Clinical Recommendations for Reducing and Preventing Food Allergies

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Presented by

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Pediatric Nutrition
CONTINUING EDUCATION FOR CLINICIANS

This activity is supported by an educational grant from
Mead Johnson Nutrition.

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Faculty Disclosures

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Research Support	National Institutes of Health
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	clinical area for above: food allergy

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Speakers Bureau	Abbott, Nutricia, Mead Johnson Nutrition
	clinical area for above: food allergy

Learning Objectives

- Develop management strategies to optimize nutrition in the allergic child and prevent allergic progression
- Interpret the latest evidence for introducing allergenic food in the first years

INTRODUCTION

- Food allergy prevalence
- The link between food allergies and poor growth

Most Common Allergens

milk

egg

fish

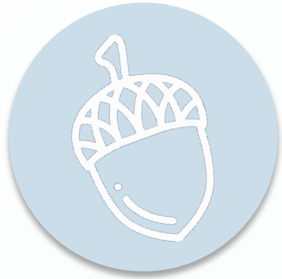
shellfish

Eight food groups account for 90% of all food allergies in the United States.

wheat

soy

peanut



tree nuts

Food Allergies Limit Growth

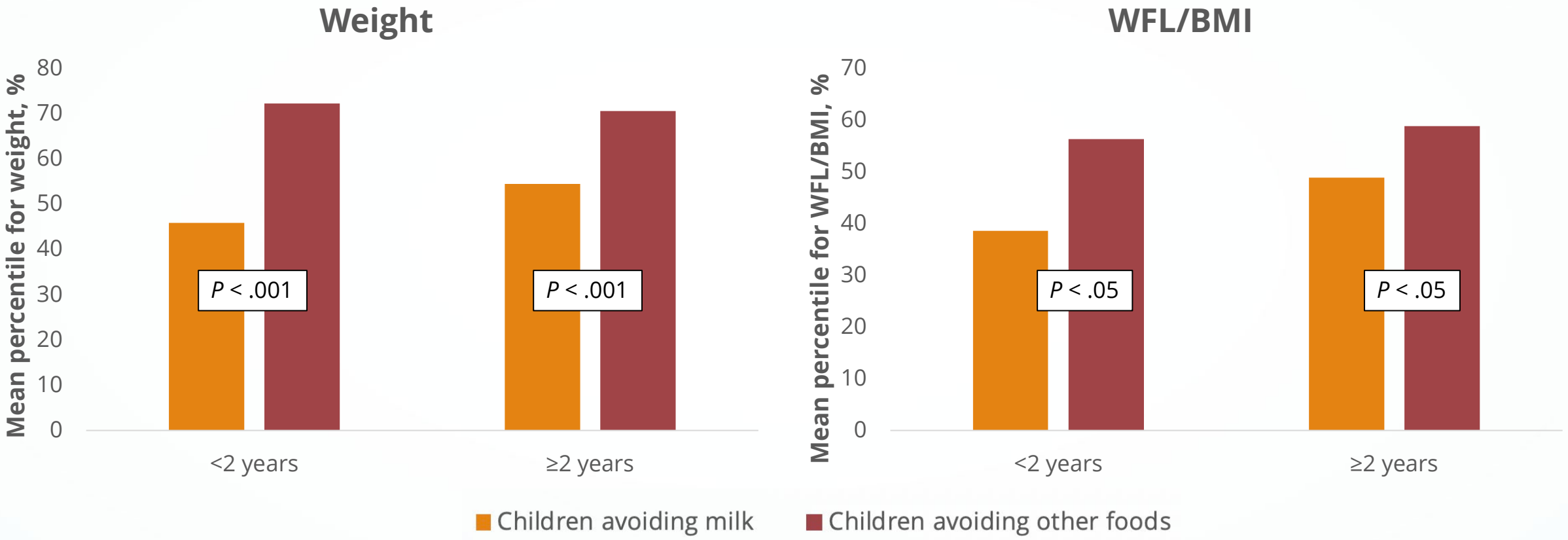
- Food allergies can negatively affect growth and food intake[1-3]
- Growth limitations are likely attributable to elimination diets and inadequate nutrient intake[1]
- Below-average weight and height persists into childhood for those with food allergies, particularly for milk allergies[4]

Height-for-Age by Allergy Status[1]

Participants	Height-for-age percentile		
	<25th	25th – 75th	>75th
Healthy controls (n = 96)	17%	56%	27%
Children with food allergy (n = 95)	28%	52%	20%
Allergic to 1 food (n = 32)	16%	50%	34%
Allergic to ≥2 foods (n = 63)	35%	52%	13%

1. Christie L, et al. *J Am Diet Assoc*. 2002;102(11):1648-1651.
2. Hobbs CB, et al. *J Allergy Clin Immunol Pract*. 2015;3(1):133–134.e1.
3. Robbins KA, et al. *J Allergy Clin Immunol*. 2014;134(6):1466–1468.e6.
4. Mehta H, et al. *J Pediatr*. 2014;165(4):842-848.

Milk Avoidance Compared With Other Food Avoidance†



†In a retrospective medical records review of children from a single center, with avoidance on the basis of real or perceived food allergies. WFL/BMI, weight for length for participants less than 2 years of age and body mass index for participants 2 years or older.

Hobbs CB, et al. *J Allergy Clin Immunol Pract*. 2015;3(1):133–4.e1.

International Survey on Growth in Children With Food Allergy[†]

- Cow's milk elimination led to lower weight-for-height Z scores than elimination of other foods
- Mixed IgE and non-IgE-mediated allergy had lower height-for-age Z scores than IgE-mediated allergy.
- Overall, the data indicated:
  - 9% were stunted
  - 6% were underweight
  - 5% were undernourished
  - 8% were overweight

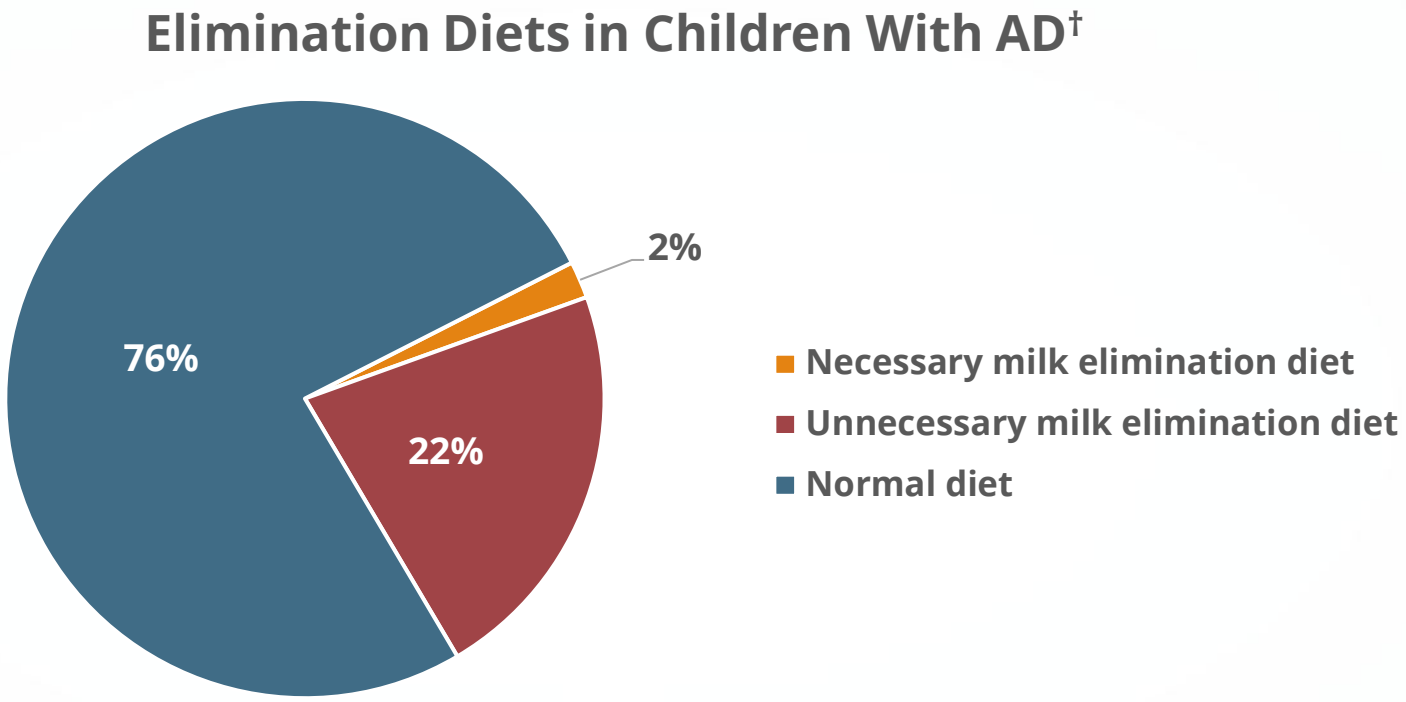
! Children particularly at risk of poor growth are those with non-IgE- and mixed IgE/non-IgE–mediated allergies, as well as those with cow's milk allergy.

[†]In a study of 430 children from 12 centers.

Meyer R, et al. *J Hum Nutr Diet*. 2019 Apr;32(2):175-184.

OPTIMIZING NUTRITION FOR THE ALLERGIC CHILD

Avoid Unnecessary Elimination Diets



Elimination diets can place children at risk for poor growth and nutritional deficiency.[1,2]

†Necessary elimination diet was one in which cow's milk allergy was confirmed with a double-blind placebo-controlled food challenge. Unnecessary elimination diet was one in which a double-blind placebo-controlled trial confirmed tolerance of cow's milk and cow's milk was successfully reintroduced.
AD, atopic dermatitis.

1. Sinagra JL, et al. *Pediatr Dermatol.* 2007;24(1):1-6.
2. Dambacher WM, et al. *Nutr J.* 2013;12:22.

Diagnosing Food Allergy: When Elimination Diets Are Necessary

- Long-term elimination diets should only be recommended by specialists for documented food allergy
- Skin prick testing results may be positive in cases where the food can be tolerated

For more information, see
Diagnosing Food Allergies in Infants and Children
with Jonathan Spergel, MD, PhD.

NIAID-Sponsored Expert Panel. *J Allergy Clin Immunol*. 2010;126(6 Suppl):S1–S58.

Food	Choose healthy infant foods*	How much/how often as part of the infant's complementary diet
BENEFICIAL for prevention When developmentally ready around 6 months of age or between 4-6 months of age if advised by your doctor due to high risk of allergy (severe eczema or egg allergy)*** **		
Peanut^	Choose peanut flour or thinned peanut butter that has no added ingredients (salt, sugar, oils) for healthier options! Peanut butter should be thinned with breastmilk, water or formula or mixed into a pureed food, eg, 2 teaspoons of peanut butter mixed with 2-3 teaspoons liquid.	About 1-2 teaspoons peanut butter/powder per serving, served 2-3 times per week as tolerated
BENEFICIAL for prevention but effective dose requires further research When developmentally ready after 4-6 months of age **		
Egg	Serve well-cooked egg mashed with pureed foods or chopped and served as finger food.	About 1/3 of a well-cooked egg, 2-3 times per week
HAVE NOT BEEN STUDIED SUFFICIENTLY to know if early introduction decreases risk of allergy, therefore doses are based on healthy feeding# There is currently no evidence of benefit to delay introduction of highly allergenic foods after 4-6 months of age and developmentally ready**		
Wheat	Infant wheat cereals (iron-fortified for the breastfed infant); whole wheat toast, pasta or crackers for older infants	½-1 oz total grains per day.
Milk	Plain, full-fat yogurt can be mixed into pureed fruit or vegetable; cow's milk should not substitute for breast milk or infant formula	2-4 fl oz per day
Sesame^	Tahini is sesame paste typically served as an ingredient in hummus or as tahini dipping sauce for finger foods like vegetables	> or = 3 teaspoons seeds/any nuts per week
Seafood	Low mercury finfish https://www.fda.gov/media/102331/download	1 oz per serving, 3 times per week (See FDA link for frequency and type of fish)
HAVE NOT BEEN STUDIED to know if early introduction decreases allergy risk, therefore doses are based on healthy feeding# There is currently no evidence of benefit to delay introduction of highly allergenic foods after 4-6 months of age and developmentally ready**		
Tree nuts^	Smooth, thinned nut butters, eg, almond, cashew, hazelnut, pistachio, walnut	> or = 3 teaspoons seeds/any nut per week
Soy	Soft tofu	2 tablespoons per serving

Added 9-August-2021

* When beginning complementary feeding, offer single ingredient foods one at a time initially to determine tolerance.
There is no prescribed number of days or feedings required to determine tolerance but we recommend only one new food per meal.

**How do I know if my infant is developmentally ready? Here are some signs:

- Holds head upright
- Closes mouth around a spoon can open mouth and lean forward to accept a spoon
- Can sit with some assistance.

Offer your baby 1-2 foods prior to offering potentially allergenic foods to ensure they are developmentally ready to eat complementary foods.

***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. The FDA has determined, however, that the evidence supporting this claim is limited to one study. If your infant has severe eczema and/or egg allergy, check with your infant's healthcare provider before feeding foods containing ground peanuts.[32]

Infant feeding

- Protein foods, modified for texture, such as peanut, tree nuts, egg, sesame, fish, and soy can be fed as healthy additions in the infant diet within this recommended framework.
- We recommend introducing potential allergenic foods early and feeding them regularly rather than a prescribed amount as long as it is within the context of healthy infant feeding.
- See Online Supplement S1 for further infant feeding guidance.

^ Peanut and Tree nuts and Sesame

- Peanut, tree nuts and sesame are protein foods with higher fat and calorie content therefore, a smaller serving size is more appropriate.
- Balance these higher fat/protein foods with lower fat foods such as fish, soy, and other proteins not considered highly allergenic such as lean meats, poultry, legumes, etc.
- Doses for tree nut prevention are not known.
- It may not fit within healthy infant feeding regimens to aim for 1-2 teaspoons of each tree nut per week.
- See mixed nut butter recipe in online Supplement S2.

Goal doses of food protein per week from EAT study- 2 g of each allergenic food protein twice each week (4 g of allergen protein per food per week). The full weekly amount for the allergenic foods consisted of 2 small 40- to 60-g portions of cow's milk yogurt, 3 rounded teaspoons of peanut butter, 1 small hard-boiled egg (<53 g), 3 rounded teaspoons of sesame paste, 25 g of whitefish, and 2 wheat-based cereal biscuits (e.g. Weetabix).[8]

A Patient-Specific Approach to Develop an Exclusion Diet to Manage Food Allergy in Infants and Children

Foods to avoid and degree of avoidance

Suitable substitutes

Self-management skills

Co-existing and cross-reacting allergens

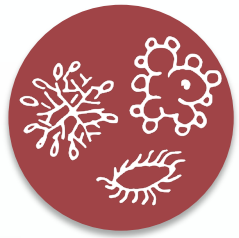
Novel allergens

Industry and environment

- Travelling and immigration
- Food and nutrition literacy
- Threshold levels and cross-contact or cross-contamination

Nutrition

- Promote optimal growth
- Prevent nutrient deficiencies
- Development of normal feeding skills
- Optimal nutrition for long-term health



Future

The role of nutrients, dietary patterns, and other food factors regarding:

- Gut microbiome
- Immune system
- Allergy prevention and tolerance development

Venter C, et al. *Clin Exp Allergy*. 2018;48(2):121-137.

Food Substitutions

Allergen	Lost nutrients	Suggested alternatives (if not allergic)
Milk	Protein, fat, calcium, riboflavin, phosphorous, vitamins A, D, B12	Meat, fish, poultry, legumes, eggs, fortified milk substitutes, calcium-fortified foods or drinks
Eggs	Protein, iron, biotin, folacin, riboflavin, vitamins A, D, E, B12, selenium	Meats, fish, poultry, legumes, dairy, leafy greens, enriched grains
Soy	Protein, thiamin, riboflavin, iron, calcium, zinc, vitamin B6	Meats, fish, poultry, legumes, eggs, dairy, fruit, vegetables, leafy greens, enriched grains
Wheat	Thiamin, niacin, riboflavin, folate, iron, fiber	Meats (iron), whole and fortified alternate grain products (oats, buckwheat, amaranth, millet, quinoa, teff, sorghum), seeds, legumes
Peanuts and tree nuts	Protein, vitamins, minerals	Meats, fish, poultry, eggs, dairy, fruit, vegetables, enriched grains, seeds
Fish and shellfish	Protein, PUFA (fatty fish) iodine, B12, A, E	Meats, poultry, eggs, fruit, vegetables, enriched grains, seeds, marine algae and seaweed

Modified from: Asthma and Allergy Foundation of America. https://www.kidswithfoodallergies.org/page/replacing-lost-nutrients.aspx. Reviewed March 2013.

Nutrients in Cow's Milk and Substitutes

Cow's milk or enriched substitute	kCal per 8 oz	Protein (g)	Fat (g)	Calcium (mg)/ Vitamin D (IU)
Cow's Milk	150	8	8	Varies based on fortification!
Pea	100	8	4.5	
Soy	100	7	4	
Oat	120	4	3	
Rice	120	1	2.5	
Coconut	80	0	4.5	
Almond	50	1	2.5	

! Milk substitutes are not nutritionally equivalent.

Encourage Breastfeeding and Ensure Adequate Maternal Nutrition

- Fatty acid composition of breast milk reflects maternal diet
- Secretion into milk is **rapidly and substantially** reduced by maternal depletion of the following nutrients:
  - Thiamin
  - Riboflavin
  - Vitamin B-6
  - Vitamin B-12
  - Choline
  - Retinol
  - Vitamin A
  - Vitamin D
  - Selenium
  - Iodine
- Maternal supplementation with these nutrients can increase breast milk concentrations and **improve infant health**

Allen L. *Adv Nutr*. 2012;3:362-369.

Hypoallergenic Formulas

- **Extensively hydrolyzed formulas** (eHF)
- **Amino acid–based formulas** (peptide-free)
- **Not Hypoallergenic**
  - Partially hydrolyzed formulas are not hypoallergenic.[1]
  - European formulas labeled “HA” are typically partially hydrolyzed.[2]
  - Soy formula is also not hypoallergenic but may be tolerated by those with cow’s milk allergy—especially those with IgE-mediated allergy—and may be used after 6 months of age.[1]

1. American Academy of Pediatrics. Committee on Nutrition. *Pediatrics*. 2000;106(2 Pt 1):346-349.
2. DiMaggio DM, et al. *J Pediatr Gastroenterol Nutr.* Published online May 9, 2019. doi:10.1097/MPG.0000000000002395

The Importance of Feeding in Infancy

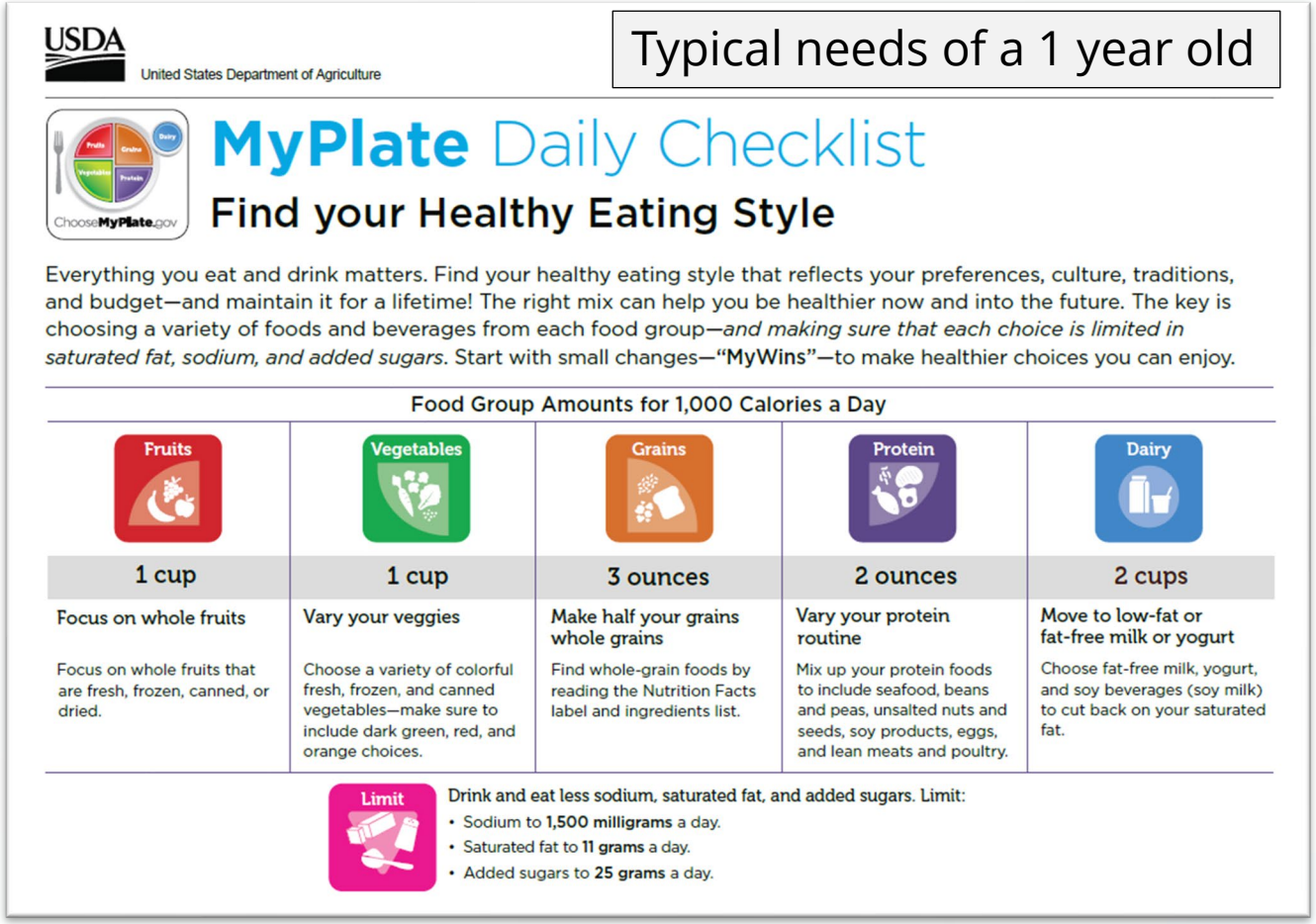
- Complementary feeding should be aligned with physiological, oral and motor skills beginning around 6 months of age (and not sooner than 4 months)
- Infants will generally accept a new flavor on the first presentation[1]
- In contrast children 2–5 years need multiple exposures to a new food[1]
- Early introduction of a variety of flavors and textures can impact long-term food acceptance
- Children introduced to lumpy solids after 9 months ate less of many food groups at 7 years of age including fruits and vegetables ($P < .05$) and were significantly more likely to have feeding problems at 7 years ($P < .05$) [2]

! There is no reason to delay introduction of complementary foods beyond 6 months, including those complementary foods thought to be highly allergenic.[3]

1. Birch LL, et al. *Appetite.* 1998;30:283-95.
2. Arlinghaus KR, et al. *Am J Clin Nutr.* 2018;108:730-6.
3. Greer FR, et al. *Pediatrics.* 2019;143(4). pii:e20190281.

Ensure That the Diet Is Balanced!

USDA MyPlate
www.choosemyplate.gov



USDA United States Department of Agriculture

Typical needs of a 1 year old

MyPlate Daily Checklist

Find your Healthy Eating Style

Everything you eat and drink matters. Find your healthy eating style that reflects your preferences, culture, traditions, and budget—and maintain it for a lifetime! The right mix can help you be healthier now and into the future. The key is choosing a variety of foods and beverages from each food group—*and making sure that each choice is limited in saturated fat, sodium, and added sugars*. Start with small changes—"**MyWins**"—to make healthier choices you can enjoy.

Food Group Amounts for 1,000 Calories a Day

Fruits	Vegetables	Grains	Protein	Dairy
1 cup	1 cup	3 ounces	2 ounces	2 cups
Focus on whole fruits	**Vary your veggies**	**Make half your grains whole grains**	**Vary your protein routine**	**Move to low-fat or fat-free milk or yogurt**
Focus on whole fruits that are fresh, frozen, canned, or dried.	Choose a variety of colorful fresh, frozen, and canned vegetables—make sure to include dark green, red, and orange choices.	Find whole-grain foods by reading the Nutrition Facts label and ingredients list.	Mix up your protein foods to include seafood, beans and peas, unsalted nuts and seeds, soy products, eggs, and lean meats and poultry.	Choose fat-free milk, yogurt, and soy beverages (soy milk) to cut back on your saturated fat.

Limit

Drink and eat less sodium, saturated fat, and added sugars. Limit:

- Sodium to **1,500 milligrams** a day.
- Saturated fat to **11 grams** a day.
- Added sugars to **25 grams** a day.

USDA MyPlate. www.choosemyplate.gov. Accessed June 17, 2019.

Dietary and Nutritional Counseling Improves Nutritional Status†

Median nutrient intake	Healthy children at baseline (n = 66)	Patients with food allergy	
		At baseline (n = 91)	6 months after counseling (n = 85)
Energy intake (kcal/kg/d)	96	91*	97.3‡
Macronutrients			
Carbohydrate (g/kg/d)	4.9	5.1	6.0*,‡
Fat (g/kg/d)	4.2	3.8	3.6*
Protein (g/kg/d)	4.6	2.2*	3.6*,‡
Micronutrients			
Fiber (g/d)	7.2	5.8	11.2*,‡
Calcium (mg/d)	848.3	314.4*	600*,‡
Iron (mg/d)	7.0	6.1	8.0*,‡
Zinc (mg/d)	4.1	3.0*	4.5‡

*$P < .01$ vs healthy children at baseline. ‡$P < .01$ vs patients with allergy at baseline.

†In a prospective, interventional study of children aged 6–36 months with food allergies.

Berni Canani R, et al. *J Acad Nutr Diet.* 2014;114(9):1432-1439.

Vitamin and Mineral Supplementation

- May be appropriate if adequate vitamin and mineral intake cannot be obtained with food substitutes
- Common supplementation needs:
  - **Cow's milk allergy:** calcium and vitamin D
  - **Multiple allergies:** individualized approach to supplementing

Recommended Dietary Intake

Age	Calcium (mg/day)	Vitamin D (IU/day)
0 to 6 months	210	400
7 to 12 months	270	400
1 to 3 years	500	600
4 to 8 years	800	600
9 to 18 years	1300	600

Dietary reference intake calculator for health care professionals: https://fnic.nal.usda.gov/fnic/dri-calculator/

Somers L. *Pediatr Ann*. 2008 Aug;37(8):559-568.

Dietary Effects of Elimination Diet

	Without eliminations	Eliminations	With substitutions
Breakfast	Waffles with syrup Strawberries Milk	~~Waffles~~ with syrup Strawberries ~~Milk~~	Gluten-free, milk-free, egg-free waffles made with buckwheat Strawberries Elemental formula (8 oz)
Lunch	Turkey on whole wheat with cheese, lettuce, and mayonnaise Carrots with ranch dressing Pudding Juice	Turkey on ~~whole wheat~~ with cheese, lettuce, and mayonnaise Carrots with ~~ranch dressing~~ ~~Pudding~~ Juice	Turkey on teff tortilla with lettuce and canola oil–based mayonnaise or cranberry sauce Carrots with hummus Alternative yogurt smoothie with frozen peaches
Snack	Corn chips with guacamole	Corn chips with guacamole	Corn chips with guacamole
Dinner	Hamburger Helper (ground beef, macaroni, cheese, tomato sauce) Spinach salad with lettuce, tomato, peppers, cheese, ranch dressing Milk	Hamburger Helper (ground beef, ~~macaroni~~, ~~cheese~~, tomato sauce) Spinach salad with lettuce, tomato, peppers, ~~cheese~~, ~~ranch dressing~~ ~~Milk~~	Lean ground beef with marinara on chick pea noodles Spinach salad with lettuce, tomato, peppers, Italian dressing Elemental formula (8 oz)
Snack	Ice cream	~~Ice cream~~	Coconut ice cream

Groetch M, et al. *J Allergy Clin Immunol Pract*. 2013;1(4):323-331.

Key Takeaways

1. Encourage breastfeeding exclusively to 4–6 months of age and continuing breastfeeding while introducing complementary foods.
2. Consider breast milk, optimal hypoallergenic formula, or beverage choice and appropriate volumes and/or vitamin/mineral supplementation as needed.
3. Encourage a healthy diet rich in fruits, vegetables, fibers in particular digestible fibers, and long chain PUFA.
4. Do not delay introduction of complementary foods.
5. Provide an otherwise individualized approach to meet nutritional needs within the context of the allergen elimination diet.

Online Patient Resources

CoFAR
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FOOD ALLERGY RESEARCH
NIH Sponsored

www.cofargroup.org

FARE
Food Allergy Research & Education

www.foodallergy.org

REDUCING THE RISK OF ALLERGY

- Milestone LEAP, EAT, and PETIT studies
- Solid food introduction and allergies
- Skin barrier maintenance and allergies

180-Degree Change in Prevention Rationale

American Academy of Pediatrics Guidelines on Preventing Food Allergy

2000[1]

Wait to introduce allergenic foods:

Milk: 1 year

Eggs: 2 years

Nuts and fish: 3 years

2008[2]

No evidence for delaying introduction of allergenic foods:

Milk, eggs, nuts, and fish: 4-6 months

2019[3]

No evidence for delaying introduction of allergenic foods:

Milk, eggs, tree nuts, and fish: 4-6 months

Early introduction of peanuts may be beneficial for infants at high risk for allergy:

Peanuts: 4-6 months

1. Zeiger RS. *Pediatrics*. 2003;111(6 Pt 3):1662-1671.
2. Greer FR, et al. *Pediatrics*. 2008;121(1):183-191.
3. Greer FR, et al. *Pediatrics*. 2019;143(4). pii:e20190281.

180-Degree Change in Prevention Rationale

American Academy of Pediatrics Guidelines on Preventing Food Allergy

2000[1]

Wait to introduce allergenic foods:

- **Milk:** 1 year
- **Eggs:** 2 years
- **Nuts and fish**: 3 years

2008[2]

No evidence for delaying introduction of allergenic foods:

- **Milk, eggs, nuts, and fish:** 4-6 months

2015

LEAP study

Early introduction of peanuts may be beneficial for infants at high risk for allergy:

- **Peanuts:** 4-6 months

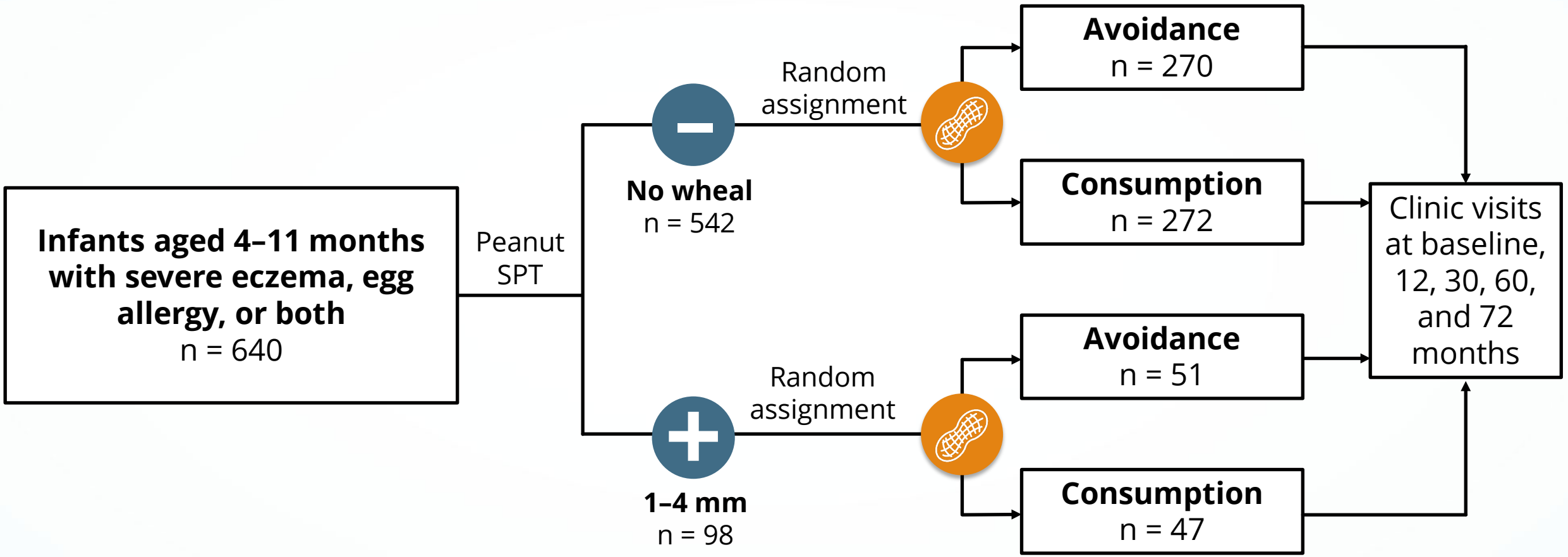
2019[3]

No evidence for delaying introduction of allergenic foods:

- **Milk, eggs, tree nuts, and fish:** 4-6 months

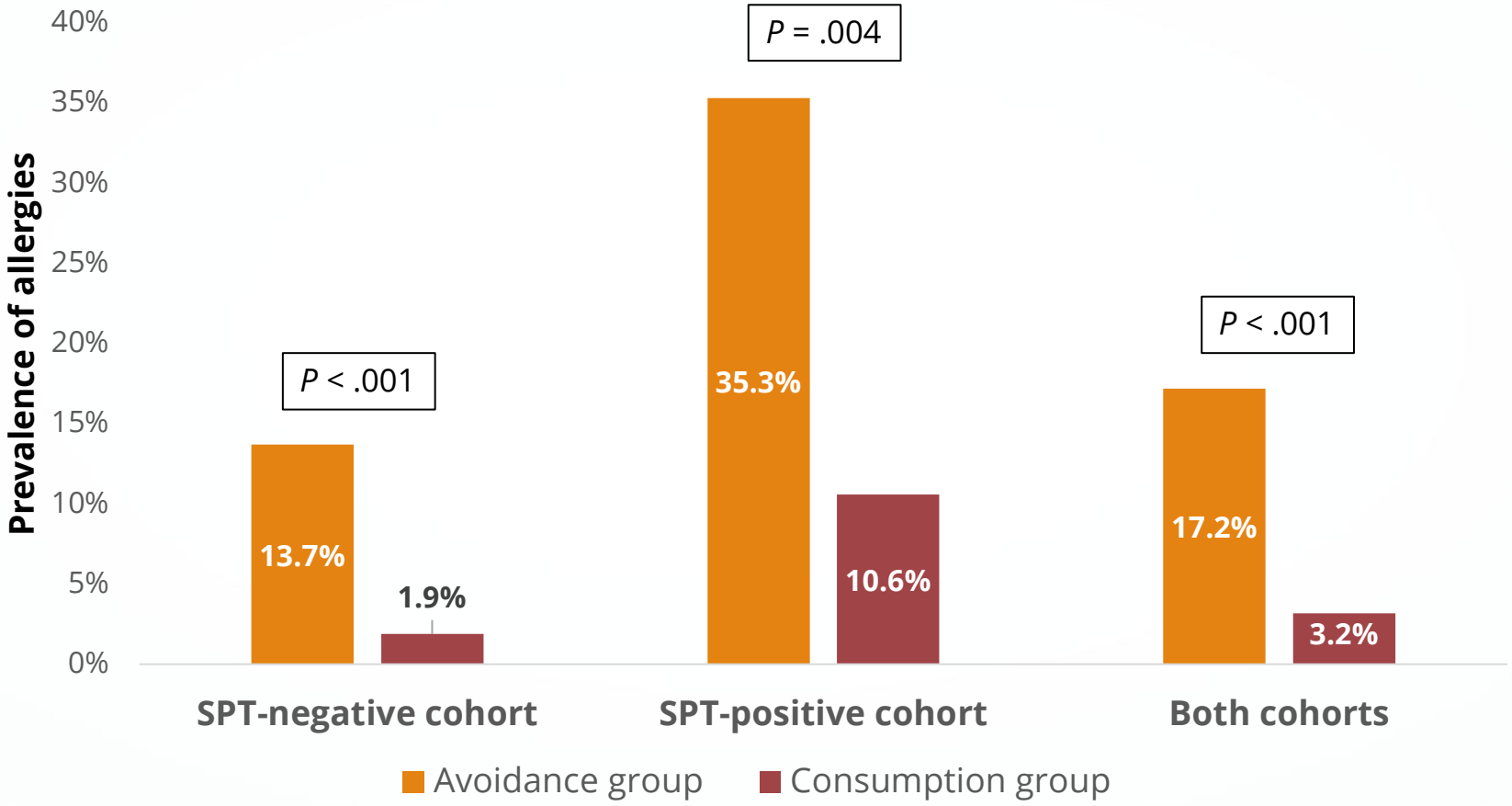
1. Zeiger RS. *Pediatrics*. 2003;111(6 Pt 3):1662-1671.
2. Greer FR, et al. *Pediatrics*. 2008;121(1):183-191.
3. Greer FR, et al. *Pediatrics*. 2019;143(4). pii:e20190281.

LEAP Study Design



SPT, skin prick test.

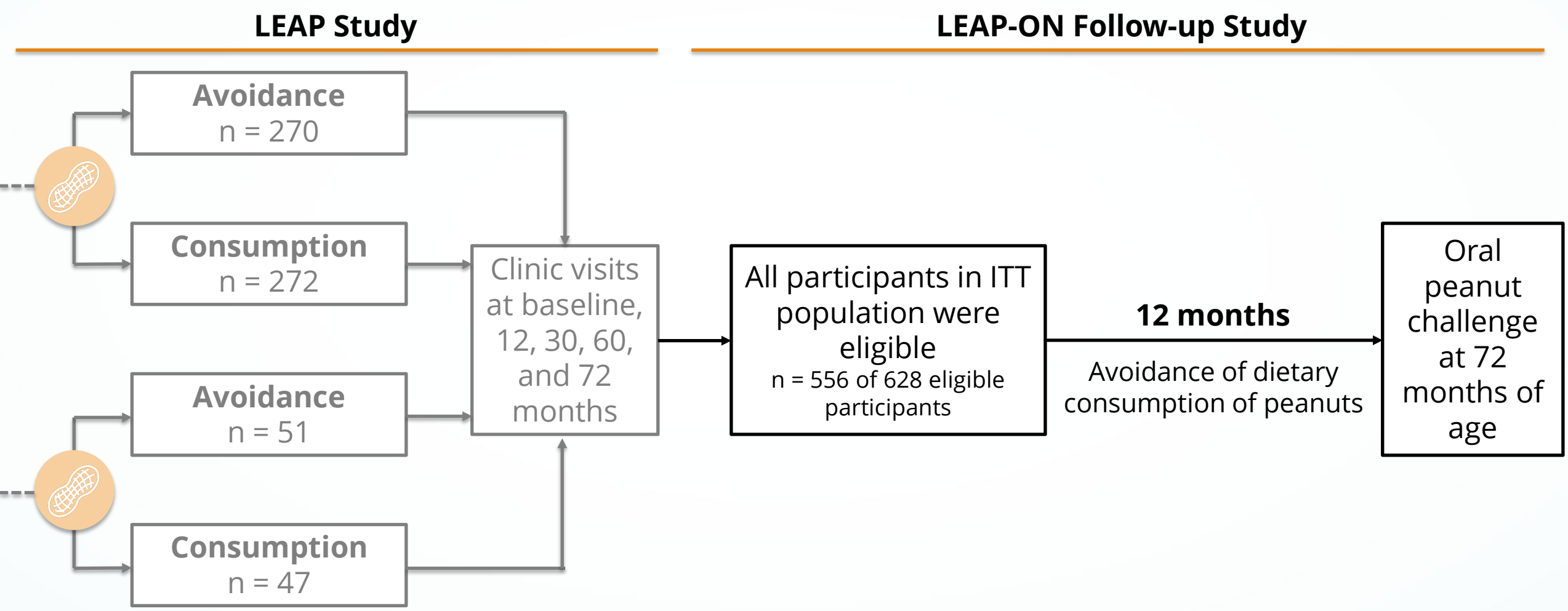
Primary and Secondary Prevention of Allergies at 60 Months†



†In the intention-to-treat analysis, as determined by an oral food challenge (96.4%) or diagnostic algorithm (1.7%).

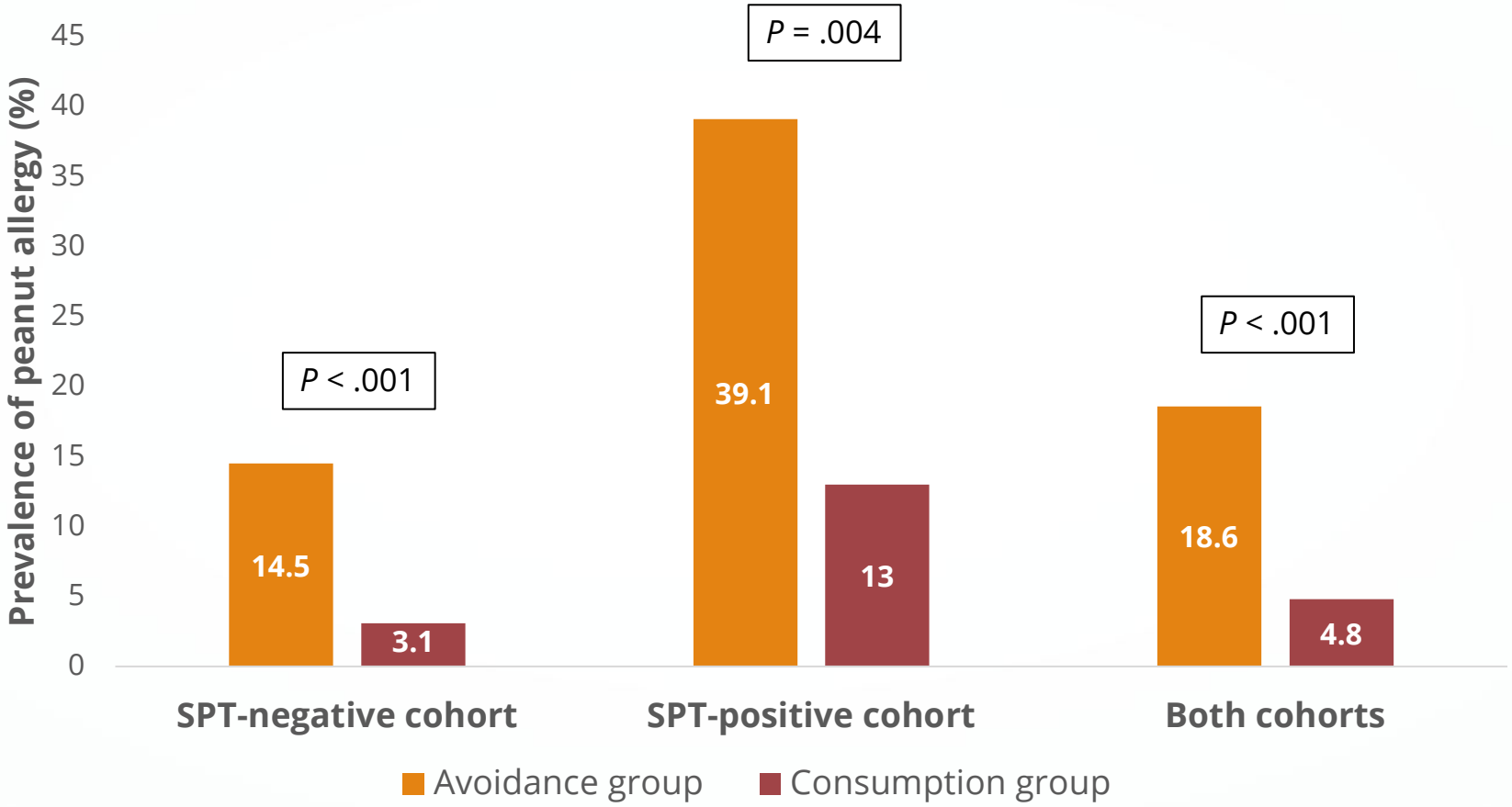
Image adapted from Du Toit G, et al. *N Engl J Med*. 2015;372(9):803-813.

LEAP-ON Follow-up Study



Du Toit G, et al. *N Engl J Med*. 2016;374(15):1435-1443.

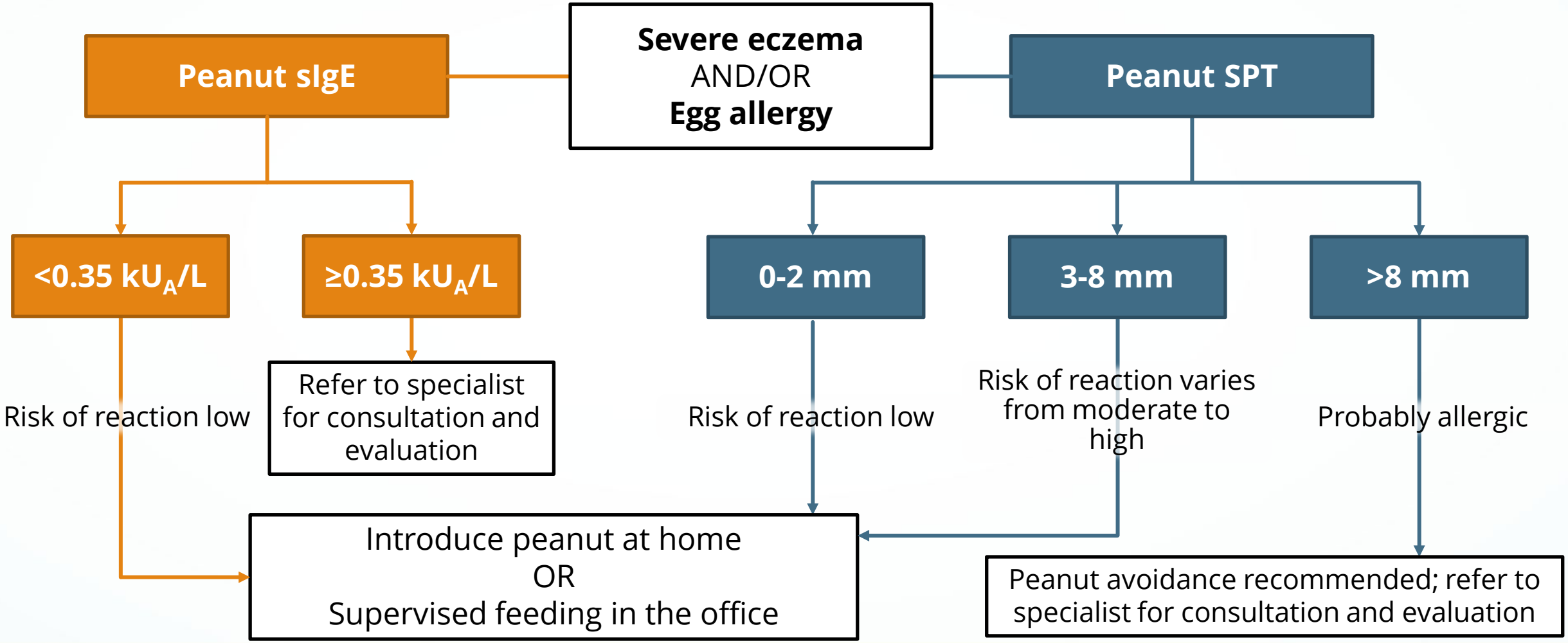
Persistence of Peanut Tolerance After Avoidance at 72 Months†



†In the enrolled participants in the follow-up study who had a peanut-allergy outcome that could be evaluated.

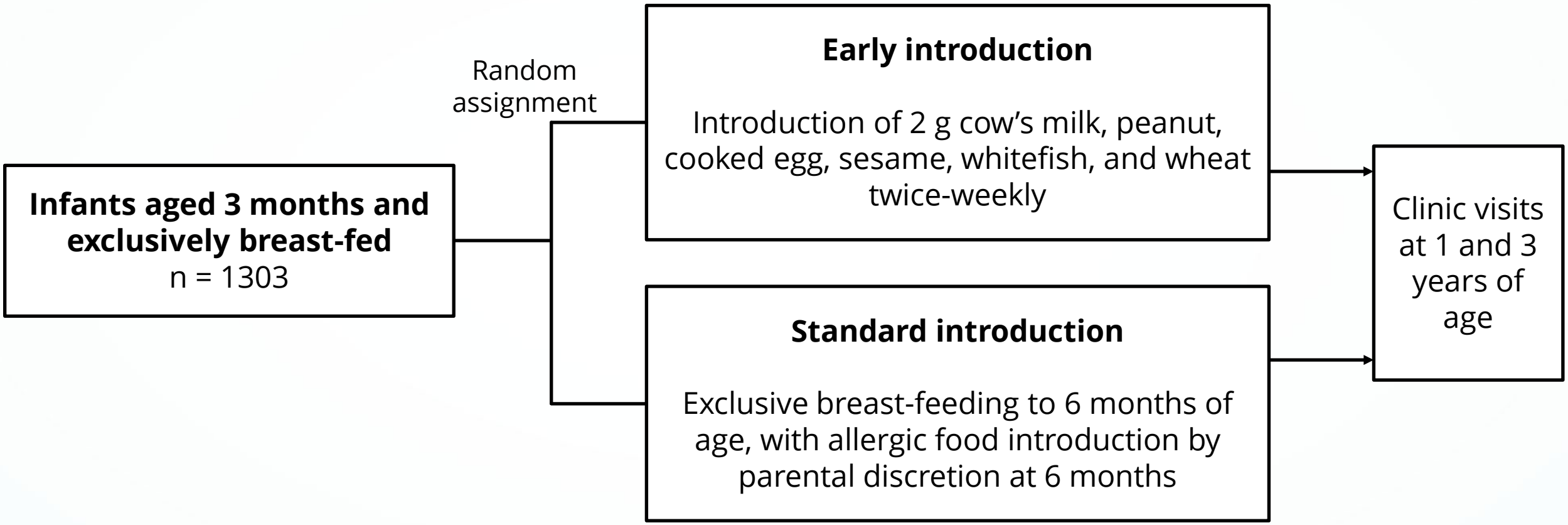
Image adapted from Du Toit G, et al. *N Engl J Med*. 2016;374(15):1435-1443.

2017 NIAID Addendum Guideline Recommendations



NIAID-Sponsored Expert Panel. https://www.niaid.nih.gov/sites/default/files/addendum-peanut-allergy-prevention-guidelines.pdf. Published 2017.

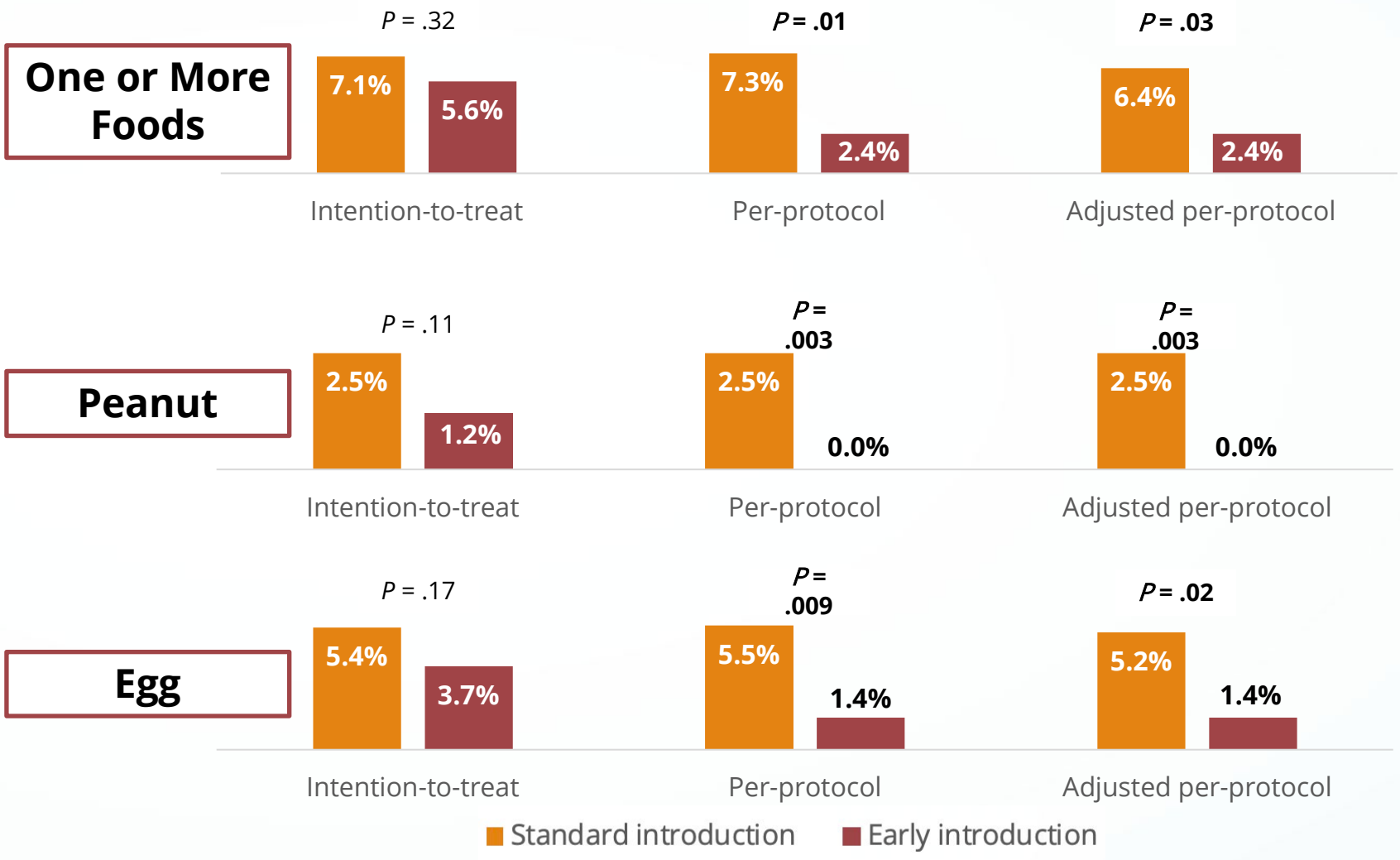
EAT Study Design



SPT, skin prick test.

Prevalence of Allergy Between 1 and 3 Years

- No significant difference in food allergy between groups by intention-to-treat analysis
- Adherence was lower for early feeding group (42.8%) than for standard feeding group (92.9%)



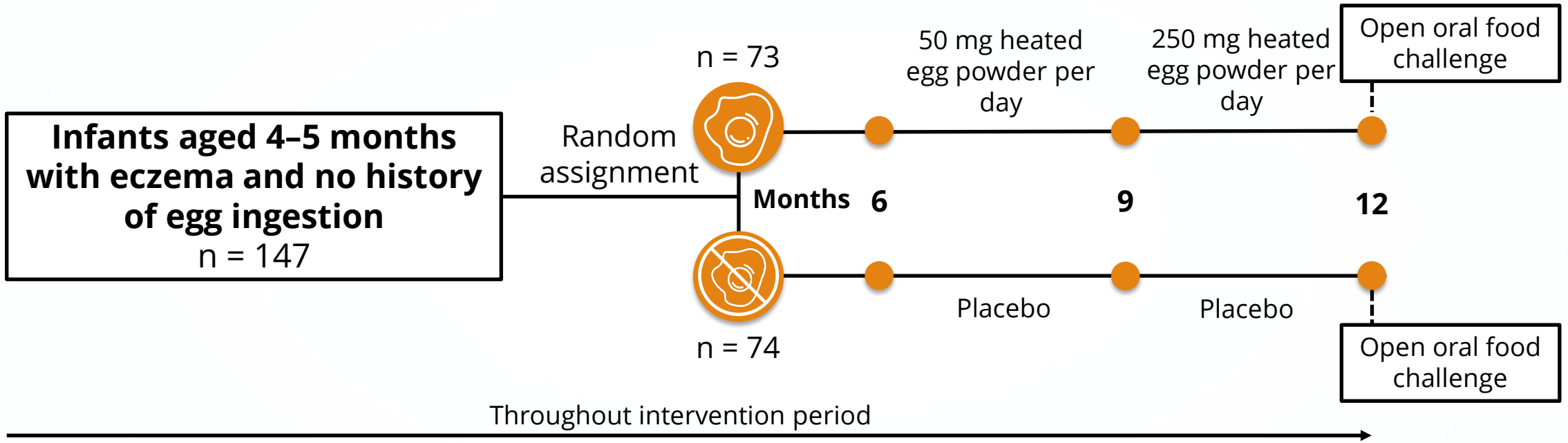
Images adapted from Perkin MR, et al. *N Engl J Med*. 2016;374(18):1733-1743.

Early Introduction of Egg and Egg Allergy: Systematic Review and Meta-analysis

- Of 416 articles identified and screened, 6 randomized controlled trials met eligibility criteria for data extraction
- Allergic outcomes evaluated in a total of 3032 participants
- A low to moderate level of evidence showed a benefit of early introduction of egg
- Consumption of less than 4 g/week of egg protein had greater preventive effect than a higher dose

Al-Saud B, Sigurdardóttir ST. *Int Arch Allergy Immunol*. 2018;177(4):350-359.

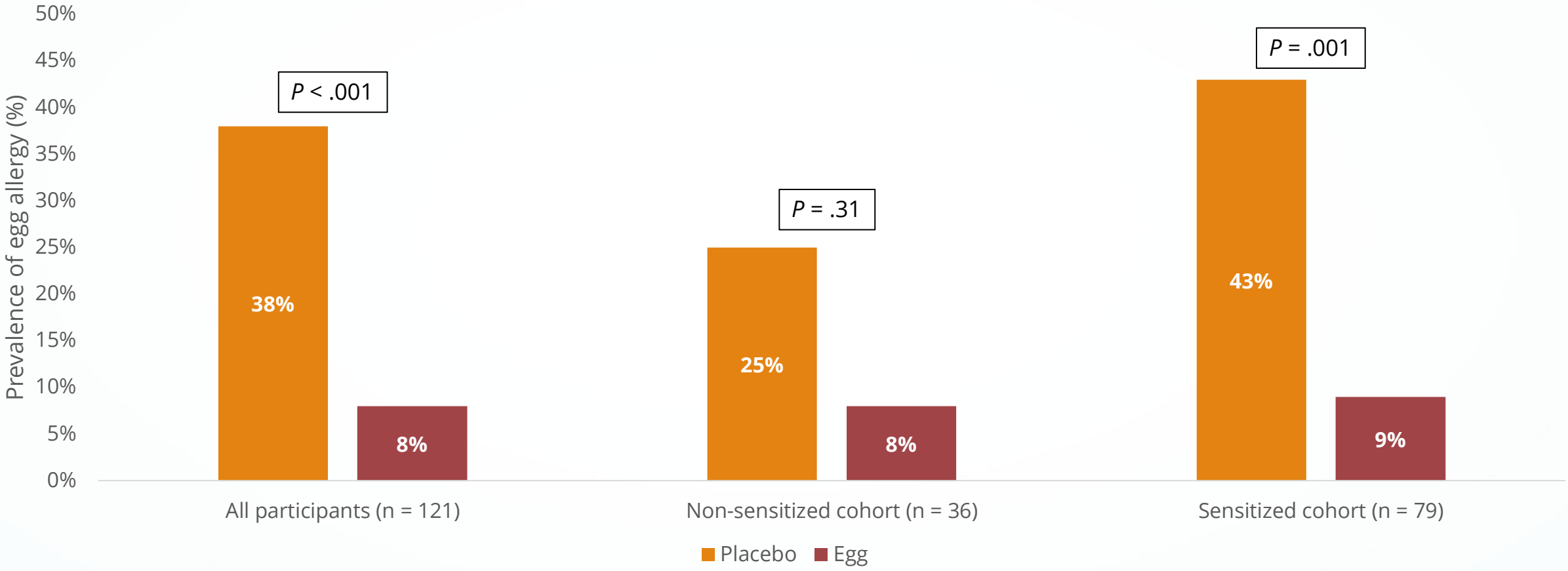
PETIT Study Design



All participants: Aggressive treatment of eczema and maintenance of control without exacerbations

Image adapted from Natsume O, et al. *Lancet*. 2017;389(10066):276-286.

Prevalence of Egg Allergy at 12 Months†



†In the primary analysis population. Sensitization cut-off was 0.35 kU_A/L of egg-white specific IgE at baseline.

Image adapted from Natsume O, et al. *Lancet*. 2017;389(10066):276-286.

Early Introduction of Cow's Milk: Observational Study

- A total of 5276 12-month-old infants were recruited from the HealthNuts longitudinal population-based food allergy study
- SPT to cow's milk allergy was performed on 2715 participants
  - Sensitization: wheal ≥2 mm
- Early exposure to cow's milk protein was determined by parental questionnaire at 1 year of age

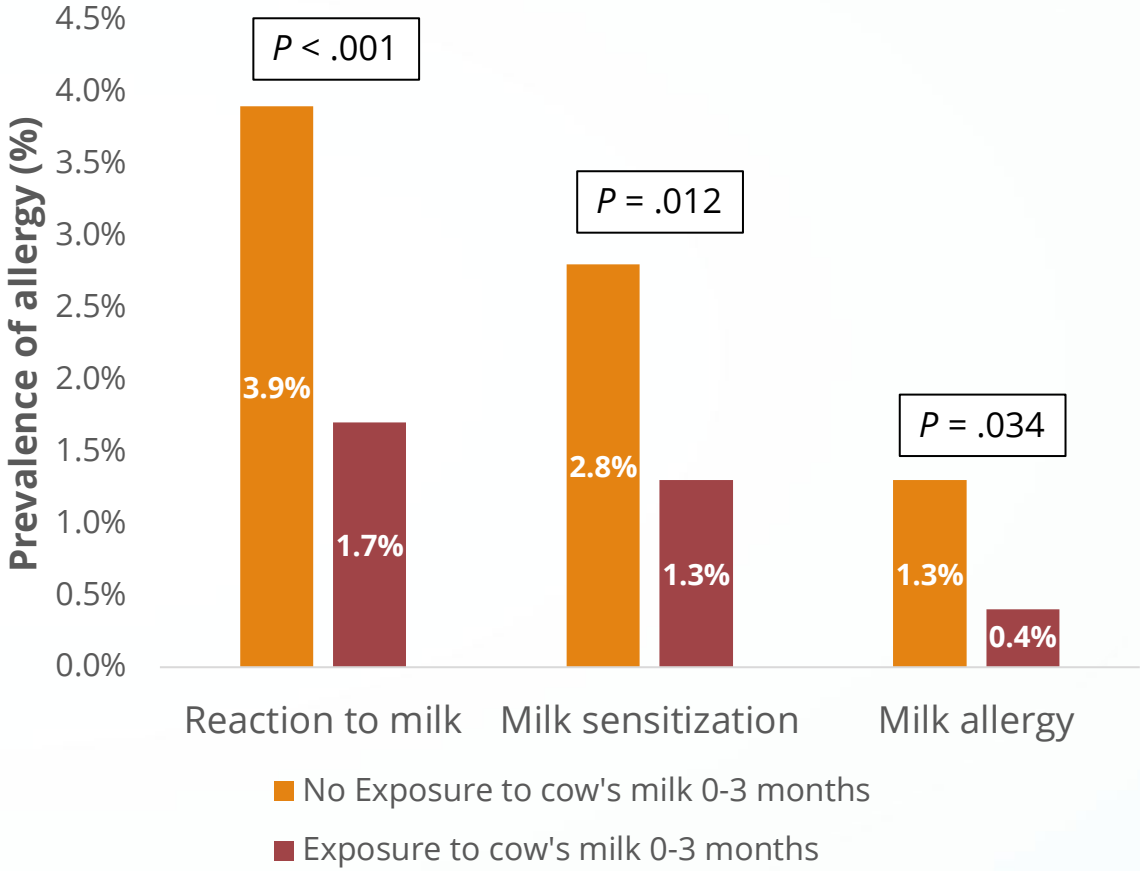


Image adapted from Peters RL, et al. *J Allergy Clin Immunol Pract*. 2019;7(2):462-470.e1.

Dietary Measures With No Proven Benefit or Insufficient Evidence

- Supplementation with vitamins A, D, E, and C; zinc; or selenium[1,2]
- Supplementation with probiotics[3]
- Introduction of hypoallergenic formulas[4]
- Exclusive breastfeeding[5]
- Maternal PUFA supplementation during pregnancy or lactation[6]

PUFA, long chain polyunsaturated fatty acids.

1. Nurmatov U, et al. *J Allergy Clin Immunol*. 2011; 127(3):724-733.e1-30.
2. di Mauro G, et al. *World Allergy Organ J*. 2016;9:28.
3. Fiocchi A, et al. *World Allergy Organ J.* 2015;8(1):4.
4. Osborn DA, et al. *Cochrane Database Syst Rev*. 2018;10:CD003664.
5. Lodge CJ, et al. *Acta Paediatr.* 2015;104(467):38-53.
6. Gunaratne AW, et al. *Cochrane Database Syst Rev.* 2015;(7):CD010085.

Rising Prevalence of Food and Skin Allergies

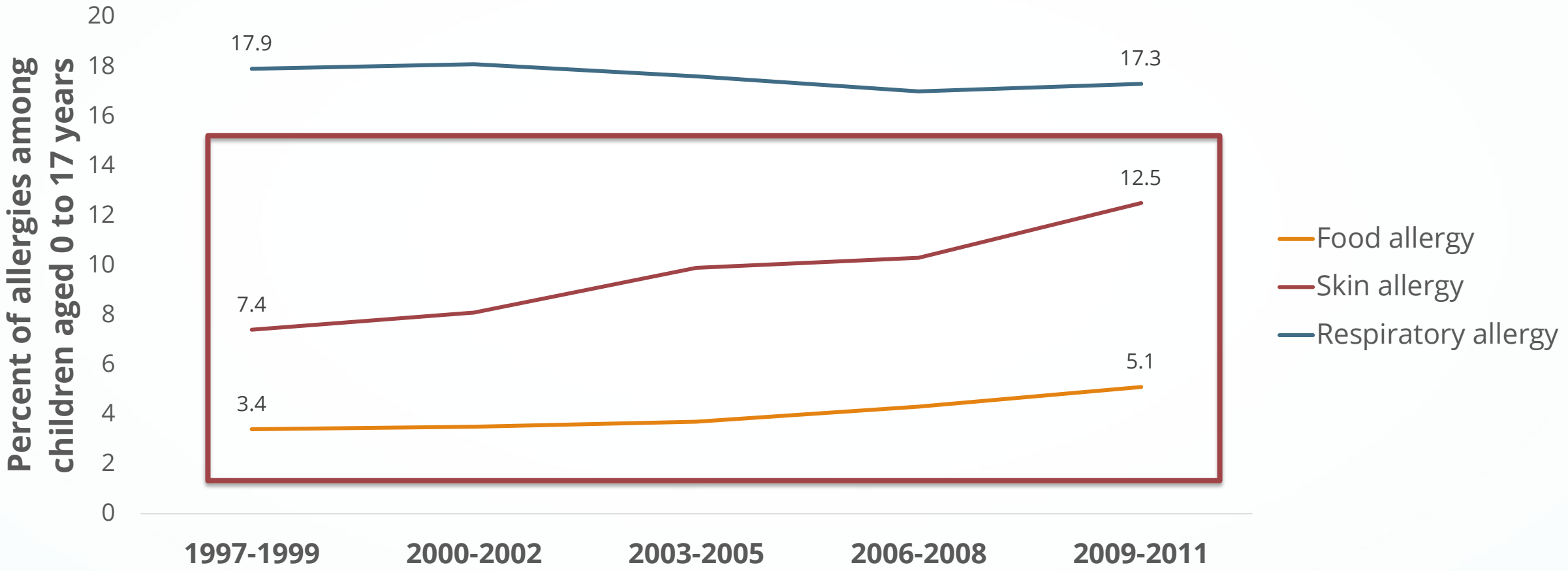
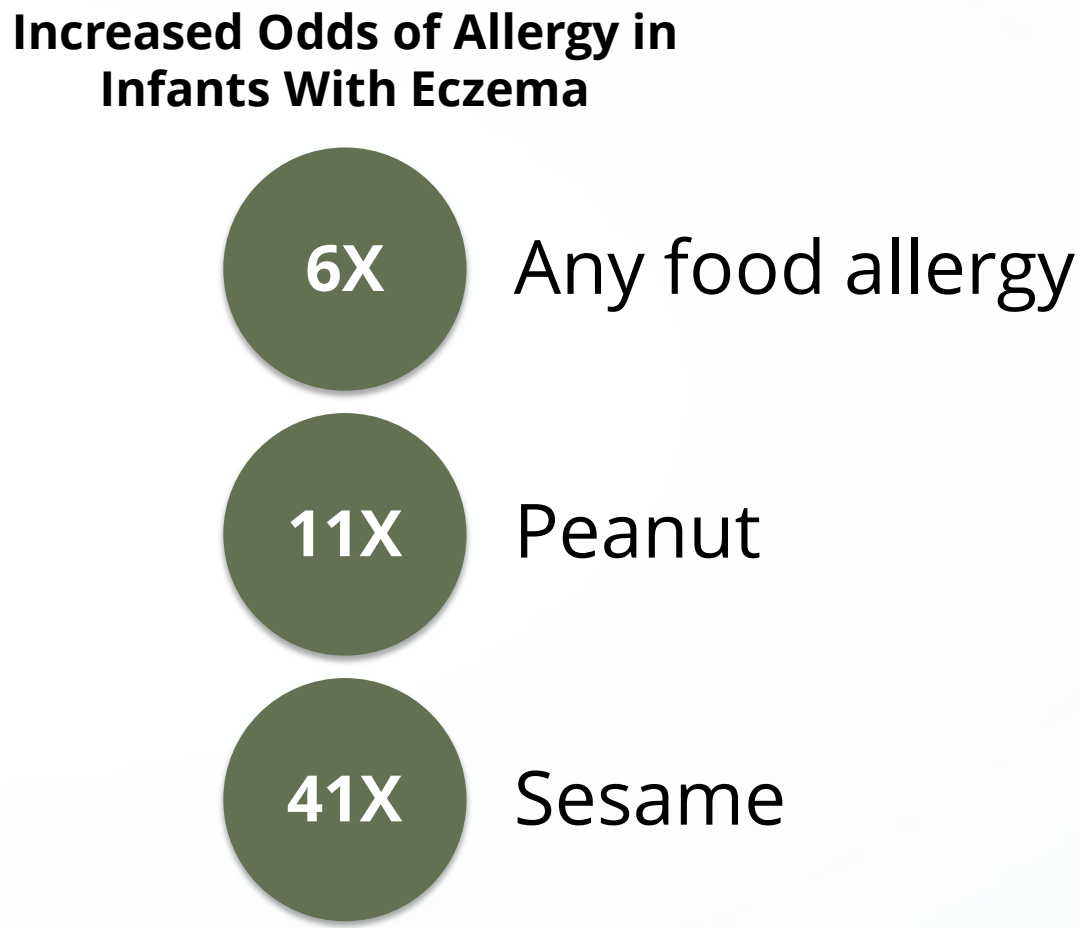


Image adapted from Jackson KD, et al. *NCHS Data Brief*. 2013;(121):1-8.

Eczema Is Associated With Development of Food Allergy

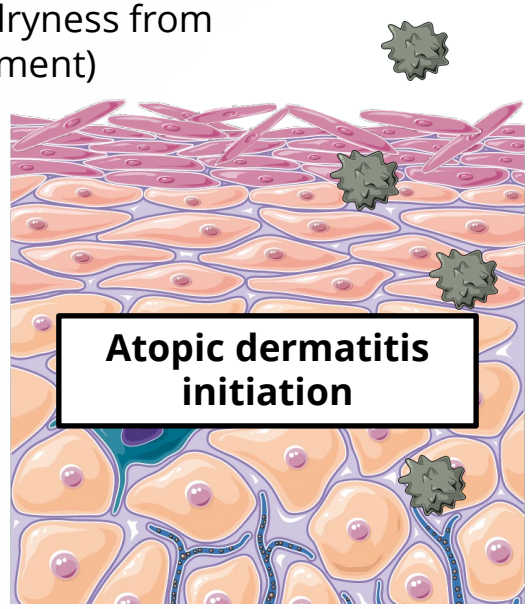
- Eczema increases the odds of developing food allergy, multiple food allergy, and specific types of food allergy
- Earlier onset eczema increases odds of food allergy
- More severe eczema increases odds of food allergy



Martin PE, et al. *Clin Exp Allergy.* 2015;45(1):255-264.

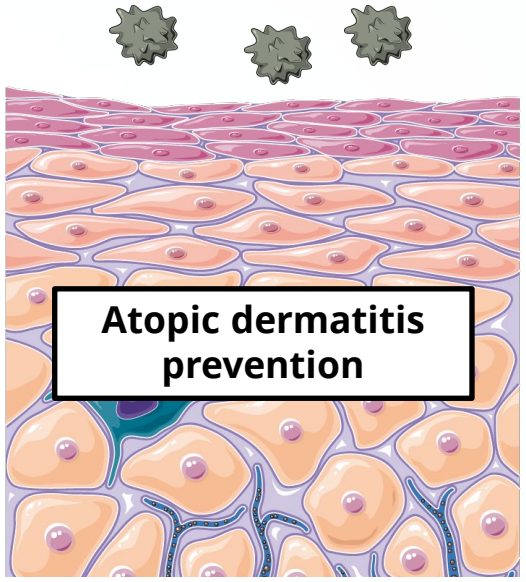
Skin Barrier Disruption Can Influence the Development of Allergies

1. Disrupted barrier (*FLG* mutation or dryness from cleansing/environment)



2. Allergen and irritant influx

3. Inflammatory T-cell responses initiated by keratinocytes (eg, TSLP) and dendritic cells



Mixed results on whether emollient therapy improves skin barrier enough to prevent allergy development

Image adapted from: Lowe AJ, et al. *Ann Allergy Asthma Immunol.* 2018;120(2):145-151.
Image components courtesy of Servier Medical Art by Servier (CC BY 3.0).

Food Allergy and Skin Barrier Disruption

Supporting evidence for allergic sensitization through skin:

- Allergic reactions to foods can occur without prior oral exposure
- Oral exposures in infancy generally lead to tolerance
- Atopic dermatitis and food allergy are highly comorbid
- Peanut allergy correlates with household peanut consumption and not individual peanut intake

Proposed Model

Skin barrier disruption

↓

Environmental exposure to allergen and epicutaneous absorption

↓

Systemic sensitization

↓

Development of food allergy

Izadi N, et al. *Children (Basel)*. 2015;2(3):382–402.

Enhancement of Skin Barrier to Prevent Atopic Dermatitis

- Protection of the skin barrier from dryness and irritation along with aggressive treatment of inflammation may prevent sensitization
- Decrease use of bathing, soaps, and anti-microbials
- Apply emollients
- Limit allergen contact exposure
- Treat inflammation aggressively

Application of Emollient to Prevent Atopic Dermatitis

- Randomized controlled trial of daily emollient application beginning by 3 weeks of age in infants at risk of atopic dermatitis[†] in the United Kingdom and United States
- Infants were randomly assigned to daily emollient treatment (n = 64) and no emollient treatment (n = 60)
- At 6 months, the **risk of atopic dermatitis was decreased by 50%** with emollient treatment relative to no treatment

  (20% vs 43%; *P* = .017)
- Did not evaluate sensitization to allergens

[†]At risk for atopic dermatitis defined as biologic parent or sibling with disease.

Simpson EL, et al. *J Allergy Clin Immunol*. 2014;134(4):818–823.

Application of Moisturizer to Prevent Atopic Dermatitis

- Enrolled neonates with one biologic parent or sibling with atopic dermatitis
- Participants were randomly assigned to receive emulsion-type moisturizer daily during the first 32 weeks of life (n = 59) or to control (n = 59)
  - All participants were prescribed petrolatum at the request of the institutional review board
- Intervention was associated with significantly lower risk of developing AD

  (*P* = .012)
- No significant difference in sensitization to egg
  - 38% vs 45% for treated vs control
  - 56% of infants who developed AD had IgE to egg (>0.7 kU_A/L)

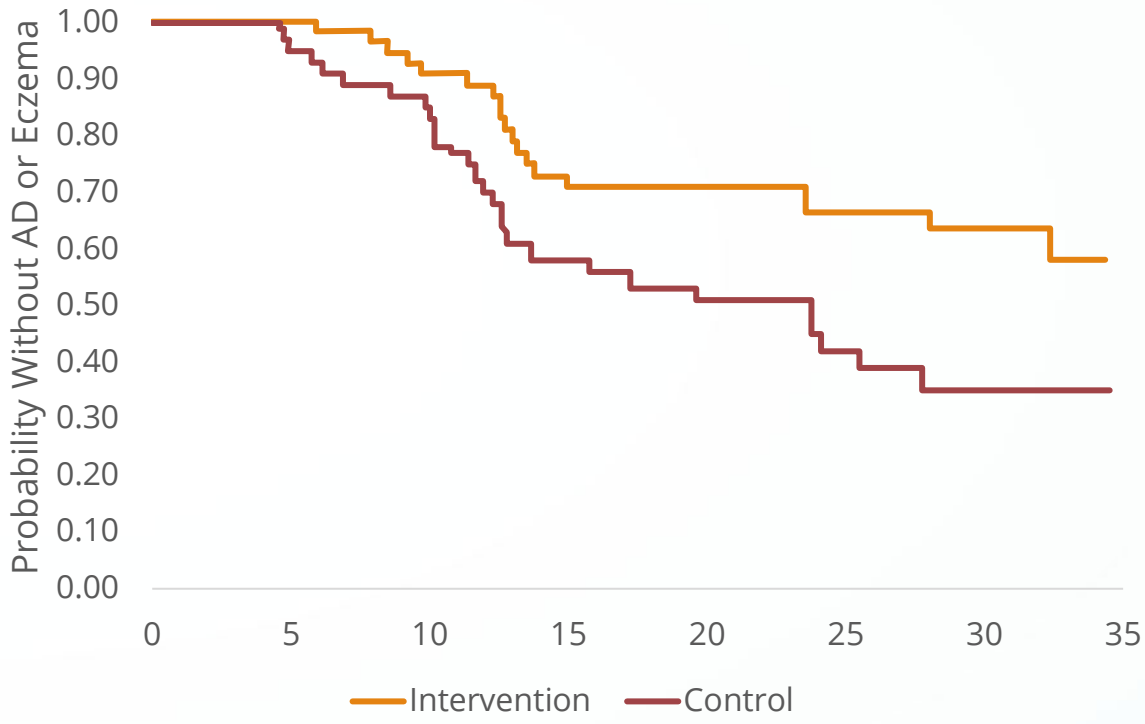


Image adapted from Horimukai K, et al. *J Allergy Clin Immunol*. 2014;134(4):824-830.e6.

Recently Released Negative Results Regarding Skin Interventions and Atopic Dermatitis

- **PreventADALL** study of 2172 infants revealed no benefit to skin or food interventions initiated at birth (and possibly risks)
  - Rates of atopic dermatitis at 12 months (*P* = .003):
    - **11.1%** in **skin intervention** group (oil baths and Ceridal cream applied to the face)
    - **9.0%** in **food intervention** group (introduction of peanut, milk, wheat, and egg between 3 and 6 months)
    - **5.3%** in **food and skin intervention** group
    - **8.1%** in **no intervention** group
- **BEEP** study of 693 high-risk babies revealed no benefit to skin intervention initiated at birth
  - Rates of eczema at 2 years (*P* = .61):
    - **23%** in **skin intervention** group (application of double-based gel or cream emollient for 12 months)
    - **25%** in **no intervention** group

Hein I. Emollient Fail to Protect Against Eczema. https://www.medscape.com/viewarticle/914051. Published June 6, 2019. Accessed June 17, 2019.

Anticipated Randomized Controlled Trial: PEBBLES

- A total of 760 infants with a family history of allergic disease will be recruited from maternity hospitals in Melbourne
- **Intervention:** Application of a ceramide-dominant emollient 2 times per day from birth to 6 months
- **Primary outcomes:** Presence of AD and food allergy in the first 12 months of life
- Phase 3 trial is underway, with results expected in 2021

NCT03667651. https://clinicaltrials.gov/ct2/show/NCT03667651. Updated October 2, 2018.

Key Takeaways: Measures to Prevent Development of Food Allergy Through Environmental Exposure

- Reduce/eliminate environmental exposure to foods
- Have to address environmental exposure and skin barrier in high-risk children
- Parental education programs (bathing and eczema care)
- Daily use of petrolatum for barrier protection
- Treat eczema or atopic dermatitis aggressively

Key Takeaways

- There is no evidence for delaying the introduction of common allergenic foods beyond 4 to 6 months
  - For infants at high risk for peanut allergy, may be beneficial to introduce peanuts at 4 to 6 months
  - Additional evidence may support early feeding of other allergenic foods
- Skin barrier dysfunction may precede development of allergies
- Evidence for reducing allergies by addressing skin barrier integrity is conflicting
  - Further studies are needed

ANY Questions?

Understanding Food Allergies in Infants and Children: The Symptoms, Diagnoses and Management

Clinical Recommendations for Reducing and Preventing Food Allergies

Hugh A. Sampson, MD, FAAAAI, and Marion Groetch, MS, RDN

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Understanding Food Allergies in Infants and Children: The Symptoms, Diagnoses and Management

1. **An Overview of Food Allergies in Children**
   Stanley A. Cohen, MD, Curriculum Chairperson

2. **Diagnosing Food Allergies in Infants and Children**
   Jonathan Spergel, MD, PhD

3. **Cow's Milk Allergy: Mechanisms, Diagnosis and Treatment**
   David Fleischer, MD, and Carina Venter, PhD, RD

4. **Guidelines for Diagnosis and Management of Food Protein-Induced Enterocolitis Syndrome**
   Anna Nowak-Węgrzyn, MD, PhD

5. **Eosinophilic Esophagitis: Practical Diagnosis and Management of Pediatric Patients with EoE**
   Mirna Chehade, MD, MPH

6. **Optimizing Nutrition in Infants at High-Risk for Developing Allergy**
   Tatyana Hofmekler, MD, MSc

7. **Clinical Recommendations for Reducing and Preventing Food Allergies**
   Hugh A. Sampson, MD, FAAAAI, and Marion Groetch, MS, RDN

Clinical Recommendations for Reducing and Preventing Food Allergies

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Pediatric Nutrition
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