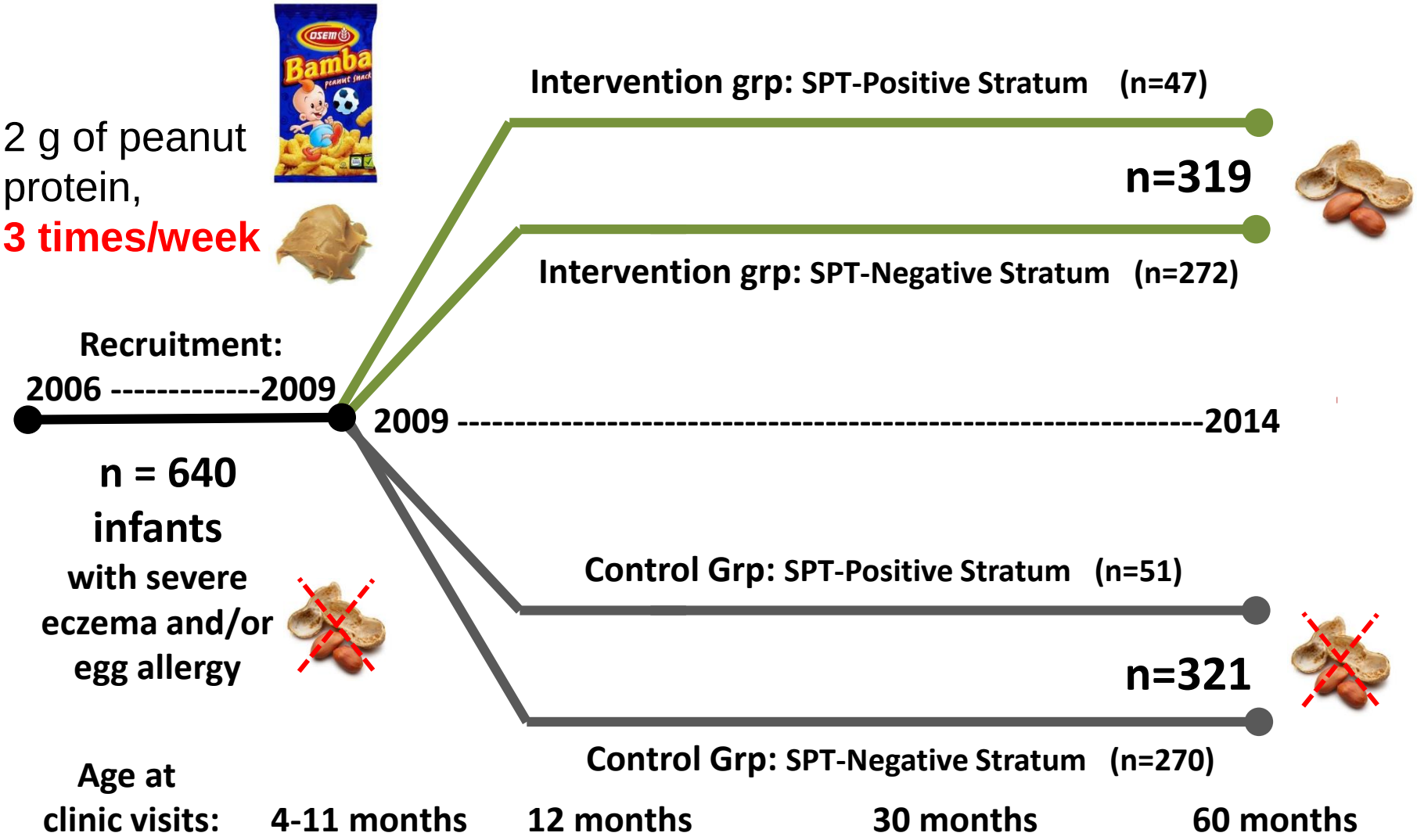
- No restriction of maternal diet is recommended during pregnancy or lactation (evidence II-2B)
- Exclusive breastfeeding for the first 6 months of life (evidence II-2B)
- Choose a hydrolyzed cow's milk–based formula, if necessary (evidence IB)
- Do not delay the introduction of any specific solid food beyond 6 months of age (evidence II-2B)
- More research is needed on the early introduction of specific foods to prevent allergy (evidence II-2B)
- Regular ingestion of newly introduced foods appears to be important for maintaining tolerance (eg, several times per week in non-choking forms). Routine skin or specific IgE blood testing before first ingestion is discouraged owing to high risk of false-positive results (evidence II-2B)

Chan ES, Cummings C. *Paediatr Child Health* 2013;18(10):545-9

Du Toit G. *J Allergy Clin Immunol* 2016; 137:998-1010

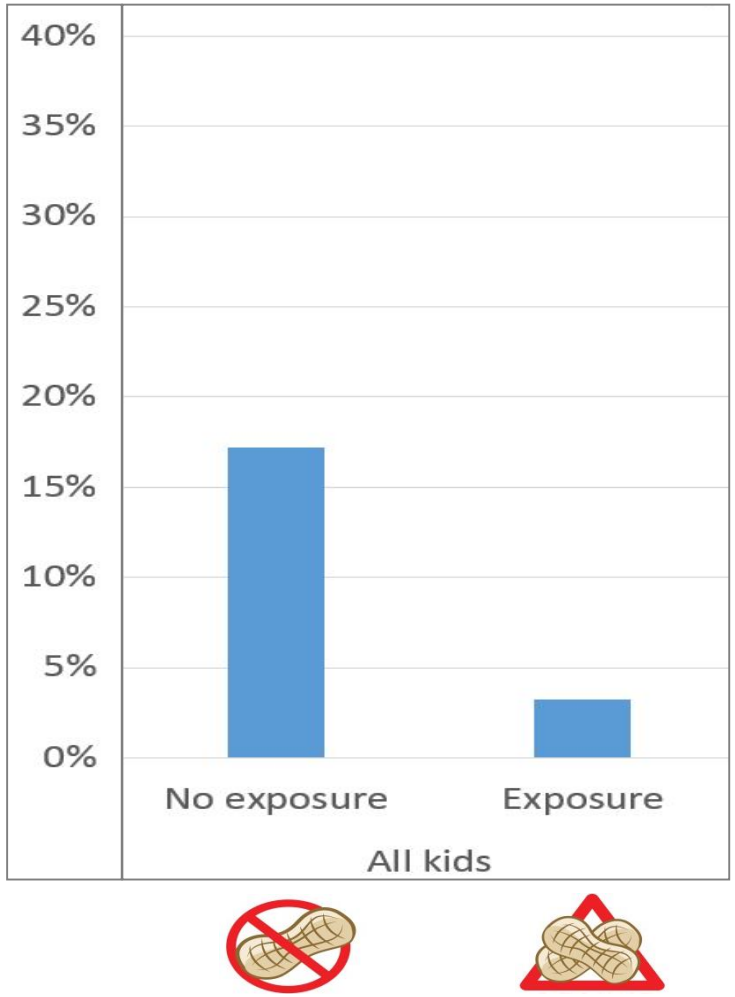
What not to do…

LEAP Trial Design

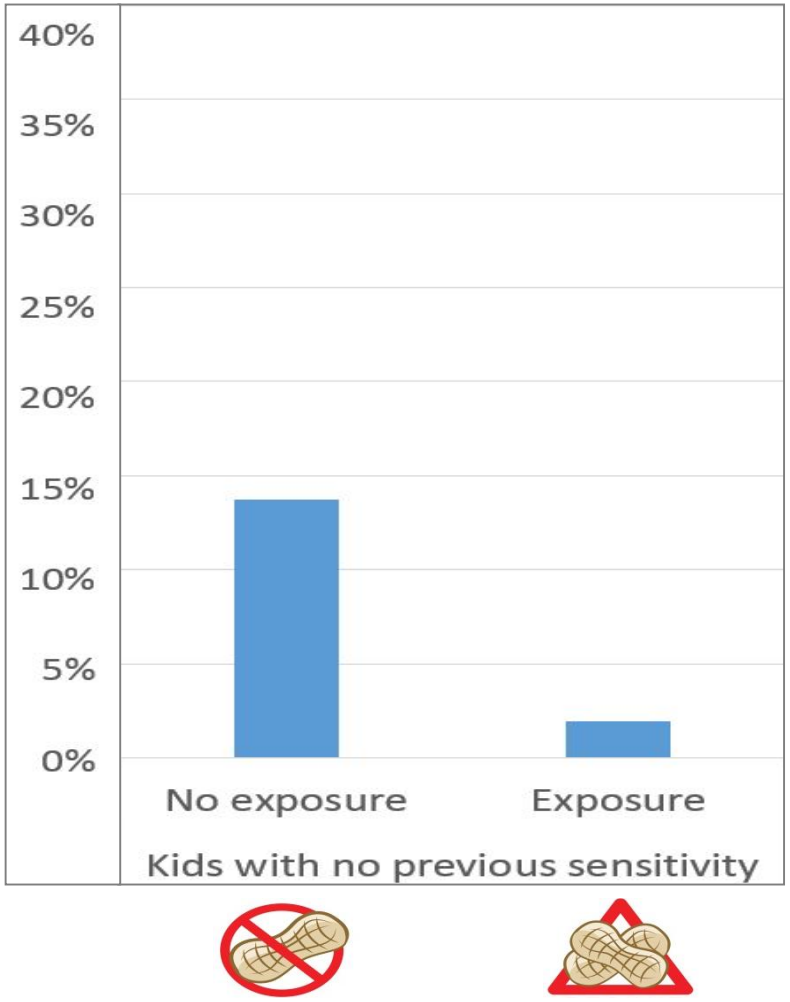


Du Toit G et al. *NEJM* 2015; 372:803-813

Percent with peanut allergy at 5 years of age (all kids)



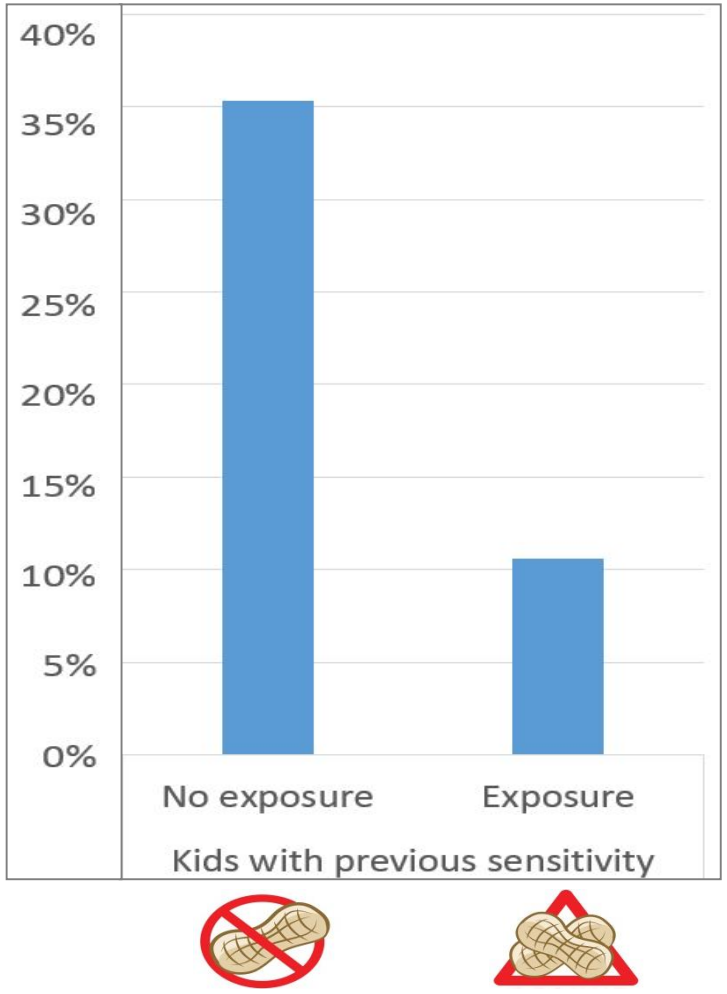
Percent with peanut allergy at 5 years of age (kids with negative skin tests)



By the numbers:

- 542 children
- 1 had a mild reaction to peanut on first introduction
- 86% relative risk reduction
- **11.8% absolute risk reduction**

Percent with peanut allergy at 5 years of age (kids with small positive skin tests)



By the numbers:

- 98 children
- 6 had a mild reaction to peanut on first introduction
- 70% relative risk reduction
- **24.7% absolute risk reduction**

Safety

- **No fatalities**
- No significant between-group difference in the incidence of serious adverse events (AE)
- AE rate not different based on sensitization
- At baseline screening:
  - 7 infants failed challenge at first randomized peanut dose
  - All 7 had mild (predominantly cutaneous) reactions, without any need for epinephrine

Du Toit G et al. N Engl J Med 2015;372:803-813

Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases–sponsored expert panel

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Bethesda, Md; McLean, Va; Cincinnati and Columbus, Ohio; Ann Arbor, Mich; San Rafael and San Diego, Calif; New Brunswick, NJ; Vancouver, British Columbia, Canada; Aurora, Colo; Lexington, Ky; Chicago and Winfield, Ill; Little Rock, Ark; Rockville, Md; Padua, Italy; Kansas City, Mo; New York, NY; Boston, Mass; Seattle, Wash; and Philadelphia, Pa

Togias A et al. J Allergy Clin Immunol. 2017 Jan;139(1):29-44.

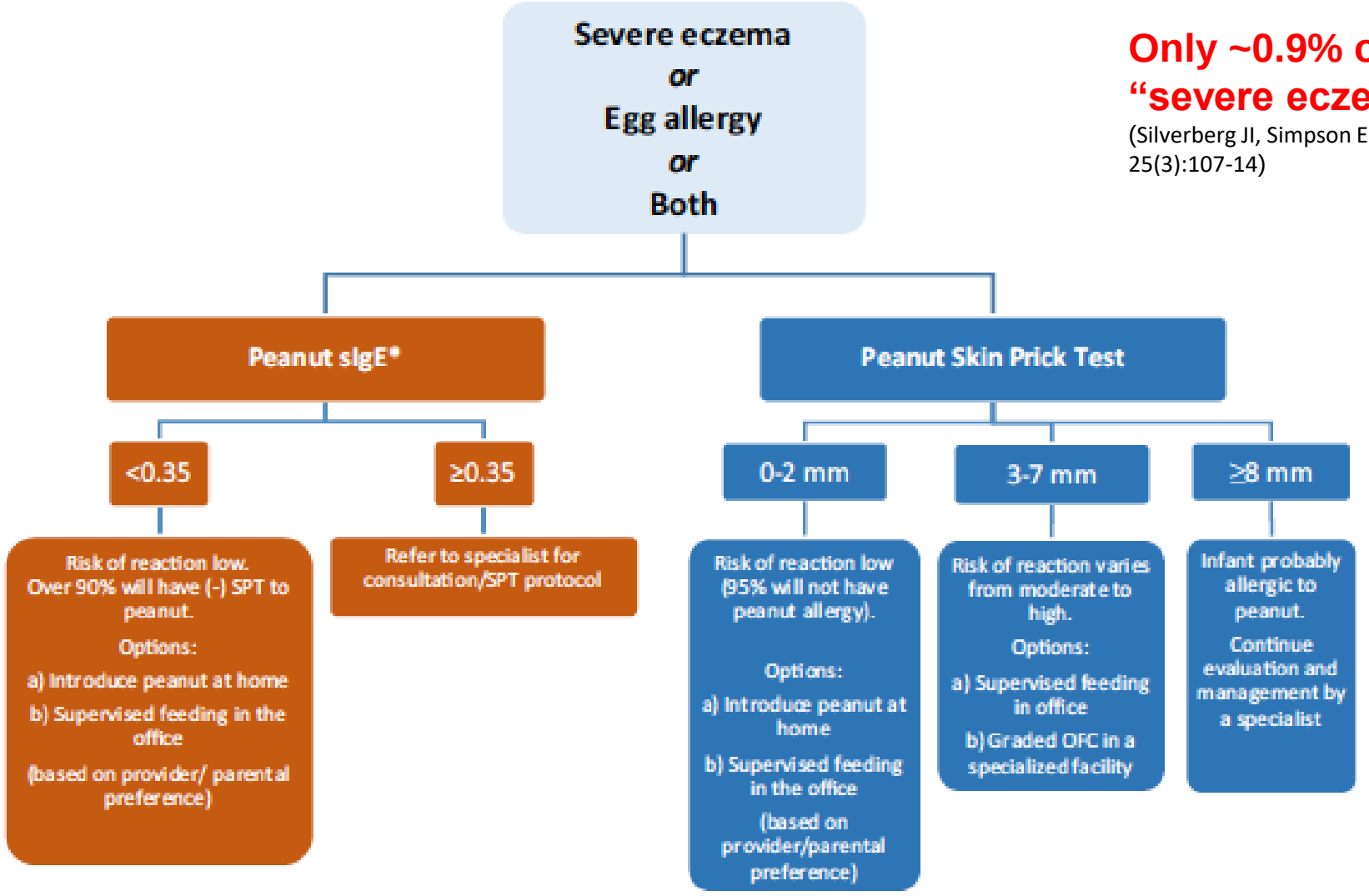
TABLE I. Summary of addendum guidelines 1, 2, and 3

Addendum guideline	Infant criteria	Recommendations	Earliest age of peanut introduction
1	Severe eczema, egg allergy, or both	Strongly consider evaluation by sIgE measurement and/or SPT and, if necessary, an OFC. Based on test results, introduce peanut-containing foods.	4-6 months
2 HOME	Mild-to-moderate eczema	Introduce peanut-containing foods	Around 6 months
3 HOME	No eczema or any food allergy	Introduce peanut-containing foods	Age appropriate and in accordance with family preferences and cultural practices

- *Severe eczema* is defined as persistent or frequently recurring eczema with typical morphology and distribution assessed as severe by a health care provider and requiring frequent need for prescription-strength topical corticosteroids, calcineurin inhibitors, or other anti-inflammatory agents despite appropriate use of emollients.

Only ~0.9% of all infants have "severe eczema"

(Silverberg JI, Simpson EL. Dermatitis. 2014 May-Jun; 25(3):107-14)



* To minimize a delay in peanut introduction for children who may test negative, testing for peanut-specific IgE may be the preferred initial approach in certain health care settings. Food allergen panel testing or the addition of sIgE testing for foods other than peanut is not recommended due to poor positive predictive value.

TABLE S-I. Typical peanut-containing foods, their peanut protein content, and feeding tips for infants

	Bamba	Peanut butter	Peanuts	Peanut flour or peanut butter powder
Amount containing approximately 2 g of peanut protein	17 g *or* ⅔ of a 28-g (1-oz) bag *or* 21 sticks	9-10 g *or* 2 teaspoons	8 g *or* ~10 whole peanuts (2½ teaspoons of grounded peanuts)	4 g *or* 2 teaspoons
Typical serving size	1 bag (28 g)	Spread on a slice of bread or toast (16 g)	2½ teaspoons of ground peanuts (8 g)	No typical serving size
Peanut protein per typical serving	3.2 g	3.4 g	2.1 g	No typical serving size
Feeding tips	For a smooth texture, mix with warm water (then let cool) or breast milk or infant formula and mash well. Pureed or mashed fruit or vegetables can be added. Older children can be offered sticks of Bamba.	For a smooth texture, mix with warm water (then let cool) or breast milk or infant formula. For older children, mix with pureed or mashed fruit or vegetables or any suitable family foods, such as yogurt or mashed potatoes.	Use blender to create a powder or paste. 2-2½ teaspoons of ground peanuts can be added to a portion of yogurt or pureed fruit or savory meal.	Mix with yogurt or apple sauce.

Notes: Bamba (Osem, Israel) is named because it was the product used in the LEAP trial and therefore has known peanut protein content and proven efficacy and safety. Other peanut puff products with similar peanut protein content can be substituted for Bamba.

Teaspoons and tablespoons are US measures (5 and 15 mL for a level teaspoon or tablespoon, respectively).

Eat 3 times / week

Controversies with NIAID guideline

- Confusing to have different ages of introduction (**4-6 vs ~6** months)
- **Screening skin tests/sIgE frequently falsely positive:**
  - No reported fatalities from exposure in 1st year of life
  - Israel has no screening, peanut introduced early, and essentially no peanut allergy
  - Lack of access to testing and oral challenges, resource limitations
- **"Screening creep":**
  - Delayed introduction due to over-diagnosis of "severe eczema" and over-testing

JAMA The Journal of the American Medical Association

Turner PJ, Campbell DE. JAMA. 2017 Feb 13

Case: Potential pitfalls of testing

- History of dry skin (no eczema), lives in Calgary
  - Peanut butter (PB) at home at 6 mo after mom heard about NIAID guidelines on TV. On 5th day some redness on face, saw family MD, peanut sIgE 2 kU/L, referred to internist, skin test results: "peanut 4, almond 3, cashew 3, sesame 3, macadamia 4, egg white 4"
- Referred to me as second opinion, seen at 8 months
  - All skin tests repeated & negative, PB challenge (observed ingestion) **same day** passed. Diagnosis of contact irritation around mouth.

    - *Message: Avoid over-diagnosis of food allergy. If lack of convincing history, don't rely on skin or blood tests.*

Practical take home messages

- 1. Food allergy is common, but also very susceptible to over-diagnosis
- 2. **Oral food challenges** are essential for diagnosis in many cases, yet under-utilized
- 3. Almost all infants should be introduced to non-choking peanut at ~ 6 months **at home**
  - Some parents may be hesitant to introduce, but few infants truly require testing before introduction
- 3. Once introduced, **give regularly**/several times per week/indefinitely

Thank you