

Supplemental Tables:

Table E1: Characteristics of Subjects requiring Repeat Almond Challenges

Subject	Almond SPT (mm) / IgE (kU/L)	Challenge 1 Outcome/Sx	Challenge 2 Outcome/Sx	Challenge 3 Outcome/Sx	Time Interval
1	SPT 6, IgE 29.2	Fail (oral itch, nasal symptoms, hives)	Pass	-	2.7 y
2	SPT 5, IgE 34.50 SPT 5, IgE 23.20	Fail (severe generalized pruritus, irritability)	Pass		4 y
3	SPT 5, IgE 8.74 SPT 10, IgE 1.13	Fail (throat itch, lip pruritus)	Pass		3.2 y
4	SPT 7, IgE 0.72 SPT 0, IgE 0.34	Fail (pruritus and flushing)	Pass		3.7 y
5	SPT 2, IgE 0.88 SPT 3, IgE 0.50	Fail (diffuse wheezing, later attributed to uncontrolled asthma)	Pass		0.4 y
6	SPT 5, IgE 0.90	Indeterminate (gagged and refused)	Pass		0.8 y
7	SPT 4, IgE 1.14 SPT 4, IgE 2.89	Pass (did not reintroduce due to intense abdominal pain hours later)	Pass		4.2 y
8	SPT 5, IgE 0.34	Pass (had eye swelling hours after challenge)	Pass		0.3 y
9	SPT 5, IgE 0.42 SPT 14, IgE 43.3	Pass (had difficulty with home introduction)	Fail (oral itch, 10-12 hives, abdominal pain)		2 y
10	SPT 0, IgE 0.34 SPT 0, IgE 0.34 SPT 4, IgE 0.43	Fail (few hives)	Indeterminate (fever, 1 hive)	Pass	3.7 y 0.4 y
11	SPT 5, IgE 0.34 SPT 0, IgE 0.44 SPT 10, IgE 0.54	Fail (several hives)	Indeterminate (1 hive)	Pass	1.2 y 3.3 y

Table E2. Sensitivity Analysis of Sensitized participants (n=475): Allergic Clinical Characteristics associated with IgE-mediated reaction. OR for specific IgE represent the increased odds for every 10 kU/L change in IgE. OR for SPT represent the increased odds for every 5 mm change in wheal.

	Unadj. OR [95% CI]	p
<u>Demographics</u>		
Age at challenge in years, mean (sd)	0.86 [0.77, 0.96]	0.009
<u>Almond History</u>		
Almond-specific IgE, mean (sd)	1.45 [1.18, 1.8]	<0.001
Almond SPT in mm, mean (sd)	2.48 [1.48, 4.15]	<0.001
<u>Allergic Sensitization</u>		
Peanut IgE, mean (sd)	1.13 [1.02, 1.26]	0.02
Pistachio IgE, mean (sd)	1.13 [0.97, 1.32]	0.12
Pecan IgE, mean (sd)	1.19 [0.96, 1.47]	0.12
Walnut IgE, mean (sd)	1.13 [0.99, 1.29]	0.08

Table E3: Specificity and Sensitivity of Almond-specific IgE (left) and Almond SPT (right) for IgE-mediated reactions. Positive predictive values (PPV), Negative Predictive values (NPV), Likelihood Ratios – positive (LR+), Likelihood Ratios – negative (LR-)

Outcome	Test	Value	Sensitivity	Specificity	PPV	NPV	LR+	LR-
Challenge Outcome	Almond SPT	7	1	0	0.05	1	1	0
		8	0.21	0.88	0.09	0.95	1.77	0.9
		9	0.21	0.94	0.17	0.95	3.61	0.84
		10	0.14	0.98	0.27	0.95	6.34	0.88
		11	0.14	0.99	0.36	0.95	9.97	0.87
		12	0.1	0.99	0.33	0.95	8.72	0.91
		14	0.07	0.99	0.29	0.95	6.98	0.94
		16	0.07	0.99	0.4	0.95	11.63	0.94
Grade 2/3 Reaction	Almond SPT	4	1	0	0.04	1	1	0
		6	0.25	0.84	0.06	0.97	1.53	0.9
		7	0.25	0.94	0.14	0.97	4.29	0.8
		8	0.2	0.97	0.21	0.97	6.87	0.82
		9	0.15	0.98	0.21	0.97	7.02	0.87
		10	0.15	0.99	0.3	0.97	11.04	0.86
		12	0.15	0.99	0.38	0.97	15.45	0.86
		13	0.1	0.99	0.33	0.97	12.87	0.91
Challenge Outcome	Almond IgE	0	1	0	0.05	1	1	0
		1	0.69	0.54	0.08	0.97	1.5	0.58
		2.25	0.31	0.71	0.06	0.95	1.08	0.97
		10	0.21	0.93	0.15	0.95	2.99	0.85
Grade 2/3 Reaction	Almond IgE	0.25	1	0	0.04	1	1	0
		1.25	0.8	0.56	0.07	0.99	1.8	0.36
		2	0.4	0.68	0.05	0.97	1.25	0.88
		10	0.25	0.93	0.12	0.97	3.39	0.81
		15	0.25	0.97	0.23	0.97	7.57	0.78

Table E4: Details of failed challenge reactions and characterization: Niggemann-Beyer reaction severity: Grade 1 (redness, swelling (not angioedema), or pruritus); Grade 2 (urticaria, angioedema, generalized flushing, abdominal pain, vomiting, or diarrhea); Grade 3 (cough, wheezing, stridor, tachycardia, decreased blood pressure, respiratory distress, shock, cardiac arrest). *patient had transient wheeze and nasal congestion at baseline, then during the challenge had worsening wheeze and sneezed three times. Supervising clinician attributed symptoms to asthma exacerbation. **patient had nasal congestion during challenge but during home introduction with exercise the next day, developed urticaria.

	N-B reaction severity	Sampson 2006	Symptoms reported	Treatment given
1	Grade 2	no	pruritus, urticaria	antihistamines
2	Grade 1	no	throat pruritus	antihistamines
3	Grade 1	no	oral pruritus	antihistamines
4	Grade 2	no	nasal congestion, urticaria (with exercise)**	none
5	Grade 1	no	oral sensitivity	antihistamines
6	Grade 1	no	oral itch, facial redness, non urticarial rash	none
7	Grade 2	no	urticaria, pruritus	none
8	Grade 1	no	oral pruritus, facial redness	antihistamines
9	Grade 1	no	facial redness, pruritus, nasal congestion	antihistamines
10	Grade 2	no	oral discomfort, urticaria	antihistamines
11	Grade 3	Anaphylaxis	pruritus, flushing, urticaria, abdominal pain, vomiting, sneezing	antihistamines, epinephrine, steroids, H2 blocker
12	Grade 3	Anaphylaxis *	wheezing*, sneezing x 3	antihistamines, albuterol
13	Grade 1	no	palmar pruritus	antihistamines
14	Grade 2	no	urticaria, sneezing, nasal congestion	none
15	Grade 2	no	urticaria, nasal congestion	antihistamines
16	Grade 2	no	oral pruritus, urticaria, mild abdominal pain	antihistamines
17	Grade 1	no	sneezing and nasal congestion	antihistamines
18	Grade 2	no	pruritus, urticaria	none
19	Grade 1	no	taste aversion, refused to consume	none
20	Grade 2	no	urticaria	antihistamines
21	Grade 2	no	urticaria, non-urticarial rash	antihistamines
22	Grade 2	no	vomiting, sneeze x 1	none
23	Grade 2	no	sneezing, congestion, throat pruritus, throat clearing	none
24	Grade 2	no	pruritus, urticaria	antihistamines
25	Grade 2	no	pruritus, urticaria	antihistamines
26	Grade 3	Anaphylaxis	nasal congestion, wheezing, urticaria	antihistamines, epinephrine,

				steroids, H2 blocker
27	Grade 2	no	urticaria, local flushing, mild lip angioedema, nasal congestion	antihistamines
28	Grade 2	no	oral itch, ear angioedema, local flushing, nasal congestion, mild abdominal pain	antihistamines
29	Grade 2	no	oral itch, vomiting	antihistamines, H2 blocker
30	Grade 2	no	urticaria	none
