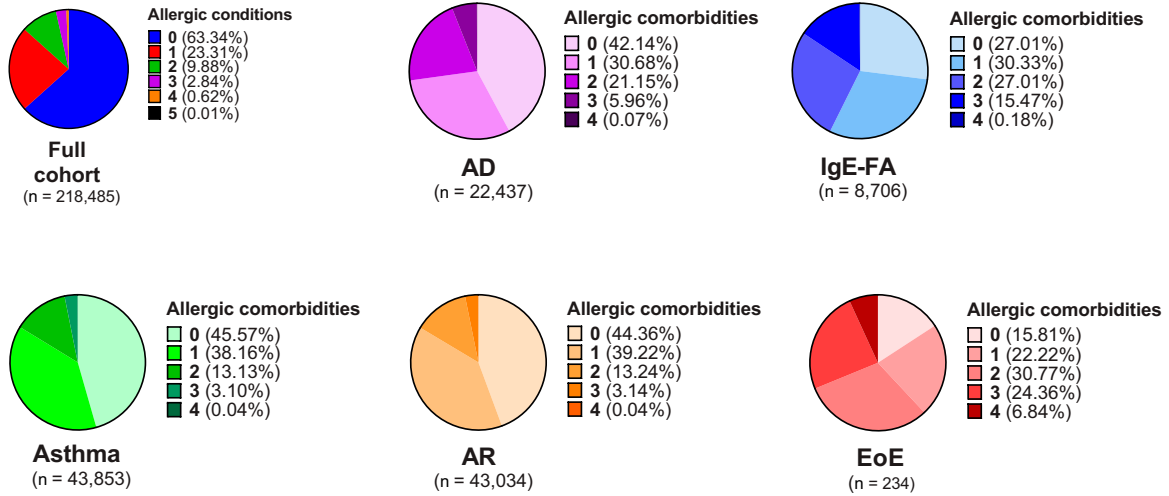


Supplemental Information



SUPPLEMENTAL FIGURE 5

Allergic multimorbidity. Percentage of subjects in the full birth cohort who had 1 to 5 allergic manifestations, and subjects in the atopic dermatitis (AD), immunoglobulin E-mediated food allergy (IgE-FA), asthma, allergic rhinitis (AR), and eosinophilic esophagitis (EoE) subcohorts who had 1 to 4 allergic comorbidities.

SUPPLEMENTAL TABLE 7 Geographic Distribution of Subjects

West			Midwest			Northeast			South			Unknown		All Regions	
State	n	%	State	n	%	State	n	%	State	n	%	n	%	n	%
Alaska	1113	0.5094	Illinois	23	0.0105	Connecticut	18	0.0082	Alabama	9	0.0041	353	0.1616	218 485	100
Arizona	21	0.0096	Indiana	14 623	6.6929	Maine	3	0.0014	Arkansas	368	0.1684				
California	34	0.0156	Iowa	7	0.0032	Massachusetts	6814	3.1187	Delaware	1420	0.6499				
Colorado	39	0.0179	Kansas	29	0.0133	New Hampshire	8	0.0037	District of Columbia	1	0.0005				
Hawaii	5	0.0023	Michigan	16	0.0073	New Jersey	15 900	7.2774	Florida	129	0.0590				
Idaho	950	0.4348	Minnesota	15	0.0069	New York	955	0.4371	Georgia	1065	0.4874				
Montana	2	0.0009	Missouri	3896	1.7832	Pennsylvania	113 375	51.8914	Kentucky	207	0.0947				
Nevada	5	0.0023	Nebraska	1	0.0005	Rhode Island	11	0.0050	Louisiana	4	0.0018				
New Mexico	51	0.0233	North Dakota	1	0.0005	Vermont	2068	0.9465	Maryland	188	0.0860				
Oregon	6180	2.8286	Ohio	26 850	12.2892				Mississippi	4	0.0018				
Utah	12	0.0055	Wisconsin	438	0.2005				North Carolina	3139	1.4367				
Washington	4049	1.8532							Oklahoma	9	0.0041				
Wyoming	1	0.0005							South Carolina	8988	4.1138				
									Tennessee	2596	1.1882				
									Texas	2440	1.1168				
									Virginia	46	0.0211				
									West Virginia	6	0.0027				
Total	12 462	5.7038		45 899	21.0078		139 152	63.6895		20 619	9.4373	353	0.1616	218 485	100

SUPPLEMENTAL TABLE 8 Rural-Urban Distribution of Subjects

RUCA Code	Description	<i>n</i>	%
1	Metropolitan area core: primary flow within an UA	195 440	89.452
2	Metropolitan area high commuting: primary flow 30% or more to an UA	4987	2.283
3	Metropolitan area low commuting: primary flow 10%–30% to an UA	97	0.044
4	Micropolitan area core: primary flow within an UC of 10 000–49 999 (large UC)	1979	0.906
5	Micropolitan high commuting: primary flow 30% or more to a large UC	117	0.054
6	Micropolitan low commuting: primary flow 10% to 30% to a large UC	80	0.037
7	Small town core: primary flow within an UC of 2500–9999 (small UC)	229	0.105
8	Small town high commuting: primary flow 30% or more to a small UC	25	0.011
9	Small town low commuting: primary flow 10%–30% to a small UC	16	0.007
10	Rural areas: primary flow to a tract outside an UA or UC	145	0.066
NA	No ZIP code information available	15 370	7.035

RUCA, rural-urban commuting code; UA, urbanized area; UC, urban cluster.

SUPPLEMENTAL TABLE 9 Allergic Disease Definitions and Criteria

Allergic Disease	ICD Code(s)	SNOMED Code	Inclusion Criteria	Exclusions
AD	691.nn, L20.nn	24079001	Minimum 180-d span of diagnosis	
IgE-FA	V15.0[1-5], 995.[6-7], 995.7, Z91.01[0-3], Z91.018, T78.1XXA	414285001	Minimum 180-d span of diagnosis; food allergen in diagnosis name (ie, egg, cow's milk, soy, wheat, peanut, walnut, pecan, pistachio, cashew, almond, hazelnut, brazil nut, sesame, fish, tuna, whitefish, salmon, shellfish, clam, crab, lobster, mussel, oyster, scallop, or shrimp); prescription of epinephrine on at least 1 occasion	Subjects with celiac disease recoded as non-wheat allergic; subjects with lactose intolerance recoded as non-milk allergic; milk protein sensitivity (SNOMED 15911003)
Asthma	493.n, J45.nn	195967001	Minimum 180-d span of diagnosis; prescription of short-acting β agonist and steroid inhalant on at least 2 separate dates after 1 y of age	Asthma diagnosis before age 1 y; exclusive diagnosis of reactive airway disease and/or postviral wheeze
AR	477.nn, J30.n	61582004	Minimum 180-d span of diagnosis	
EoE	530.13, K20.0	735455001	Minimum 1 occasion	

AD, atopic dermatitis; AR, allergic rhinitis; EoE, eosinophilic esophagitis; IgE-FA, immunoglobulin E-mediated food allergy.

SUPPLEMENTAL TABLE 10 Search Terms for Individual IgE-Mediated Food Allergies

Food Allergens	Search Terms	Exclusions
Egg	'egg ^egg'	'family history drug eggplant eggnog'
Milk	'milk.*allerg allerg.*milk'	'family history intoleran'
Soy	'soy'	'family history intoleran'
Wheat	'wheat'	'family history buckwheat intoleran'
Fish	'fish tuna whitefish salmon'	'shell jelly <i>Salmonella</i> Salmon patch poison toxic trisomy family history'
Shellfish	'shellfish clam, clam clam\$ crab, crab crab\$ lobster, lobster\$ mussel oyster scallop shrimp'	'poison toxic family history'
Peanut	'peanut'	'family history flavor'
Tree nut	'tree.*nut'	'family history flavor'
Walnut	'walnut'	'family history flavor'
Pecan	'pecan'	'family history flavor'
Pistachio	'pistachio'	'family history flavor'
Almond	'almond'	'family history flavor'
Brazil nut	'brazil'	'family history flavor'
Hazelnut	'hazelnut'	'family history flavor'
Cashew	'cashew'	'family history flavor'
Sesame	'sesame'	'family history flavor'

For each food allergen, the terms were searched for within the condition source description.

SUPPLEMENTAL TABLE 11 Distribution of Subjects by Observation Time

Duration (y)	<i>n</i>	% of Total
5	32 583	14.9
6	30 662	14.0
7	25 799	11.8
8	22 862	10.5
9	19 444	8.9
10	16 450	7.5
11	17 721	8.1
12	14 860	6.8
13	12 939	5.9
14	10 851	5.0
15	7 104	3.3
16	4 351	2.0
17	2 057	0.9
18	802	0.4

SUPPLEMENTAL TABLE 12 Most Common Combinations of Food Allergens in Subjects With Multiple Immunoglobulin E–Mediated Food Allergies								
2 Food Allergens			<i>n</i>	%	3 Food Allergens			
Peanut, tree nut			324	21.0	Egg, milk, peanut		123	19.3
Egg, peanut			310	20.1	Peanut, fish, shellfish		74	11.6
Peanut, shellfish			161	10.4	Egg, peanut, tree nut		60	9.4
Egg, milk			108	7.0	Egg, peanut, shellfish		51	8.0
Peanut, sesame			106	6.9	Peanut, tree nut, sesame		39	6.1
Total, top 5 combinations			1009	65.3	Total, top 5 combinations		347	54.4
Total, subjects with 2 allergens			1546	100.0	Total, subjects with 3 allergens		638	100.0
4 food allergens			<i>n</i>	%	≥5 food allergens			
Egg, peanut, fish, shellfish			30	13.2	Egg, milk, peanut, fish, shellfish		19	12.3
Egg, milk, peanut, shellfish			18	7.9	Egg, milk, peanut, tree nut, sesame		8	5.2
Egg, milk, peanut, sesame			17	7.5	Egg, milk, soy, peanut, shellfish		8	5.2
Egg, milk, peanut, fish			16	7.0	Egg, milk, soy, peanut, tree nut		6	3.9
Egg, milk, peanut, tree nut			16	7.0	Egg, soy, peanut, fish, shellfish		5	3.2
Total, top 5 combinations			97	42.7	Total, top 5 combinations		46	29.7
Total, subjects with 4 allergens			227	100.0	Total, subjects with ≥5 allergens		155	100.0

SUPPLEMENTAL TABLE 13 Age at Diagnosis of Immunoglobulin E–Mediated Tree Nut Allergies														
Age Range (mo)	Walnut		Pecan		Pistachio		Almond		Brazil Nut		Hazelnut		Cashew	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
0–<6	2	0.7	0	0.0	2	0.9	1	0.7	0	0.0	1	0.6	7	1.7
6–<12	5	1.7	0	0.0	1	0.4	2	1.4	0	0.0	2	1.3	4	1.0
12–<18	9	3.1	5	3.3	7	3.1	8	5.8	0	0.0	2	1.3	17	4.2
18–<24	9	3.1	3	2.0	1	0.4	5	3.6	1	8.3	4	2.5	21	5.2
24–<30	21	7.1	9	5.9	7	3.1	10	7.2	0	0.0	8	5.1	40	10.0
30–<36	22	7.5	7	4.6	17	7.5	8	5.8	0	0.0	3	1.9	29	7.2
36–<42	17	5.8	8	5.3	11	4.8	9	6.5	1	8.3	12	7.6	25	6.2
42–<48	15	5.1	10	6.6	13	5.7	8	5.8	1	8.3	5	3.2	16	4.0
48–<54	29	9.9	20	13.2	18	7.9	13	9.4	1	8.3	10	6.3	34	8.5
54–<60	17	5.8	6	3.9	13	5.7	3	2.2	1	8.3	9	5.7	20	5.0
≥60	148	50.3	84	55.3	138	60.5	71	51.4	7	58.7	102	64.6	188	46.9
Total	294	100.0	152	100.0	228	100.0	138	100.0	12	100.0	158	100.0	401	100.0

SUPPLEMENTAL TABLE 14 Cumulative Incidences of Immunoglobulin E–Mediated Tree Nut Allergies														
Age Range (y)	Walnut		Pecan		Pistachio		Almond		Brazil Nut		Hazelnut		Cashew	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
0–<3	100	0.05	42	0.02	59	0.03	51	0.02	3	0.00	37	0.02	159	0.07
0–<5	192	0.09	91	0.04	113	0.05	79	0.04	8	0.00	80	0.04	251	0.11
0–<11	272	0.12	139	0.06	215	0.10	117	0.05	12	0.01	145	0.07	370	0.17
0–<14	291	0.13	149	0.07	225	0.10	138	0.06	12	0.01	156	0.07	398	0.18
0–18	294	0.13	152	0.07	228	0.10	138	0.06	12	0.01	158	0.07	401	0.18