Oral Immuno therapy for treatmen of Food allergy Evidence base

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Children's Hospital number 2
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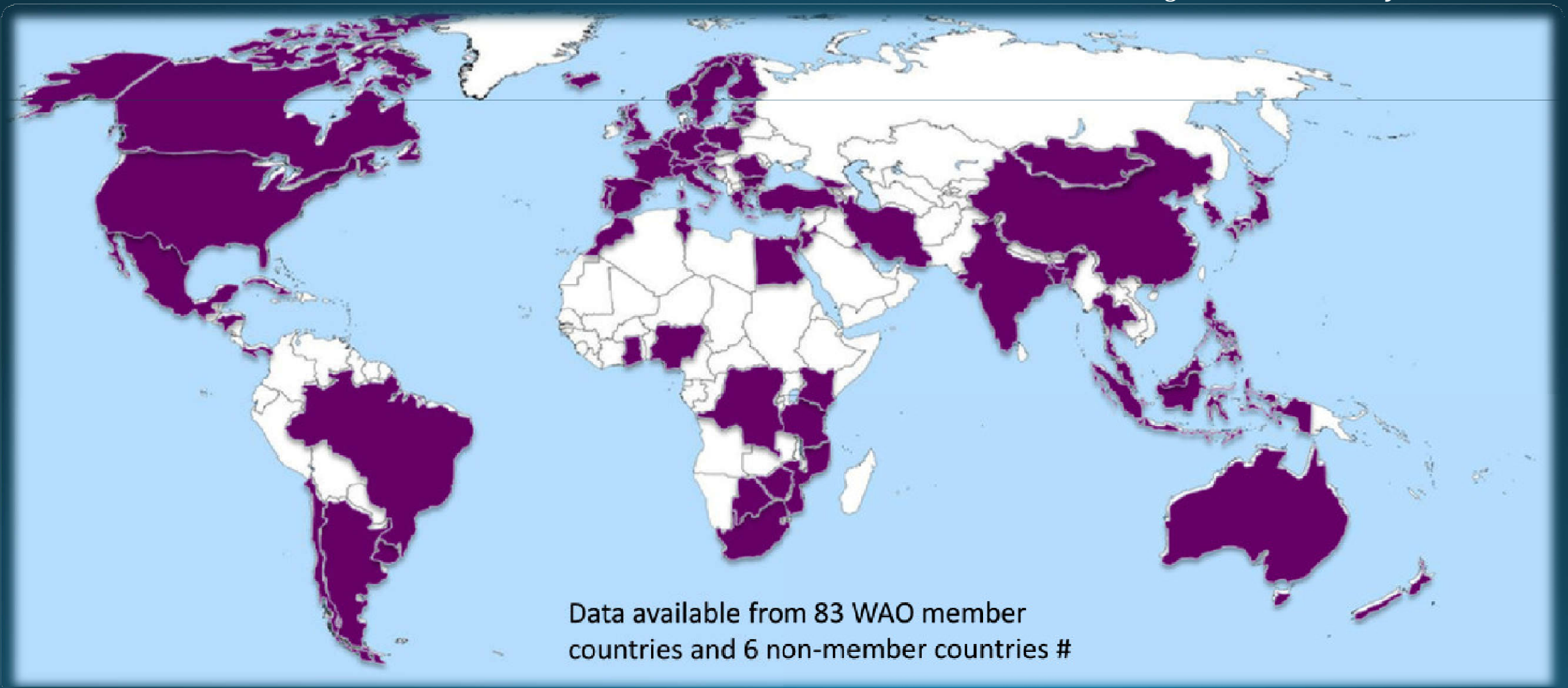
WAO journal
WORLD ALLERGY ORGANIZATION

Original 16th February 2013



Epidemiology

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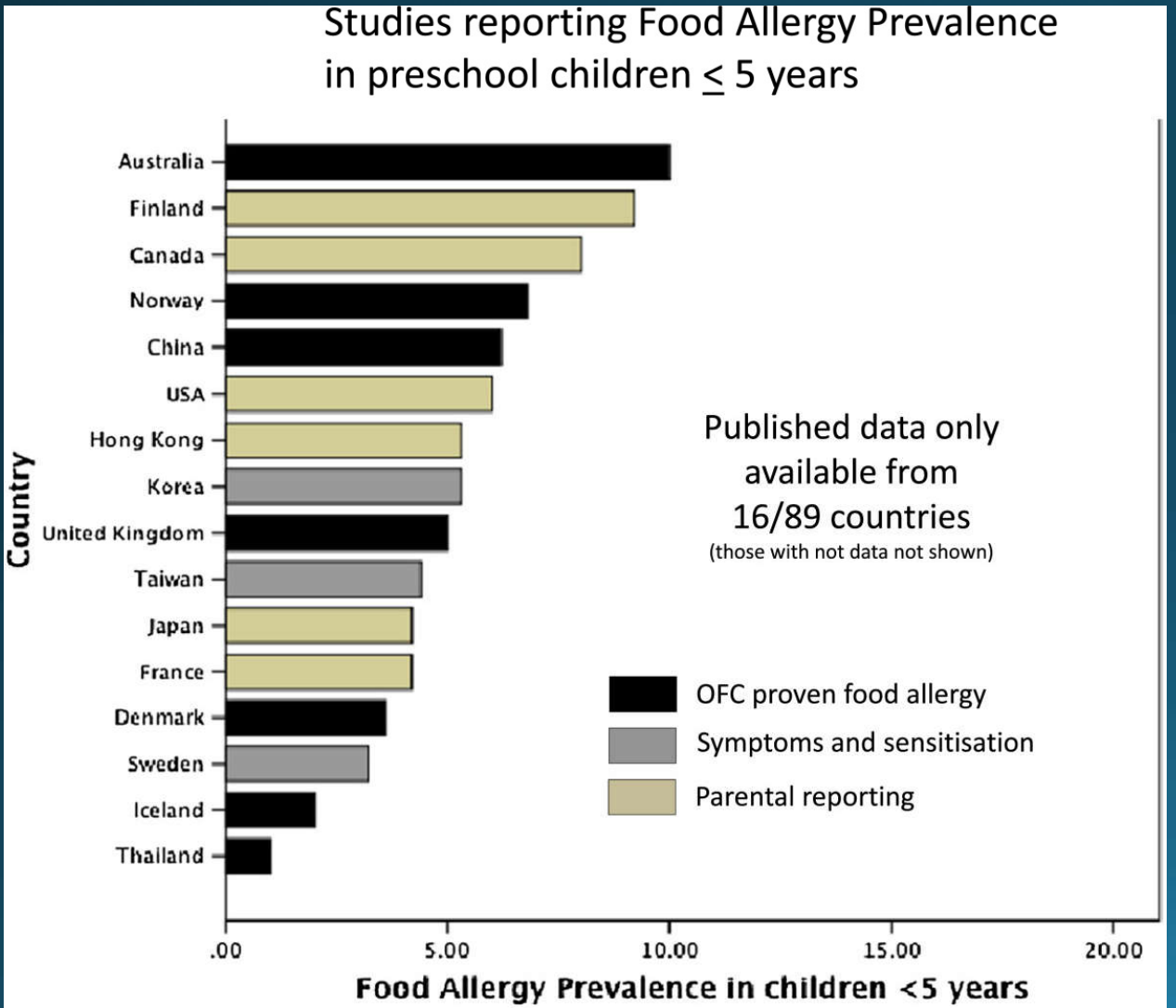

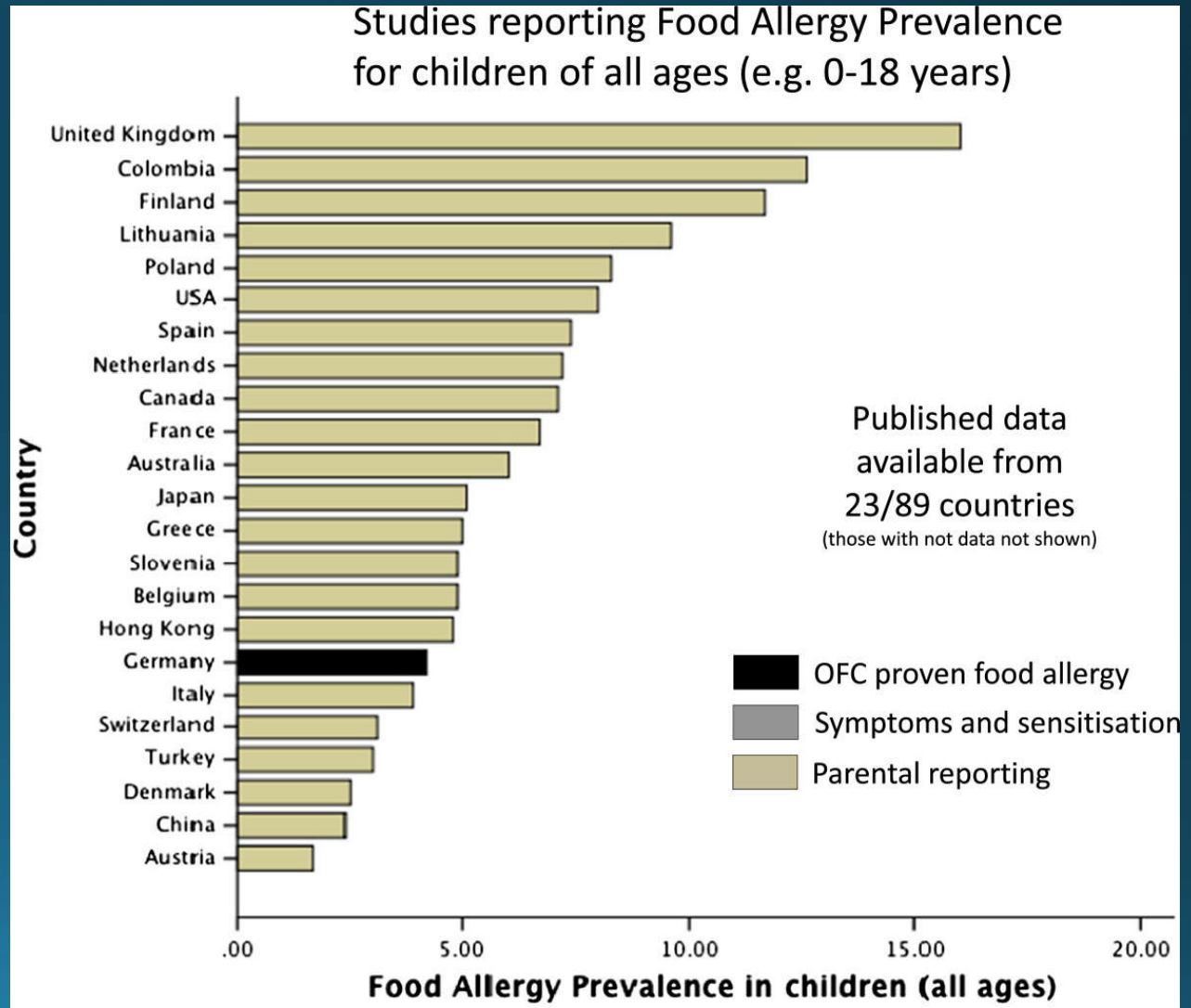

Prevalence of food allergy in Viet Nam

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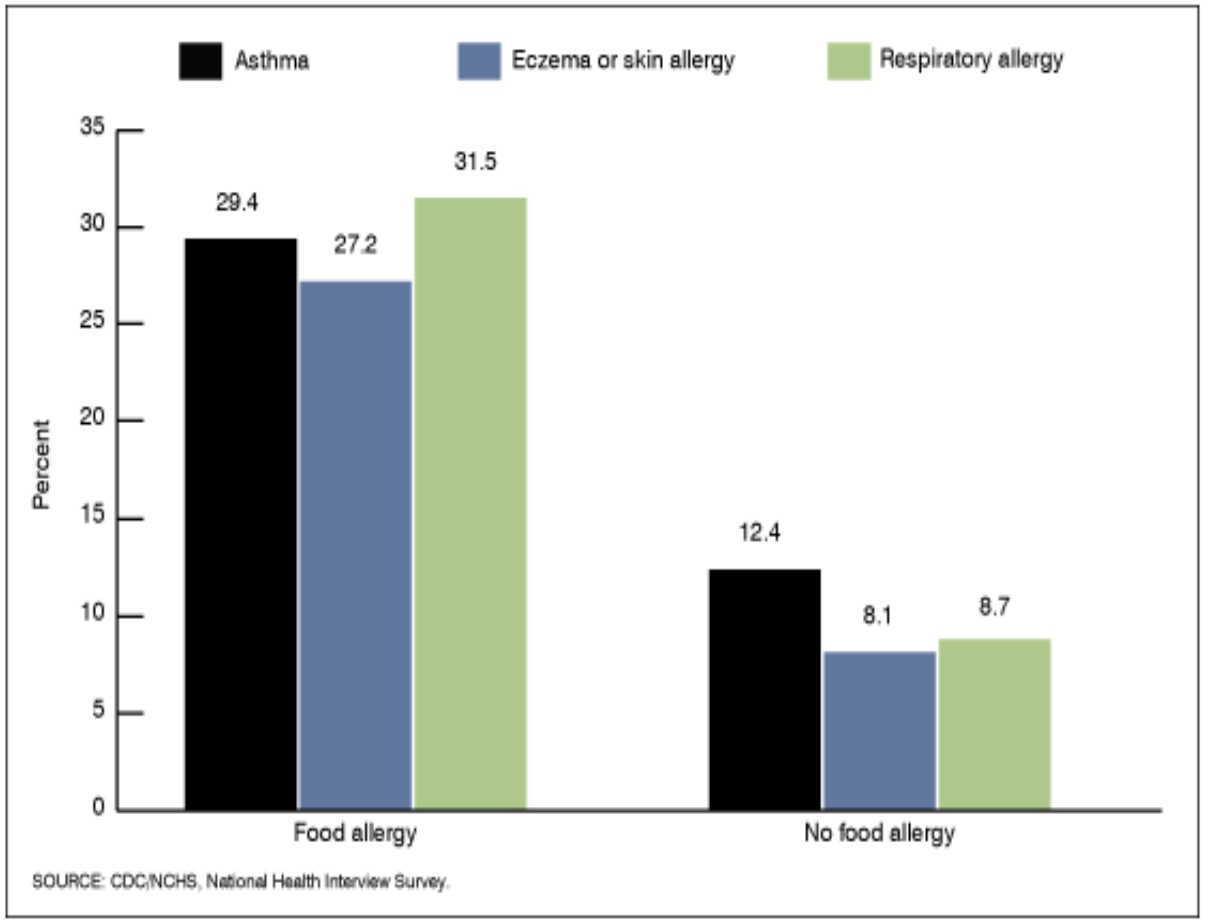
Country	Prevalence of clinical food allergy in last 10 years (%)			Method of determining prevalence, population size (and reference to support response if available)	Change in prevalence in last 10 years?	Age group most affected by any change?
	All ages	< 5 year olds	≥ 5 year olds			
Vietnam	-	-	-	**No population prevalence data reported/found	-	-
India	-	-	-	**No population prevalence data reported/found	-	-
Hong Kong	4.8%[21]	4.6%[7] - 5.3%[21]	4.5%[21]	[21] Population based survey of 7,393 children aged 0-14 years. History of convincing adverse reactions to foods. [7] Community survey of 3827 preschool children (2–7 yr), parent-reported reactions (8.1%) and parent-reported doctor diagnosed reactions (4.6%)	Increased*	1-5 years*
Singapore	-	1.2% (shellfish); 0.7%[22] (nuts)	0.3%[23] (fish); 5.2% (shellfish); 0.54%[22] (nuts)	No data found on overall FA prevalence. [22] Nut and shellfish allergy prevalence in 4-6 year olds (n=4390 and 14-16 year olds (n=6450) participating in regional survey [23] Fish allergy prevalence in the same population study.	Increased*	1-5 years*
Philippines	-	-	2.3%[23] (fish); 5.1% (shellfish); 0.7%[22] (nuts)	No data found on overall FA prevalence. [23] Fish allergy prevalence in 11,434 14-16 year olds participating in regional survey [22] Nut and shellfish allergy prevalence in the same population study	Increased*	1-5 years*

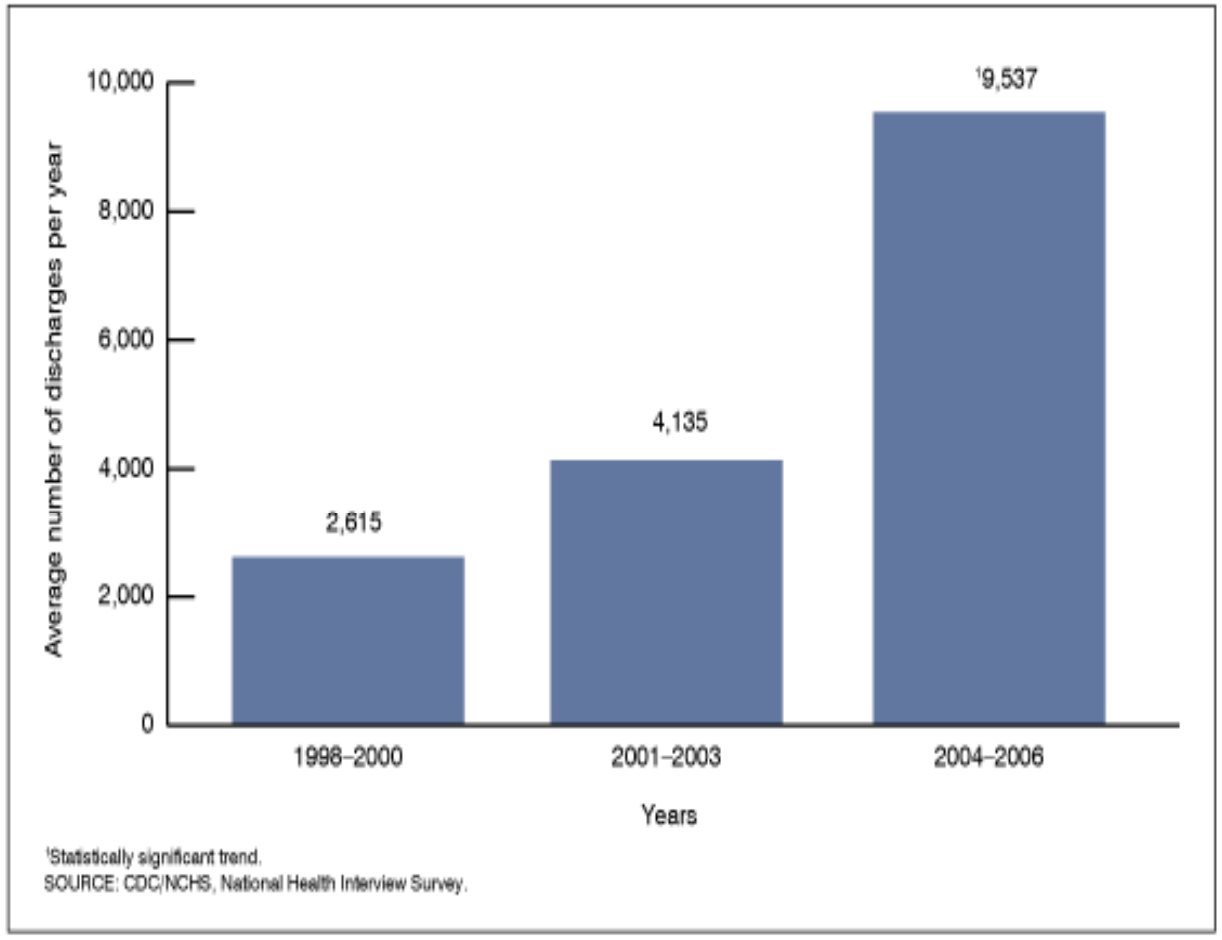
CDC anoun about food allergy

Figure 3. Percentage of children under age 18 years with asthma or other reported allergic conditions in the previous 12 months, by reported food allergy status: United States, 2007



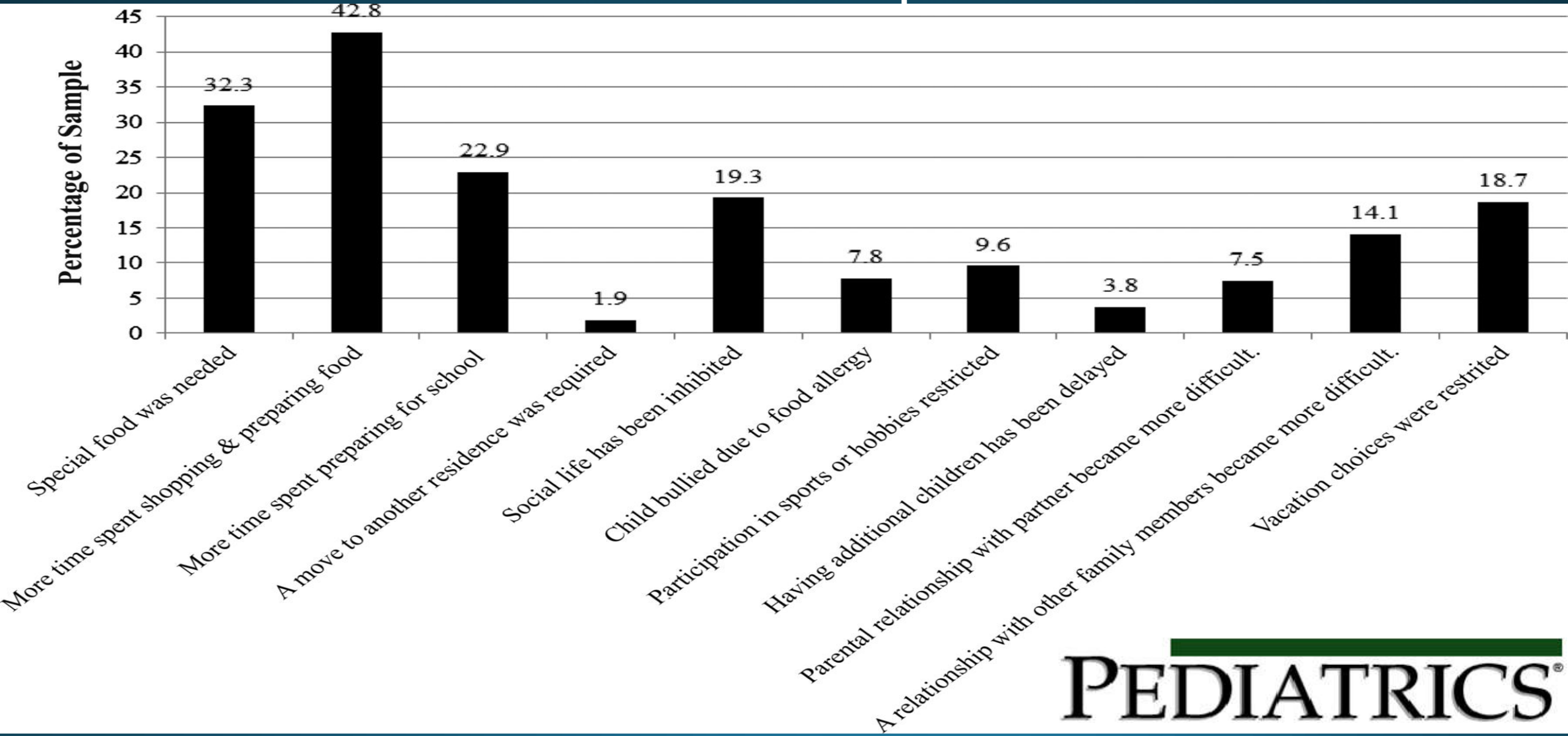
SOURCE: CDC/NCHS, National Health Interview Survey.

Figure 4. Average number of hospital discharges per year among children under age 18 years with any diagnosis related to food allergy: United States, 1998–2006



[1]Statistically significant trend.
SOURCE: CDC/NCHS, National Health Interview Survey.

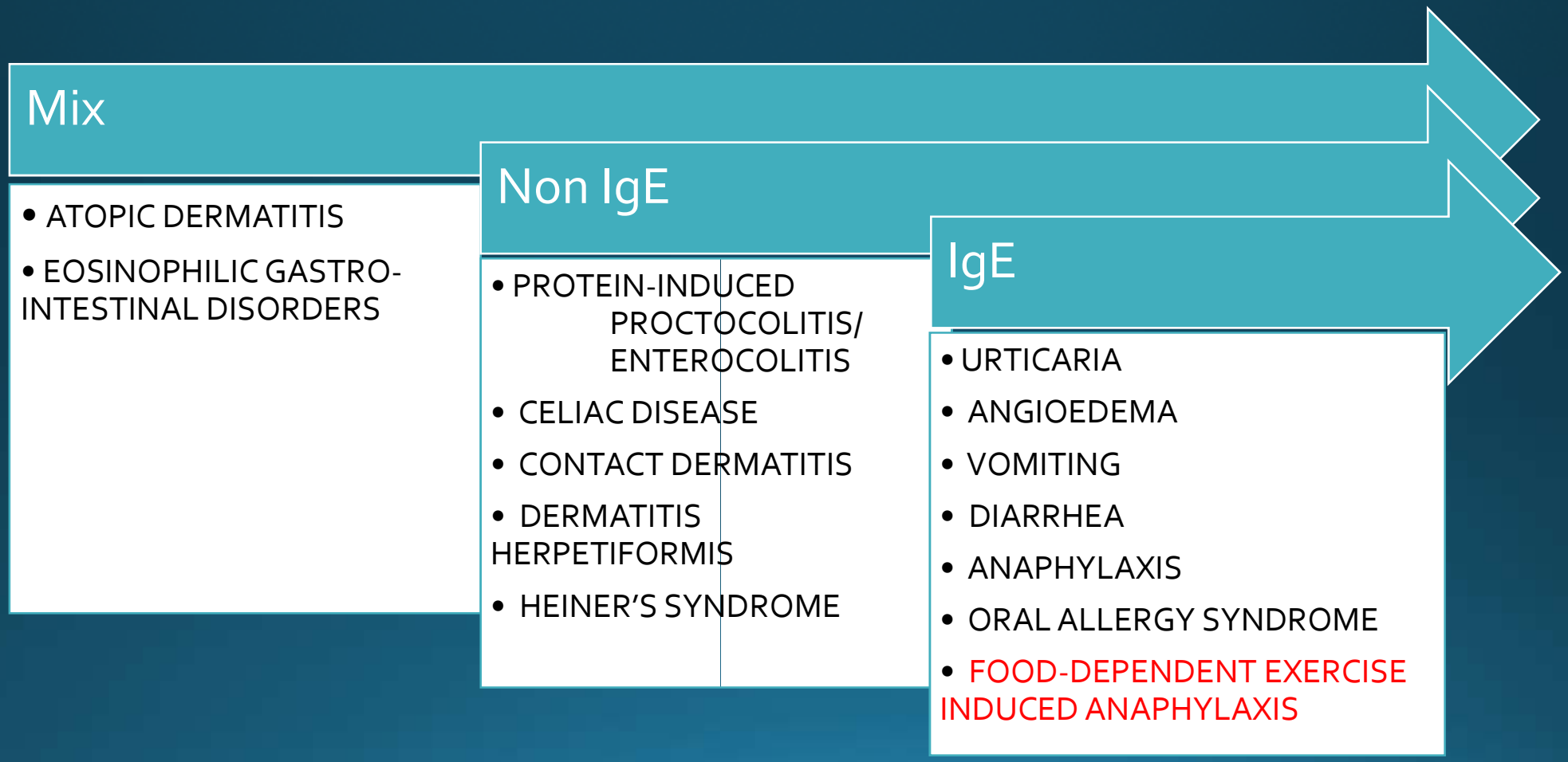
Percentage of children with caregiver report of specific allergy-related needs and problems.



PEDIATRICS®

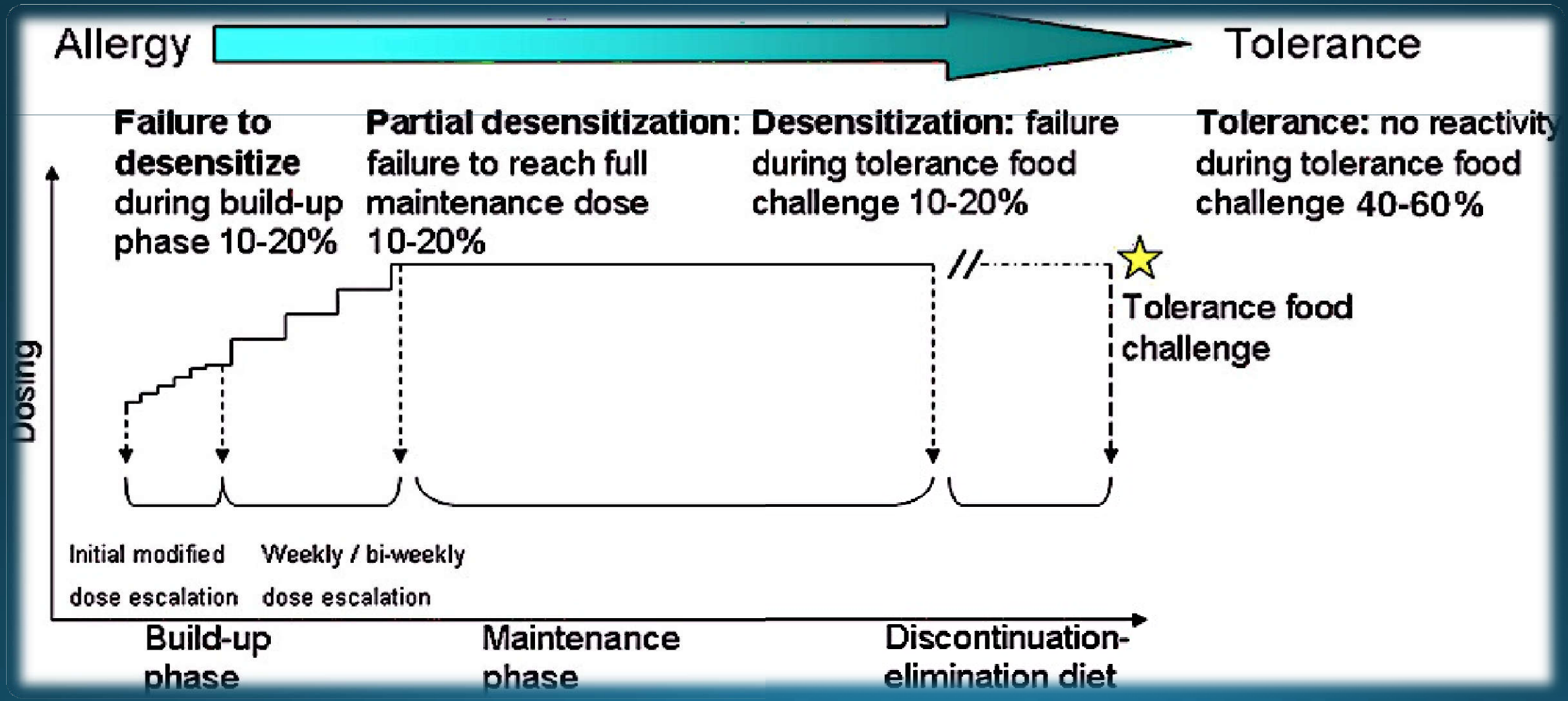
Lucy A. Bilaver et al. Pediatrics doi:10.1542/peds.2015-3678

Food Allergy: Immune System mediated Adverse Food Reaction




Milk
Fish
Soybeans
Tree Nuts
TOP 8
FOOD
ALLERGENS
Peanuts
Eggs
Shellfish
Wheat

Patterns of response to food OIT



Nowak-Wegrzyn JACI March 2011

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oral Immunotherapy for Treatment of Egg Allergy in Children

A. Wesley Burks, M.D., Stacie M. Jones, M.D., Robert A. Wood, M.D., David M. Fleischer, M.D., Scott H. Sicherer, M.D., Robert W. Lindblad, M.D., Donald Stablein, Ph.D., Alice K. Henning, M.S., Brian P. Vickery, M.D.,

- Double-blind, randomized, placebo-controlled study, 55 children, 5 to 11 years of age, with egg allergy received oral immunotherapy (40 children) or placebo (15).
- Initial dose-escalation, build-up, and maintenance phases were followed by an oral food challenge with egg-white powder at 10 months and at 22 months
- Children who successfully passed the challenge at 22 months discontinued oral immunotherapy and avoided all egg consumption for 4 to 6 weeks.
- Children who passed this challenge at 24 months were placed on a diet with ad libitum egg consumption and were evaluated for continuation of sustained unresponsiveness at 30 months and 36 months

Double-blind, randomized, placebo-controlled study

N Engl J Med 2012; 367:233-243 July 19, 2012

Long-term treatment with egg oral immunotherapy enhances sustained unresponsiveness that persists after cessation of therapy

Stacie M. Jones, MD,[a] A. Wesley Burks, MD,[b] Corinne Keet, MD,[c] Brian P. Vickery, MD,[b] Amy M. Scurlock, MD,[a] Robert A. Wood, MD,[c] Andrew H. Liu, MD,[d] Scott H. Sicherer, MD,[e] Alice K. Henning, MS,[f] Robert W. Lindblad, MD,[f] Peter Dawson, PhD,[f] Cecilia Berin, PhD,[e] David M. Fleischer, MD,[d] Donald Y. M. Leung, MD,[d] Marshall Plaut, MD,[g] and Hugh A. Sampson, MD,[e] for the Consortium of Food Allergy Research (CoFAR) *Little Rock, Ark, Chapel Hill, NC, Baltimore, Rockville, and Bethesda, Md, Denver, Colo, and New York, NY*

Food challenge–defined clinical outcomes with longterm eOIT

Time from eOIT initiation	Desensitization	SU
Year 2*	30/40 (75%)	11/40 (27.5%)
Year 3	31/40 (77.5%)	18/40 (45.0%)
Year 4	31/40 (77.5%)	20/40 (50.0%)

*Previously reported in Burks et al.[9]
Among the 22 eOIT-treated subjects treated after 2 years, 41% (95% CI, 21% to 64%) achieved SU. One eOIT-treated subject in whom the 2-year tolerance OFC failed did not resume eOIT dosing.

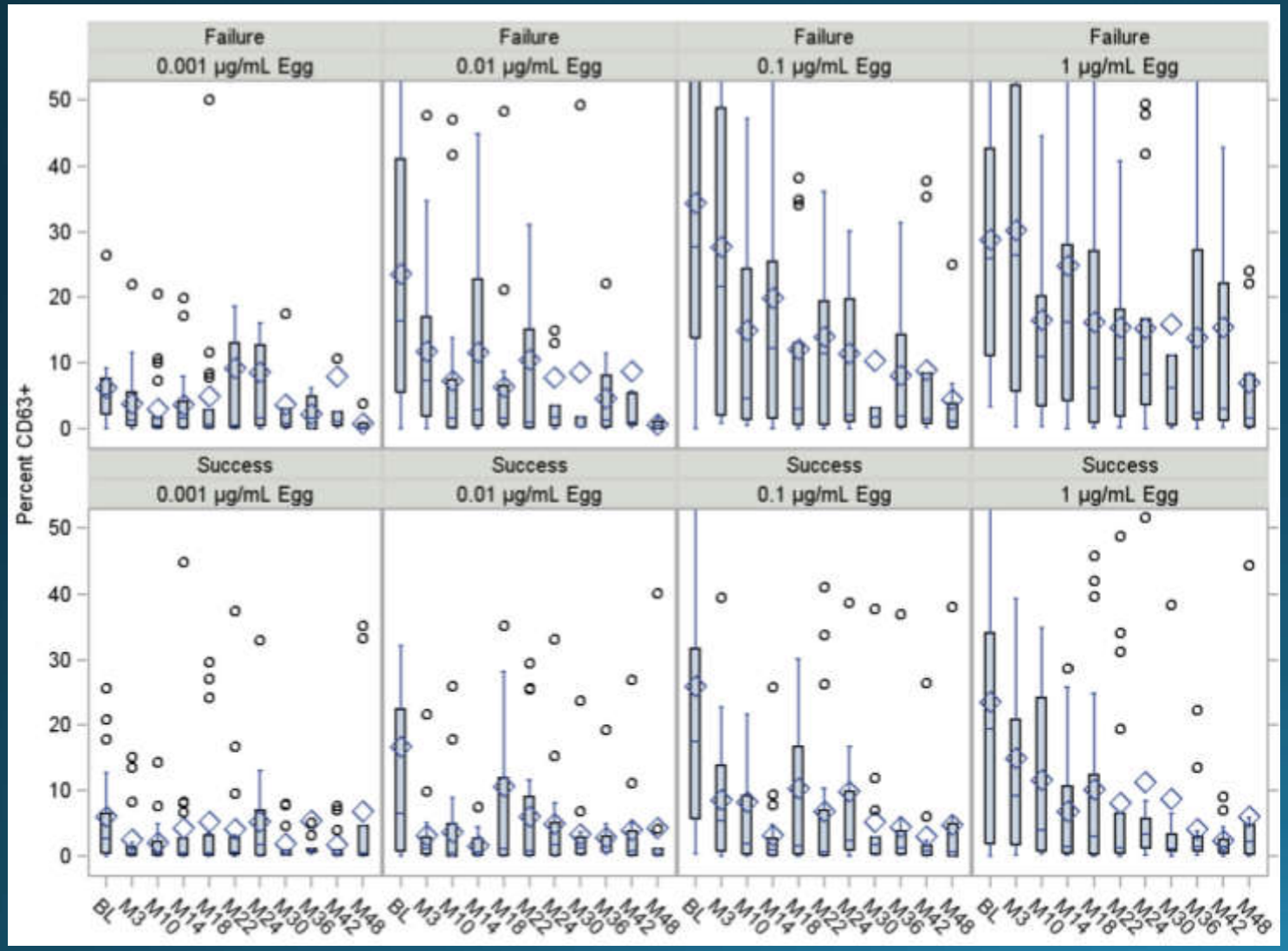
J Allergy Clin Immunol 2016;137:1117-27.

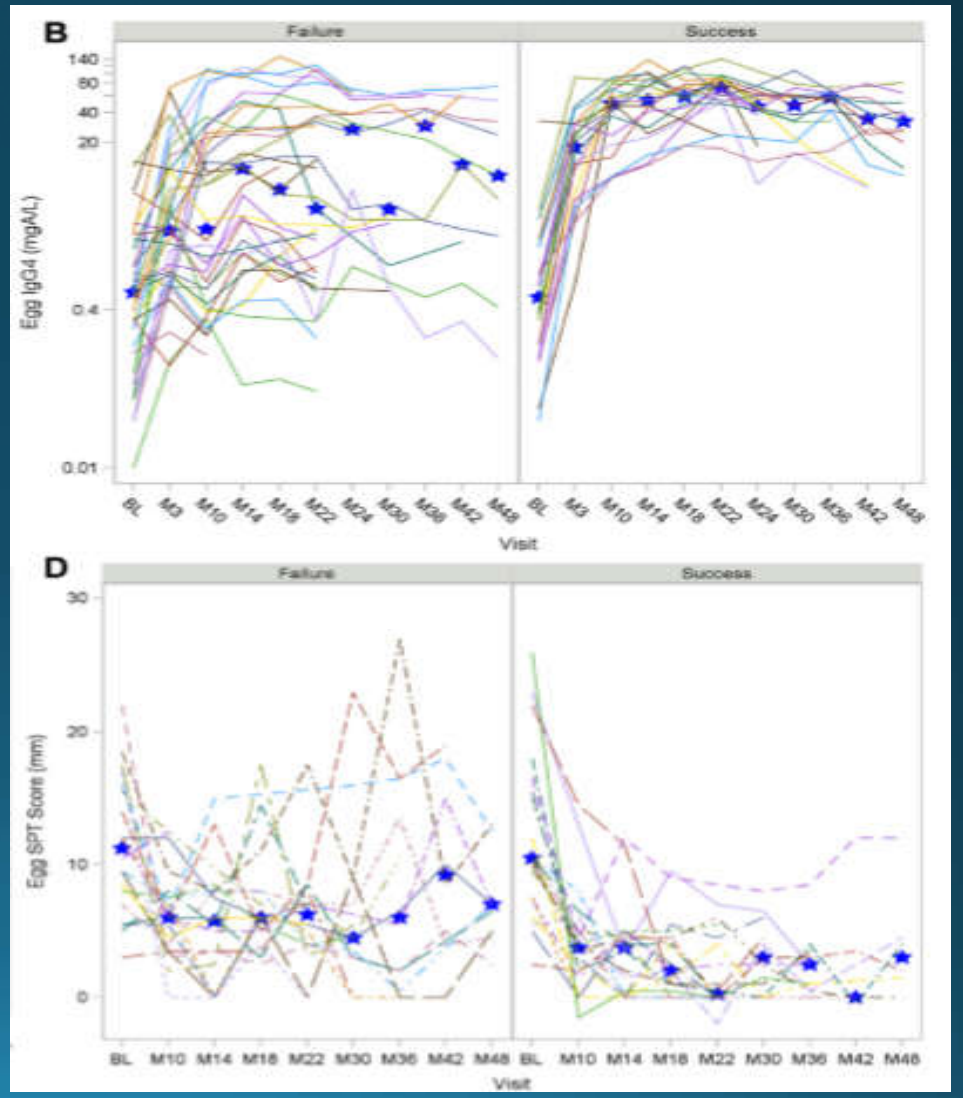
Identify immunologic markers associated with the treatment

Table 3. Median Levels of Immune Markers in the Oral-Immunotherapy Group, According to the Responses to Three Oral Food Challenges.

Variable	Month 10			Month 22			Month 24		
	Pass (N=22)	Fail (N=18)*	P Value	Pass (N=30)†	Fail (N=10)‡	P Value	Pass (N=11)§	Fail (N=29)¶	P Value
Month 10									
Wheal diameter on skin-prick testing (mm)	3.8	6.0	0.10	4.0	7.0	0.03	4.0	5.5	0.32
Egg-specific IgG4 antibody (mg/liter)	52.0	14.2	0.007	42.6	7.6	0.005	54.8	22.4	0.02
Total IgE antibody (kU/liter)	1205.9	926.4	0.68	1177.6	859.6	0.77	1246.5	915.2	0.67
Egg-specific IgE antibody (kU/liter)	7.5	6.1	0.38	5.3	13.3	0.02	5.2	6.8	0.35
CD63+ basophils (%)									
0.1 μg of egg extract	2.1	9.7	0.05	1.9	29.3	0.008	2.5	2.8	0.70
0.01 μg of egg extract	1.0	2.7	0.19	0.5	6.1	0.04	1.4	0.9	0.62

Identify immunologic markers associated with the treatment





Oral Immunotherapy With Cow's Milk

Safety and Efficacy Profile and Immunological Changes Associated With Oral Immunotherapy for IgE-Mediated Cow's Milk Allergy in Children: Systematic Review and Meta-analysis

- The 6 studies were randomized controlled trials conducted between 2007 and 2012
- 138 patients
- IgE-mediated allergy was confirmed by double-blind placebo-controlled food challenge in 4 of the studies

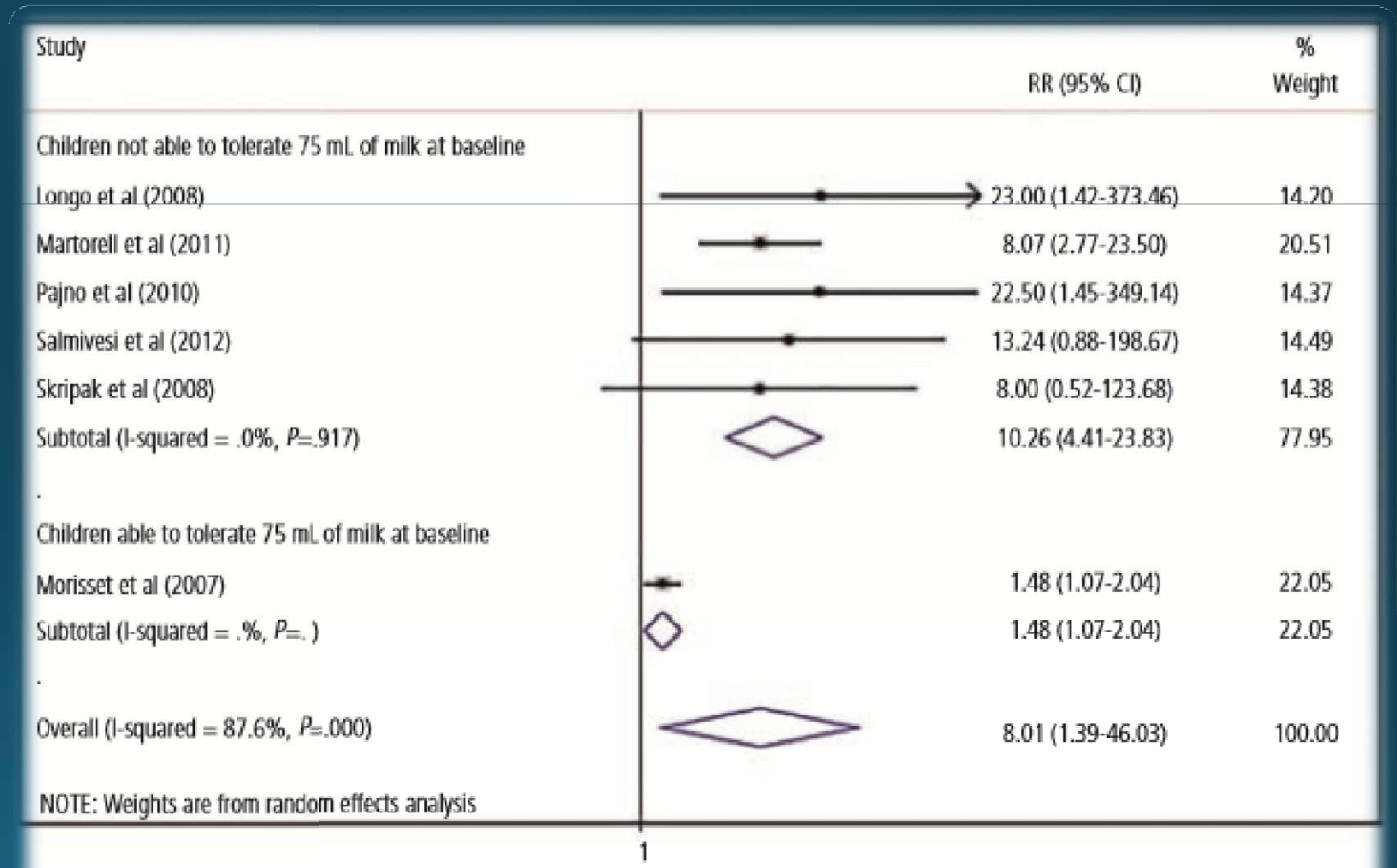


Figure 3. Results of effectiveness of oral immunotherapy with cow's milk.

C Martorell Calatayud,1 A Muriel García,2 A Martorell Aragonés,3 B De La Hoz Caballer4

Safety of food OIT

Table 4. Oral Doses Associated with Symptoms during the First 10 Months, According to Study Group and Phase of Therapy.*

Group and Phase of Therapy†	Total Doses	Any Symptom	Symptom Type					Duration of >30 Min	Treated	Severity‡		
Oral-immunotherapy group												
Initial-day dose escalation	347	27.4	13.8	8.1	9.8	9.5	3.5	8.4	7.2	16.7	3.7	
Build-up	730	35.9	19.7	5.8	13.4	8.8	3.2	4.5	3.7	22.1	1.9	
Maintenance	10,783	24.2	15.1	4.2	7.4	5.1	2.1	4.7	3.5	13.7	0.6	
All	11,860	25.0	15.4	4.4	7.8	5.5	2.2	4.8	3.6	14.3	0.7	

* GI denotes gastrointestinal.
† Doses for the initial-day dose escalation and build-up phases were given at the clinic under medical observation. Doses for the maintenance

TABLE II. OIT doses (percentages)* associated with symptoms during years 3 and 4 of the study

Visit type	No. of doses	Any symptom	Symptom type					Persist >30 min	Treated	Symptom severity		
			Oral/pharyngeal	Skin	Respiratory	Gastrointestinal	Other			Mild	Moderate	Severe
Clinic	194	14.9	11.3	0.5	1.5	1.0	1.5	0.0	1.0	4.1	0.0	0.0
Home	8731	4.7	2.2	1.1	2.1	0.2	0.2	2.0	1.6	3.0	0.0	0.0
All	8925	5.0	2.4	1.1	2.1	0.3	0.2	1.9	1.6	3.0	0.0	0.0

*With the exception of number of doses, values are percentages of doses.

Bégin et al. Allergy, Asthma & Clinical Immunology 2014, 10:1
http://www.aacijournal.com/content/10/1/1

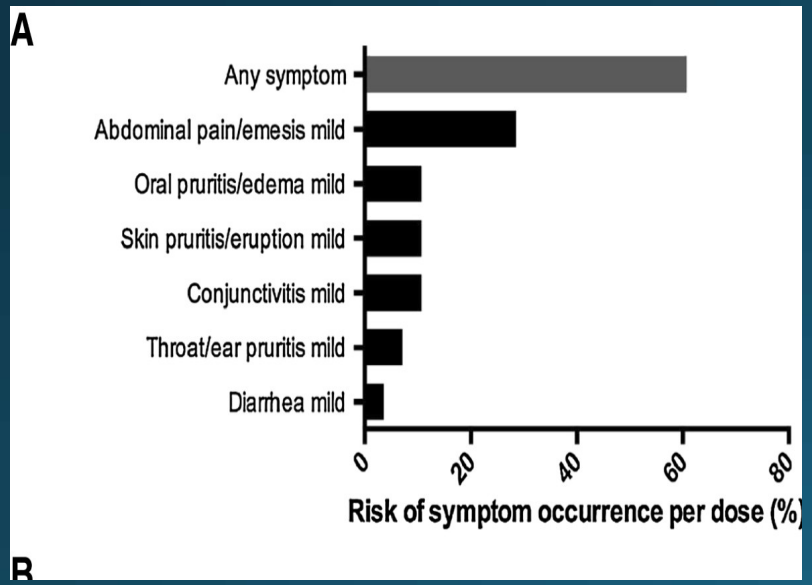
ALLERGY, ASTHMA & CLINICAL IMMUNOLOGY

RESEARCH Open Access

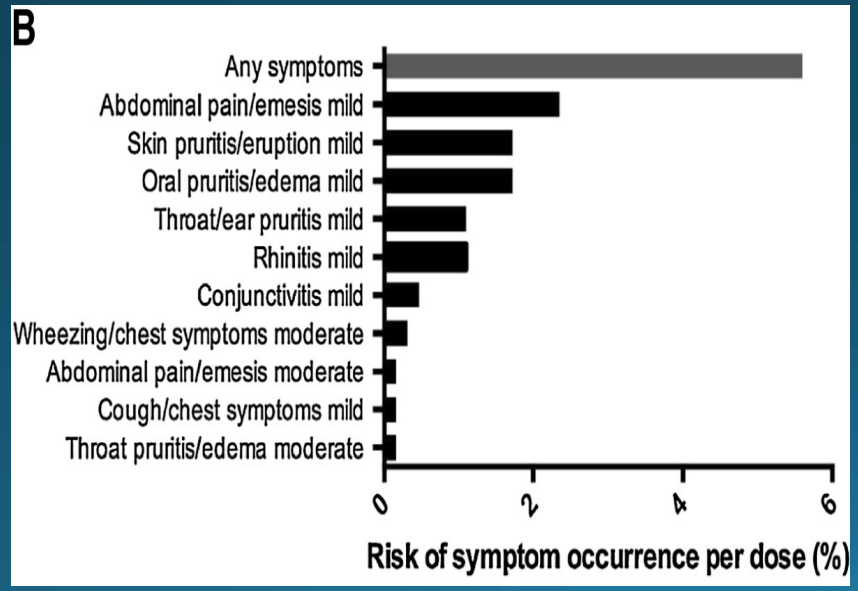
Safety and feasibility of oral immunotherapy to multiple allergens for food allergy

Philippe Bégin[1*], Lisa C Winterroth[1], Tina Dominguez[1], Shruti P Wilson[1], Liane Bacal[1], Anjuli Mehrotra[1],

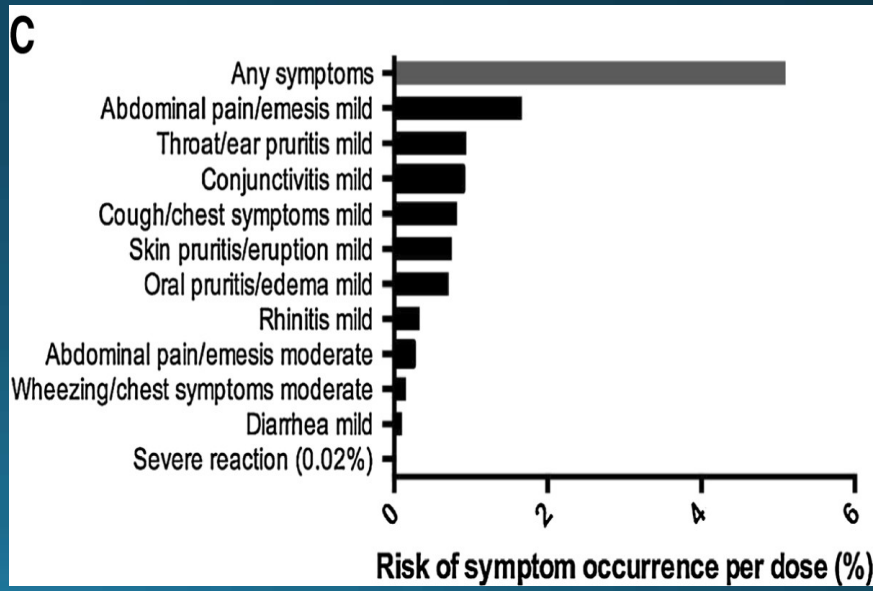
Participants underwent double-blind placebo-controlled food challenges (DBPCFC) up to a cumulative dose of 182 mg of food protein to peanut followed by other nuts, sesame, dairy or egg



Initial escalation day



Dose escalations



home dosing during OIT to multiple foods.

Improving the safety of oral immunotherapy for food allergy.

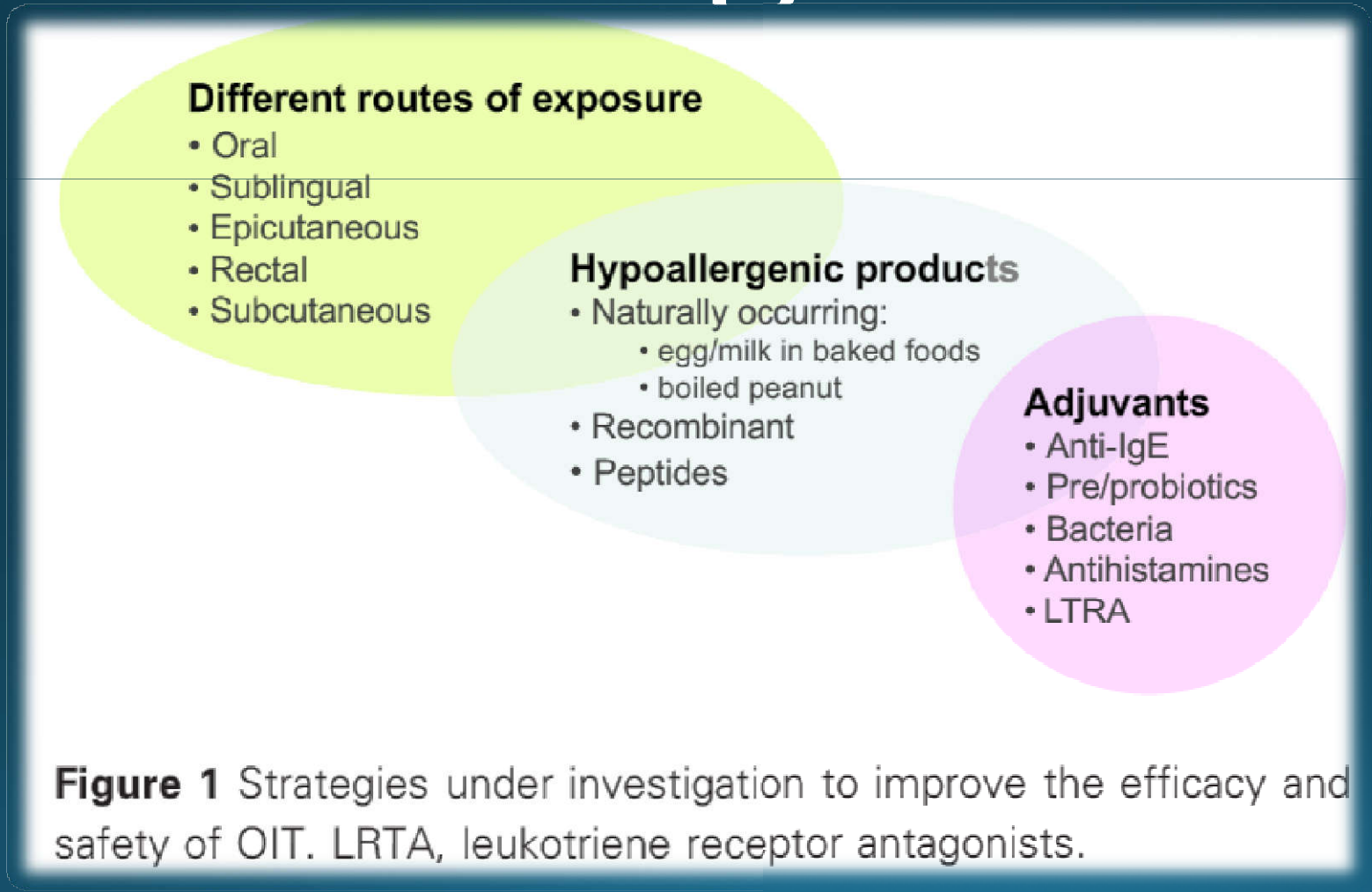


Figure 1 Strategies under investigation to improve the efficacy and safety of OIT. LRTA, leukotriene receptor antagonists.

Pediatr Allergy Immunol. 2016 Mar;27(2):117-25. doi: 10.1111/pai.12510. Epub 2015 Dec 22.
Improving the safety of oral immunotherapy for food allergy.
Vazquez-Ortiz M[1], Turner PJ[1,2].

Improving the safety of oral immunotherapy for food allergy.

Pediatr Allergy Immunol. 2016 Mar 22. doi: 10.1111/pai.12567

Anti-IgE-assisted desensitization to egg and cow's milk in patients refractory to conventional oral **immunotherapy**.

Martorell-Calatayud C, Michavila-Gómez A, Martorell-Aragonés A, Molini-Menchón N, Cerdá-Mir JC, Félix-Toledo R, De Las Marinas-Álvarez MD.

J Allergy Clin Immunol. 2016 Apr;137(4):1103-1110.e11. doi: 10.1016/j.jaci.2015.10.005. Epub 2015 Nov 12.

A randomized, double-blind, placebo-controlled study of omalizumab combined with oral immunotherapy for the treatment of cow's milk allergy.

Wood RA1, Kim JS2, Lindblad R3, Nadeau K4, Henning AK3, Dawson P3, Plaut M5, Sampson HA6.

Clin Exp Allergy. 2015 Jun;45(6):1071-84. doi: 10.1111/cea.12528.

Identification of novel peptide biomarkers to predict safety and efficacy of cow's milk oral immunotherapy by peptide microarray.

Martínez-Botas J[1,2], Rodríguez-Álvarez M[3], Cerecedo I[4], Vlaicu C[4], Diéguez MC[4], Gómez-Coronado D[1,2], Fernández-Rivas M[3], de la Hoz B[4].

Omalizumab improvements in measurements of safety but not in outcomes of efficacy

TABLE III. Percentage of doses per subject with dosing symptoms during the escalation period

	Treatment group						
	Omalizumab (n = 27)			Placebo (n = 28)			
MOIT dose-related symptoms	Median	Lower quartile	Upper quartile	Median	Lower quartile	Upper quartile	*P* value
Total no. of doses	198.0	190.0	209.0	225.0	200.0	239.0	.008
Any symptoms	2.1	0.5	12.0	16.1	7.8	38.9	.0005
Any symptoms excluding oral/pharyngeal	0.5	0.0	3.3	8.6	4.1	18.9	.0001
Duration >30 min	0.4	0.0	1.0	3.0	1.2	4.3	.0001
Treatment used	0.0	0.0	1.6	3.8	1.5	5.8	.0008
Oral/pharyngeal symptoms	0.6	0.0	10.9	8.8	2.7	29.5	.0025
Skin symptoms	0.0	0.0	0.5	1.1	0.6	2.5	.0004
Respiratory symptoms	0.0	0.0	1.4	2.5	1.7	4.8	<.0001
GI symptoms	0.0	0.0	1.9	3.0	1.2	7.3	.001
Other symptoms	0.0	0.0	0.5	1.4	0.2	4.0	.008
Mild symptoms	0.5	0.0	3.3	7.9	3.5	18.1	.0001
Moderate symptoms	0.0	0.0	0.0	0.5	0.2	1.3	.0005
Severe symptoms	0.0	0.0	0.0	0.0	0.0	0.0	.35
Treated with epinephrine	0.0	0.0	0.0	0.0	0.0	0.0	.052

GI, Gastrointestinal.

J Allergy Clin Immunol. 2016 Apr;137(4):1103-1110.e11. doi: 10.1016/j.jaci.2015.10.005. Epub 2015 Nov 12.
A randomized, double-blind, placebo-controlled study of omalizumab combined with oral immunotherapy for the treatment of cow's milk allergy.
Wood RA1, Kim JS2,

OIT ready for standard clinical practice?

- Effective and reasonably safe alternative to the avoidance diet
- Best safest and most efficacious clinical protocol has not yet been established

Thank you for your attention