# Food SLIT:
# Data 2025 Version

# (249 reasons why you should be doing SLIT!)

David Fitzhugh, MD

ALLERGY PARTNERS
www.allergypartners.com

# Goals

- Review data for food SLIT safety and efficacy
- Peanut vs. other allergens
- Discuss extract-based vs. food-based SLIT
- Answer common practical questions:
  - What is target goal for protection?
  - How long does it take to get there?
  - Can you achieve “full” desensitization?
  - What is youngest age?
- Review typical escalation protocols
- SLIT —> OIT “bridge” (hybrid approach)
- Single vs. multi-allergen SLIT
- What is success?  How do we monitor this?

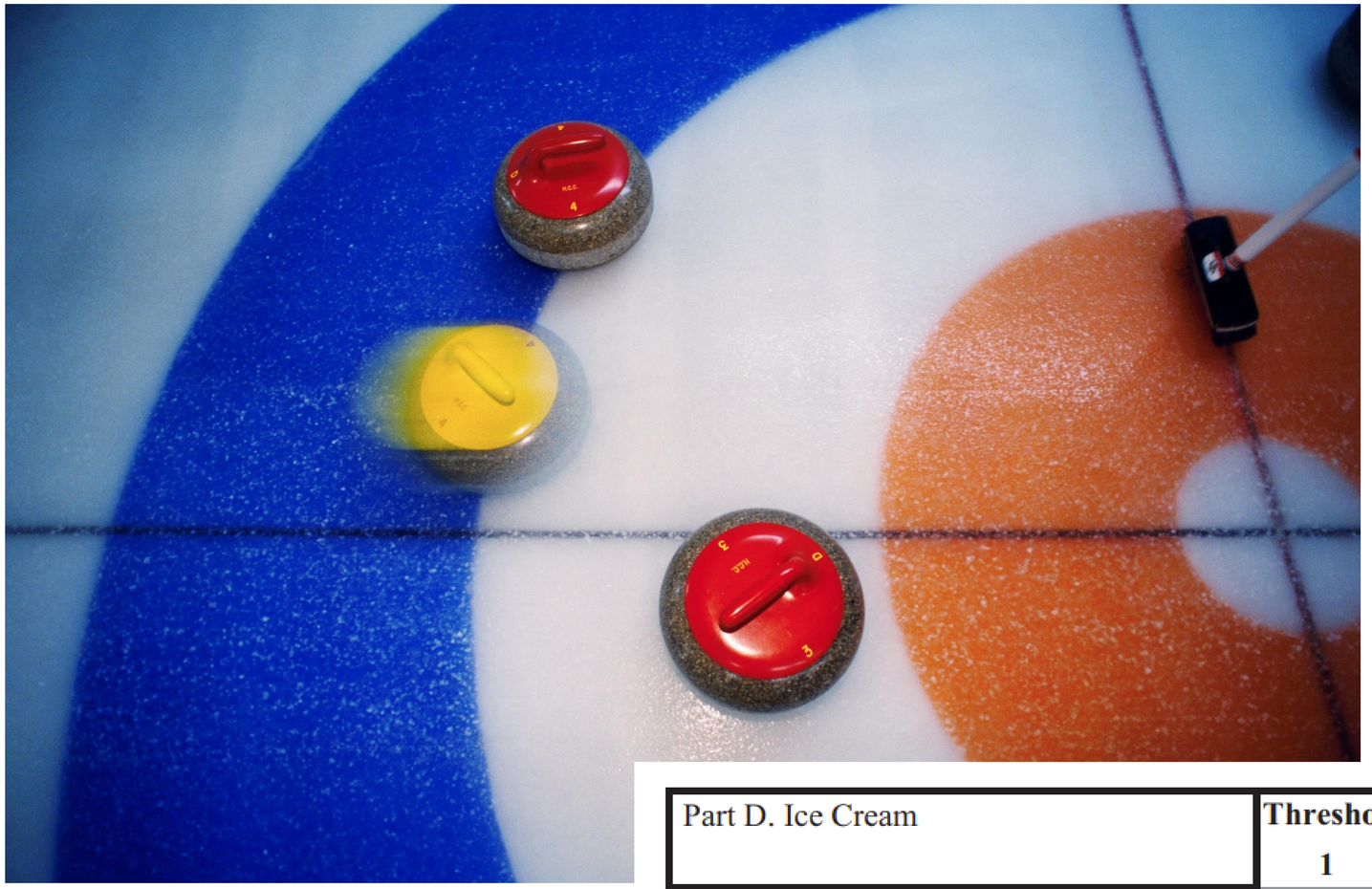
# Highlights of OIT vs. SLIT

| | OIT | SLIT |
|---|---|---|
| Office visits | Every 2 weeks | Every 2 months (4 total visits) |
| Home dosing | Daily | Daily |
| Time to achieve protection | 6 - 12 months | 1 - 2 years (maybe longer) |
| Rest period after dosing | 2 hours | none |
| Possible to achieve dietary inclusion | Yes | Not with SLIT alone (SLIT followed by OIT possible) |
| Side effects | GI symptoms relatively frequent; needing EpiPen can occur but very uncommon (1:2000 doses delivered) | Mainly mild oral side effects (itch, tingling in mouth). |
| Dosing range | 2 mg -> 1000 mg | 2 mcg -> 2 mg |
| Age restriction | Best if < 12 years old | Any age (3 or older) |
| Multiple allergens at same time | No | Possible but likely limited to 4 |
| Best for: | Younger age, relatively moderate IgE values | Higher risk patients (asthma history, very high IgE values) but possible with most patients |

- High-level overview for patients/parents
- Many parents come assuming OIT is the preferred route

# Summary of published SLIT data
# (~~2~~ 4 other important papers I'll review in a bit)

| Study (year) | Allergen | Total N (active + placebo) | Target Maintenace Dose) | Duration | Primary End Point | Results |
|---|---|---|---|---|---|---|
| Enrique (2005) | Hazelnut | 23 | 13 mg | 12 weeks | Increase reaction threshold | 2.29 g > 11.5 g (5-fold increase) |
| | | | | | | 3.49 g > 4.14 g (no change) |
| Keet *(2012) | Milk | 30 | 7 mg SLIT | 60 weeks | 8 gram challenge | SLIT 7 mg 10% |
| (OIT vs. SLIT) | | | 1000 mg OIT, 2000 mg OIT | | | OIT 1000 mg 60% |
| | | | | | | OIT 2000 mg 80% |
| Fleischer (2013) | Peanut | 40 | 4 mg | 44 weeks | **5 gram PN challenge or** | **70% active** |
| | | | | | **10X baseline increase** | **15% placebo** |
| Narisety (2015) | Peanut | 21 (no placebo) | 3.7 mg SLIT | 12 months | **Increase reaction threshold** | **21 mg>496 mg PP (24x fold increase)** |
| (OIT vs. SLIT) | | | 2000 mg OIT | | | 21 mg>7246 mg PP (345x fold increase) |
| Kim (2011) | Peanut | 18 | 2 mg | 12 months | **Increase reaction threshold** | **1710 mg median SCD PN SLIT** |
| | | | | | | **85 mg median SCD placebo** |
| Kim (2019) | Peanut | 48 (no placebo) | 2 mg | 3-5 years | **750 mg PN challenge** | **67%** |
| | | | | | **5 gram PN challenge** | **25%** |
| Kim (2023) | Peanut | 47 (no placebo) | 4 mg | 48 months | **Increase in SCD** | **48.4 mg>2723 mg PP** |
| | | | | | "Successfully Consumed Dose" | **70% achieved 800 mg SCD** |
| | | | | | | **36% achieved 5000 mg SCD** |



- Increasing clinical threshold to 300 mg peanut protein estimated to provide greater than 95% risk reduction

- A clinical threshold of 1,000 mg peanut protein increased risk reduction to 99%

| Part D. Ice Cream | | Threshold Dose - Post Immunotherapy Treatment (mg of peanut protein) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 1 | 3 | 10 | 30 | 100 | 300 | 1000 |
| Baseline Threshold Dose (mg of peanut protein) | 1 | 0% | 22.7% | 46.8% | 68.7% | 90.4% | 99.5% | 99.9% |
| | 3 | | 0% | 31.1% | 59.5% | 87.6% | 99.4% | 99.9% |
| | 10 | | | 0% | 41.2% | 82.0% | 99.1% | 99.9% |
| | 30 | | | | 0% | 69.5% | 98.5% | 99.9% |
| | 100 | | | | | 0% | 94.9% | 99.9% |
| | 300 | | | | | | 0% | 98.6% |
| | 1000 | | | | | | | 0% |

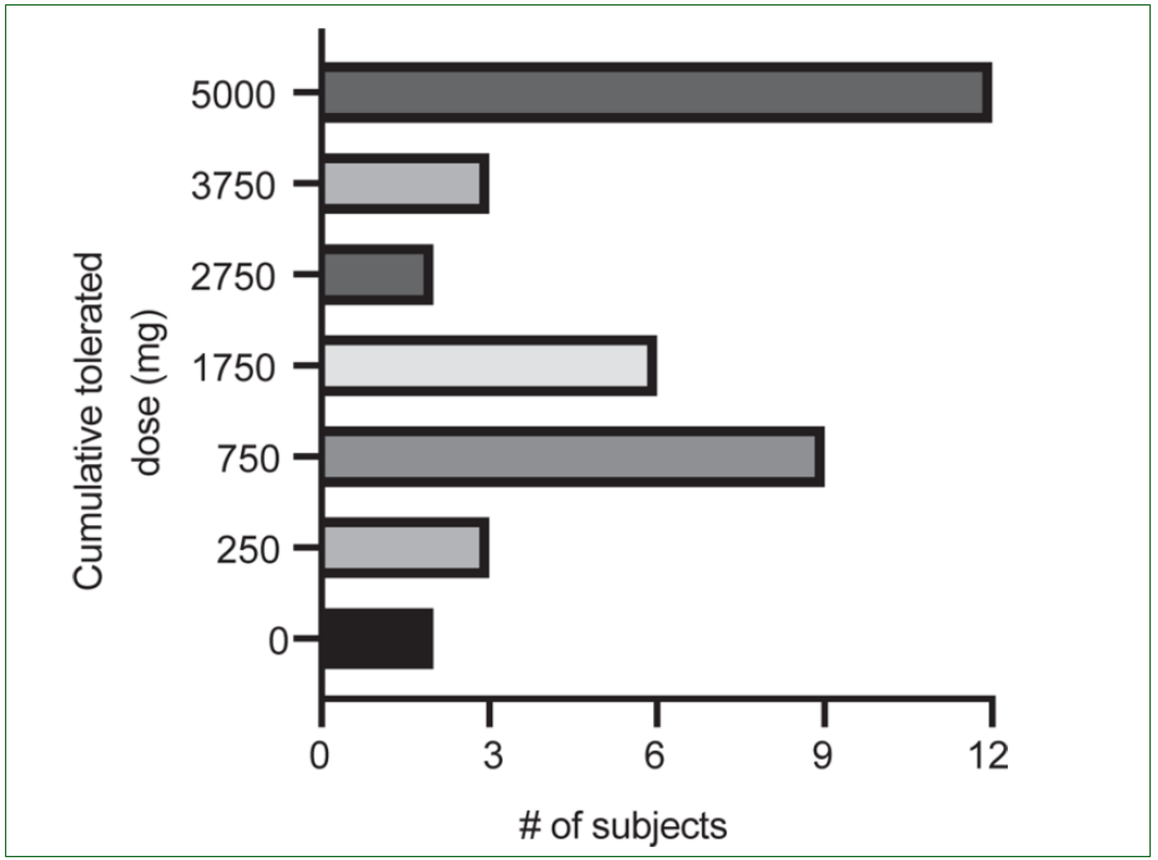
Risk Reduction Scale

Highest Risk → Lowest Risk

Baumert JL et al. 2018

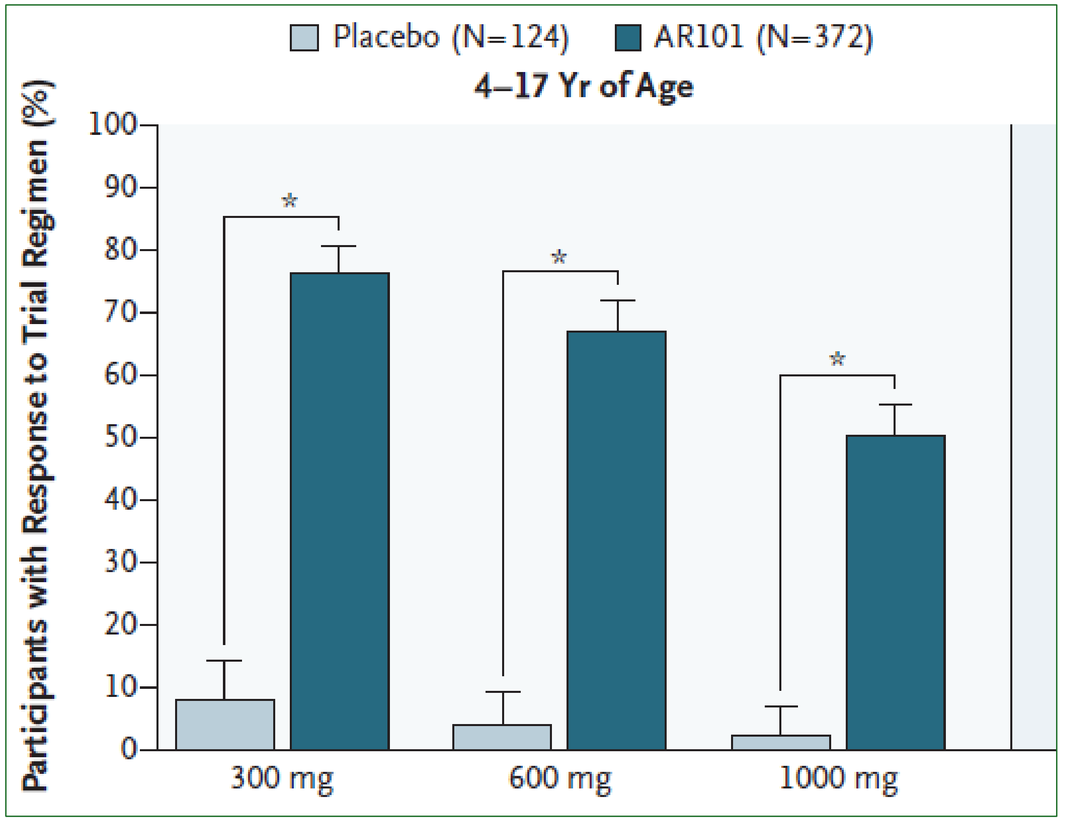
# Clinically Meaningful Desensitization

*Kim EH 2019: 2 mg peanut protein/day*



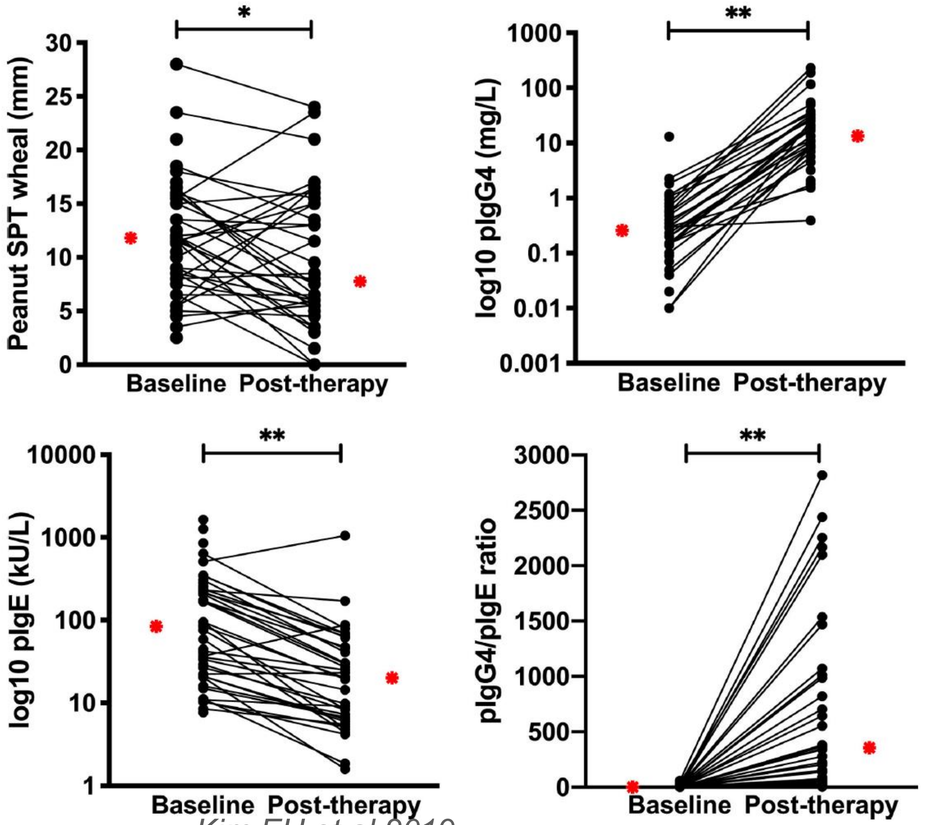

**67% tolerated at least 750 mg (3-5 years)**

*PALISADE NEJM 2018: 300 mg peanut protein/day*

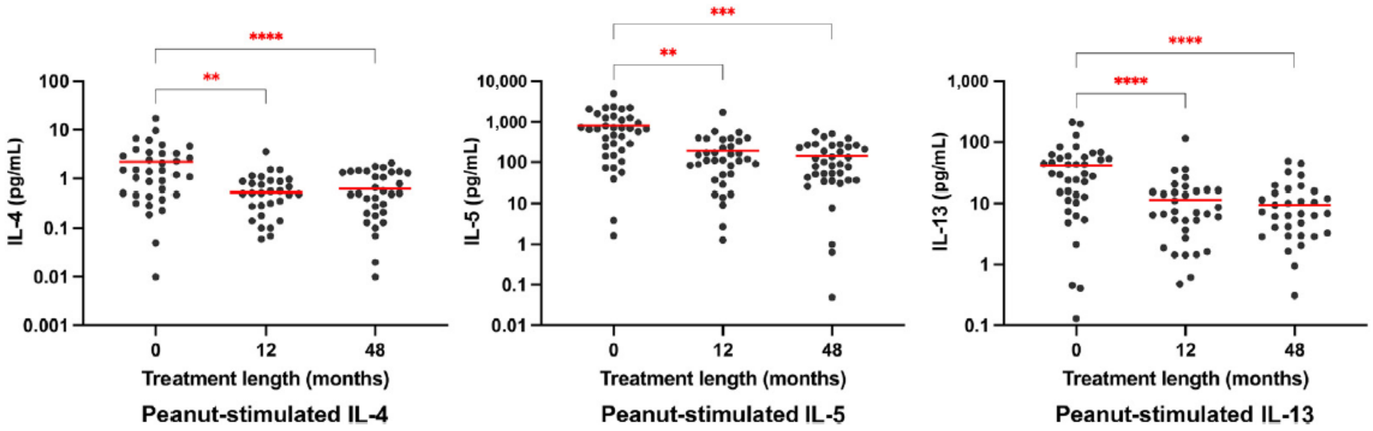



**67.2% tolerate 1043 mg (12 months)**

# Alterations in both humoral and cell-mediated responses on SLIT



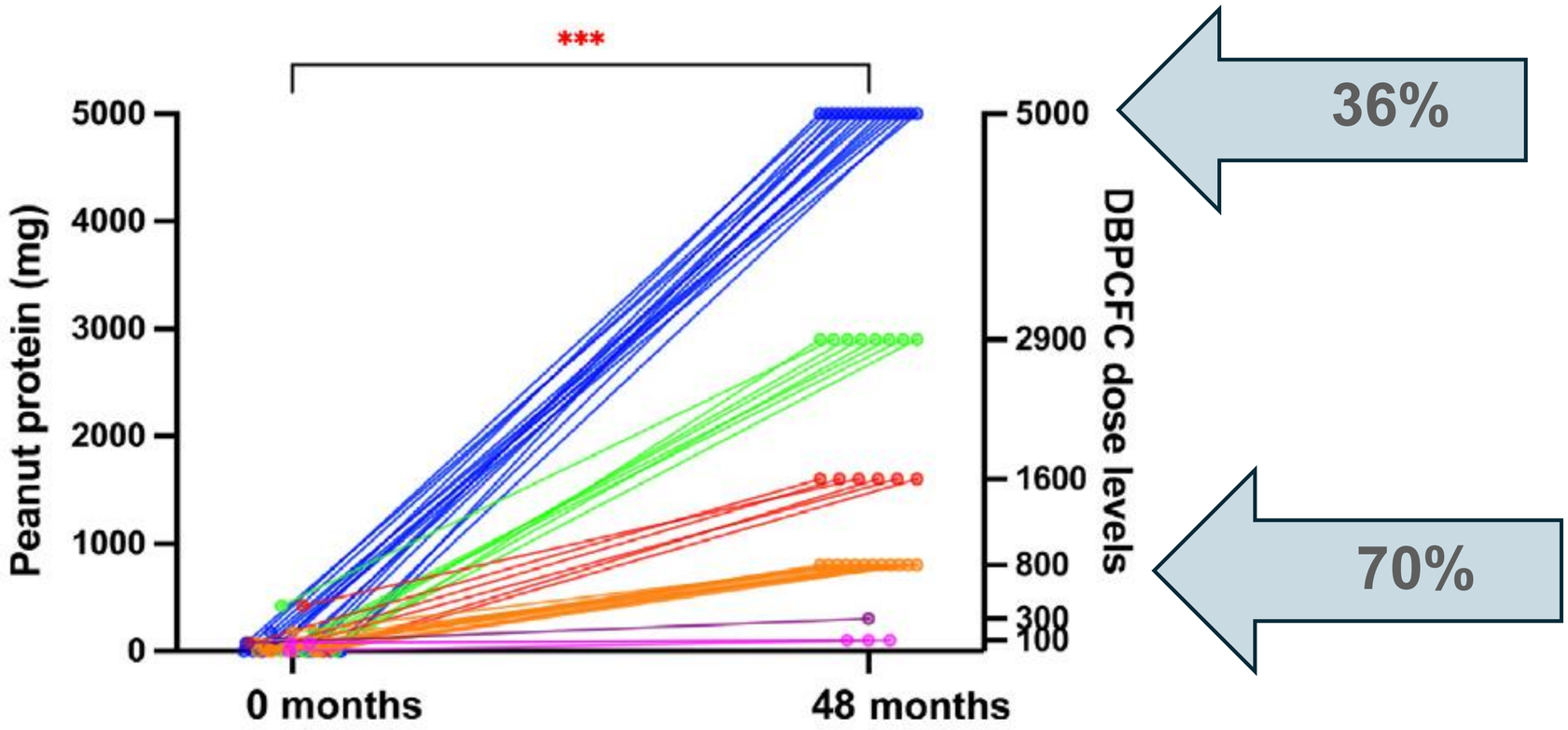

*Kim EH et al 2019*




*Kim EH et al 2023*

# 4 mg/day peanut Maintenance Dosing

**Mean baseline PN sIgE 212.3 kU/L, median 84.3 kU/L**




*Kim EH 2023*

# 48-month open label Safety data

- 81,301 dosing days (97.6% taken)
  - Median rate of reaction per person per dose is 0.49%
  - Side effects reported with about 4% of total doses delivered
  - Of those, 90% were oral itching
  - No ETRs!

| Dosing | Peanut SLIT (n = 54) |
|---|---|
| Total dosing days | 81,031 |
| Missed doses | 2,019 (2.49) |
| Total doses taken | 79,012 (97.51) |
| Dosing symptoms, n (% doses taken) | 3,203 (4.05) |
| Local | |
| Oropharyngeal pruritus | 2,841 (3.60) |
| Lip swelling | 50 (0.06) |
| Skin | 113 (0.14) |
| Upper respiratory tract | 7 (0.01) |
| Lower respiratory tract | 28 (0.03) |
| Abdominal | |
| Belly pain | 89 (0.11) |
| Vomiting | 18 (0.02) |
| Diarrhea | 5 (0.01) |
| Treatment administered, n (% doses taken) | |
| Antihistamine | 143 (0.18) |
| Epinephrine | 0 |

*Kim EH 2023*

# Summary of Peanut SLIT data (Kim et al)

- In a very highly peanut allergic population (mean peanut IgE > 200, median 84), SLIT was very successful and safe.
- Majority (70%) tolerated at least 800 mg PP at 4 years
- A non-trivial minority (36%) actually were completely desensitized (tolerated 5000 mg PP)
- Safety profile extremely reassuring:
  - < 4% of doses elicited any reaction and of those, 90% were minimal oral symptoms
  - No epinephrine usage at all across 4 years of the study
  - No EoE was observed
- Broad modulation of both humoral and cell-mediated responses on SLIT

# SLIT to OIT bridge

Original Article

## 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*

- Canadian allergists are quite progressive
- They also appear to really like Las Vegas! (NAPAAC attendance)

# OIT to SLIT bridge

- 188 pts, ages 4 - 18
- Specifically chose “high-risk” patients relative to OIT:
  - Moderate/severe reaction history
  - Specific IgE > 50
- Very large variety of foods (PN, TNs, sesame, CM, egg, soy, legumes, wheat, fish, SF)
- Aggressive build protocol (either 3 or 5 steps total)
- Target 2 mg protein each allergen

# OIT to SLIT bridge, results

- 70% of patients tolerated 300 mg protein challenge at 2 years, who were all converted to 300 mg OIT
- A further 18% did not tolerated 300 mg challenge, but were rescued with low-dose OIT (starting at 80 mg and completed “self-escalation” at home to 300 mg maintenance)
- Thus, this translates to an overall success rate of 88% (in terms of bypassing OIT build)
- The remaining 12% of patients reacted <80 mg on challenge and were advised to continue SLIT for 1-2 additional years before re-challenging at 300 mg

# OIT to SLIT bridge, safety

- Did report ETRs (4 total, 2.1% of patients) during build
- No ETRs during maintenance SLIT
- ***Much*** more aggressive protocol than Kim:
  - (0.1 mg, 0.3 mg), 0.5 mg, 1 mg, 2 mg  -> just 3 total steps!

A 3-dose buildup protocol was selected for most of the patients, whereas a 5-dose buildup protocol was created for those with particularly severe features such as a history of grade 4 reaction, epinephrine intravenous infusion, intensive care unit admission, and/or OFC threshold of less than 1 mg protein.

- q4 week escalation, so most patients at maintenance in literally 2 months
- For reference, this is about 3 months faster and starts about 200 times higher than Kim SLIT peanut build (500 ug vs. 2.5 ug)

# Real food SLIT: Windom experience

- 50 patients in 2 cohorts
- Median age 11, but included adults
- Cohort 1:
  - Started at 1:1000 (7 dosing visits)
- Cohort 2:
  - Started at 1:100 (4 dosing visits)
- Solutions prepared in 50% glycerin (either diluting milk, egg white liquid, or tree nut milks) or from peanut, sesame, wheat flours, ranging 4-11 mg final dosing
- Also addressed whether exercise restriction is necessary and stability of extracts at RT vs. refrigeration as well as freezing of whole foods

# Real food dosing

**TABLE I.** Food sources with protein content and maintenance, or top, dose features

| Food | Source | Protein content | Top dose (mL) | Top dose (mg protein) |
|---|---|---|---|---|
| Peanut | Light roasted 12% fat (Byrd Mill),* flour solution, 40 mg/mL | 50% | 0.3 | 6 |
| Egg | Egg white liquid (Egglands) | 111 mg/mL | 0.1 | 11 |
| Milk | Whole or 2% milk | 33.3 mg/mL | 0.3 | 10 |
| Cashew | Cashew milk (Elmhurst) | 16.7 mg/mL | 0.3 | 5 |
| Walnut | Walnut milk (Elmhurst) | 12.5 mg/mL | 0.3 | 3.8 |
| Hazelnut | Hazelnut milk (Pacific) | 8.3 mg/mL | 0.5 | 4.2 |
| Wheat | Vital wheat gluten, flour solution, 30 mg/mL | 77% | 0.3 | 6.9 |
| Sesame | organic sesame (Kevala), flour solution, 35 mg/mL | 50% | 0.3 | 5.3 |
| Sunflower seed | Sunflower milk (Lattini) | 8.3 mg/mL | 0.5 | 4.2 |

*Byrd Mill not currently offering peanut flour.

Target dosing: 4 - 11 mg protein

Windom, 2024

# Real food dosing schedules

**TABLE II.** SLIT dosing schedules for cohorts 1 and 2

| | Cohort 1 | | Cohort 2 | |
|---|---|---|---|---|
| **Visit** | **Dilution** | **Doses (mL)** | **Dilution** | **Doses (mL)** |
| Day 1 | 1:1000 | 0.05, 0.1, 0.2 | 1:100 | 0.1, 0.2, 0.3 |
| Updose 1 | 1:100 | 0.05, 0.1, 0.2 | 1:10 | 0.1, 0.2, 0.3 |
| Updose 2 | 1:10 | 0.05, 0.1 | 1:1 | 0.05, 0.1 |
| Updose 3 | 1:10 | 0.15, 0.25 | 1:1 | 0.1, 0.3 |
| Updose 4 | 1:1 | 0.05, 0.05 | | |
| Updose 5 | 1:1 | 0.05, 0.1 | | |
| Updose 6 | 1:1 | 0.1, 0.2 (weekly increase 0.25, 0.3 at home) | | |

Serial doses at each visit administered 20 min apart.
Exceptions to this schedule: egg white liquid—due to high protein content there are 2 visits at 1:10 and a single 1:1 visit of 0.05 and 0.1 in cohort 2 and for cohort 1, the updose 5 was last visit; hazelnut and sunflower milk—due to lower protein content, top dose is 0.5 mL.

- Only 4-7 office visits
- Minimum 1 week at each dose
- Median time to maintenance: 14 weeks cohort 1; 7 weeks cohort 2

Windom, 2024

# Questions answered by Windom study

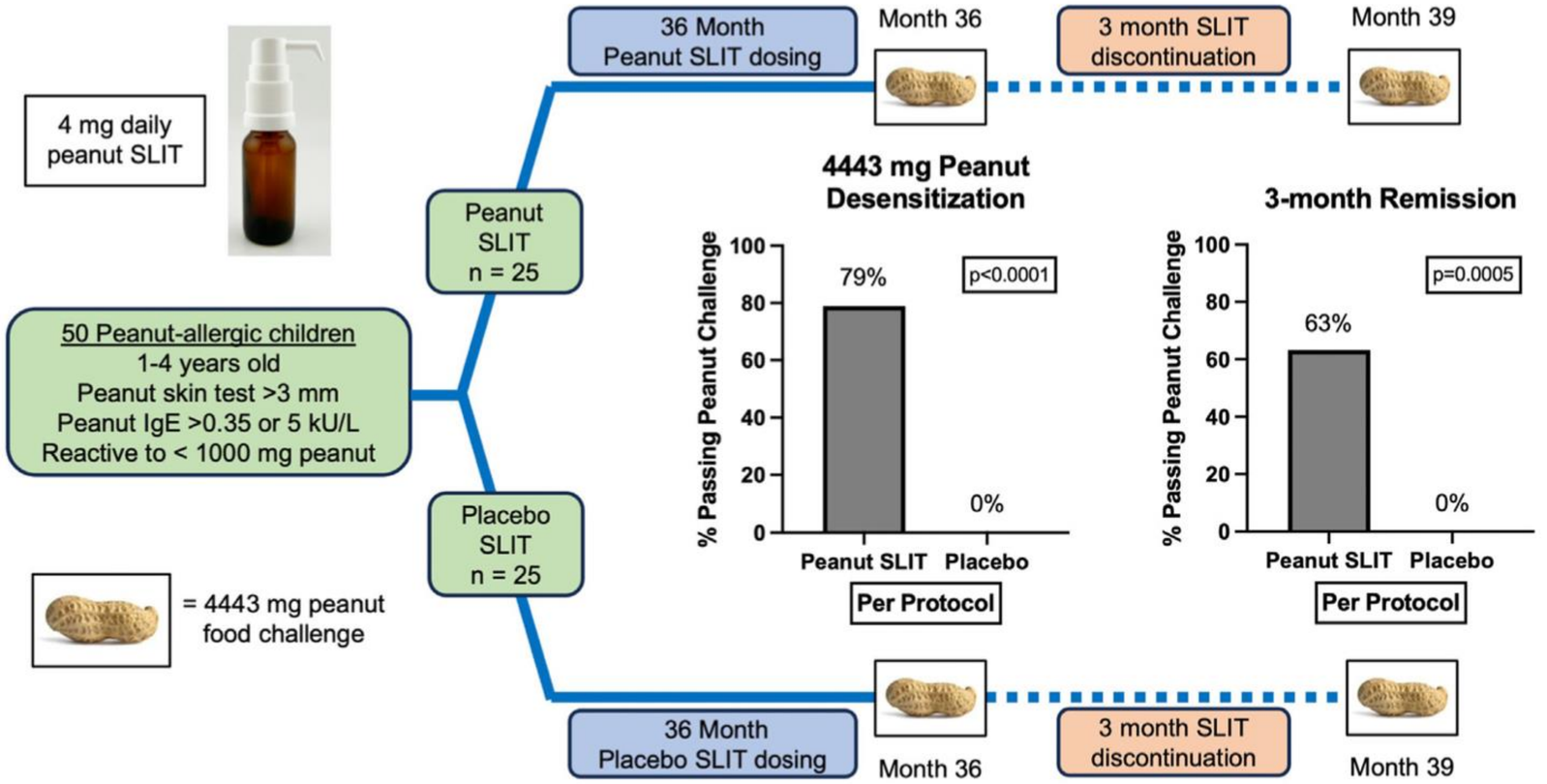
- No differences in skin test responses to fresh peanut solution in 50% glycerin, RT x 3 months, or refrigerated x 6 months
- No differences in skin test response between fresh foods (tree nut milk, egg white liquids) between fresh and frozen x 1 month
- Post-dose exercise challenge performed in 12 patients, no evidence of exercise-augmented reaction
- Similar to Kim 2023, no treatment-related ETRs

# Protocol comparisons

| | Starting dose | Maintenance dose | Time to achieve maintenance | Epi-needing reactions |
|---|---|---|---|---|
| Kim 2023 | 2.5 ug | 4 mg | 5 months | No |
| Chan 2024 | 500 ug | 2 mg | 2 months | Yes |
| Windom 2024 (cohort 1) | 1 ug | 6 mg | 3.5 months | No |
| Windom 2024 (cohort 2) | 20 ug | 6 mg | 2 months | No |

- Relatively similar study populations
- Perhaps Kim protocol excessively conservation
- Chan maybe too aggressive?
- Windom in the sweet spot?

# Early SLIT?




- Markedly less sensitized than in prior cohort (median PN-sp IgE 4.3 vs. 84.3 in earlier cohort (ages 1-11)
- Much of this likely reflects natural history of disease (usually less sensitized at early age)
- Early intervention advantage: trend towards greater remission in 1-2 yo vs. 2-3 or 3-4 yo groups

Kim, 2024

# BAT as early monitoring for food SLIT?

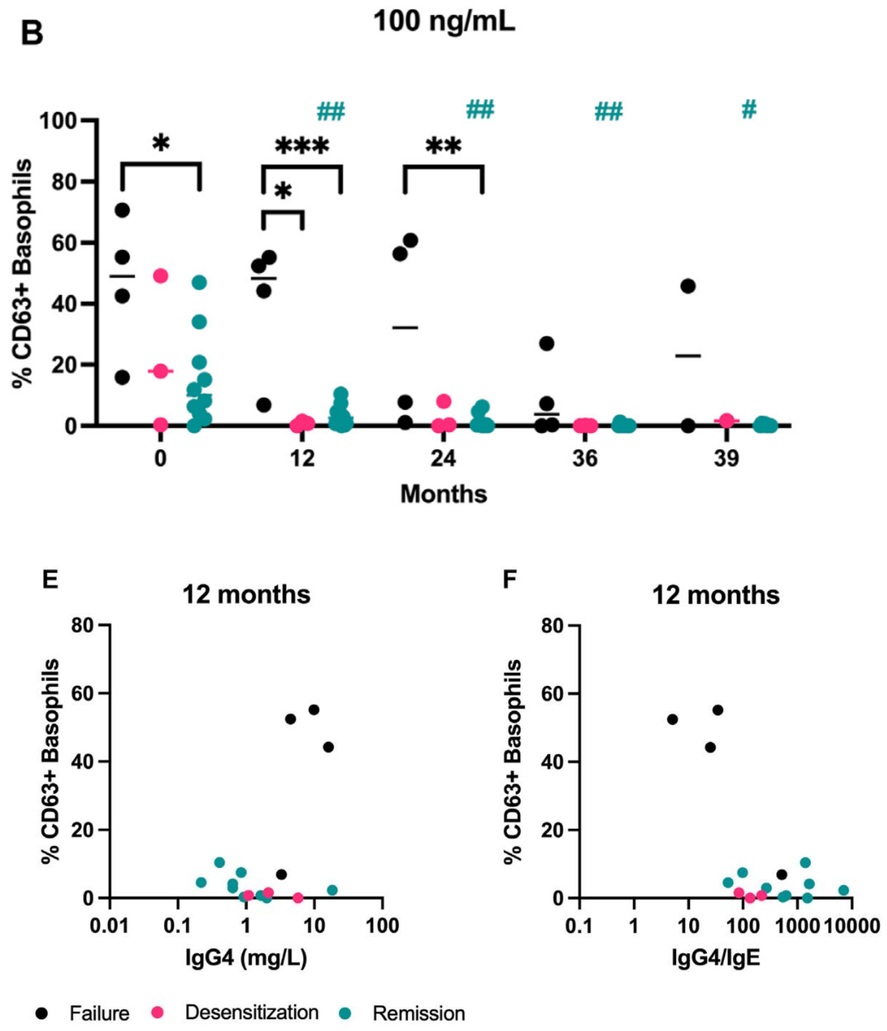
Brief report

## Baseline basophil activation and early suppression is associated with clinical outcome after peanut sublingual immunotherapy

Jessica R. Humphrey, MS,[a,b] Rishu Guo, PhD,[a] Xiaohong Yue, MS,[a] Corinne A. Keet, MD, PhD,[a] Yamini V. Virkud, MD, MPH,[a] J. Andrew Bird, MD,[c] A. Wesley Burks, MD,[a] Edwin H. Kim, MD, MS,[a] Johanna M. Smeekens, PhD,[a,b]* and Michael D. Kulis, PhD[a]* *Chapel Hill, NC, and Dallas, Tex*

In press, JACI 2025

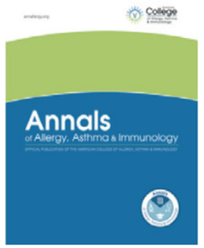
# BAT for SLIT monitoring




- <u>Lower basophil activation at baseline and suppression at 12 months may be a key predictor of SLIT success</u>
- sp IgG4 alone is not a great predictor (can still make plenty of IgG4 and not get basophil suppression)
- sp IgG4/IgE ratio does seem to correlate with reduced BAT activation

# Real-world “grocery store” SLIT

Contents lists available at ScienceDirect




## The use of grocery-sourced real-food solutions in sublingual immunotherapy for food allergies

Brock A. Williams, PhD[*,†]; Ally Baaske, BSc[*]; Lianne Soller, PhD[*]; Stephanie C. Erdle, MD[*,†]; Tiffany Wong, MD[*,†]; Raymond Mak, MD[*,†]; Nikhila D. Schroeder, MD[‡]; Edmond S. Chan, MD[*,†]

[*] *Division of Allergy, Department of Pediatrics, Faculty of Medicine, The University of British Columbia, Vancouver, British Columbia, Canada*
[†] *BC Children’s Hospital Research Institute, Vancouver, British Columbia, Canada*
[‡] *Allergenuity Health, Huntersville, North Carolina*

Annals 2025

# Real-world “grocery store” SLIT results

- 305 active food SLIT pts
- 99% satisfaction rate
- 82% consistently taking dose
- 70% passed low-dose (300 mg) challenge at 1-2 years
- Maintenance dose 2-4 mg protein

# Sample protocol “Grocery Store”

**Table 1**
Sample Sublingual Immunotherapy 5-Dose Protocols and Recipes for Build-Up of Real-Food Powder-Based and Liquid-Based Allergens (Peanut, Cow’s Milk, Cashew, Egg, and Sesame) to a 2- to 4-mg Maintenance Dose[a,b]

| Sample protocol: peanut (powder) | | | | | |
|---|---|---|---|---|---|
| Dose number[c] | Protein (mg) | Peanut powder for mixture* (g) | Water for mixture* (mL) | Daily volume (mL) | Interval |
| 2 mg maintenance dose | | | | | |
| 1 (Optional) | 0.1 | 0.2 | 80 | 0.1 | 4 wk |
| 2 (Optional) | 0.3 | 0.2 | 26 | 0.1 | 4 wk |
| 3 | 0.5 | 0.2 | 16 | 0.1 | 4 wk |
| 4 | 1 | 0.2 | 8 | 0.1 | 4 wk |
| 5 | 2 | 0.2 | 4 | 0.1 | Continue daily long term |
| 4 mg maintenance dose | | | | | |
| 1 (Optional) | 0.3 | 0.2 | 26 | 0.1 | 4 wk |
| 2 (Optional) | 0.5 | 0.2 | 16 | 0.1 | 4 wk |
| 3 | 1 | 0.2 | 8 | 0.1 | 4 wk |
| 4 | 2 | 0.2 | 4 | 0.1 | 4 wk |
| 5 | 4 | 0.2 | 4 | 0.2 | Continue daily long term |

*Make fresh mixture daily for powder-based mixtures. Mix well before giving. Calculations based on a powdered peanut butter with 6 g of protein per 15-g serving (eg, similar to PB&Me Original Powdered Peanut Butter; note that variations exist in protein and/or serving size by product).

# Extract-based vs. real food SLIT

- Extract-based:
  - Temperatures stability
  - Very long shelf life - Expiry at least 1 year for Greer extracts
  - Ease of use
  - Cost an issue
  - Greer can mix these for you (for a price)

- Real food SLIT:
  - Much cheaper
  - More customizable (could go to higher concentration more easily)
  - Can make glycerinated dilutions, which gets around shelf-life
  - Can freeze whole food liquids with no apparent degradation
  - Need to have mixing capacity in-house

# Peanut vs. other allergens

| Type of food treated, n (%) | |
|---|---|
| Peanut | 149 (79.3) |
| Cashew/pistachio | 97 (51.6) |
| Walnut/pecan | 73 (38.8) |
| Hazelnut | 59 (31.4) |
| Almond | 24 (12.8) |
| Sesame | 15 (8.00) |
| Egg | 15 (8.00) |
| Cow's milk | 10 (5.32) |
| Soy | 10 (5.32) |
| Pea | 8 (4.26) |
| Chickpea | 7 (3.72) |
| Lentil | 7 (3.72) |
| Salmon/cod | 6 (3.19) |
| Wheat | 5 (2.66) |
| Pine nut | 4 (2.13) |
| Shrimp | 4 (2.13) |

best studied

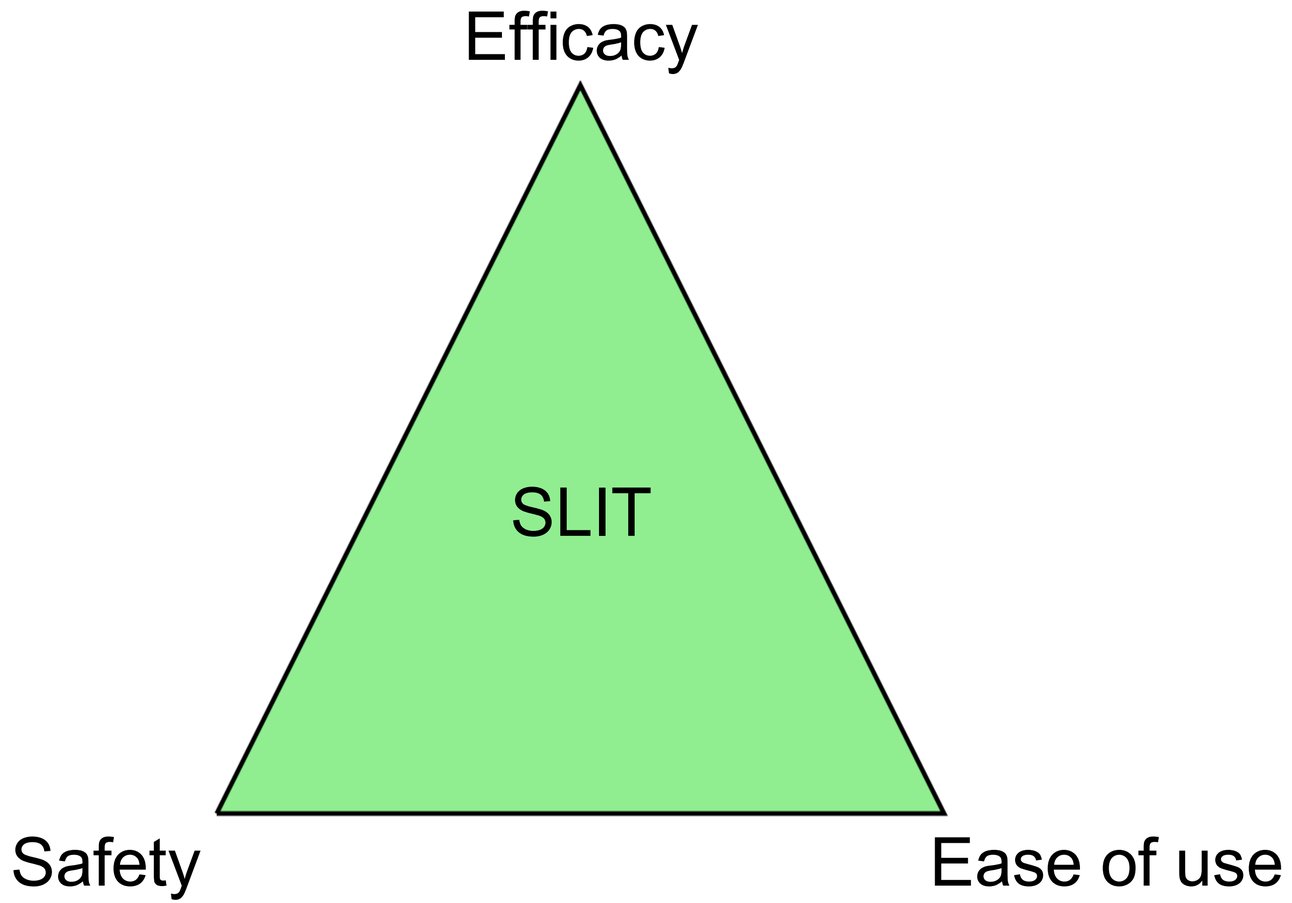
cy at 2 mg maintenance dosing for a very wide
hallenge at 1 year)

Chan, 2024

# Single vs. multi-allergen SLIT

- To date, only 2 studies with multi-allergen SLIT studied (Chan and Windom)
- Neither noted increase in safety signals with multiple allergens vs. single
- Of note, both dosed allergens individually, with no waiting period between dosing (beyond 1-2 min SLIT absorption time)
- Allergens could be mixed together but may be hard to achieve adequate concentration due to dilution effects
- No EoE was observed, even with multi-allergen.  (Chan included known EoE patients and no EoE flares were noted).

# SLIT in the sweet spot



# Take-home nuggies for SLIT

- SLIT has an extremely favorable safety profile, with almost no serious reactions observed
- SLIT has shown clear efficacy for peanut and other allergens
- Time to desensitization guideposts:
  - 2 year: 300 mg for most
  - 4 years: 800 mg for most (a minority may tolerate full serving at this time)
- Unlike OIT, no onerous dosing restrictions (particularly exercise)
- Can consider even in infants/toddlers
- SLIT is ideal for higher-risk patients (asthma, highly sensitized)
- Real-food SLIT is approachable if you can mix in-house; extract-based easy but expensive
- ~~No perfect biomarker, but sp IgG4 may be worth tracking~~ BAT (CD63) +/- sp IgG4/IgE ratio may be worth tracking
- If possible, annual challenges would be ideal (consider sub-threshold challenges)

# We don’t do enough challenges…

| OFC performed in practice (per month), total number | Percent reporting (513 answered) |
|---|---|
| 0 | 5.46% (28) |
| 1-5 | 58.09% (298) |
| 6-10 | 19.30% (99) |
| 11-15 | 7.21% (37) |
| 16-20 | 9.94% (51) |

*OFC*, Oral food challenge.

Greiwe et al, AAAAI Work Group Report: Trends in Oral Food Challenge Practices Among Allergists in the United States, 2020

# References


- Bajowala SS. Sublingual immunotherapy as an option for effective food allergy treatment. J Food Allergy. 2022;4:106-111
- Schworer SA, Kim EH. Sublingual immunotherapy for food allergy and its future directions. Immunotherapy. 2020;12:921-931.
- Baumert JL et al. Quantitative assessment of the safety benefits associated with increasing clinical peanut thresholds through immunotherapy. J Allergy Clin Immunol Pract. 2018;6:457-65.
- Kim EH et al. Long-term sublingual immunotherapy for peanut allergy in children: clinical and immunologic evidence of desensitization. J Allergy Clin Immunol. 2019;144(5):1320-1326.
- Vickery BP et al. AR101 Oral Immunotherapy for peanut allergy. N Engl J Med 2018; 379:1991-2001.
- Narisety et al. A randomized, double-blind, placebo-controlled pilot study of sublingual versus oral immunotherapy for the treatment of peanut allergy. J Allergy Clin Immunol. 2015;135:1275-82.
- Kim EH et al. Open-label study of the efficacy, safety, and durability of peanut sublingual immunotherapy in peanut-allergic children.  J Aller Clin Immunol 2023; 151:1558-65
- Burks AW et al. Sublingual immunotherapy for peanut allergy: long-term follow up of a randomized multicenter trial. J Allergy Clin Immunol. 2015;135:1240-8.
- Soller, L., Williams, B. A., Mak, R., Wong, T., Erdle, S. C., Chomyn, A., Tetreault, B., Morrison, K., Gaudet, L., & Chan, E. S. (2024). Safety and Effectiveness of bypassing oral immunotherapy buildup with an initial phase of sublingual immunotherapy for higher-risk food allergy. *Journal of Allergy and Clinical Immunology. In Practice*
- Kim, E. H., Bird, J. A., Keet, C. A., Virkud, Y. V., Herlihy, L., Ye, P., Smeekens, J. M., Guo, R., Yue, X., Penumarti, A., Qaqish, B., Li, Q., Kulis, M. D., & Burks, A. W. (2024). Desensitization and remission after peanut sublingual immunotherapy in 1- to 4-year-old peanut-allergic children: A randomized, placebo-controlled trial. *the Journal of Allergy and Clinical Immunology*
- Windom, R. R., Seitz, S., Ly, J. B., Dunn, N., Fergeson, J., & Windom, H. H. (2024). Food Sublingual immunotherapy: Safety and simplicity of a real food updosing protocol. *Journal of Allergy and Clinical Immunology. In Practice*
- Humphrey, J. R., Guo, R., Yue, X., Keet, C. A., Virkud, Y. V., Bird, J. A., Burks, A. W., Kim, E. H., Smeekens, J. M., & Kulis, M. D. (2025). Baseline basophil activation and early suppression is associated with clinical outcome after peanut sublingual immunotherapy. Journal of Allergy and Clinical Immunology. https://doi.org/10.1016/j.jaci.2025.04.010
- Williams, B. A., Baaske, A., Soller, L., Erdle, S. C., Wong, T., Mak, R., Schroeder, N. D., & Chan, E. S. (2025). The use of grocery-sourced real-food solutions in sublingual immunotherapy for food allergies. Annals of Allergy, Asthma & Immunology. https://doi.org/10.1016/j.anai.2025.03.001

# SLIT is amazing!!

Juliette Fitzhugh, astonished by the power of food SLIT!!