

Literature Review

(and random stuff 😊)

Tom Chacko

www.chackoallergy.com

Atlanta Area

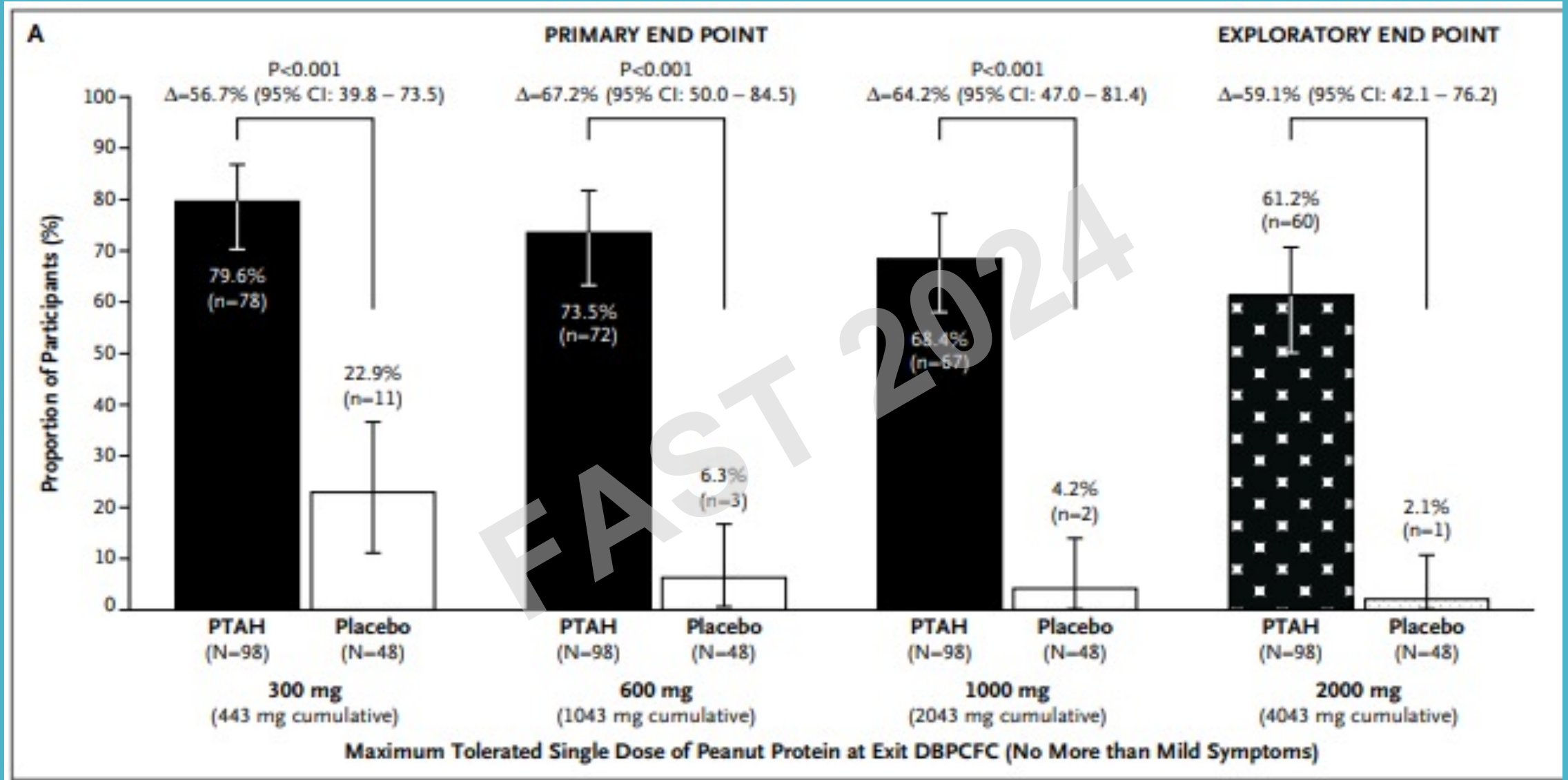
FAST 2024

ORIGINAL ARTICLE

Oral Immunotherapy for Peanut Allergy in Children 1 to Less Than 4 Years of Age

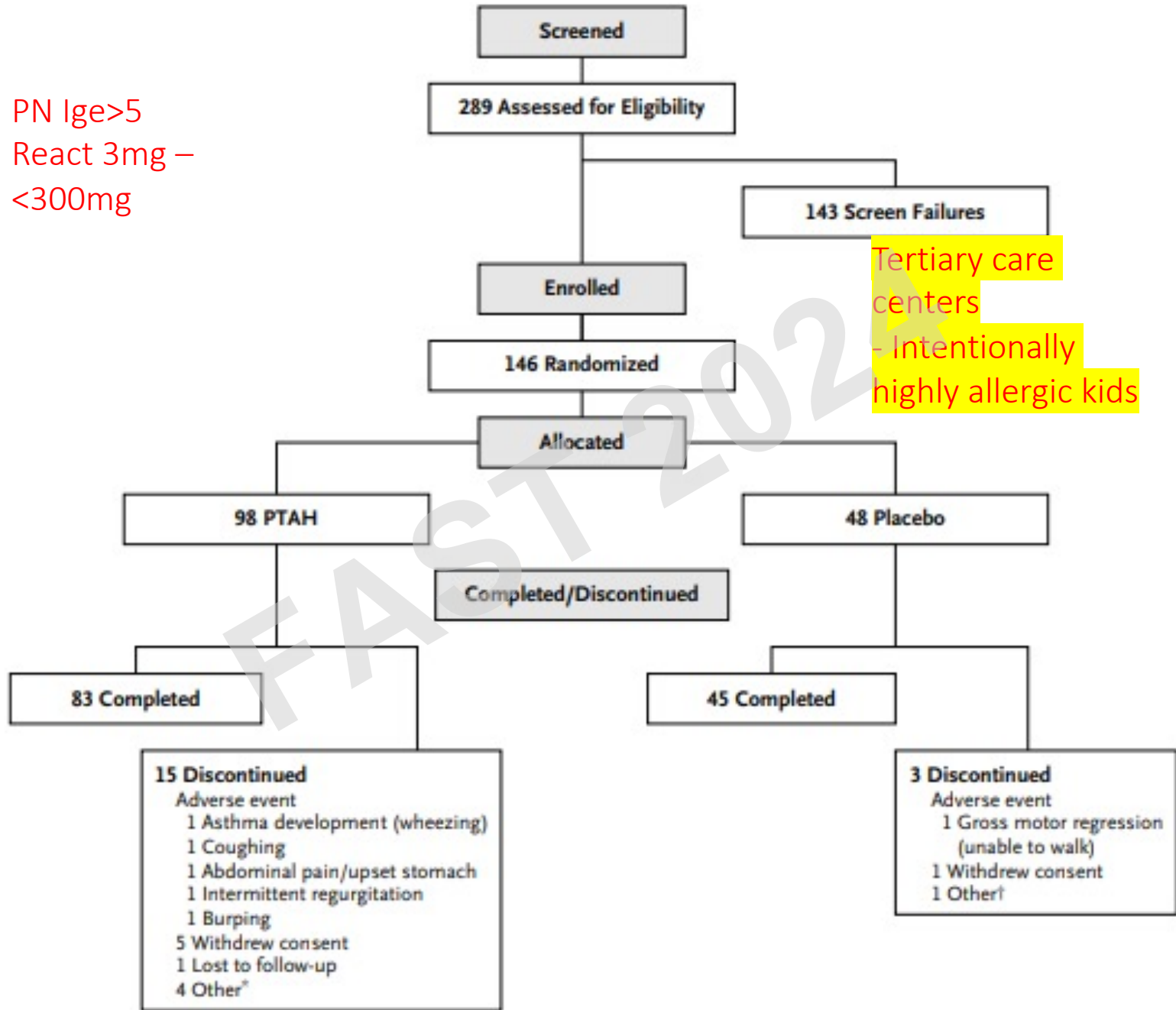
George Du Toit, M.B., B.Ch.,¹ Kari R. Brown, M.D.,² Andrea Vereda, M.D., Ph.D.,³ Anne-Marie Irani, M.D.,² Stephen Tilles, M.D.,² Anoshie Ratnayake, M.D.,² Stacie M. Jones, M.D.,⁴ and Brian P. Vickery, M.D.,⁵ for the POSEIDON Study Group*

- 1-<4 yo failed a challenge of 300mg Peanut Protein or less (less than 1 peanut)
- 12 month peanut allergy powder (PTAH) versus placebo
- End point- - Tolerate 600mg or more
 - 73% met the endpoint in treatment vs 6.3 in placebo
 - mild/moderate reactions 92.9% PTAH vs 93.8% placebo
 - 3 treatment related systemic adverse events- none severe in 2 PTAH pts (2%)
- Conclusion- Children 1-<4 yo when treated , then vast majority can then tolerate 600mg peanut protein



Only treatment for a year and starting at high IgEs, likely if doing longer, IgEs likely go down with time and could tolerate higher amounts

PN Ige>5
React 3mg –
<300mg



Not Really Typical Patients We see in Clinic- More Severe
 Not infants- more so toddlers 2-3 years old

Age	PTAH (N=98)	Placebo (N=48)	Total (N=146)
Median — years (range)	2.0 (1–3)	2.0 (1–3)	2.0 (1–3)
1 to <2 years — no. of patients (%)	33 (33.7)	16 (33.3)	49 (33.6)
2 to <3 years — no. of patients (%)	35 (35.7)	15 (31.3)	50 (34.2)
3 to <4 years — no. of patients (%)	30 (30.6)	17 (35.4)	47 (32.2)
History of allergic disease — no. of			

Table 1. (cont.)

Demographic or Characteristic	PTAH (N=98)	Placebo (N=48)	Total (N=146)
Immunologic markers — median (Q1, Q3 [range])			
Total IgE (IU/ml)	162.5 (52, 453 [5–3324]); n=86	175.0 (41, 343 [9–5508]); n=45	164.0 (51, 422 [5–5508]); n=131
psIgE (kUA/l)	6.8 (2.28, 33.5 [0.01–100]); n=87	30.0 (2.12, 69.7 [0.06–100]); n=45	10.1 (2.23, 51.5 [0.01–100]); n=132
Ara h 2 IgE (kUA/l)	5.19 (1.26, 25.4 [0.01–100]); n=86	14.2 (1.79, 54.7 [0.05–100]); n=45	6.27 (1.37, 38.2 [0.01–100]); n=131
Peanut SPT wheal mean diameter (mm)	9.0 (7.0, 13.5 [4.0–36.0]); n=95	9.75 (6.75, 13.0 [2.0–26.5]); n=48	9.5 (7.0, 13.0 [2.0–36.0]); n=143
MTD peanut protein at screening DBPCFC — median mg (Q1, Q3 [range])	30 (10, 100 [1–100])	30 (10, 30 [1–100])	30 (10, 100 [1–100])

* DBPCFC denotes double-blind, placebo-controlled food challenge; IgE, immunoglobulin E; MTD, maximum tolerated dose; psIgE, peanut-specific immunoglobulin E; PTAH, peanut (*Arachis*)

On entry, higher IgEs, reacting at less than ½ bamba stick

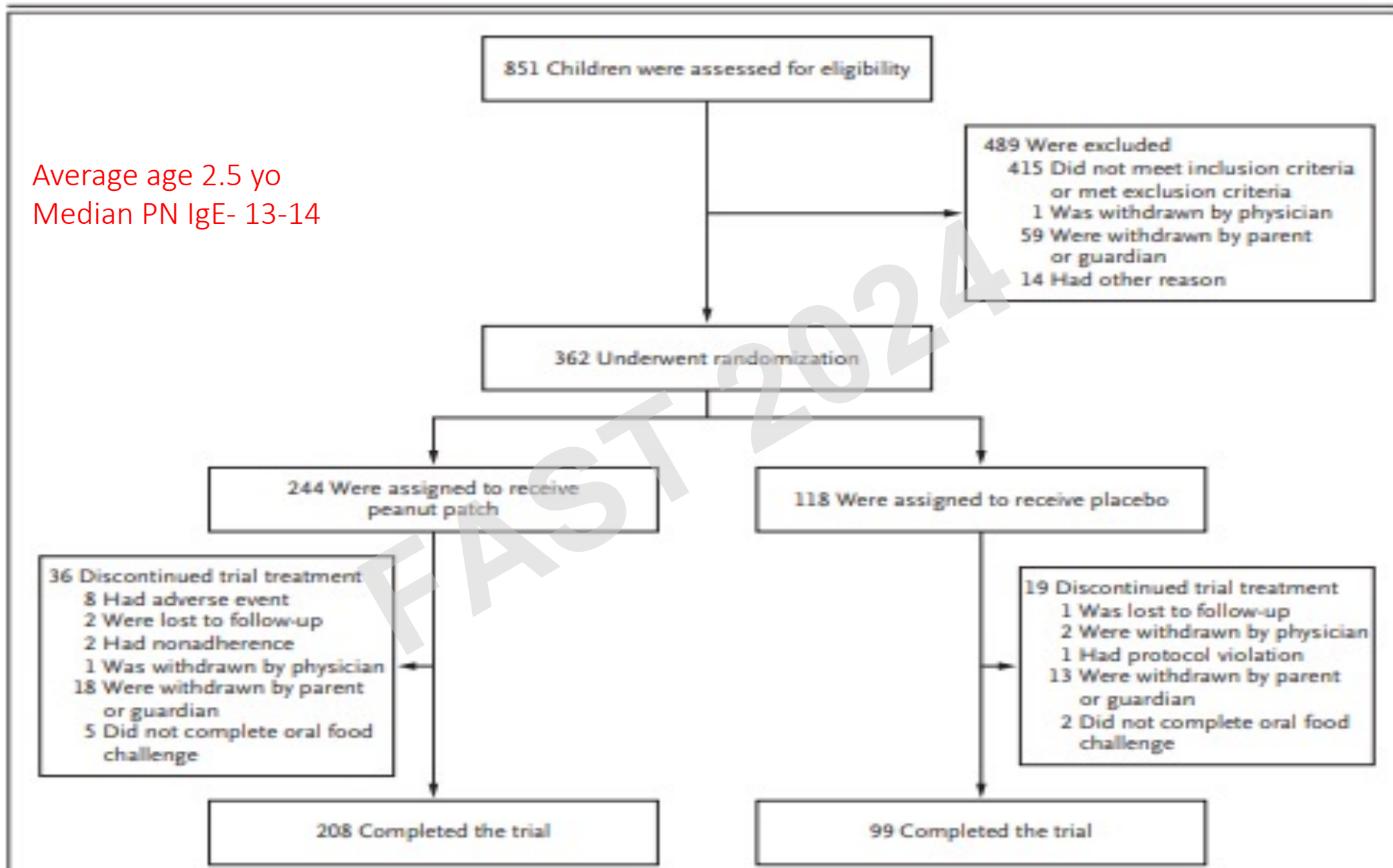
Take home: Good results but in clinical practice, should be easier as intentionally skewed highly allergic population in study

Phase 3 Trial of Epicutaneous Immunotherapy in Toddlers with Peanut Allergy

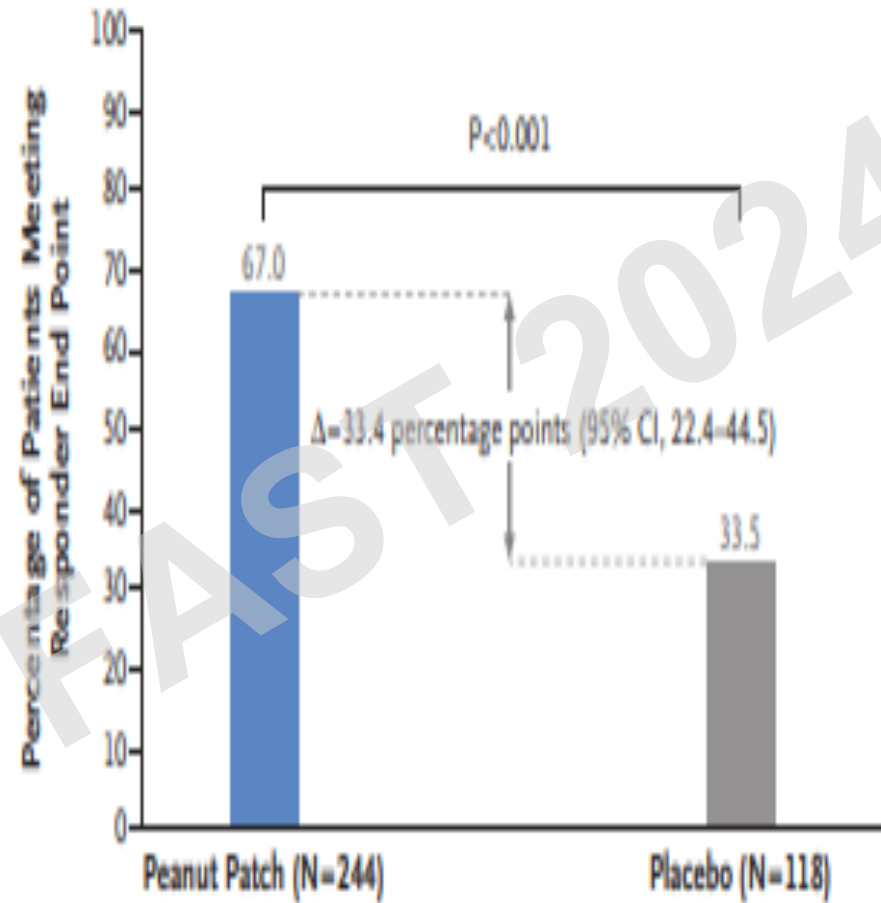
M. Greenhawt, S.B. Sindher, J. Wang, M. O'Sullivan, G. du Toit, E.H. Kim,
D. Albright, S. Anvari, N. Arends, P.D. Arkwright, P. Bégin, K. Blumchen,
T. Bourrier, T. Brown-Whitehorn, H. Cassell, E.S. Chan, C.E. Ciaccio,
A. Deschildre, A. Divaret-Chauveau, S.L. Dorris, M.J. Dorsey, T. Eiwegger,

- May 2023 NEJM
- Children 1-3 yo Peanut Allergy with received placebo or patch of 250 micrograms (0.25 milligrams) daily 12 months
- Primary endpoint- Increase in treatment response of eliciting dose after 12 month
- Conclusion:
- 64 % of intervention able to consume at least 1000mg vs 29% of placebo

Average age 2.5 yo
Median PN IgE- 13-14



A Primary Analysis



My take homes for EPIT in toddlers

- Wasn't geared for infants
- Most somewhat later in age, higher IgEs
- Tolerated well....seems to work
- Do we need it?
- Expensive, well funded
- Lose window to make cheap, long term intervention
- Recent review EPIT with milk (Woods, April 2024 JAMA Peds)- 50% improvement in treatment arm vs 35% placebo, no dose response (300 microgram worked, not higher)

Safety and effectiveness of peanut oral immunotherapy in children under 12 months



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Jaclyn Bjelac, MD^b, Leigh Ann Kerns, MD^b,
Ahila Subramanian, MD, MPH^b, Alice E.W. Hoyt, MD^c,
Rachel Whitsel, APRN, CNP^b, and Sandra J. Hong, MD^{b,*}

JACI in Practice Nov 2023

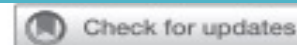
Clinical Implications

Peanut oral immunotherapy is an option for the treatment of peanut allergy. Our study suggests that peanut oral immunotherapy in children aged less than 12 months is safe and effective.

-Retrospective Chart Review Cleveland Clinic

- Started 18 mg PP and build to 500 mg PP
- 22 patients
- 9.2 months old
- Mean Peanut IgE 6.8 (high?-tertiary care center)
- 1 discontinue (recurrent illnesses/logistics)
- - 2/3 mild symptoms- most self resolved
- 10 negative full dose peanut challenges
- Conclusion- All patients tolerated 500mg PP and high % of patients tolerated full PN servings

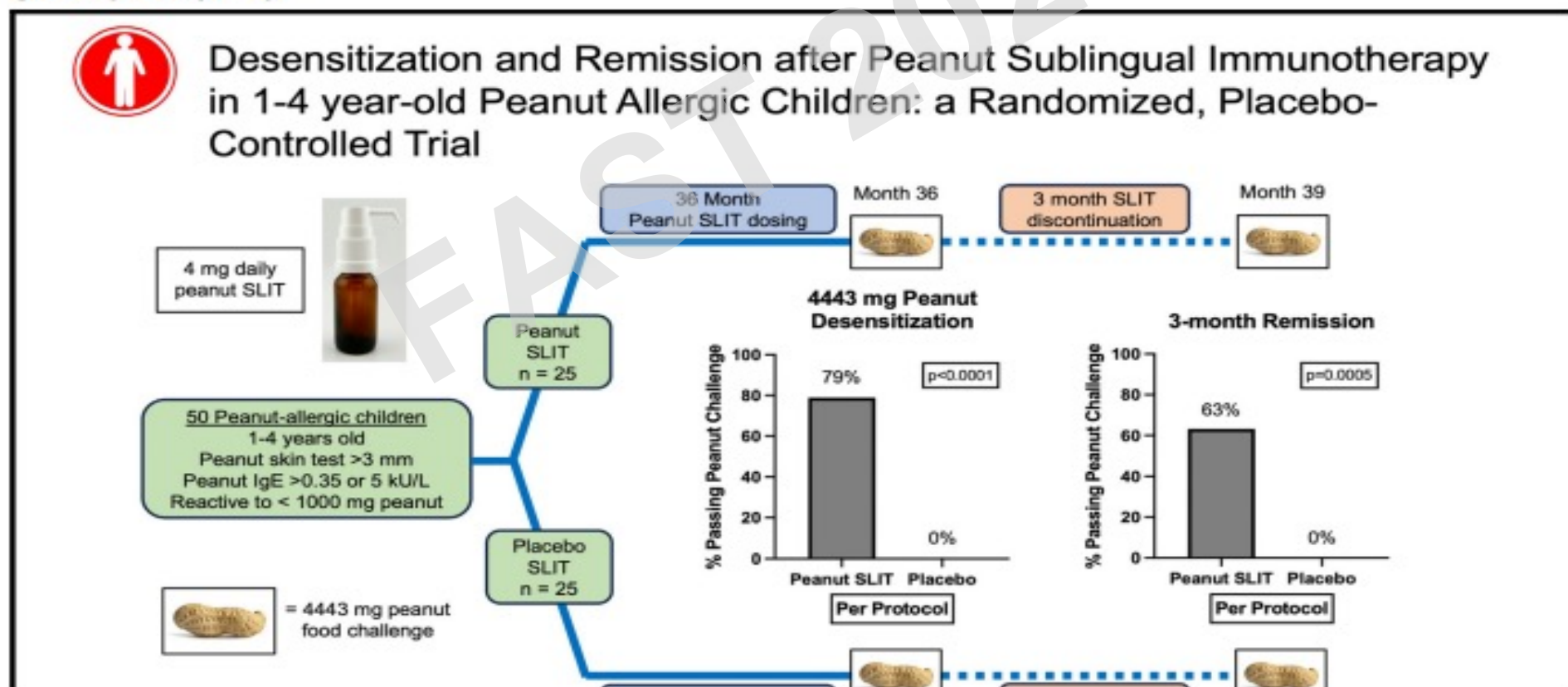
Desensitization and remission after peanut sublingual immunotherapy in 1- to 4-year-old peanut-allergic children: A randomized, placebo-controlled trial



Edwin H. Kim, MD, MS,^a J. Andrew Bird, MD,^c Corinne A. Keet, MD, PhD,^a Yamini V. Virkud, MD, MPH,^a Lauren Herlihy, DNP,^a Ping Ye, PhD,^a Johanna M. Smeekens, PhD,^a Rishu Guo, PhD,^a Xiaohong Yue, MS, DDS,^a Anusha Penumarti, PhD,^a Bahjat Qaqish, PhD,^b Quefeng Li, PhD,^b Michael D. Kulis, PhD,^a and A. Wesley Burks, MD^a
Chapel Hill, NC, and Dallas, Tex

JACI January 2024

GRAPHICAL ABSTRACT



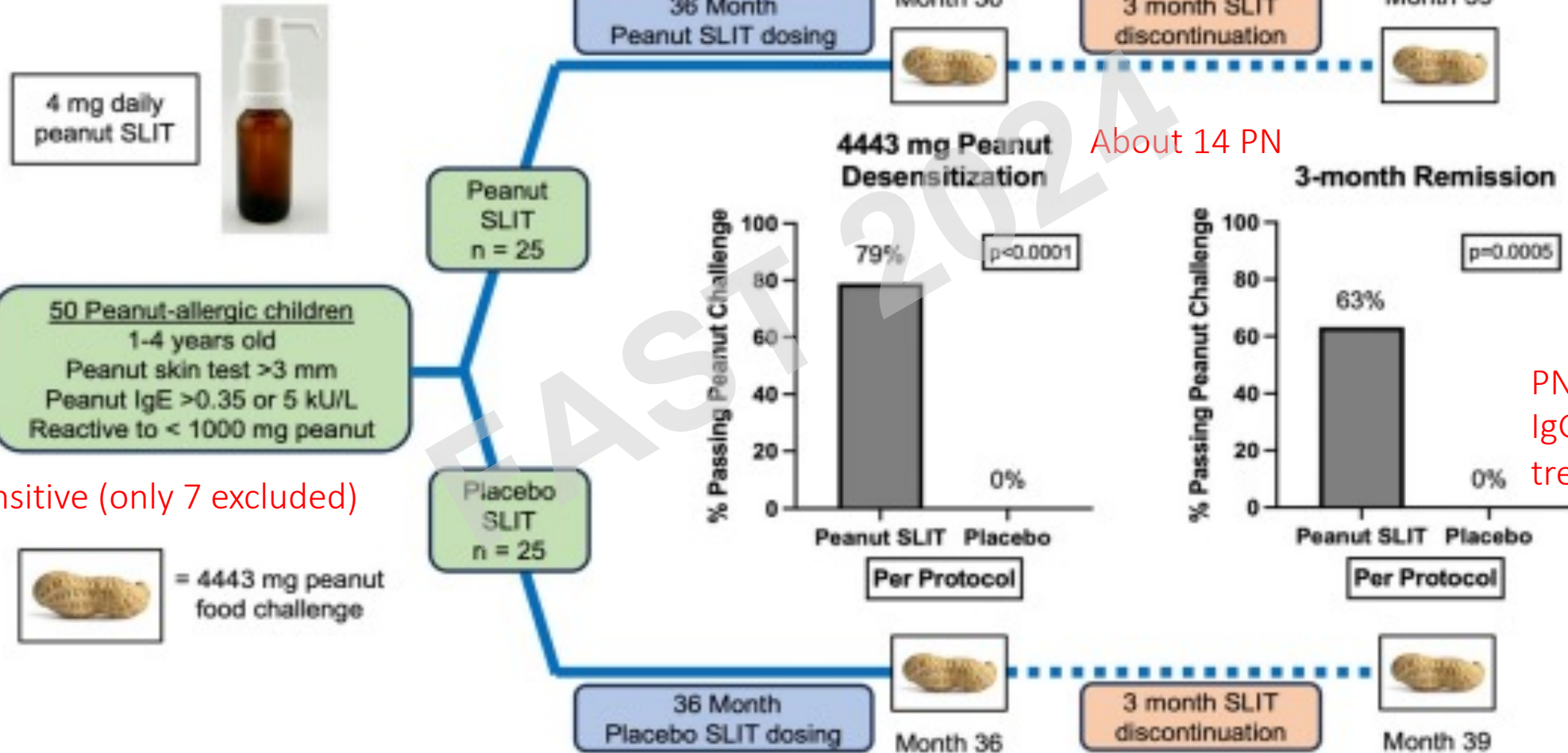
Disclosure

-I am not a SLITer

FAST 2024



Desensitization and Remission after Peanut Sublingual Immunotherapy in 1-4 year-old Peanut Allergic Children: a Randomized, Placebo-Controlled Trial



Peanut SLIT 1-4 yo

- 25 participants each arm
- ½ the participants between 1-2 years old (let's go 😊)
- Hold under 2 minutes and then swallow
- Little kids this is higher volume so many broken up in 2 doses

Impressions

- “First in toddlers” SLIT
- Large effect size for both desensitization & remission
- Apparently safe (only TRAEs reported)
 - No epi use or EoE/ELOR
 - 2 WD with only mild AEs
- 17/50 (34%) withdrew before month 39
 - 7 active, 10 pbo
- Proof of concept only
- Essentially single-center
- Primary analysis not shown?
- Imbalance in IgE parameters suppressed PBO response
 - Powered for 60% between group diff w/ 20% PBO response rate
- Underpowered for age comparisons & not stratified
- 1000 mg entry threshold; 2 dose-level improvement for response

Slide Courtesy of Brian Vickery, MD-
CHOA/Emory Journal Club

Is this just low-dose OIT? If not, why not?

Safety and Effectiveness of Bypassing Oral Immunotherapy Buildup With an Initial Phase of Sublingual Immunotherapy for Higher-Risk Food Allergy

Lianne Soller, PhD, Brock A. Williams, PhD, Raymond Mak, MD, Tiffany Wong, MD, Stephanie C. Erdle, MD, Alanna Chomyn, MD, Brittany Tetreault, BScN, Kelly Morrison, BScN, Lisa Gaudet, BScN, and Edmond S. Chan, MD
Vancouver, BC, Canada

JACI in Practice- In Press... email chain from David Fitzhugh ☺

What is already known about this topic? Oral immunotherapy (OIT) is safe and effective in preschoolers, but the risk of severe reaction is higher in older children and adults. Sublingual immunotherapy (SLIT) has been shown to be safer and better tolerated than OIT, with lower effectiveness.

What does this article add to our knowledge? An initial phase of multifoed SLIT to bypass OIT buildup is safe and effective in a real-world setting.

How does this study impact current management guidelines? For patients and families desiring treatment when OIT would be of higher risk, SLIT may be a safer alternative by allowing patients to skip the OIT buildup phase.

SLIT to OIT Bridge

- Based out of Canada (clinical practice- Not industry sponsored - love Canadian studies 😊)
- Multi-food SLIT with goal of bypassing OIT build up
- 4 to 18 years old (not infants- good 😊)
- 2 mg protein SLIT over 3 to 5 visits supervised
- 1-2 years SLIT → low dose challenge 300 mg protein

SLIT to OIT Bridge

Results

- 188 patients enrolled
- 11 year (median age)
- Well tolerated, 2.1% received epi but no severe reactions
- 70% pass OFC to 300 mg protein
- Conclusion: SLIT option to bypass OIT build up in high risk patients

SLIT to OIT Bridge

Details/Thoughts

- Median age 11 year old (great option)
- Specific median IgE – 28.4
- 188 patient treated → 149 PN (80%), 97 TN (51%), egg 15 (8%), milk 10 (5%)
- No entry level challenge (cool with that-real life trial)- low dose tolerant/high dose reacted?
- Overall- More so SLIT helpful for PN/TN

Home > 'Very Low-Dose' Peanut Oral Immunotherapy Helps Desensitize

'Very Low-Dose' Peanut Oral Immunotherapy Helps Desensitize

By: Jenifer Goodwin in Food Allergy, Food Allergy News
Published: February 28, 2023

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Very Low-Dose OIT Shows Efficacy for Peanut-Allergic Kids

— Plus, for sesame-allergic kids, oral desensitization effective with crushed sesame seeds, tahini

How low can we go: preliminary efficacy of low dose peanut OIT

Upton et al. Abstract AAAAI 2023

- Ongoing Trial- 49/51 enrolled 45 randomized
- Children reactive to <443 mg PP (DBPCFC)
- OIT 30 mg PP (VLOIT) or 300mg or placebo
- Challenge- > 443 mg PP and >1043 mg PP

How low can we go: preliminary efficacy of low dose peanut OIT

Upton et al. Abstract AAAAI 2023

Results

- Median age 10 yo
- PP tolerant 44 mg on entry (older, likely higher IgEs)
- VLOIT- 12/15 completed 1 year,
- 300mg OIT- 9/15 complete 1 year
- VLOIT- 10/12 tolerated 443mg, 5/12 tolerated >1043 mg
- Conclusion- VLOIT increased threshold of reactions and may allow for the simplified OIT regiments
- Waiting further data but clinically makes sense to me



Retail Food Equivalents for Post-Oral Immunotherapy Dosing in the Omalizumab as Monotherapy and as Adjunct Therapy to Multi-Allergen Oral Immunotherapy in Food-Allergic Children and Adults (OUtMATCH) Clinical Trial

Marion Groetch, MS, RDN^a, Kim Mudd, MSN, RN^b, Margaret Woch, RDN^c, Allison Schaible, MS, RDN^a, Brianna E. Gray, MS, RDN^d, Denise C. Babineau, PhD^e, J. Andrew Bird, MD^f, Stacie Jones, MD^g, Edwin H. Kim, MD, MS^h, Bruce J. Lanser, MD, MPHⁱ, Julian Poyser, FNP, MPA, MS^j, Nicole Rogers, BS^o, Wayne Shreffler, MD, PhD^d, Scott Sicherer, MD^a, Amanda K. Rudman Spergel, MD^l, Jonathan Spergel, MD^k, Brian P. Vickery, MD^l, R. Sharon Chinthrajah, MD^{c,*}, and Robert Wood, MD^{b,*} *New York, NY; Baltimore and Bethesda, Md; Stanford, Calif; Boston, Mass; Dallas, Texas; Little Rock, Ark; Chapel Hill and Durham, NC; Denver, Colo; Philadelphia, Pa; and Atlanta, Ga*

JACI in Practice Feb 2023.












What is already known about this topic? Although foods are increasingly being used for therapeutic purposes in food allergy, only limited guidance on retail food protein equivalent doses has been published.

What does this article add to our knowledge? We describe a process by which multiple retail food equivalents and participant-oriented educational materials were developed for a posttreatment clinical research trial for the allergens of peanut, milk, egg, wheat, cashew, hazelnut, and walnut.

How does this study impact current management guidelines? Our results provide extensive guidance and retail food equivalent variety to research participants and a method to estimate retail food equivalents systematically for the maintenance of home feeding of daily allergen protein quantities.

TABLE III. Milk food protein equivalents

Food	300 mg	600 mg	1,000 mg	2,000 mg	4,000 mg	6,000 mg
Fluid cow's milk Dairy Pure 1% Fat Milk	2 tsp	1 tbsp plus $\frac{1}{2}$ tsp	2 tbsp	$\frac{1}{4}$ cup	$\frac{1}{2}$ cup	$\frac{3}{4}$ cup
Mozzarella cheese Sargento String Cheese	$\frac{1}{24}$ of cheese stick	$\frac{1}{12}$ of cheese stick	$\frac{1}{6}$ of cheese stick	$\frac{7}{24}$ of cheese stick	$\frac{7}{12}$ of cheese stick	$\frac{5}{6}$ of cheese stick
Shredded mozzarella cheese Kraft Natural Mozzarella Shredded low- moisture part skim	$\frac{1}{2}$ tsp	1 tsp	$1\frac{3}{4}$ tsp	1 tbsp plus $\frac{1}{2}$ tsp	2 tbsp plus 1 tsp	$3\frac{1}{2}$ tbsp
Parmesan cheese grated Kraft	$\frac{1}{5}$ tsp	$\frac{2}{3}$ tsp	1 tsp	2 tsp	1 tbsp plus 1 tsp	2 tbsp
Cream cheese Philadelphia Regular Cream Cheese	1 tsp	$1\frac{3}{4}$ tsp	1 tbsp	2 tbsp	4 tbsp ($\frac{1}{4}$ cup)	6 tbsp
Whipped cream cheese Philadelphia Whipped Cream Cheese	2 tsp	1 tbsp plus $\frac{1}{2}$ tsp	2 tbsp	4 tbsp	8 tbsp ($\frac{1}{2}$ cup)	12 tbsp
Nonfat plain Greek yogurt Chobani (no fruit flavors)	$\frac{3}{4}$ tsp	$1\frac{1}{2}$ tsp	$2\frac{1}{4}$ tsp	$1\frac{1}{2}$ tbsp	3 tbsp	$4\frac{1}{2}$ tbsp
Regular yogurt Yoplait Original	2 tsp	1 tbsp plus $\frac{3}{4}$ tsp	2 tbsp	4 tbsp	4 oz or $\frac{1}{2}$ cup	1 single serve (6 oz) ($\frac{3}{4}$ cup)
Instant nonfat dry milk Carnation	$\frac{1}{2}$ tsp	$\frac{1}{4}$ tsp plus $\frac{2}{3}$ tsp	$1\frac{1}{2}$ tsp (or $\frac{1}{2}$ tbsp)	1 tbsp	2 tbsp	3 tbsp
Ice cream Classic Vanilla Bean Edy's or Dryer's	1 tbsp plus $\frac{1}{2}$ tsp	2 tbsp plus $\frac{1}{2}$ tsp	$\frac{1}{4}$ cup (or 4 tbsp)	$\frac{1}{4}$ cup plus 3 tbsp	$\frac{3}{4}$ cup plus 2 tbsp	$1\frac{1}{3}$ cups
Milk chocolate chips Hershey's	16 chips	32 chips	53 chips	109 chips ($3\frac{1}{2}$ tbsp)	217 chips ($\frac{1}{4}$ cup plus 3 tbsp)	325 chips ($\frac{1}{2}$ cup plus $2\frac{1}{2}$ tbsp)

Consume one or these foods every day. The amount listed is the MINIMUM amount to eat. Many ingredients contribute to the total protein content of a food. The amount to eat is based on the specific allergen protein content and not the total protein content.		Amount to eat
Peanut Butter* Skippy or Jif		1/2 teaspoon
Peanut butter* Teddie Organic All Natural Creamy		1/2 teaspoon You will need to stir this product and then refrigerate, as the oil will separate from the nut butter and make measuring the serving size more difficult.
Peanuts* Planters Cocktail or Hampton Farms Peanuts in the shell Peanuts can be eaten with or without the skin.		 Whole peanut Half peanut 1 and 1/2 peanuts (Choose 1 whole + 1 half peanut OR 3 half peanuts)
Peanut Flour Golden or Byrd Mill 12% Light Roast		1/3 teaspoon
Bamba Osam brand		3 pieces
PB2 Powdered Peanut Butter Original PB2 and Organic PB2		1/3 teaspoon
Reese's Peanut Butter Cups Miniatures (Wrapped)		1/2 Miniature
Peanut M&Ms		2 peanut M&Ms
Reese's Peanut Butter Cups Unwrapped Minis		1 and 1/2 Minis
Reese's Pieces Candies		4 Reese's Pieces

Peanut Protein- 300mg Peanut Protein

- Who licked the M&Ms?
- Long way from Academy protocol exchanges

Flex-IT! Applying “Platform Trials” Methodology to Immunotherapy for Food Allergy in Research and Clinical Practice

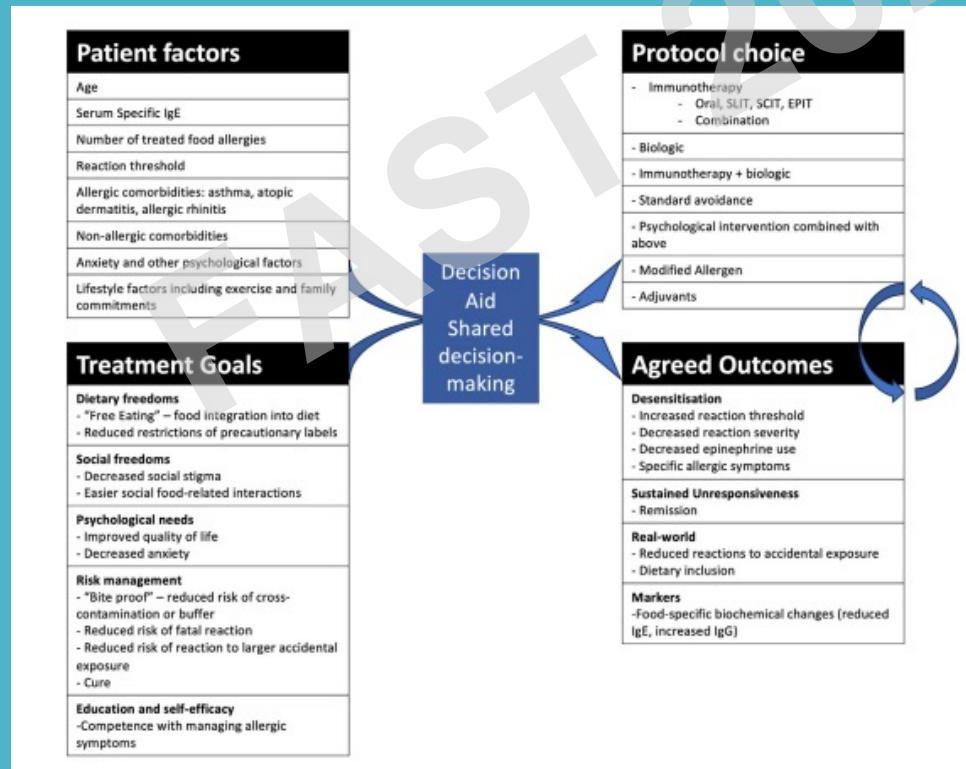
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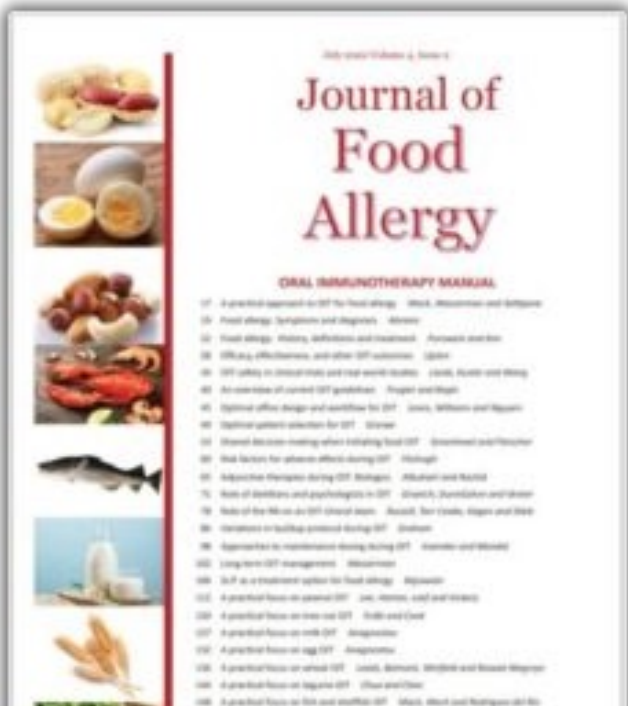


Douglas P. Mack, MD^a, Julia Upton, MD^{b,c}, Nandinee Patel, MD, PhD^d, and Paul J. Turner, FRCPCH, PhD^d *Hamilton and Toronto, Ontario, Canada; and London, United Kingdom*

There is an increasing trend in the management of food allergy toward active treatment using allergen immunotherapy (AIT). Although AIT is efficacious, treatment-related adverse events are

approach as flexible immunotherapy. However, there is little evidence to inform clinicians as to what changes to treatment are most likely to result in treatment success. Classical clinical trials





o A practical focus on oral immunotherapy to tree nuts

pp. 120-126(7)

Authors: Erdle, Stephanie; Cook, Victoria E.

o A practical focus on milk oral immunotherapy

pp. 127-131(5)

Author: Anagnostou, Aikaterini

o A practical focus on egg oral immunotherapy

pp. 132-135(4)

Author: Anagnostou, Aikaterini

o A practical focus on wheat oral immunotherapy

pp. 136-143(8)

Authors: Leeds, Stephanie; Belmont, Ami; Winfield, Holly; Nowak-Wegrzyn, Anna

o A practical focus on legume oral immunotherapy

pp. 144-147(4)

Authors: Chua, Gilbert T.; Chan, Edmond S.

o A practical focus on fish and shellfish oral immunotherapy

pp. 148-150(3)

Authors: Mack, Douglas P.; Woch, Margaret; Rodríguez del Río, Pablo

o A practical focus on sesame allergy and a brief review of other seed allergies

pp. 151-157(7)

No.	WP, mg	cooked orzo grains§	approximation)	Interval	Increase
1	2.6 mg	1/2	—	Day 1	100
2	5.2 mg	1	—	Day 1	100
3	10.4	2	—	2 wk	100
4	20.8	4	—	2 wk	100
5	41.6	8	—	2 wk	100
6	52.0	10	—	2 wk	25
7	62.4	12	—	2 wk	20
8	83.2	16 (1/4 tsp)	—	2 wk	33
9	114.4	22 (1/3 tsp)	1 oyster cracker¶	2 wk	37.5
10	166.4	32 (1/2 tsp)	—	2 wk	45.5
11	249.6	48 (3/4 tsp)	—	2 wk	50
12	332.8	64 (1 tsp)	3 oyster crackers	2 wk	33.3
13	416	80 (1 tsp and 1/4 tsp)	2 saltine crackers or 4 oyster crackers	2 wk	25
14	582.4	96 (1 tsp and 1/2 tsp)	3 saltine crackers or 6 oyster crackers	2 wk	40
15	665.6	128 (2 tsp)	7 oyster crackers	2 wk	14.3
16	800	154 (2 tsp and 1/3 tsp and 4 grains)	4 saltine crackers or 8 oyster crackers	2 wk	20
17	998.4	192 (3 tsp [1 tbsp])	5 saltine crackers or 10 oyster crackers	2 wk	24.8
18	1331.3	4 tsp (leveled)	6 saltine crackers or 13 oyster crackers	2 wk	33.3
19	1664	5 tsp (leveled)	8 saltine crackers or 16 oyster crackers	2 wk	25
20	1996.8	6 tsp (= 2 tbsps = 1 oz) (leveled)	10 saltine crackers or 20 oyster crackers or one slice of white bread**	2 wk	20

OIT = Oral immunotherapy; WP = wheat protein.

Wheat OIT- Vital Wheat Powder, David's Awesome Bagel, Orzo grains?



Organic Peanut Butter Puffs

Amount of peanut protein

Per 42g pouch: 7 grams peanut protein

Per 7g serving (approx 27 puffs): 1.17 grams peanut protein

Per puff: 43 mg peanut protein

Approx # puffs for 500 mg peanut protein: 12 puffs

Mixed Nut Butter Puffs

Approx amount of protein from each nut (peanut, cashew, walnut, hazelnut, almond) and total nuts is below.

Per 42g pouch: 1 gram protein per nut = 5 grams total nut protein

Per 7g serving (33 puffs): 167 mg per nut = 833 mg total nut protein

Per puff: 5 mg per nut = 25 mg total nut protein

Approx # puffs for 500 mg protein from each nut (including peanut): 100 puffs (half a pouch)

Table 3 Sample TN-OIT dosing schedule

Dose*	Food Protein Dose, mg	Cashew Flour (5 g protein/28 g cashew flour), mg#	Walnut Meal (5 g protein/30 g walnut flour), mg#	Hazelnut Flour (5 g protein/28 g hazelnut flour), mg#	Almond Flour (6 g protein/28 g almond flour), mg#
1§	1	5.6	6	5.6	4.8
	2.5	14	15	14	12
	5	28	30	28	23
	10	56	60	56	47
2	20	112	120	112	93
3	40	224	240	224	187
4	80	448	480	448	373
5	120	672	720	672	560
6	160	896	960	896	750
7	240	1344	1440	1344	1120
8	300	1680	1800	1680	1400

TN – Tree nut; OIT – oral immunotherapy

-Gideon Lack founder with Atlanta family (JJ Jackson)

- Based out of Atlanta
- CHOA/Emory uses for their OIT for Peanut

- We've come a long way in since our first FAST meeting
- Started with 8PN or more for maintenance- now lower OIT dose, VLOIT, SLIT, same stuff?
- Palforzia is now.....just peanut flour
- EPIT, commercial SLIT, biologics.....protect from accidents...suck on 1 Mightyme TN puff (5mg peanut protein?)
- Always thanks to the OGs

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22. 9 month old with hives after 1/2 teaspoon of peanut butter. Bloodwork shows total IgE 5, IgE Peanut 2.0 Ara H2- 1.25. Do you?

① Start presenting to display the poll results on this slide.

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23. 17 yo boy with history of PN allergy heading to college. Reacted as a baby and avoided since. Total IgE 200, PN IgE 80 Ara H2- 50. Child seems fine but parents want to do "something" to protect before he goes away to college and come to you for some treatment. They know you offer OIT as well as have heard about Xolair. Do you?

i Start presenting to display the poll results on this slide.