



Peanut Allergy

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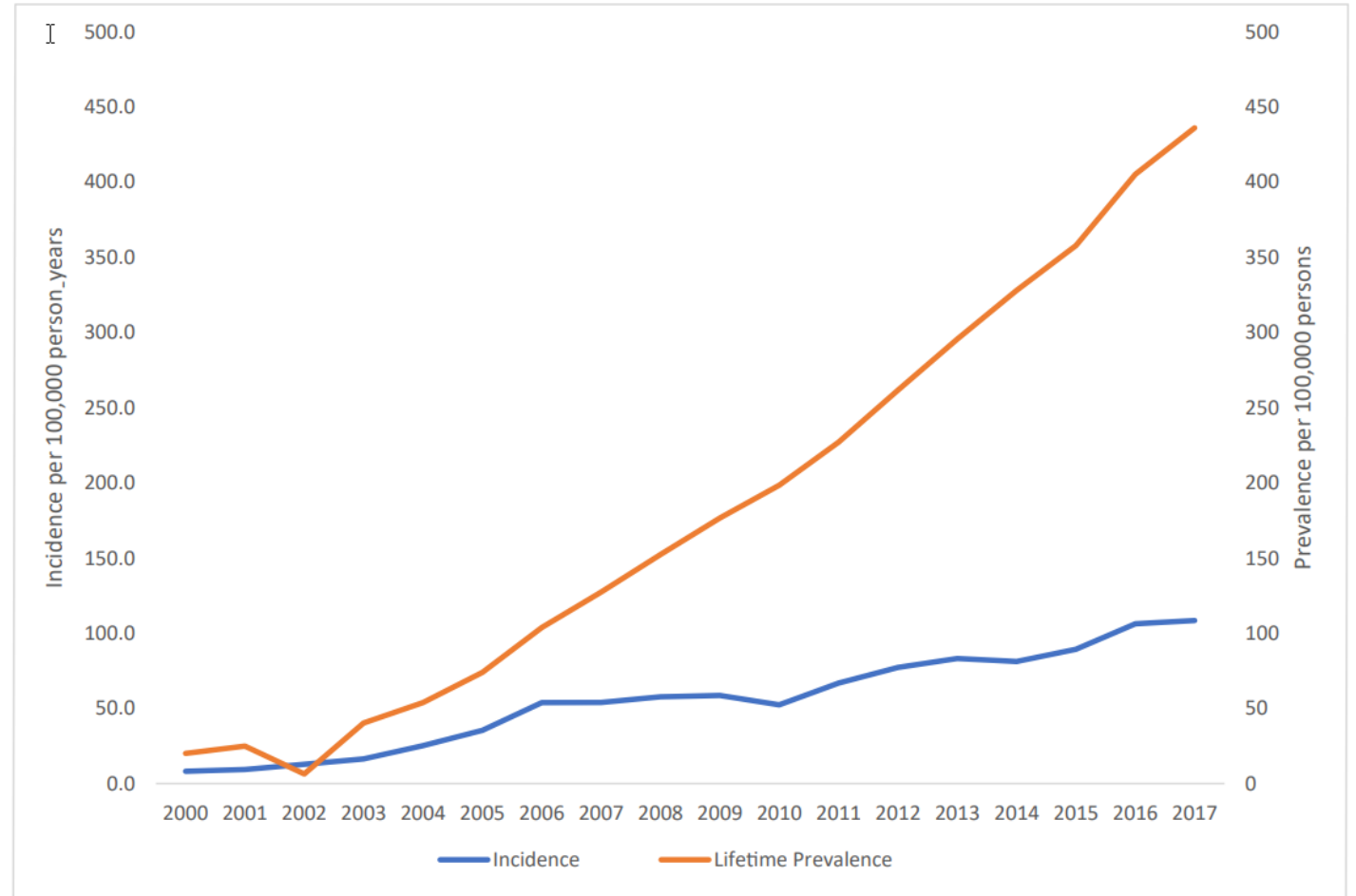
Medical Director, JHACH Food Allergy Clinic

Learning Objectives

- 1 Describe **natural history** of peanut allergy
- 2 Select appropriate **tools** for diagnosing peanut allergy
- 3 Discuss **treatment options** for patients with peanut allergy
- 4 Assess **outcomes** of recent peanut allergy clinical trials

What Do We Know?

Increasing prevalence of FA
8% of children (<3 years)



**Increasing incidence and prevalence of food allergy diagnoses
in active component US Armed Forces, 2000-2017**

If you could choose.....

Patient 1

<input type="checkbox"/>	D. farinae	* < 0.35
<input type="checkbox"/>	D. pteronyssinus	* < 0.35
<input type="checkbox"/>	Bermuda Grass	* < 0.35
<input type="checkbox"/>	Peanut	* H 91.10
<input type="checkbox"/>	Cat Antigen	* < 0.35
<input type="checkbox"/>	Johnson Grass	* < 0.35
<input type="checkbox"/>	Penicillium N	* < 0.35
<input type="checkbox"/>	Cladosporidium	* < 0.35
<input type="checkbox"/>	A. fumigatus	* < 0.35
<input type="checkbox"/>	Alternaria	* < 0.35
<input type="checkbox"/>	Elm	* < 0.35
<input type="checkbox"/>	Common Ragweed	* < 0.35
<input type="checkbox"/>	Dog Dander	* < 0.35
<input type="checkbox"/>	Bahia Grass	* < 0.35
<input type="checkbox"/>	Meadow Grass	* < 0.35
<input type="checkbox"/>	Cockroach	* < 0.35
<input type="checkbox"/>	Pecan Tree	* < 0.35
<input type="checkbox"/>	Pine, Australian (Beefwood)	* < 0.35
<input type="checkbox"/>	Oak, White	* < 0.35
<input type="checkbox"/>	Pigweed	* < 0.35

Patient 2

	11/14/2019 1714	3/15/2019 1643	10/4/2018 1654	3/20/2018 1512	3/9/2017 0740
ALLERGEN					
Banana (F92) IgE				0.87 *	
Beef Antibody	6.54 *	7.64 *	12.80 *	15.10 *	20.40 *
Allergen Casein/Co...	2.35 *	3.27 *	4.30 *	3.70 *	
Chicken Meat (F83)...					< 0.35 *
Allergen Class	Test Deleted *				
Allergen Corn Result				< 0.35 *	
Allergen Oat IgE	5.38 *	7.06 *	9.94 *	12.50 *	20.30 *
Macadamia Nut (Rf3...	1.55 *	1.40 *	2.66 *	1.55 *	
Sesame Seed (F10) IgE	5.77 *	7.97 *	8.33 *	5.74 *	11.40 *
Tomato (F25) IgE					0.78 *
Allergen,Miscellan...	Test Deleted *				
Almond (F20) IgE	23.20 *	35.70 *	41.10 *	48.60 *	> 100.00 *
F018-IgE Brazil Nut	3.99 *	3.51 *	3.82 *	5.29 *	5.21 *
F202-IgE Cashew Nut	25.00 *	26.00 *	24.50 *	16.80 *	1.84 *
Cinnamon (F220) IGE					0.40 *
Coconut (F36) IgE	1.63 *	1.84 *	2.04 *	3.05 *	7.80 *
Egg White (F1) IgE	33.70 *	47.30 *	57.50 *	47.10 *	
Egg Yolk (F75) IgE	17.00 *			9.53 *	
Hazelnut (F17) IgE	6.72 *	7.61 *	8.27 *	4.96 *	8.09 *
F002-IgE Milk	16.80 *	19.60 *	25.50 *	30.30 *	
Orange (F33) IgE					< 0.35 *
Peanut (F13) IgE	19.10 *	41.40 *	59.80 *	68.70 *	
Pecan Nut (F201) IgE	0.77 *	0.82 *	< 0.35 *	< 0.35 *	< 0.35 *
Pistachio Nut F203...	31.20 *	33.60 *	33.50 *	21.50 *	5.33 *
Soybean (F14) IgE	4.00 *	5.02 *	4.52 *	2.81 *	
F256-IGE WALNUT	3.68 *	1.88 *	2.11 *	< 0.35 *	
Ovalbumin (F232) IgE	30.00 *	33.90 *	44.40 *	37.40 *	



At Panera Bread



Checking Peanut Allergy Status



Skin prick test



Blood test



Tolerating peanuts

All forms

Any amount

Any time



Paradigm Shift in *Food Allergy* Management

**Prior to
2008**

Delayed food introduction

2010's

Prevention strategies



- Early food introduction (LEAP, EAT studies)
- Prevention and intensive treatment of eczema
- Microbial exposure

Education

Immunotherapy and Biologic trials



In one study, **77%** of patients sensitized to peanut are not at risk of a severe reaction

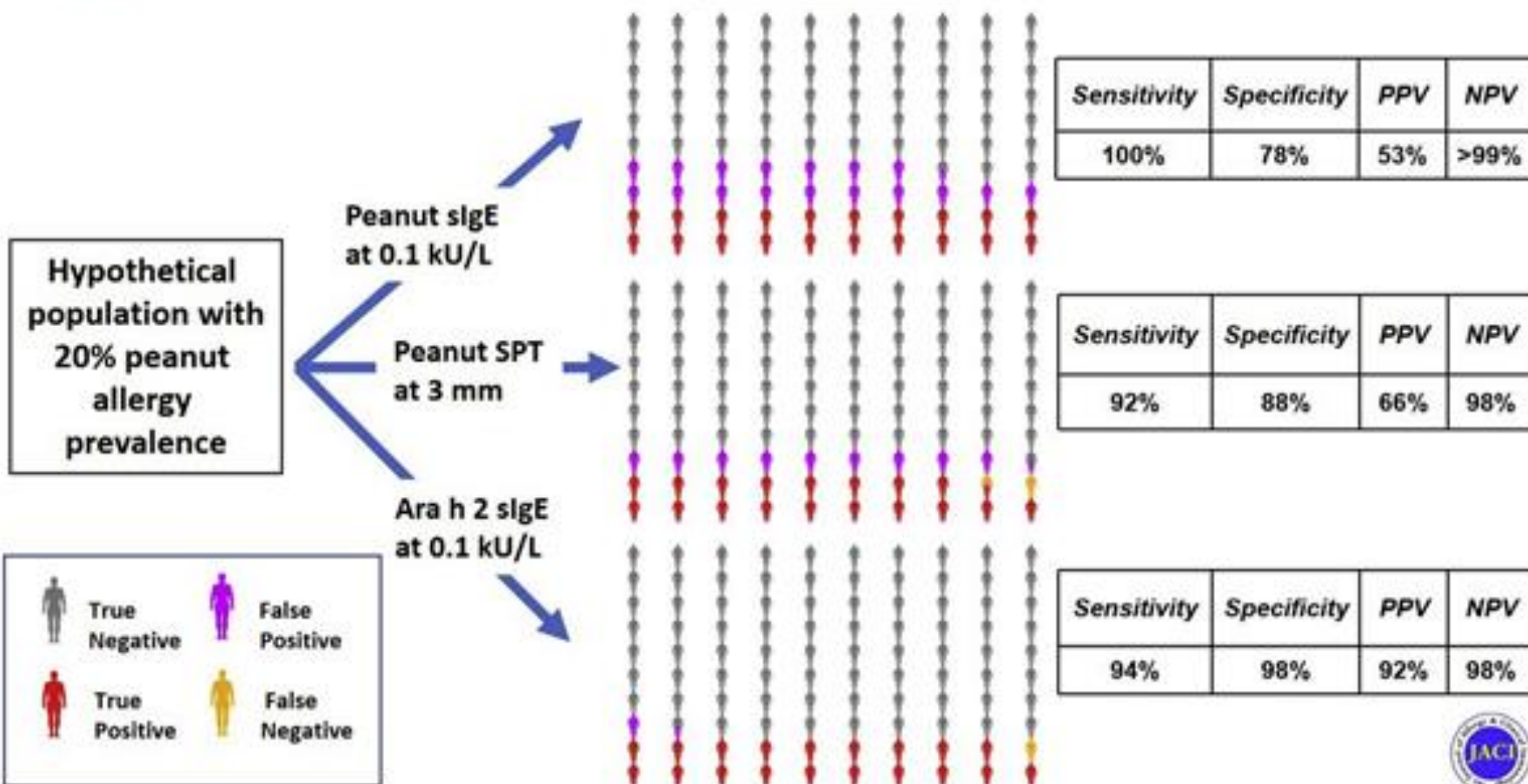
	CCD	PROFILIN	PR-10	LTP	STORAGE PROTEINS
 Peanut	MUXF3*	Bet v 2**	Ara h 8	Ara h 9	Ara h 1 Ara h 2 Ara h 3 Ara h 6
 Hazelnut			Cora 1	Cora 8	Cora 9 Cora 14
 Walnut				Jugr 3	Jugr 1
 Brazil Nut					Ber e 1
 Cashew					Ana o 3

Component Testing



Ara h 2-specific IgE is superior to whole peanut IgE or SPT for diagnosis of peanut allergy in infancy

Screening Test Results



Peanut Components

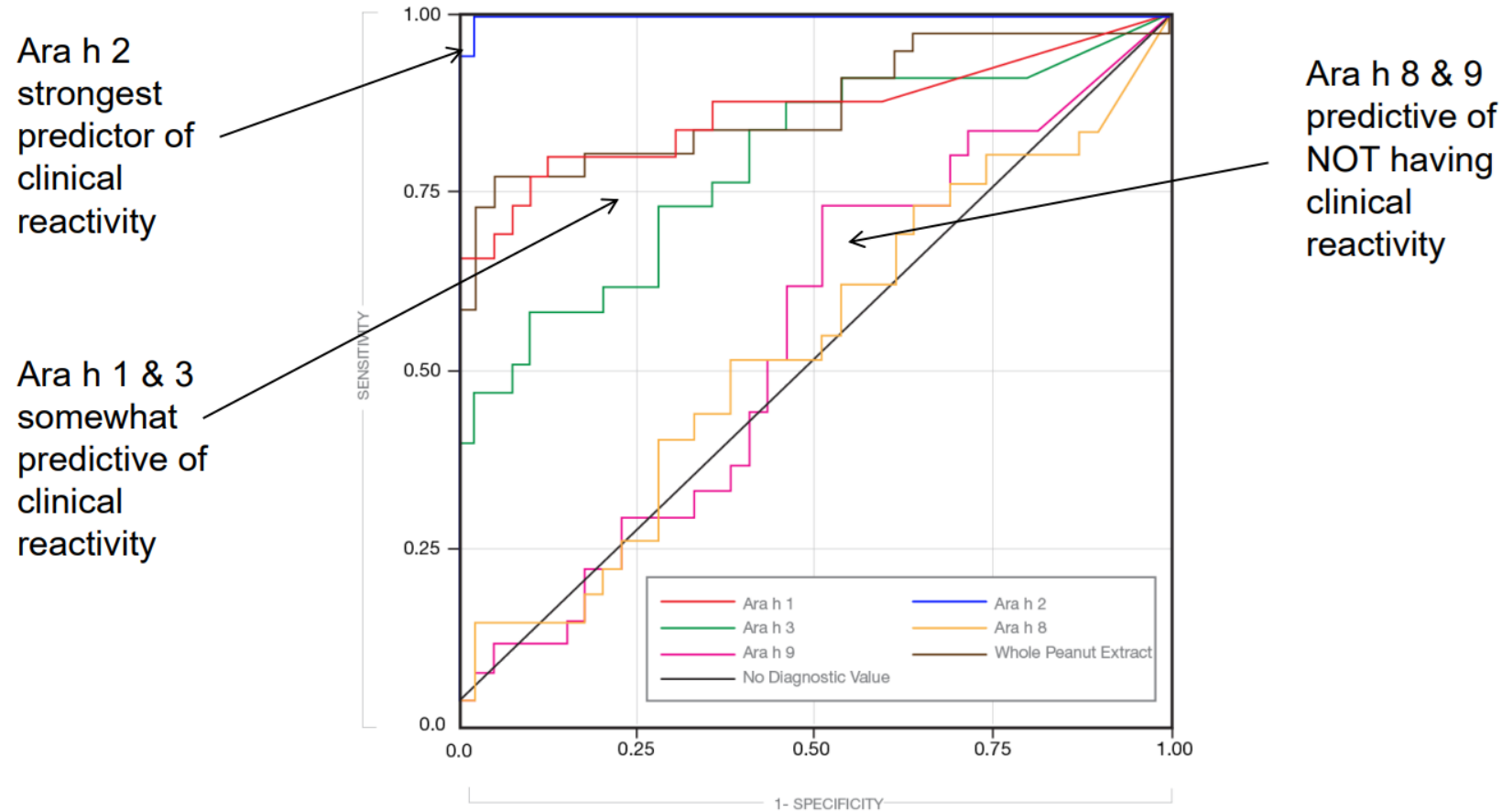


FIG 1. ROC curves showing the true-positive rate (*Sensitivity*) plotted in function of the false-positive rate (*1-Specificity*) for different cutoff points of the quantified components Ara h 1,2,3,8 and 9 and whole peanut extract. Ara h 2 is the component with the highest accuracy for discriminating between allergy or tolerance to peanut. Analysis included 66 subjects with all available data (27 with peanut allergy and 39 peanut-tolerant).

Basophil Activation Test (BAT)

1. Stimulation



Whole blood + Stimulants

Allergen
 Negative control
 Positive controls

2. Staining



- Stop degranulation (EDTA + variation in temperature to 4°C)
- Staining (with antibodies conjugated to fluorochromes)

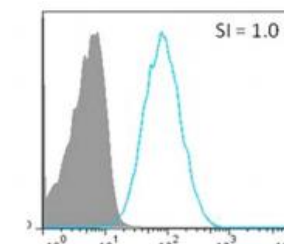
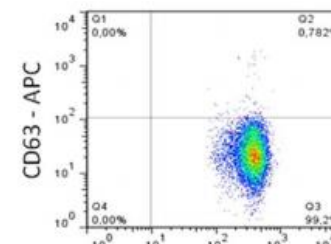
3. Red blood cell lysis



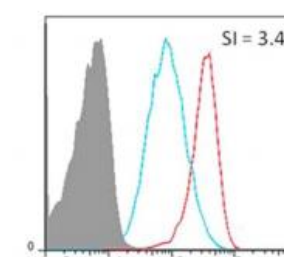
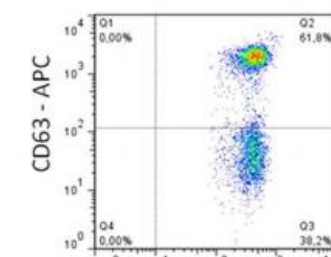
- Red blood cell lysis
- Cell suspension ready for analysis

4. Flow cytometry

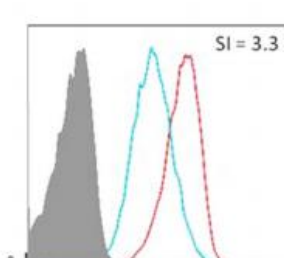
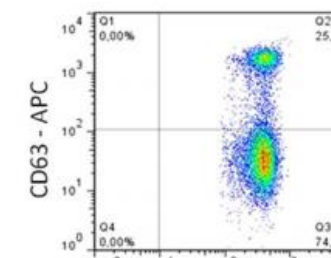
No stimulation



Peanut extract
10 ng/ml



Anti-IgE
1 µg/ml



Legend:

- Isotype control
- Unstimulated basophils
- Stimulated basophils

The Use of *BAT* in Food Allergy Diagnosis



Food	Author year	N	Cut-offs	Sensitivity	Specificity
Peanut	Santos 2014 [15]	N = 104	≥4.78 % CD63+	97.6 %	96.0 %
		Validation population N = 65		83.3 %	100 %
	Glaumann 2012 [12]	N = 38	ND	92 %	77 %
	Javaloyes 2012 [16]	N = 26	ND	92 %	95 %
	Ocmant 2009 [17]	N = 75	≥9.1 % CD63+	87 %	94 %
Hazelnut	Brandström 2015 [28]	N = 40	CD-sens > 1.7	100 %	97 %
Egg	Ocmant 2009 [17]	N = 67	≥5 % CD63+	77 %	100 %
Cow's milk	Sato 2010 [19]	N = 50	SI CD203c ≥ 1.9	89 %	83 %
Wheat	Tokuda 2009 [22]	N = 58	≥14.4 % CD203c+	85 %	77 %
Apple (PFS)	Ebo 2005 [34]	N = 61	Vs sensit. ≥17 % CD63+ Vs NA ≥10 %	Vs sensit. = 88 % Vs NA = 100 %	Vs sensit. = 75 % Vs NA = 100 %
Hazelnut (PFS)	Erdmann 2003 [33]	N = 30	≥6.7 % CD63+	85 %	80 %
Celery (PFS)			≥6.3 % CD63+	85 %	80 %
Carrot (PFS)			≥8.9 % CD63+	85 %	85 %

N number of study participants, PFS pollen-food syndrome, ND not determined, Vs versus, Sensit. sensitised but tolerant, NA non-sensitised non-allergic, SI stimulation index

Basophil Activation Test (BAT)

Requires fresh whole blood

5–10% non-responsive rate to IgE-mediated stimulation

Test ordering?

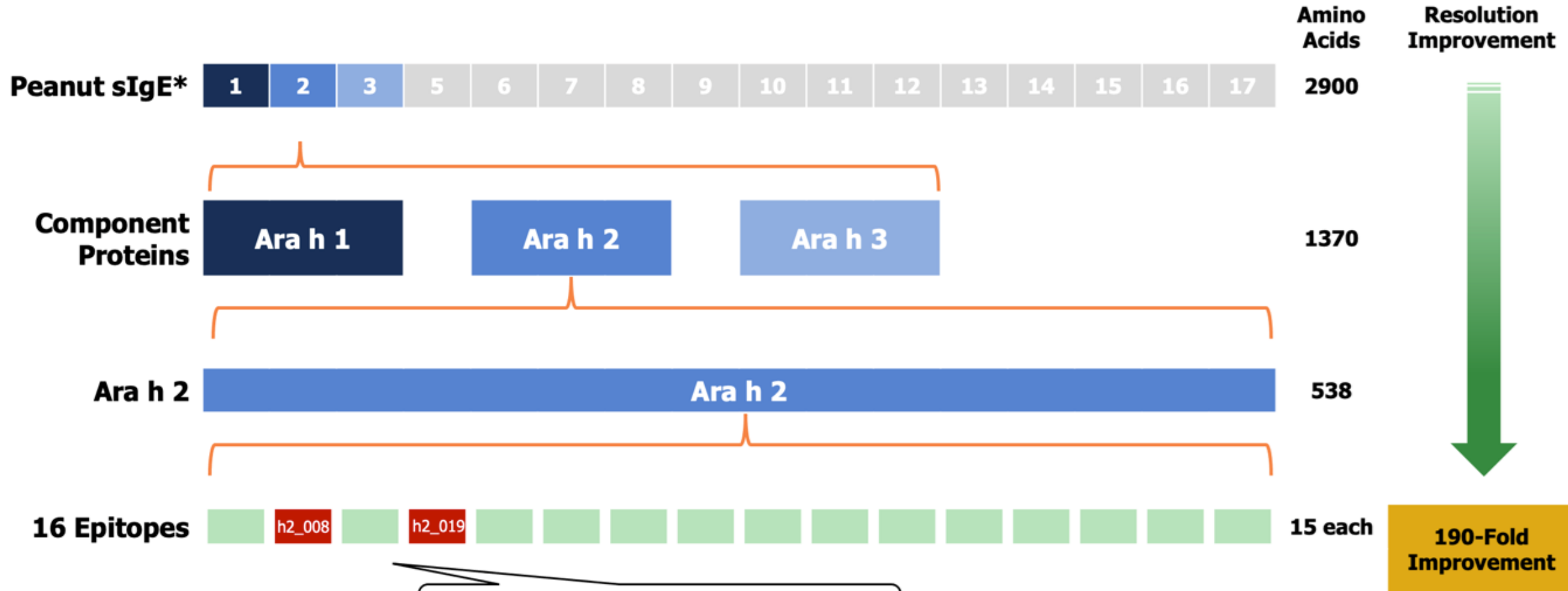
Issues with insurance coverage?



Epitope Testing

The resolution of Epitope Mapping eliminates the biological noise associated with sIgE and Component-resolved Diagnostics

Testing at the epitope level **improves resolution by 190-fold** by allowing the measurement of epitope level antibody binding (1 Ab: 1 epitope)



*The allergen Ara h 4 was renamed Ara h 3.02 and the number 4 is not available for future peanut allergen designations to avoid confusions with the already existing literature (Radauer et al., 2014).

1 patient & ordering provider information

2 easy to read

Color coded allergy status results allow for quick interpretation of the binary allergy status.. Results can be either Likely Allergic or Unlikely Allergic. If allergic, a patient would fall into 1 of 3 epitope reactivity levels.

3 allergic patient results

If patient is allergic, the test returns the epitope reactivity level and the percentage of patients that tolerated each dose as determined by an OFC.

final report

patient

NAME:
DOB:
GENDER:
MEDICAL RECORD/ID#:

provider

PROVIDER:
NPI:
CENTER:
ADDRESS:
PHONE:
ACCOUNT:
OTHER PROVIDER:

specimen

SPECIMEN ID#:
COLLECTION DATE:
REPORT DATE:
SPECIMEN TYPE:
RECEIVED DATE:



Bead-Based Epitope Assay (BBEA)^{1,2}

allergy status

likely allergic

description

Patient is likely allergic:

- Post test probability of patient being allergic to peanuts is greater than or equal to 91%.¹
- Results should be considered in conjunction with patient's history and other applicable information.

epitope reactivity level

level 1

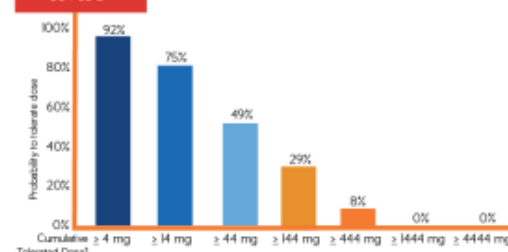
level 2

level 3

description

On the scale from 1 to 3, a level 1 patient can only tolerate very low levels of peanut. Patient may react to low levels of peanut protein. The higher the level, the more peanut that a patient can consume before having a reaction.

level 1



description

Cumulative Tolerated Doses (CTD) shown for a Level 1 peanut allergic patient. A CTD of at least 14 mg would be tolerated by approximately 75% of patients in this level, as determined by a standardized oral food challenge.²⁻³



Actions and management of food allergies are best managed by a board certified allergist, or those licensed providers with extensive training in food allergy.

references

1. Suarez-Farinas M, Suprun M, Kearney P, Getts R, Grishina G, Hayward C, Lutz D, Porter A, Wilmer M, du Toit G, Lack G, Chinthrajah R, Galli S, Nadeau K, Sampson H. Accurate and Reproducible Diagnosis of Peanut Allergy Using Epitope Mapping. 15 May 2021. *Allergy*. <https://doi.org/10.1016/j.all.2021.04.005>
2. Data on file, available upon request.
3. Sampson H, Gerth van Wijk R, MD, Bindsvær-Jensen C, Sicherer S, Teuber S, Burks W., MD, Dubois A, Beyer K, Eigenmann P, Spergel J, Wierfel T, Chinchilli V. PRACTALL consensus report. 2012. *JACI* 130:6

notes:

DOC #:
04-Jan2022-Vir 2-MPO_FRT

2801 Sterling Drive
Hatfield, PA 19440
1 of 2

Benjamin Gerson, M.D.
Laboratory Director

4 level comparison

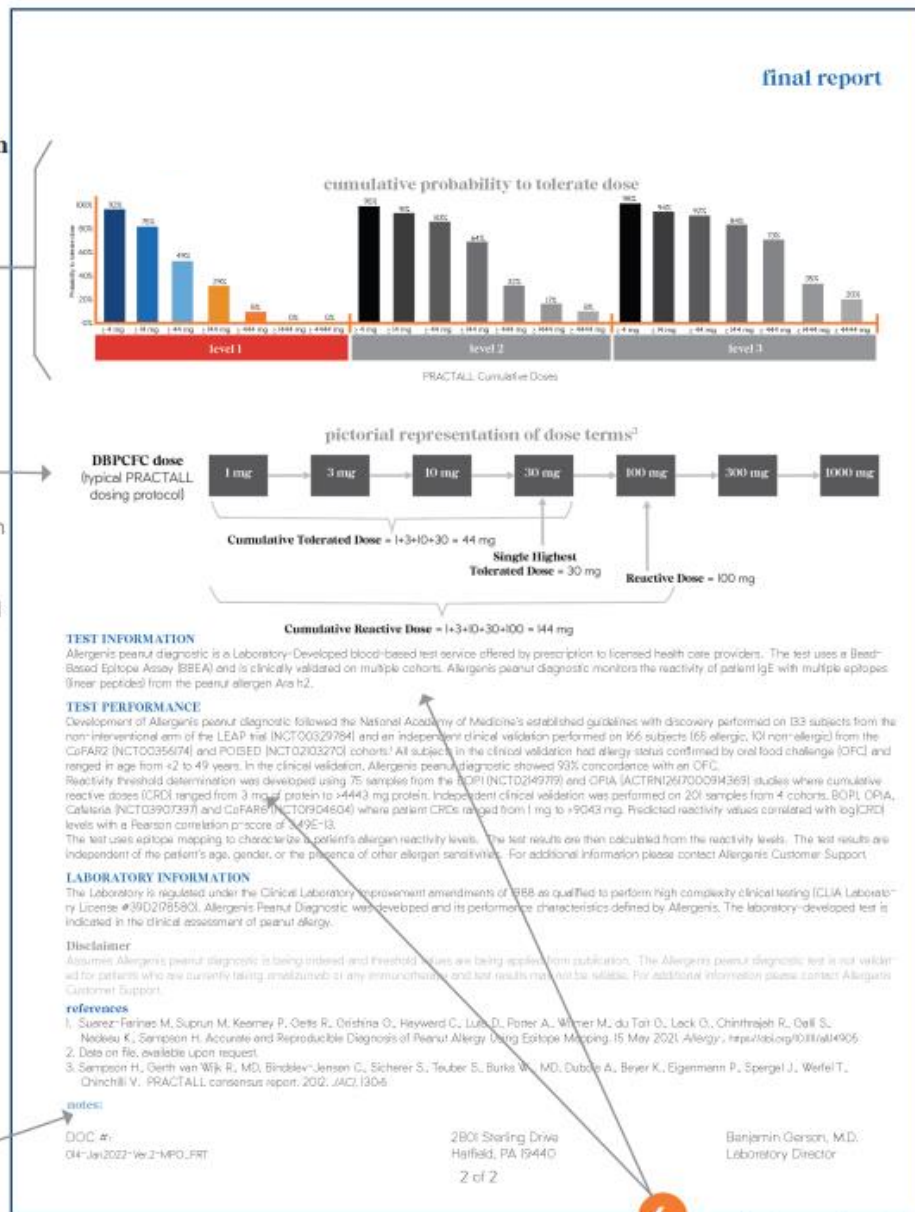
Test report provides a comparison to the other levels.

5 dose terms

Report provides a pictorial representation of dose terminology to help patients and caregivers understand the differences in the values.

7 notes

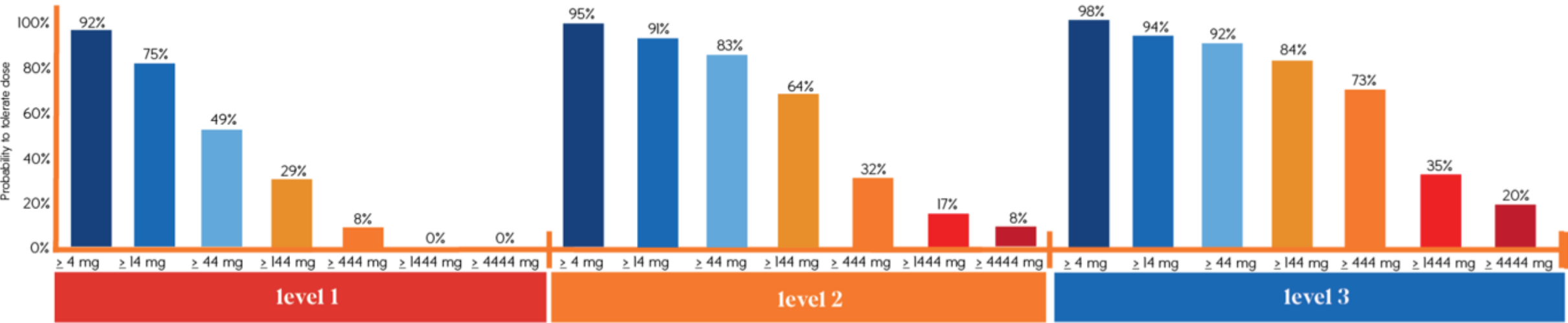
Any additional information from Allergenics about the specimen when it was received.



6 test information & performance details

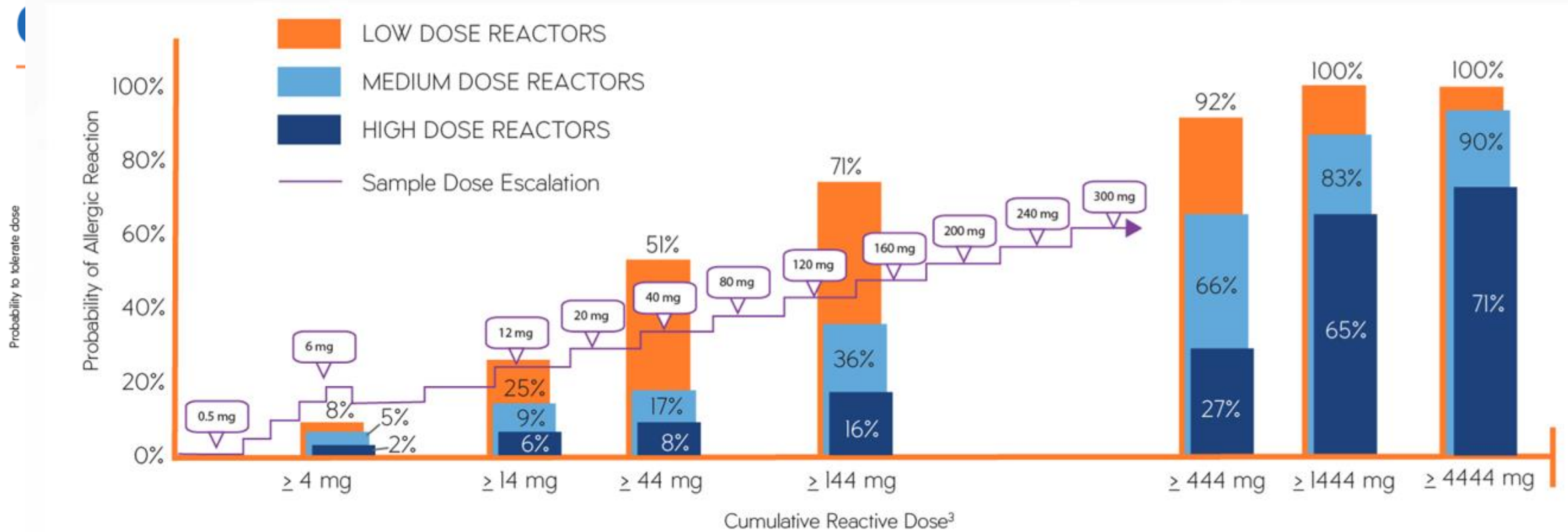
Provides further information on the validation of the algorithms used in the Allergenics Peanut Diagnostic and the performance criteria of the test.

CLINICAL CONSIDERATIONS BY LEVEL



PRACTALL Cumulative Tolerated Dose Levels³

Cumulative reactive dose by reactor type

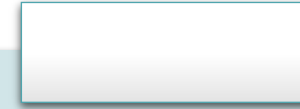


Epitope Testing



Pros

- High Spec, Sens, PPV and NPV
- Provides a probability that a patient can tolerate specific amounts of PN
- Results can be superimposed with OIT dosing schedule / Palforzia ladder



Cons

- Does not predict the severity of reaction
- May result in a false negative if no serum IgE is detectable
- Not recommended for patients on omalizumab or OIT currently
- Requires phlebotomy

Food Allergy Immunotherapy Approaches



Oral IT (OIT)



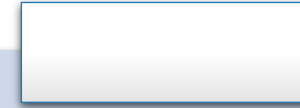
**Epicutaneous IT
(EPIT)**



Sublingual IT (SLIT)



Commercially Available Peanut OIT



Pros

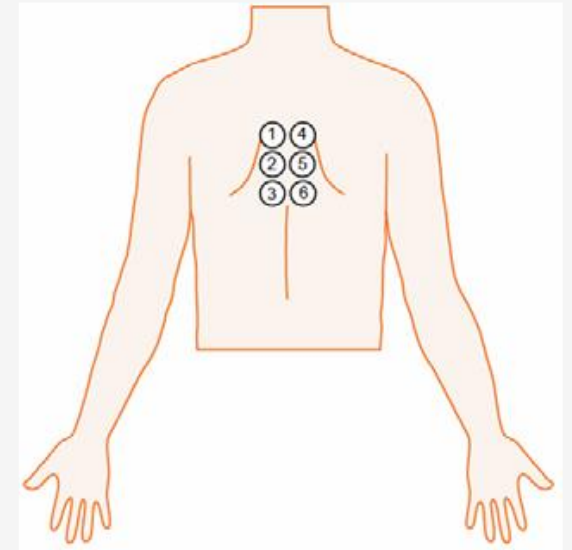
- Standardized
- Well researched
- Affordable (commercial and Medicaid)
- Easy to prepare/administer
- Great for allergists starting OIT

Cons

- Limited to semi solid foods (no liquids)
- Grittiness
- Logistics/pharmacy delays
 - Multiple phone calls
 - Weather delays
- Products not always immediately available for shipping (due to insurance not wanting to pay) depending on when it was last shipped
- Obtaining PA can be a cumbersome



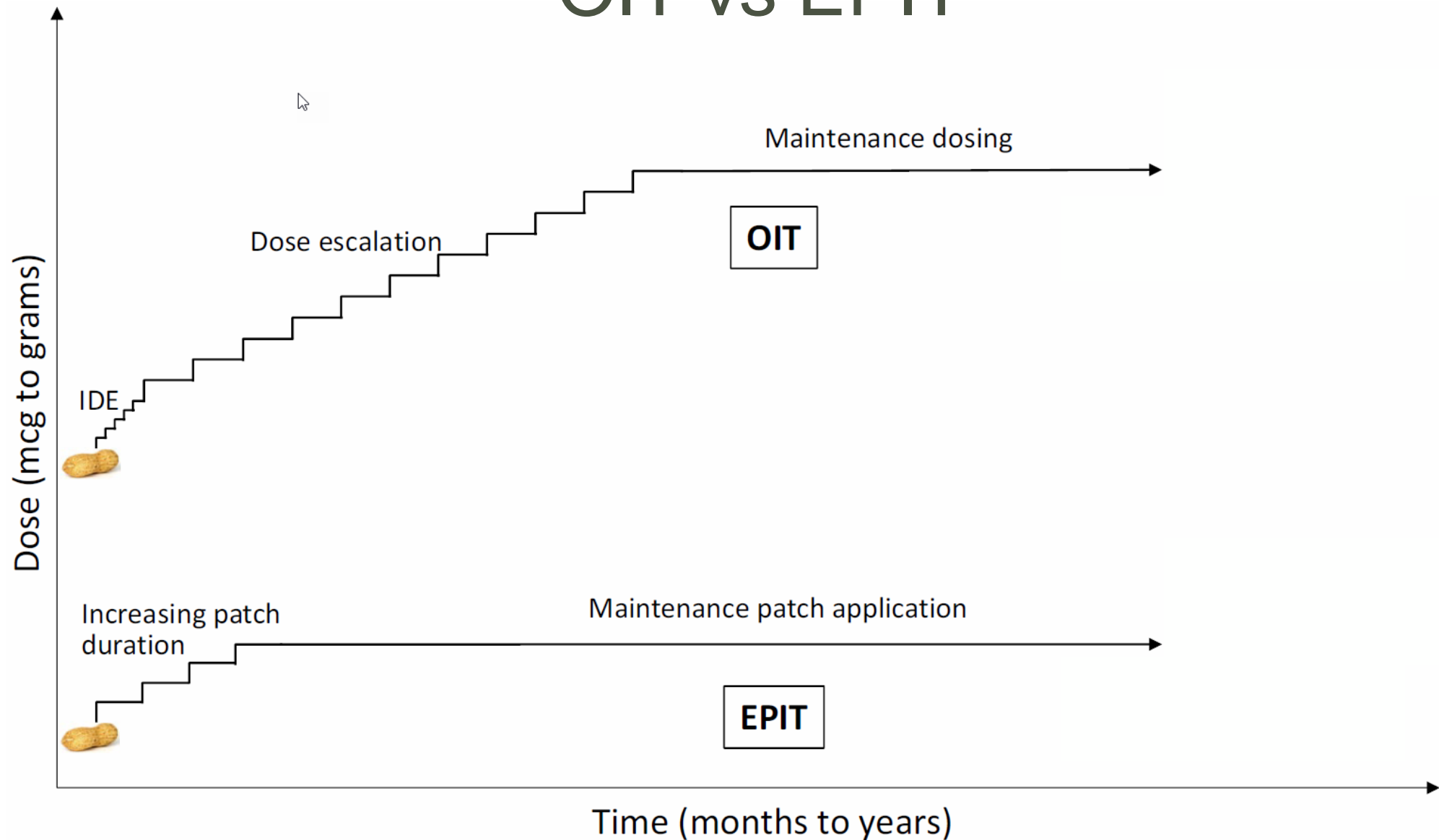
How Does EPIT Work?



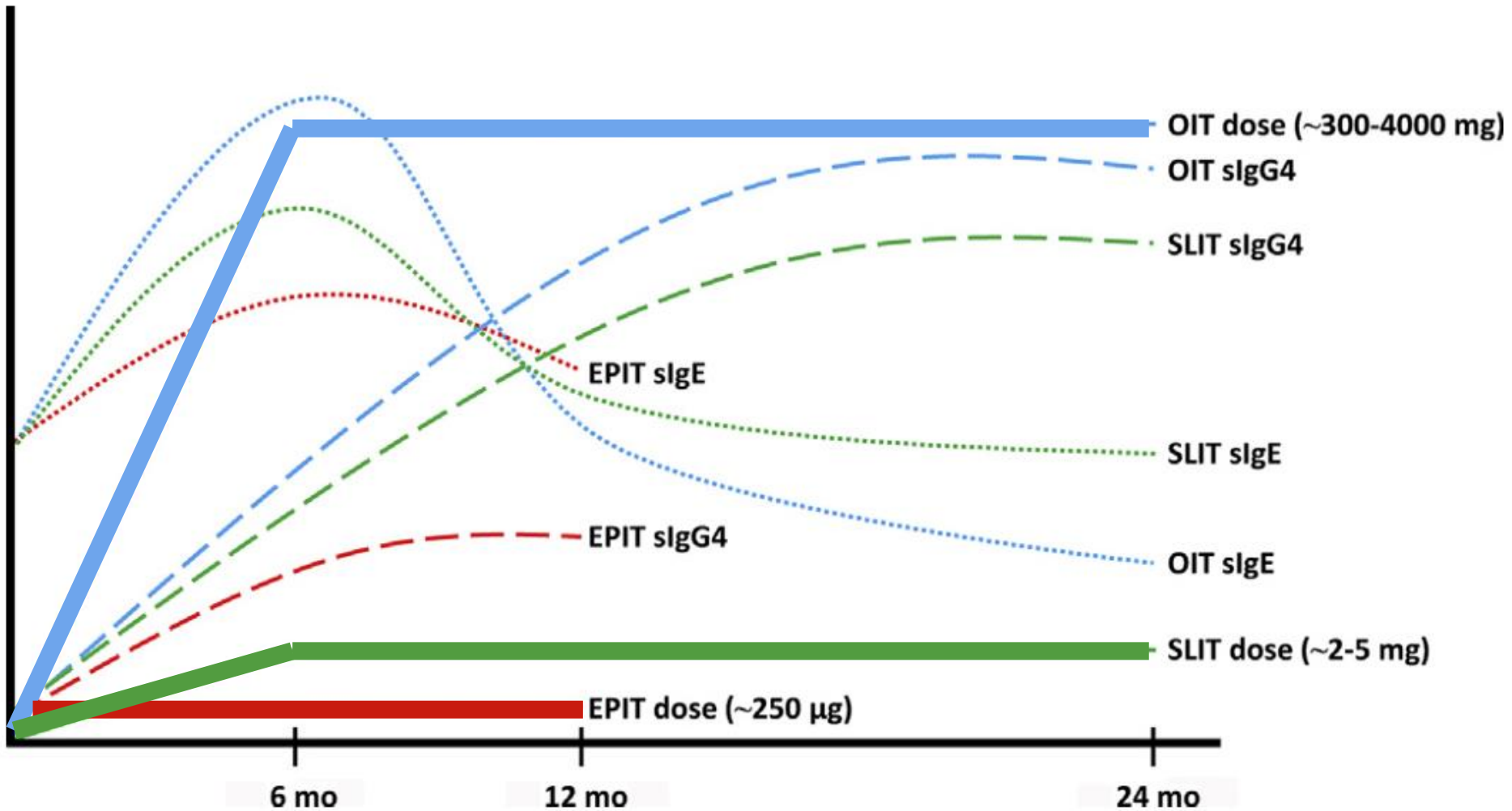
Comparison of Food Allergen Immunotherapy

	OIT	SLIT	EPIT
Daily dose (protein)	300-4000 mg	2-7 mg	50-500 µg
Side effects	Gastrointestinal, oral (systemic when associated with fever, URI, exercise)	Oral-pharyngeal (local)	Skin (local)
Desensitization	Large effect	Moderate effect	Ongoing investigation
Long-term tolerance	Variable response	Ongoing investigation	Unknown
Immune modulation	Significant	Present	Present in mice; ongoing investigation in human subjects

OIT vs EPIT



OIT, SLIT, and EPIT



RESEARCH SUMMARY

Phase 3 Trial of Epicutaneous Immunotherapy in Toddlers with Peanut Allergy

Greenhawt M et al. DOI: 10.1056/NEJMoa2212895

CLINICAL PROBLEM

Treatments for peanut allergy are not approved for children <4 years of age. However, treatment at younger ages may be more effective than at older ages.

CLINICAL TRIAL

Design: A phase 3, multicenter, double-blind, randomized, placebo-controlled trial compared responses to a peanut food challenge among children 1 to 3 years of age after epicutaneous immunotherapy with a peanut patch or placebo for 12 months.

Intervention: 362 toddlers with peanut allergy elicited by ≤ 300 mg of peanut protein were assigned, in a 2:1 ratio, to receive an interscapular patch, containing either 250 μg of peanut protein or a placebo, daily for 12 months. The primary outcome was desensitization to oral peanut-protein challenge, defined as a symptom-eliciting dose of ≥ 1000 mg of peanut protein (equivalent to approximately 3 to 4 peanuts) for those with baseline responses to >10 mg or ≥ 300 mg of peanut protein (equivalent to approximately 1 peanut) for those with baseline responses to ≤ 10 mg.

RESULTS

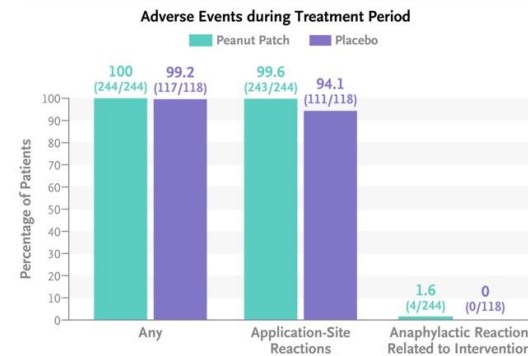
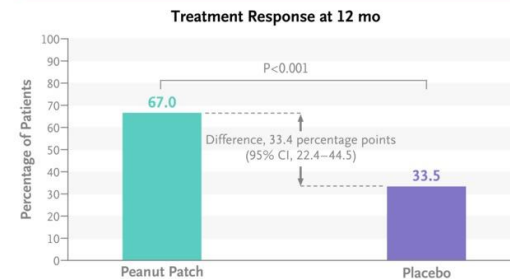
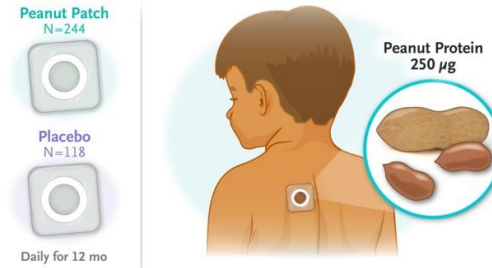
Efficacy: Significantly more toddlers in the intervention group had a response at 12 months than in the placebo group.

Safety: All the patients who received the peanut patch and 99.2% of those who received placebo had adverse events during treatment, primarily treatment-site reactions in the first 3 months. Serious adverse events occurred in more patients in the intervention group than in the placebo group, including mild-to-moderate anaphylaxis.

LIMITATIONS AND REMAINING QUESTIONS

- Patients with a history of severe anaphylactic response to peanuts were excluded.
- A lack of racial diversity among patients may limit generalizability.
- The appropriate duration of peanut-patch use remains unknown.

Links: [Full Article](#) | [NEJM Quick Take](#) | [Editorial](#)

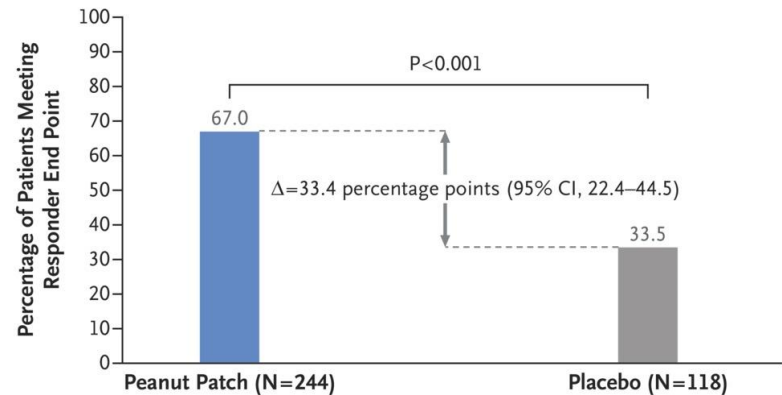


CONCLUSIONS

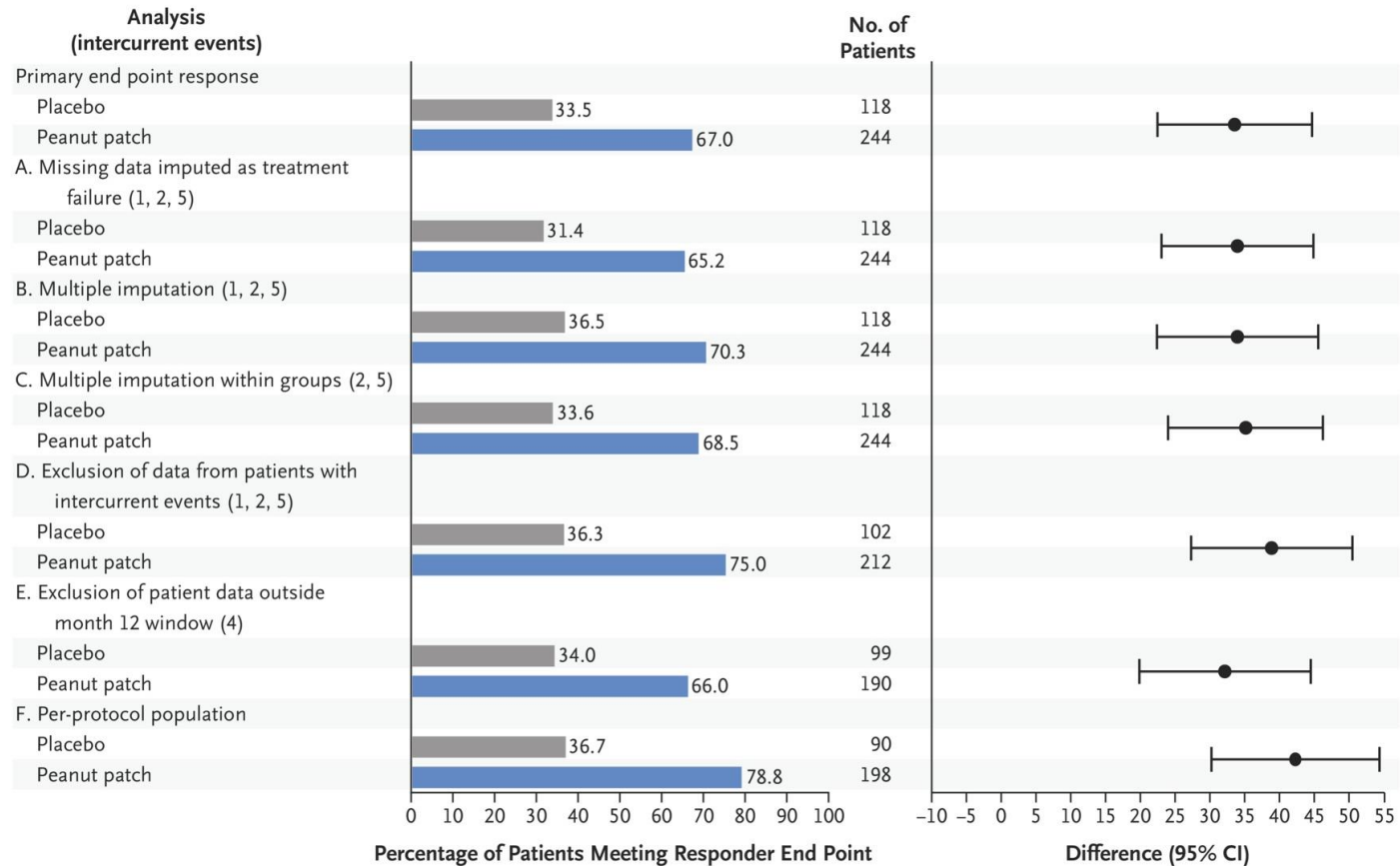
As compared with a placebo patch, a 250- μg peanut patch used daily for 12 months led to peanut desensitization in significantly more children 1 to 3 years of age with peanut allergy.

Primary and Sensitivity Analyses of the Primary End Point

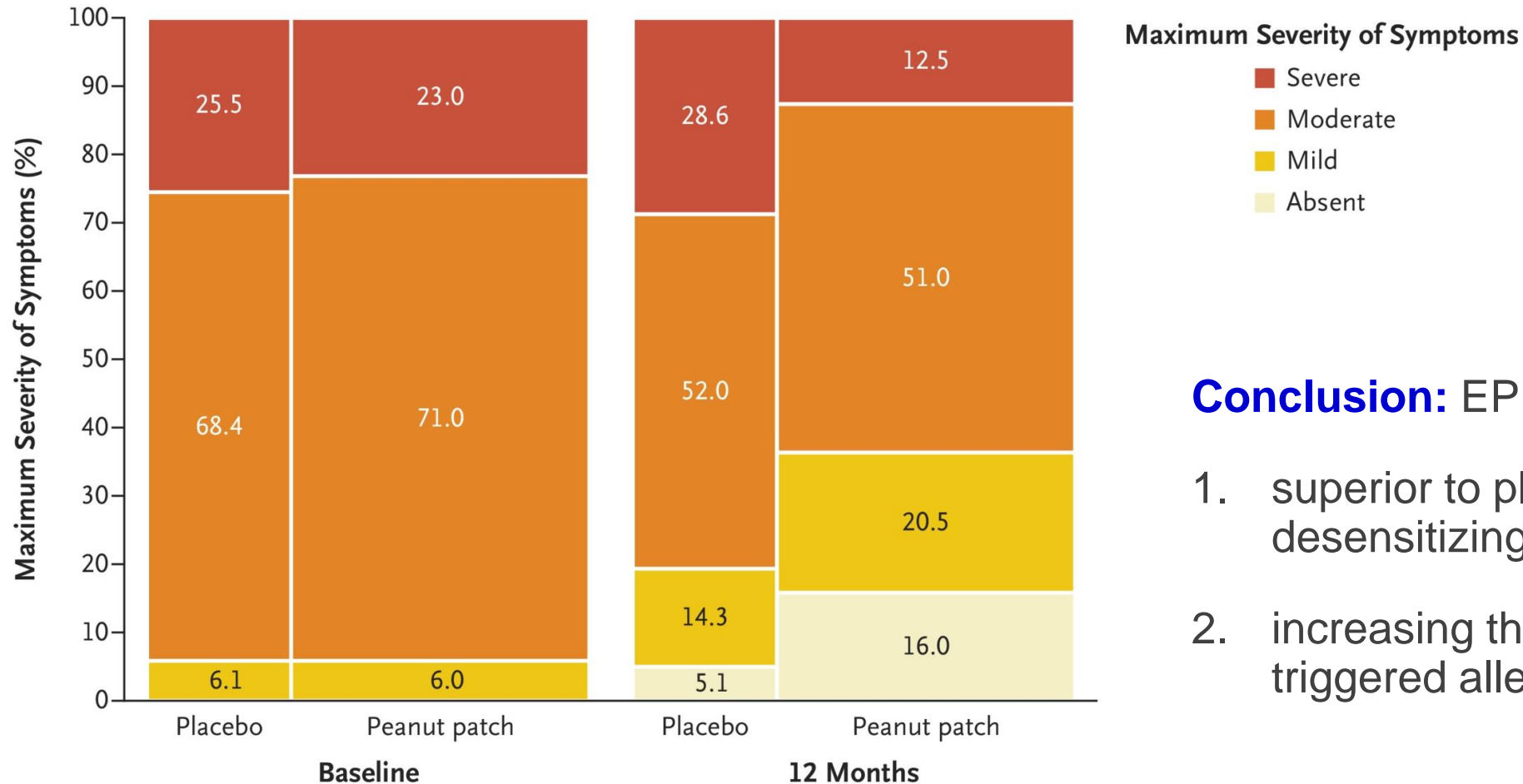
A Primary Analysis



B Sensitivity Analyses



Maximum Symptom Severity during Oral Food Challenge



Conclusion: EPIT for 12 months was:

1. superior to placebo in desensitizing children to peanuts
2. increasing the peanut dose that triggered allergic symptoms

Biologics for treatment of Food Allergy

Omalizumab

- **Most studied** biologic in food allergy
 - Used as an adjunct therapy in multi-food OIT, **enabling safe and rapid desensitization** (Andorf et al, The lancet. Gastroenterology & hepatology, 2018)
 - Being evaluated in several OIT trials

Ligelizumab (binds to the Cε3 domain of the IgE with higher affinity than omalizumab)

- FDA-granted Breakthrough Therapy for CSU
- Being evaluated in a peanut trial

Biologics for treatment of Food Allergy

Dupilumab (targets IL4R α , blocks IL-4/IL-13 signaling)

- Two ongoing randomized placebo controlled phase II clinical trials evaluating Dupilumab in food allergy
 - As a monotherapy (NCT03793608)
 - As an adjunct therapy to peanut OIT (NCT03682770)

Anti-IL-5 (mepolizumab, reslizumab, benralizumab)

- No reported trials in food allergy

Therapeutic Agents	Clinical Trials in Food Allergy	References or NCT Number
Anti-IgE		
Omalizumab (Anti-IgE mAb)	Monotherapy for peanut allergy	Savage et al, ¹⁸ 2012 Sampson et al, ¹⁹ 2011 Fiocchi et al, ²⁰ 2019 Leung et al, ⁶⁷ 2003
	Adjunct to peanut, milk or multi-food OIT	Nadeau et al, ²¹ 2011 MacGinnitie et al, ²² 2017 Schneider et al, ²³ 2013 Wood et al, ²⁴ 2016 Andorf et al, ²⁵ 2017; Andorf et al, ²⁶ 2018
Anti-IL 4R		
Dupilumab (Anti-IL4-R mAb)	Monotherapy for peanut allergy	Phase II (NCT03793608)
	Adjunct to peanut OIT	Phase II (NCT03682770)
Th1 adjuvants		
Glucopyranosyl lipid A (GLA)	Adjunct to peanut SLIT	Phase I (NCT03463135) (Trial has been terminated prematurely)
Anti-TSLP and IL-33		
Etokimab (anti-IL-33 Ab)	Peanut allergy	Phase II (NCT02920021)
DNA vaccines		
ASP0892 (ARA-LAMP-vax)	Peanut allergy	Phase I (NCT03755713) Phase I (NCT02851277)
Modified food allergen proteins		
Encapsulated, recombinant modified peanut proteins Ara h 1, Ara h 2, and Ara h 3 (EMP-123)	Peanut allergy	Wood et al, ⁵⁹ 2013
HAL-MPE1	Peanut allergy	Phase I (NCT02991885)
Anti- Sialic acid binding immunoglobulin like lectin (Siglec-8) Antibody (AK002)	Eosinophilic gastritis and/or eosinophilic gastroenteritis	Phase II (NCT03496571)
Ibrutinib (Bruton's tyrosine kinase inhibitor)	Peanut allergy	Dispenza et al, ⁶⁸ 2018
Targeting the microbiome		
Probiotics	Cow's milk allergy	Berni Canani et al, ⁶¹ 2012; Berni Canani et al, ⁶⁹ 2017 Hol et al, ⁶² 2008 Zhang et al, ⁶³ 2016
Probiotic with peanut oral immunotherapy	Peanut allergy	Tang et al, ⁶⁴ 2015
Fecal microbiota transplantation (FMT)	Peanut allergy	Phase I (NCT02960074)

Investigational Therapies for Food Allergy



The product is intended to significantly raise a patient's immune threshold through daily use of OMIT toothpaste beyond what has triggered a potentially dangerous allergic reaction via accidental exposure. This additional protection helps relieve the persistent anxiety of peanut allergic individuals toward accidental exposure.

Peanut INT301



Peanut INT301: Phase 1 Clinical Trial

The Unknowns of Food Immunotherapy

- ▶ How long does desensitization from immunotherapy last?
- ▶ Without a food challenge, how do determine success?
- ▶ Best age to start?
- ▶ Is immunotherapy safer than avoidance?
- ▶ Do the benefits outweigh the risks?

Thank You

