should consider the experiences of other countries where management practices (e.g., training of stakeholders or developing anaphylaxis plans) have been standardized.

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Appendix A

Open Session Agendas

The committee held data-gathering sessions that were open to the public in Washington, DC, on June 22, 2015, and August 31-September 1, 2015. The open session agendas for the public meetings and a workshop are presented below:

Committee on Food Allergies: Global Burden, Causes, Treatment, Prevention, and Public Policy

Keck Center of the National Academies
500 Fifth Street NW, Washington, DC
Room 201

MONDAY, JUNE 22, 2015

OPEN SESSION

11:30-11:35 a.m. Welcome and Introductions
Virginia Stallings and Committee

11:35 a.m.-12:30 p.m.	**Sponsor Perspectives on the Study** *Mary Jane Marchisotto, Food Allergy Research & Education* *Stefano Luccioli & Patricia Hansen, Center for Food Safety and Applied Nutrition, Food and Drug Administration* *Daniel Rotrosen, National Institute of Allergy and Infectious Diseases, National Institutes of Health* *Charlsia Fortner, Food and Nutrition Service, U.S. Department of Agriculture* *Bob Parker, National Peanut Board*
12:30-1:30	Lunch Break Cafeteria on the Third Floor
1:30-2:30	**Sponsor Perspectives on the Study** *Tia Rains, Egg Nutrition Center* *Barbara Blakistone, National Fisheries Institute* *Ari Mayer Mackler, International Tree Nut Council Nutrition Research & Education* *Jill Nicholls, National Dairy Council* *Alison Kretser, International Life Sciences Institute North America* *Meryl Bloomrosen, Asthma and Allergy Foundation of America*
2:30-3:00	Questions from the Committee
3:00-3:15	Break
3:15-3:30	Discussion with Advisory Panel *Bryan Bunning* *Monika Biller Harris* *Dan Cicero* *Karen Hemmerdinger* *Jill Mindlin* *Caroline Moassessi* *Karin Tegila*
3:30 p.m.	End of Open Session

Committee on Food Allergies: Global Burden, Causes, Treatment, Prevention, and Public Policy

Public Workshop
August 31-September 1, 2015

Keck Center of the National Academies
500 Fifth Street NW, Washington, DC
Room 100

Workshop Goals

- Review current knowledge, research, and trends in food allergy
- Explore strategies for understanding, measuring, preventing, and diagnosing food allergy
- Identify public settings of concern for individuals with food allergy
- Evaluate approaches to address the unique needs and challenges of individuals with food allergy
- Discuss existing food allergy legislation and regulatory issues

MONDAY, AUGUST 31, 2015

12:15-12:40 p.m. Registration and Check-In

12:40-12:45 Welcome Remarks
Virginia Stallings, Committee Chair

Session I: Context, Basic Mechanisms, and Diagnostics
Moderator: Stephen Galli

12:45-1:05 Food Allergies in Socioecological Contexts of Human Adaptation and Development
Ann Masten, University of Minnesota

1:05-1:35 Mechanisms of Food Allergy
Wayne Shreffler, Massachusetts General Hospital

1:35-1:55	Cellular and Molecular Diagnostics and Prognostics in Food Allergy *Kari Nadeau, Stanford University School of Medicine*
1:55-2:10	Panel Discussion
	Session II: Early Determinants of Food Allergy Moderator: Anna Maria Siega-Riz
2:10-2:30	Genetic and Epigenetics Effects for Allergy-Related Diseases and Traits *Liming Liang, Harvard School of Public Health*
2:30-2:50	Infant Gut Microbial Markers of Food Sensitization at Age 1 *Anita Kozyrskyj, Pediatrics, University of Alberta*
2:50-3:10	Nutritional and Lifestyle Early Life Determinants *Katie Allen, Murdoch Children's Research Institute*
3:10-3:30	Panel Discussions
3:30-3:50	Break
	Session III: Prevention and Urgent Care of Food Allergy Moderator: Hugh Sampson
3:50-4:25	Food Allergy Prevention (Peanuts) *Gideon Lack, King's College London/St. Thomas' Hospital*
4:25-4:45	Research on Early Introduction of Hen's Egg and Cow's Milk *Johanna Bellach, Charité Hospital, University of Berlin*
4:45-5:05	Emergency Anaphylaxis Management: Opportunities for Improvement *Ronna Campbell, Mayo Clinic*
5:05-5:25	Panel Discussion
5:25 p.m.	Adjourn

TUESDAY, SEPTEMBER 1, 2015

7:30-7:55 a.m.	Coffee, Tea, and Juice Served
7:55-8:00	Welcome Remarks *Virginia Stallings, Committee Chair*
	Session IV: International Perspectives Moderator: Virginia Stallings
8:00-8:25	Food Allergy in Japan *Motohiro Ebisawa, World Allergy Organization/ Sagamihara National Hospital*
8:25-8:50	Management of Food Allergy in Europe—an Overview Using Germany as an Example *Johanna Bellach, Charité University Hospital Berlin*
8:50-9:15	Food Allergies in Australia/Food Advisory Labeling *Katie Allen, Murdoch Children's Research Institute*
9:15-9:35	Break
	Session V: Patient-Centered Concerns Moderator: Scott Sicherer
9:35-9:55	Reimbursement/Insurance *Paul Campbell, Amplify Public Affairs*
9:55-10:15	Causes, Treatment, Prevention, and Public Policy: A Psychological Perspective on Food Allergy *Audrey DunnGalvin, University College Cork*
10:15-10:35	Primary Care Management of Food Allergy and General Public Knowledge and Beliefs *Ruchi Gupta, Northwestern University Feinberg School of Medicine; Ann & Robert H. Lurie Children's Hospital of Chicago*
10:35-10:55	Challenges in Managing Food Allergy in Vulnerable Groups *Hemant Sharma, Children's National Medical Center*

10:55-11:25	Dietary Intake and Nutritional Status *Marion Groetch, Jaffe Food Allergy Institute, Icahn School of Medicine at Mount Sinai*
11:25-11:55	Panel Discussion
11:55 a.m- 12:55 p.m.	Lunch Cafeteria on Third Floor

Session VI: Food Industry and Regulatory Environment
Moderator: Stephen Taylor

12:55-1:15	Bioguided Food Processing *Bruce German, University of California*
1:15-1:35	State and National Policymaking on Food Allergies: Changes Sweeping (some of) the Nation *Lynn Morrison, Washington Health Advocates*
1:35-1:55	Assessing Risks of Exposure to Allergens from Foods *Joe Baumert, University of Nebraska*
1:55-2:15	The Allergen Journey: Developing Best Practice Solutions for Industry *Sue Estes, Pepsico*
2:15-2:45	Practical Regulatory Issues *Steven Gendel, IEH Laboratories and Consulting Group*
2:45-3:15	Panel Discussion
3:15-3:30	Break

Session VII: Public Settings of Concern
Moderator: Wesley Burks

3:30-3:50	Food Allergy Management in the School Setting *Sally Schoessler, Allergy and Asthma Network*
3:50-4:10	Food Allergies in Higher Education

	Lindsay Haas, University of Michigan
4:10-4:30	Food Allergies: Bridging the Accommodation Gap in Food Service *David Crownover, National Restaurant Association*
4:30-4:50	Food Marketing/Retail *Hilary Thesmar, Food Marketing Institute*
4:50-5:10	Flying with Food Allergies: Concerns and Opportunities *Laurel Francoeur, Attorney and Food Allergy Advocate*
5:10-5:40	Panel Discussion
5:40-6:00	Public Comment *Karin Teglia* *Bryan Bunning* *Lianne Mandelbaum* *Kristen Spotz* *Rachel Clark* *Scott Riccio* *Meryl Bloomrosen*
6:00 p.m.	Closing Remarks and Adjourn *Virginia Stallings*

Appendix B

Food Allergy Prevalence Literature Search Strategy

Two literature searches were conducted to assess the current prevalence of food allergy both nationally and internationally, including overall population prevalence, food-induced anaphylaxis, and the prevalence of allergy to specific foods. The searches were conducted in the online databases Medline and EMBASE and were not limited by country. Peanut, nut, milk, wheat, egg, soy, fish, shellfish, and sesame were included in the initial search. An additional search was conducted that included the previous foods as well as specific types of fish (tuna, salmon, cod), molluscs (clams), nuts (almond, macadamia nut, Brazil nut, pecan, cashew, pine nut, chestnut, pistachio, hazelnut, walnut), seeds (sesame, mustard, sunflower, poppy, pumpkin), coconut, litchi, lupin, fruits, and vegetables. Articles were excluded if they were written in a language other than English, had nonhuman subjects, or were case studies/series, notes, conference abstracts, nonsystematic reviews, or opinion pieces. The searches yielded 767 unduplicated articles. The abstracts of these articles were then screened for food allergy or anaphylaxis population prevalence estimates. Of these, 707 articles did not provide an estimate and were excluded, leaving 60 articles for full text review. These were supplemented by 13 articles suggested by committee members or found through reference mining. This process is illustrated in Figure B-1, and the search terms used are listed in Tables B-1 and B-2. A summary of studies that reported prevalence of food allergy is found in Table B-3. Summary tables of systematic reviews on the prevalence of food allergy are found in Table B-4.

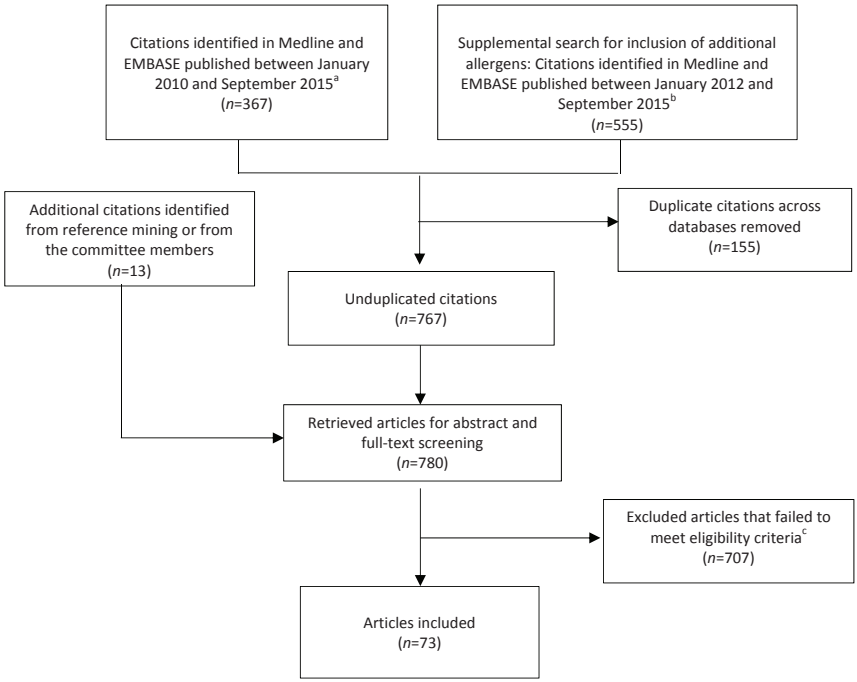

FIGURE B-1 Literature search and selection process.

[a] Search was designed to capture studies measuring the prevalence of food allergy and anaphylaxis to peanut, nut, milk, wheat, egg, soy, fish, shellfish, or sesame, and was not limited by country.

[b] Supplemental search was designed to capture studies measuring the prevalence of food allergy and anaphylaxis to additional allergens not included in initial search (see text for complete list) and was not limited by country.

[c] Articles were excluded if they did not give food allergy or anaphylaxis population prevalence estimates.

TABLE B-1 Search Terms to Identify Relevant Literature on Global Prevalence of Food Allergy for Medline and EMBASE

Search Number	Search Terms
	a. Medline Search
1	Food hypersensitivity/
2	Peanut hypersensitivity/
3	Nut hypersensitivity/
4	Milk hypersensitivity/
5	Wheat hypersensitivity/
6	Egg hypersensitivity/
7	Soybean allergy.mp
8	Soy allergy.mp
9	Fish allergy.mp
10	Shellfish allergy.mp
11	Sesame allergy.mp
12	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13	Prevalence/
14	Anaphylaxis/
15	Life threatening food allergy.mp
16	13 or 14 or 15
17	12 and 16
	b. EMBASE Search
1	Food allergy/
2	Food allergen/
3	Peanut allergy/
4	Nut allergy/
5	Milk allergy/
6	Wheat allergy/
7	Egg allergy/
8	Soy allergy.mp
9	Soybean allergy.mp
10	Fish allergy.mp
11	Shellfish allergy.mp
12	Sesame allergy.mp
13	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14	Prevalence/
15	Anaphylaxis/
16	Food allergy prevalence.mp
17	Life threatening food allergy.mp
18	14 or 15 or 16 or 17
19	13 and 18

NOTES: Search terms were mapped to Subject Headings when available; otherwise searched as Keyword (.mp). Searches limited to 2010 to Current.

TABLE B-2 Search Terms to Identify Relevant Literature on Global Prevalence of Food Allergy to Additional Allergens for Medline and EMBASE

Search Numbers	Search Terms
	a. Medline
1	Prevalence/
2	limit 1 to (English language and humans and yr="2012 -Current")
3	Incidence/
4	limit 3 to (English language and humans and yr="2012 -Current")
5	Hypersensitivity/
6	limit 5 to (English language and humans and yr="2012 -Current")
7	Food Hypersensitivity/
8	limit 7 to (English language and humans and yr="2012 -Current")
9	Skin Tests/
10	Immunoglobulin E/
11	2 or 4
12	6 or 8 or 9 or 10
13	11 and 12
14	Milk/
15	13 and 14
16	Egg Hypersensitivity/
17	13 and 16
18	Milk Hypersensitivity/
19	13 and 18
20	Fishes/
21	Tuna/
22	Salmon/
23	Gadiformes/
24	20 or 21 or 22 or 23
25	13 and 24
26	Nut Hypersensitivity/
27	Prunus/
28	Macadamia/
29	Bertholletia/
30	Carya/

TABLE B-2 Continued

Search Numbers	Search Terms
31	Anacardium/
32	Nuts/
33	Pistacia/
34	Corylus/
35	Juglans/
36	pine nut.mp.
37	chestnut.mp.
38	26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37
39	13 and 38
40	Peanut Hypersensitivity/
41	13 and 40
42	Wheat Hypersensitivity/
43	13 and 42
44	Soybeans/
45	13 and 44
46	Seeds/
47	Sesamum/
48	Mustard Plant/
49	Helianthus/
50	Papaver/
51	Cucurbita/
52	46 or 47 or 48 or 49 or 50 or 51
53	13 and 52
54	Cocos/
55	13 and 54
56	Litchi/
57	13 and 56
58	Lupinus/
59	13 and 58
60	Fruit/
61	Vegetables/
62	Fragaria/

continued

TABLE B-2 Continued

Search Numbers	Search Terms
63	60 or 61 or 62
64	13 and 63
65	Mollusca/
66	Bivalvia/
67	65 or 66
68	13 and 67
	Results from 15, 17, 19, 25, 39, 41, 43, 45, 53, 55, 57, 59, 64, and 68 combined
	b. EMBASE Search
1	Prevalence/
2	limit 1 to (human and English language and yr="2012 -Current")
3	incidence/
4	limit 3 to (human and English language and yr="2012 -Current")
5	hypersensitivity/
6	limit 5 to (human and English language and yr="2012 -Current")
7	food allergy/
8	limit 7 to (human and English language and yr="2012 -Current")
9	skin test/
10	immunoglobulin E/
11	2 or 4
12	6 or 8 or 9 or 10
13	11 and 12
14	milk allergy/
15	egg allergy/
16	fish/
17	salmon/
18	tuna/
19	Atlantic cod/
20	Crustacea/
21	shellfish/
22	shrimp/
23	lobster/
24	crab/
25	mollusc/

TABLE B-2 Continued

Search Numbers	Search Terms
26	clam/
27	nut allergy/
28	almond/
29	Macadamia/
30	Brazil nut/
31	pecan/
32	cashew nut/
33	pine nut.mp.
34	chestnut/
35	hazelnut/
36	pistachio/
37	walnut/
38	peanut allergy/
39	wheat allergy/
40	soybean/
41	plant seed/
42	sunflower/
43	sesame/
44	Papaver/
45	mustard/
46	squash/
47	coconut/
48	lychee/
49	lupin/
50	fruit/
51	vegetable/
52	14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51
53	13 and 52

NOTES: Search terms were mapped to Subject Headings when available; otherwise searched as Keyword (.mp). Searches limited to human studies, English language, and published 2012 to Current.

TABLE B-3 Summary of Food Allergy Prevalence Studies

Reference	Country	Study Design	Number Invited or Eligible Participants	Participation Rate N (%)
Grabenhenrich et al., 2016	Europe	Cross-sectional	N/A	1,970 (reports of anaphylaxis)
McGowan et al., 2016	US	Cross-sectional	N/A	NHANES III (1988-1994): 4,995 NHANES (2005-2006): 2,901
Xepapadaki et al., 2016	Europe	Cohort	12,049	9,336 (77%)
Datema et al., 2015	Europe	Cross-sectional	Not indicated	731
Le et al., 2015	Europe (The Netherlands)	Cross-sectional	6,600	3,864 (59%)

Age of Participants	Food Allergens	Method of Outcome Assessment	Estimated Prevalence of Food Allergy, % (95% CI)
<18 years	Hen egg, cow milk, nuts	Report of anaphylaxis in the European Anaphylaxis Registry	Food-related anaphylaxis: 66% of reports
6-19 years	Peanut, milk, egg, shrimp	sIgE	Food sensitization NHANES III: 24.3 (22.1-26.5) NHANES 2005-2006: 21.6 (19.5-23.7) Shrimp sensitization NHANES III: 11.2 (10.0-12.5) NHANES 2005-2006: 6.1 (4.5-7.7)
2 years	Hen egg	sIgE, SPT, DBPCOFC	Mean raw incidence: 0.84 (0.67-1.03) Adjusted mean incidence: 1.23 (0.98-1.51) (Adjusted for eligible children who were not challenged)
Mean age: 32.3 ± 14.8 (SD) years	Hazelnut	SPT sIgE DBPCOFC (N=124)	77.4 83.7 70.2
20-54 years	Hen egg, cow milk, peanut, hazelnut, celery, apple, peach, fish, or shrimp	Self-report Clinical evaluation, medical history, sIgE DBPCOFC	10.8 4.1 3.2

continued

TABLE B-3 Continued

Reference	Country	Study Design	Number Invited or Eligible Participants	Participation Rate N (%)
Schoemaker et al., 2015	Europe	Cohort	12,049	9,336 (77%) 358 eligible for DBPCOFC; 248 agreed to at least 1 challenge
Soller et al., 2015	Canada	Cross-sectional	12,762 households	5,734 households/ 15,022 individuals (45%) (full participants) 524 households (4%) (partial participants)
Winberg et al., 2015	Sweden	Cohort	Not indicated	2,612 (96%)

Age of Participants	Food Allergens	Method of Outcome Assessment	Estimated Prevalence of Food Allergy, % (95% CI)
12 and 24 months	Cow milk	Parent-report, clinical examination, sIgE or SPT, DBPCOFC	Raw incidence: 0.54 (0.41-0.70) Adjusted incidence: 0.74 (0.56-0.97) (Adjusted for children who were eligible but not challenged, were placebo reactors, or who had inconclusive challenge outcomes, or who were lost to follow up)
Adults and children	Peanut, tree nuts, fish, shellfish, sesame, milk, egg, wheat, and/or soy	Self-report, convincing history, physician diagnosis	Self-reported food allergy to any food Full participants: 6.4 (6.0-6.8) (unweighted) 7.5 (6.9-8.1) (weighted) Partial participants: 2.1 (1.4-2.9) (unweighted)
11-12 years	Milk, egg, cod, wheat	Parent-report	Reported food allergy: 4.8 (4-6)
		Clinical evaluation + sIgE	Clinically evaluated food allergy: 1.4 (1-2)
		DBPCOFC	DBPCOFC-proven food allergy: 0.6 (0-1)

continued

TABLE B-3 Continued

Reference	Country	Study Design	Number Invited or Eligible Participants	Participation Rate N (%)
Bunyavanich et al., 2014	US	Cohort study	1,277	616 (48.2)
Burney et al., 2014	Europe	Cross-sectional	28,269	17,366 (54.6)
Gaspar-Marques et al., 2014	Portugal	Cross-sectional	2,228	1,225 (55.0) participated 1,217 (54.6) included in analysis
Salo et al., 2014	US	Cross-sectional	10,348	10,348
Wood et al., 2014	US	Cross-sectional (patient survey)	1,651	1,059 (64%)

Age of Participants	Food Allergens	Method of Outcome Assessment	Estimated Prevalence of Food Allergy, % (95% CI)
7-10 years	Peanut	Self-reported symptoms, sIgE levels, clinical information, and combinations of these variables	Self-reported food allergy: 4.6 (2.9-6.3) Clinical food allergy based on sIgE: 5.0% (3.5-7.1) Peanut sIgE ≥0.35 kU/L and prescribed epi auto-injector: 4.9 (3.2-6.7) Peanut sIgE ≥14 kU/L: 2.9 (1.6-4.3) Peanut sIgE ≥14 kU/L and prescribed epi auto-injector: 2.0 (0.9-3.2)
20-54 years	Various	Self-report, physician diagnosis, sIgE (≥0.35 kU_A/L)	Self-report: 21.0 Physician diagnosis: 4.4 IgE to any foods: 15.81
0-3 years 4-6 years	Various	Self-report	*Ever had a food allergy* 0-3 years: 8.6 (6.4-11.5) 4-6 years: 12.1 (10.0-14.7) Total: 10.8 (9.1-12.6) *Current food allergy* 0-3 years: 4.7 (3.1-7.0) 4-6 years: 6.4 (4.9-8.4) Total: 5.7 (4.6-7.2)
≥1 year	Egg white, cow milk, peanut, shrimp	sIgE	Prevalence of food sensitization: 28
Adults (median age 52 years)	Not specified	Self-report of anaphylaxis to food	Reported anaphylaxis: 31

continued

TABLE B-3 Continued

Reference	Country	Study Design	Number Invited or Eligible Participants	Participation Rate N (%)
Kaya et al., 2013	Turkey	Cross-sectional	11,233	10,096 (89.9)
Gupta et al., 2012	US	Cross-sectional	40,104	38,465 (96)
Gupta et al., 2011, 2013	US	Cross-sectional	40,104	38,480 (96)

Age of Participants	Food Allergens	Method of Outcome Assessment	Estimated Prevalence of Food Allergy, % (95% CI)
11-15 years	Various	Parent-report Confirmation by: clinical history, sIgE, SPT, OFC, DBPCOFC	Lifetime parent-reported: 11.3 (10.7-11.9) Parent-reported point prevalence: 3.6 (3.2-3.8) Confirmed food allergy: 0.15 Confirmed peanut: 0.05 Confirmed tree nut: 0.05
0-17 years	All allergens (peanut, shellfish, milk, fin fish, egg, tree nuts, wheat, soy)	Parent report of physician diagnosis, sIgE, SPT, OFC, reaction history	Urban centers: 9.8 (8.6-11.0) Metro cities: 9.2 (8.4-10.1) Urban outskirts: 7.8 (7.0-8.6) Suburban areas: 7.6 (6.9-8.2) Small towns: 7.2 (5.7-8.6) Rural areas: 6.2 (5.6-6.8) P<0.0001
0-17 years	Egg, fin fish, milk, peanut, shellfish, soy, tree nuts, wheat, or strawberry	Parent report of physician diagnosis, sIgE, SPT, OFC, reaction history	All allergens: 8.0 (7.7-8.3) Egg: 0.8 (0.7-0.9) Fin fish: 0.5 (0.4-0.6) Milk: 1.7 (1.5-1.8) Peanut: 2.0 (1.8-2.2) Shellfish: 1.4 (1.2-1.5) Soy: 0.4 (0.3-0.4) Tree nuts: 1.0 (0.9-1.2) Wheat: 0.4 (0.3-0.5) Strawberry: 0.4 (0.4-0.5)

continued

TABLE B-3 Continued

Reference	Country	Study Design	Number Invited or Eligible Participants	Participation Rate N (%)
Osborne et al., 2011	Australia	Cohort	3,898	2,848 (73)
Sicherer et al., 2010	US	Cross-sectional	12,658 households	5,300 households (13,534 subjects) (42)
Venter et al., 2010	UK	Cohort	Cohort A: 1,456 Cohort B: 2,858 Cohort C: 969	Cohort A: 1,218 (84) Cohort B: 1,273 (44) Cohort C: 891 (92)
Ben-Shoshan et al., 2009	Canada	Cross-sectional	8,039	(64)
Branum and Lukacs, 2009	US	Cross-sectional	Not indicated	Not indicated

NOTE: CI = confidence interval; DBPCOFC = double-blind, placebo-controlled oral food challenge; IgE = immunoglobulin E; N/A = not applicable; OFC = oral food challenge; SE = standard error; sIgE = food-specific serum IgE; SPT = skin prick test; UK = United Kingdom; US = United States.

Age of Participants	Food Allergens	Method of Outcome Assessment	Estimated Prevalence of Food Allergy, % (95% CI)
12 months	Raw egg, peanut, sesame, shellfish, or cow milk	SPT, DBPCOFC Shellfish and milk: no food challenge performed	Overall prevalence (raw egg, peanut or sesame): 10.4 (9.3-11.5) Raw egg: 8.9 (7.8-10.0) Peanut: 3.0 (2.4-3.8) Sesame: 0.8 (0.5-1.1)
<18 years	Peanut, tree nuts, sesame	Self-report	Peanut: 1.4 (1.0-1.9) Tree nuts: 1.1 Sesame: 0.1 (0-0.2)
3-4 years	Peanut	Cohort A: clinical history Cohorts B and C: SPT and clinical history or OFC	Cohort A: 0.5 Cohort B: 1.4 Cohort C: 1.2
K-grade 3 students	Peanut	Clinical history, SPT, sIgE, DBPCOFC	1.62 (1.31-1.98)
0-17 years	Not indicated	Parent-report	3.9 ± 0.3 (SE)
	Peanut, egg, milk, shrimp (in children ≥6 years)	sIgE	Proportion estimate ± SE sIgE (peanut): 9.3 ± 0.8 sIgE (egg): 6.7 ± 0.6 sIgE (milk): 12.2 ± 0.9 sIgE (shrimp): 5.2 ± 0.6
		Food allergy-related ambulatory care visits to hospital facilities and physician offices and hospitalizations	317,000 (95% CI: 196,000-438,000) visits per year

TABLE B-4 Prevalence of Food Allergy: Systematic Review Summaries

Author, year	McWilliam et al., 2015
Aims/Key questions	To provide a comprehensive, up-to-date systematic review of the population prevalence of tree nut allergy in children and adults, including details of all individual tree nuts in various regions of the world
Study eligibility criteria	Inclusion criteria: • Types of studies: Population, cross-sectional, and cohort studies. • Types of participants: Adults and children; no age restrictions. • Primary outcomes: All forms of allergic reactions (primary and secondary IgE-mediated and non-IgE-mediated reactions) were included. All tree nut allergy outcomes were included for both individual and combined tree nut allergies. Included eligible studies that reported tree nut allergy based on self-report, sensitization (sIgE or SPT), OFC/DBPCOFC or convincing clinical history. Exclusion criteria: • Types of studies: Reviews, case reports, and studies without full-text. • Types of participants: Selected patient groups or those performed in hospital or allergy clinic settings.
Literature search dates or year range	January 1996 to December 2014
Number of food allergy studies included	36
Synthesis methods	Summary tables, narrative text, meta-analysis

TABLE B-4 Continued

Key findings	Confirmed food allergy: Seven studies (all in children) using OFC (or convincing recent history of allergic reaction together with positive allergen-specific IgE) to determine a prevalence range of 0-1.6%. Probable food allergy: Nine studies combined self-reported food allergy with additional objective assessment (e.g., specific details regarding doctor diagnosis or sensitization details [sIgE/SPT]) and were classified as probable food allergy for this review. The overall probable tree nut allergy prevalence range was 0.05-4.9%, with only one study reporting adult data. Self-reported food allergy: Twenty studies based on self-report found tree nut allergy prevalence range was wider for adults (0.18-8.9%) and those studies including both adults and children (0.4-11.4%) than for those studies including only children (0-3.8%). Overall self-reported tree nut allergy prevalence ranged from 0 to 11.4%. Pollen-associated food allergy: Prevalence estimates that included pollen-associated food allergy reactions to tree nut were significantly higher (8-11.4%) and were predominantly from Europe. Geographic Differences: Prevalence of individual tree nut allergies varied significantly by region, with hazelnut the most common tree nut allergy in Europe; walnut and cashew the most common in the US; and Brazil nut, almond, and walnut the most common in the UK.
Limitations	Small number of studies reporting challenge-confirmed tree nut allergy prevalence. Unable to pool the prevalence estimates due to the large heterogeneity between the studies. Data are largely limited to European, US, and UK studies.
AMSTAR rating	
An a priori design?	Y
Duplicate study selection and data extraction?	Y
Comprehensive literature search?	Y
Status of the publication as an inclusion criterion?	Y (limited to English-language articles)
List of studies (included and excluded) provided?	Y/N (no list of excluded studies)
Characteristics of included provided?	Y
Scientific quality of the included studies assessed and reported?	Y
Scientific quality used in formulating conclusions?	Y

continued

TABLE B-4 Continued

Methods used to combine the findings appropriate?	Y
Likelihood of publication bias assessed?	N
Conflict of interest (COI) stated?	Y/N (COI of the systematic review authors was provided but not provided for included studies)

Author, year	Umasunthar et al., 2015
Aims/Key questions	To quantify the risk of anaphylaxis for food-allergic people
Study eligibility criteria	Inclusion criteria: • Study design: Prospective or retrospective registries, databases or cohort studies. • Participants: People with a medically diagnosed food allergy or a defined population where an assumed population rate of food allergy could be applied. • Follow-up: To enable calculation of total person-years of observation, the authors included studies that specified either total population and duration of data collection or anaphylaxis incidence rate. • Outcomes: The authors included reports of number of food anaphylaxis events during the follow-up period. Anaphylaxis determined by self-report, medical coding, or anaphylaxis admission to hospital. Exclusion criteria: • Food-allergic reactions reported were not anaphylactic, or severity was not defined. • Time period not defined. • Population in which food anaphylaxis cases occurred could not be quantified.
Literature search dates or year range	January 1946 to September 5, 2012
Number of food allergy studies included	34
Synthesis methods	Summary tables, narrative text, meta-analysis

TABLE B-4 Continued

Key findings	Self-reported food anaphylaxis in food allergic people: • Based on data from 10 studies, meta-analysis gave an incidence of 4.93 (95% CI: 2.78-8.74; range 0.60-57.89) per 100 person-years for people ages 0-19 years. • For peanut allergic people meta-analysis of data from four studies gave an incidence rate of 2.64 (95% CI: 1.13-6.17; range 1.64-8.90) per 100 person-years. Medically coded food anaphylaxis in food-allergic people: • Based on nine studies, the incidence rate was 0.14 per 100 person-years (95% CI: 0.05-0.35; range 0.01-1.28). • Based on nine studies, the incidence rate for people ages 0-19 years was 0.20 (95% CI: 0.09-0.43; range 0.01-2.55; sensitivity analysis 0.08-0.39). • In sensitivity analysis using different estimated food allergy prevalence, the incidence varied from 0.11 to 0.21 per 100 person-years. • The incidence rate of up to 7.00 per 100 person-years has been reported for children ages 0-4 years. Hospital admission due to food anaphylaxis in food-allergic people: • Based on four studies, the incidence rate was 0.09 (95% CI: 0.01-0.67; range 0.02-0.81) per 1,000 person-years. • Based on eight studies, the incidence rate for people ages 0-19 years was 0.20 (95% CI: 0.10-0.43; range 0.04-2.25). • Based on six studies, the incidence rate for children agse 0-4 years was 0.50 (95% CI: 0.26-0.93; range 0.08-2.82).
Limitations	High heterogeneity between study results, possibly due to variation in study populations, anaphylaxis definition, and data collection methods. Some uncertainty exists about the precision of the risk estimates, so mean estimates should be interpreted with caution. The rate of self-reported anaphylaxis varied widely across studies. Study quality was generally rated as low for studies of self-reported anaphylaxis. It is likely that studies of self-reported anaphylaxis overestimate the true incidence of anaphylaxis. The rate of medically coded anaphylaxis also varied widely between studies. These data may underestimate food anaphylaxis occurrence.

continued

TABLE B-4 Continued

AMSTAR rating	
An a priori design?	Y
Duplicate study selection and data extraction?	Y
Comprehensive literature search?	Y
Status of the publication as an inclusion criterion?	Y
List of studies (included and excluded) provided?	Y/N (no list of excluded studies)
Characteristics of included provided?	Y
Scientific quality of the included studies assessed and reported?	Y
Scientific quality used in formulating conclusions?	Y
Methods used to combine the findings appropriate?	Y
Likelihood of publication bias assessed?	Y
Conflict of interest stated?	Y/N (COI of the systematic review authors was provided but not provided for included studies)

Author, year	Katz et al., 2014
Aims/Key questions	To identify the adjusted prevalence of IgE-mediated soy allergy in children and perform a secondary analysis of the impact of age (less than and more than 6 months).
Study eligibility criteria	Inclusion criteria: • Types of studies: analytical transversal studies, studies of cases and controls, cohort studies, and clinical trials. • Types of participants: infants and children up to 19 years old, including newborns. • Primary outcomes: prevalence of sensitization or allergy to soy identified by clinical manifestations, parent reports, serum concentrations of sIgE, SPT, or an OFC. Exclusion criteria: • Types of studies: narrative reviews; studies of people older than age 19 years; studies lacking sufficient congruence and/or yield between what was described in the objectives and what was reported.
Literature search dates or year range	1909 to March 2013
Number of food allergy studies included	40
Synthesis methods	Summary tables, meta-analysis

TABLE B-4 Continued

Key findings	Ten studies reported OFC-proven soy protein allergy in the general population (i.e., the referred population). Quality of evidence was low or moderate. • The weighted prevalence for the general population: 0.27 (95% CI: 0.1%-0.44%) (N/total=4/1,946) • The weighted prevalence for the referred population: 1.9 (95% CI: 1.1%-2.7%) (N/total=35/1,807) • The weighted prevalence for atopic children: 2.7 (95% CI: 1.8%-3.3%) (N/total=19/708) Six studies reported the prevalence of self-reported soy allergy in the general population. The quality of evidence was low. • The prevalence was 0.2 (95% CI: 0.0%-0.30%) (N/total=39/19,732) Twelve studies reported the prevalence of allergy to soy after the use of infant formula with soy-based protein. Quality of evidence was low to moderate. • The weighted prevalence of OFC-proven soy allergy was 2.5% (95% CI: 2.1%-8.3%) (N/total=18/720) Six studies reported prevalence of self-reported soy allergy after use of soy-based formula. Quality of evidence was moderate except for one study. • Weighted prevalence was 4.4% (95% CI: 0%-5.6%) (N/total=108/2,439)
Limitations	All four positive cases of OFC-proven soy allergy in the general population originated from one study. Cutaneous signs were noted in only one of these cases.

AMSTAR rating	
An a priori design?	Y
Duplicate study selection and data extraction?	Y
Comprehensive literature search?	Y
Status of the publication as an inclusion criterion?	Y
List of studies (included and excluded) provided?	Y/N (no for excluded studies)
Characteristics of included provided?	Y
Scientific quality of the included studies assessed and reported?	Y
Scientific quality used in formulating conclusions?	Y
Methods used to combine the findings appropriate?	Y
Likelihood of publication bias assessed?	Y
Conflict of interest stated?	N

continued

TABLE B-4 Continued

Author, year	Keet et al., 2014
Aims/Key questions	To determine the prevalence of self-reported food allergy in children in the US, and explore sources of variation in prevalence estimates, including case definition, changes over time, and racial/ethnic differences.
Study eligibility criteria	Inclusion criteria: • Types of studies: national surveys; population-based original reports. • Types of participants: US general population; children. • Primary outcomes: self-reported food allergy. Exclusion criteria: • Types of studies: studies without individual level data; abstracts only. • Types of participants: adults.
Literature search dates or year range	Up to February 2012
Number of food allergy studies included	27 survey administrations (20 survey administrations were used in the meta-regression)
Synthesis methods	Summary tables, narrative text, meta-analysis with meta-regression

TABLE B-4 Continued

Key findings	Seven surveys reported self-reported food allergy (National Maternal and Infant Health Survey; NHANES III; National Survey of Children's Health 2003 and 2007; NHIS 1997-2011; NHANES 2007-2008 and 2009-2010). Prevalence: It appears that the prevalence of self-reported food allergy is between 3 and 6 percent. Prevalence (current versus ever): Compared to estimates of prevalence of self-reported current food allergy, the prevalence of self-reported history of food allergy ever was considerably higher, even after adjusting for year of study (difference: 2.5 percentage points between current and ever/time undefined food allergy, 95% CI: 1.5%-3.4%; P<0.001 for all children). Change over time: The self-reported prevalence of food allergy among children was estimated to have increased by 1.2 percentage points per decade during 1988-2011 (95% CI: 0.7%-1.6%). Racial/ethnic differences: The rate of increase in self-reported food allergy prevalence varied significantly by race/ethnicity; the estimated increase in food allergy prevalence per decade among Black children was 2.1 percentage points (95% CI: 1.5%-2.7%) compared to 1.2 percentage points among Hispanics (95% CI: 0.7%-1.7%) and 1.0 percentage points (95% CI: 0.4%-1.6%) among whites (P=0.01 for comparison of trends between blacks and whites, and P=0.04 for comparison between blacks and Hispanics).
Limitations	Surveys included in meta-regression were limited to those conducted by the CDC. The studies have too much heterogeneity to calculate a summary measure of food allergy prevalence. All outcomes were based on self-report.
AMSTAR rating	
An a priori design?	Y
Duplicate study selection and data extraction?	Y
Comprehensive literature search?	Y
Status of the publication as an inclusion criterion?	Y (English-only)
List of studies (included and excluded) provided?	Y/N (no list of excluded studies)
Characteristics of included provided?	Y
Scientific quality of the included studies assessed and reported?	Y
Scientific quality used in formulating conclusions?	Y
Methods used to combine the findings appropriate?	Y

continued

TABLE B-4 Continued

Likelihood of publication bias assessed?	Y
Conflict of interest stated?	Y/N (COI of the systematic review authors was provided but not provided for included studies)
Author, year	Nwaru et al., 2014
Aims/Key questions	To provide up-to-date estimates of the prevalence of allergy to cow milk, egg, wheat, soy, peanut, tree nuts, fish, and shellfish in Europe.
Study eligibility criteria	Inclusion criteria: • Types of studies: Systematic reviews and meta-analyses, cohort studies, case-control studies, cross-sectional studies, and routine health care studies published in Europe. • Types of participants: All ages; population-based. • Primary outcomes: Allergy to cow milk, egg, wheat, soy, peanut, tree nuts, fish, and shellfish. Assessments based on self-report, SPT, sIgE, OFC/DBPCOFC, or convincing clinical history (i.e., outcomes confirmed by a convincing clinical judgment by a physician without food challenge). Exclusion criteria: • Types of studies: Review and discussion papers, non-research letters and editorials, case studies and case series, animal studies, and all randomized controlled trials.
Literature search dates or year range	January 2000 to September 30, 2012
Number of food allergy studies included	65 (based on 50 primary studies)
Synthesis methods	Summary tables, narrative text, meta-analysis
Key findings	Self-reported food allergy: The overall pooled estimates for all age groups of self-reported lifetime prevalence of allergy to cow milk, egg, wheat, soy, peanut, tree nuts, fish, and shellfish were 6.0% (95% CI: 5.7%-6.4%), 2.5% (2.3%-2.7%), 3.6% (3.0%-4.2%), 0.4% (0.3%-0.6%), 1.3% (1.2%-1.5%), 2.2% (1.8%-2.5%), and 1.3% (0.9%-1.7%), respectively. Food-challenge-defined food allergy: The prevalence of food-challenge-defined allergy to cow milk, egg, wheat, soy, peanut, tree nuts, fish, and shellfish was 0.6% (0.5%-0.8%), 0.2% (0.2%-0.3%), 0.1% (0.01%-0.2%), 0.3% (0.1%-0.4%), 0.2% (0.2%-0.3%), 0.5% (0.08%-0.8%), 0.1% (0.02%-0.2%), and 0.1% (0.06%-0.3%).

TABLE B-4 Continued

Limitations	Significant heterogeneity between the studies. Limited generalizability (limited to European studies published after 2000).
AMSTAR rating	
An a priori design?	Y
Duplicate study selection and data extraction?	Y
Comprehensive literature search?	Y
Status of the publication as an inclusion criterion?	Y
List of studies (included and excluded) provided?	Y/N (no list of excluded studies)
Characteristics of included provided?	Y
Scientific quality of the included studies assessed and reported?	Y
Scientific quality used in formulating conclusions?	Y
Methods used to combine the findings appropriate?	Y
Likelihood of publication bias assessed?	N
Conflict of interest stated?	Y/N (COI of the systematic review authors was provided but not provided for included studies)
Author, year	Greenhawt et al., 2013
Aims/Key questions	To understand the racial and ethnic disparities in food allergy in the US.
Study eligibility criteria	Inclusion criteria: • Types of studies: English-language articles with data from the US and research that presented original data related to racial/ethnic disparity in reported or diagnosed food allergy (including food sensitization), prevalence, treatment, or clinical course. Exclusion criteria: • Types of studies: Systematic reviews, meta-analyses, abstracts, gray literature, and non-US studies.
Literature search dates or year range	Not provided
Number of food allergy studies included	20
Synthesis methods	Summary tables, narrative text

continued

TABLE B-4 Continued

Key findings	None of the studies used OFC/DBPCOFC to assess food allergy.
	In 12 studies, blacks (primarily children) had significantly increased adjusted odds of food sensitization or significantly higher proportion or odds of food allergy by self-report, discharge codes, or clinic-based chart review than did white children.
Limitations	Major differences in study methodology and reporting precluded calculation of a pooled estimate of effect.
	Food allergy outcomes were measured indirectly.
	Low AMSTAR rating.
AMSTAR rating	
An a priori design?	Y
Duplicate study selection and data extraction?	Y
Comprehensive literature search?	N (did not state the literature search dates or range)
Status of the publication as an inclusion criterion?	N
List of studies (included and excluded) provided?	Y/N (list of excluded studies not provided)
Characteristics of included provided?	Y
Scientific quality of the included studies assessed and reported?	N
Scientific quality used in formulating conclusions?	N
Methods used to combine the findings appropriate?	N
Likelihood of publication bias assessed?	N
Conflict of interest stated?	Y/N (COI of the systematic review authors was provided but not provided for included studies)

TABLE B-4 Continued

Author, year	Lee et al., 2013
Aims/Key questions	To summarize the current literature on food allergy in Asia and compare it with Western populations.
Study eligibility criteria	Inclusion criteria: • Types of studies: Reviews, epidemiological/prevalence studies, clinical studies, anaphylaxis studies, case series/reports. • Types of participants: Asian populations. • Outcomes: Food allergy determined by self-report, SPT, food elimination testing, DBPCOFC, convincing history, food avoidance, sIgE, physician diagnosis, or OFC. Exclusion criteria: • Types of studies: Articles from the Middle East and Turkey; non-English studies.
Literature search dates or year range	January 2005 to December 2012
Number of food allergy studies included	53
Synthesis methods	Summary table, narrative text
Key findings	The overall prevalence of food allergy in Asia is somewhat comparable to the West. However, the types of food allergy differ in order of relevance. Shellfish is the most common food allergen from Asia. The prevalence of peanut allergy in Asia is extremely low compared to the West. Among young children and infants, egg and cow milk allergy are the two most common food allergies, with prevalence data comparable to Western populations. Wheat allergy, though uncommon in most Asian countries, is the most common cause of anaphylaxis in Japan and Korea, and is increasing in Thailand.
Limitations	Low AMSTAR rating
AMSTAR rating	
An a priori design?	Y
Duplicate study selection and data extraction?	N
Comprehensive literature search?	N (did not supplement the database searches)
Status of the publication as an inclusion criterion?	N
List of studies (included and excluded) provided?	Y/N (did not include list of excluded studies)

continued

TABLE B-4 Continued

Characteristics of included provided?	Y/N (not for all 53 studies)
Scientific quality of the included studies assessed and reported?	N
Scientific quality used in formulating conclusions?	N
Methods used to combine the findings appropriate?	Not applicable (findings were not combined)
Likelihood of publication bias assessed?	N
Conflict of interest stated?	N

Author, year	Panesar et al., 2013
Aims/Key questions	To understand and describe the epidemiology of anaphylaxis from any cause in Europe and describe how these characteristics vary by person, place, and time.
Study eligibility criteria	Inclusion criteria: • Types of studies: Systematic reviews and/or meta-analyses, cohort studies, cross-sectional studies, case-control studies, and routine health care studies. • Primary outcomes: Incidence, prevalence, and trends over time of anaphylaxis in Europe. Exclusion criteria: • Types of studies: Reviews, discussion papers, nonresearch letters and editorials, case studies, and case series plus animal studies.
Literature search dates or year range	January 1, 2000, to September 30, 2012
Number of food allergy studies included	49 (3 included in meta-analysis) Only 10 were food allergy studies and none of these was in the meta-analysis
Synthesis methods	Summary tables, narrative text, meta-analysis
Key findings	Meta-analysis yielded a pooled estimated prevalence of anaphylaxis, due to any cause, of 0.3% (95% CI 0.1%-0.5%). Ten studies found that the proportions of food allergy reactions that resulted in anaphylaxis ranged from 0.4% to 39.9%. One study of 163 children found the food allergens that most commonly resulted in anaphylaxis were cow milk (29%), hen egg (25%), hazelnut (5%), peanut (4%), kiwi (4%), walnut (4%), pine nut (3%), fish (3%), wheat (2%), soy (2%), shrimp (2%), apricot (2%), and sesame (2%).

TABLE B-4 Continued

Limitations	No discussion of how food allergy was determined. Very few studies were on food allergy. Limited to European populations.	
AMSTAR rating		
An a priori design?		Y
Duplicate study selection and data extraction?		Y
Comprehensive literature search?		Y
Status of the publication as an inclusion criterion?		Y
List of studies (included and excluded) provided?		Y
Characteristics of included provided?		Y
Scientific quality of the included studies assessed and reported?		Y
Scientific quality used in formulating conclusions?		Y
Methods used to combine the findings appropriate?		Y
Likelihood of publication bias assessed?		N
Conflict of interest stated?		Y/N (COI of the systematic review authors was provided but not provided for included studies)
Author, year	Umasunthar et al., 2013	
Aims/Key questions	To estimate the incidence of fatal food-induced anaphylaxis for people with food allergy and relate this to other mortality risks in the general population.	
Study eligibility criteria	Inclusion criteria: • Study design: Registries, databases, or cohort studies including ≥1 case of fatal food anaphylaxis. • Participants: A defined population where an assumed population rate of food allergy could be applied. • Follow-up: To enable calculation of total person-years of observation, the authors included studies that specified either total population and duration of data collection or anaphylaxis incidence rate. • Outcomes: Reports of number of fatal food anaphylaxis events during the follow-up period. Exclusion criteria: • Fatalities neither probably nor definitely due to anaphylaxis, in the judgment of the original study authors. • Time period not defined. • Population in which food anaphylaxis cases occurred could not be quantified.	

continued

TABLE B-4 Continued

Literature search dates or year range	January 1946 to September 5, 2012
Number of food allergy studies included	13
Synthesis methods	Summary table, meta-analysis
Key findings	Meta-analysis estimates the incidence rate of fatal food anaphylaxis in a food-allergic person as: • 1.81 (95% CI: 0.94-3.45; range 0.63-6.68) per million person-years (micromorts) based on 10 studies • 3.25 (95% CI: 1.73-6.10; range 0.94-15.75) micromorts in those ages 0 to 19 based on 10 studies • 2.13 (95% CI: 1.09-4.16; range 1.03-8.77) micromorts for peanut allergy based on seven studies In sensitivity analysis with different estimated food allergy prevalence, the incidence varied from 1.35 to 2.71 per million person-years.
Limitations	Study quality was mixed, and study results had high heterogeneity, possibly due to variation in food allergy prevalence and data collection methods. Study authors were unable to exclude the possibility of a systematic bias operating across different studies, in either the acquisition and coding of fatal food anaphylaxis data or the estimation of food allergy prevalence.
AMSTAR rating	
An a priori design?	Y
Duplicate study selection and data extraction?	Y
Comprehensive literature search?	Y
Status of the publication as an inclusion criterion?	Y
List of studies (included and excluded) provided?	Y/N (list of excluded studies was not provided)
Characteristics of included provided?	Y
Scientific quality of the included studies assessed and reported?	Y
Scientific quality used in formulating conclusions?	Y
Methods used to combine the findings appropriate?	Y
Likelihood of publication bias assessed?	Y
Conflict of interest stated?	Y/N (COI of the systematic review authors was provided but not provided for included studies)

TABLE B-4 Continued

Author, year	Chafen et al., 2010
Aims/Key questions	To systematically review the evidence on the prevalence of food allergies.
Study eligibility criteria	Inclusion criteria: • The initial inclusion criteria were broad and included prior systematic reviews, meta-analyses, or both, and studies presenting original data related to the prevalence, diagnosis, management, or prevention of food allergy. After assessing the relative quantities of studies on these topics, the authors restricted studies of prevalence to those with population-based samples (and systematic reviews of such studies); studies of diagnostic tests to those that presented sufficient data to calculate both sensitivity and specificity, had a prospective, defined study population, and used food challenge as a criterion standard; and studies of management and prevention to those that were either controlled trials (both randomized and nonrandomized) or systematic reviews.
Literature search dates or year range	January 1988 to September 2009
Number of food allergy studies included	6 studies on prevalence of food allergy
Synthesis methods	Narrative text

continued

TABLE B-4 Continued

Key findings	One meta-analysis on incidence and prevalence. • The pooled estimate of prevalence of cow milk allergy was 3.5% (95% CI: 2.9%-4.1%) by self-report; 0.6% to 0.9% from SPT, sIgE, and DBPCOFC. • The pooled estimates (%, 95% CI) for self-report and other methods were: 1.3% (95% CI: 1.0%-1.6%) versus 0.3% to 0.9% (egg); 0.75% (95% CI: 0.6%-0.9%) versus 0.75% (peanut); 0.6% (95% CI: 0.5%-0.7%) versus 0.2% to 0.3% (fish); and 1.1% (95% CI: 1.0%-1.2%) versus 0.6% (shellfish). Three population-based studies on change in prevalence over time in the UK, Canada, and the US. • The UK study found the parent-reported prevalence of peanut allergy increased from 0.5% in 1989 to 1.0% in 1994-1996 (P=0.20), and the prevalence of IgE antibodies increased from 1.1% to 3.3% (P=0.001). • In Canada, prevalence of peanut allergy was 1.5% in 2000-2002 and increased to 1.63% in 2005-2007 (non-significant difference) (based on parent-report, SPT, sIgE, and food challenge). • In the US, authors estimated that 3.3% of US children had food allergies in 1997 versus 3.9% in 2007 (statistically significant difference). Overall Findings: • Food allergy affects more than 1% to 2% but less than 10% of the population. • It is unclear whether the prevalence of food allergies is increasing.
Limitations	• Heterogeneity in the criteria used for the diagnosis of food allergy made comparisons of prevalence across studies dependent on the methods used for the diagnosis and prevented data pooling. • Authors were unable to perform formal evaluations for publication bias due to the heterogeneity of the included studies.

AMSTAR rating	
An a priori design?	Y
Duplicate study selection and data extraction?	Y
Comprehensive literature search?	Y
Status of the publication as an inclusion criterion?	Y (limited to English-only articles)
List of studies (included and excluded) provided?	N
Characteristics of included provided?	N
Scientific quality of the included studies assessed and reported?	Y
Scientific quality used in formulating conclusions?	Y

TABLE B-4 Continued

Methods used to combine the findings appropriate?	Not applicable (findings on prevalence were not combined)
Likelihood of publication bias assessed?	N
Conflict of interest stated?	Y/N (COI of the systematic review authors was provided but not provided for included studies)

Author, year	Zuidmeer et al., 2008
Aims/Key questions	To assess the prevalence of allergies to plant food according to the different subjective and objective assessment methods.
Study eligibility criteria	Inclusion criteria: • Types of studies: Population-based cross-sectional and cohort studies. • Primary outcomes: Food allergy (OFC/DBPCOFC), food sensitization (SPT, sIgE), or perceived food allergy (parent-/self-report). Exclusion criteria: • Types of studies: Case-control studies; studies in selected patient groups (e.g., asthma or eczema patients); studies performed in clinical settings; studies that had enriched study samples with patients with allergy (for further clinical studies); or articles that did not report the sample size.
Literature search dates or year range	January 1990 to December 2006
Number of food allergy studies included	36 (33 publications)
Synthesis methods	Summary tables, meta-analysis

continued

TABLE B-4 Continued

Key findings	Based on 4 studies using food challenge tests, the prevalence of allergy to fruits ranged from 0.1% to 4.3%. Based on 2 studies using food challenge tests, the prevalence of allergy to vegetables ranged from 0.1% to 0.3%. Based on 3 studies using food challenge tests, the prevalence of allergy to nuts ranged from 0.1% (almond) to 4.3% (hazelnut). Both for challenge tests and for sensitization assessed by SPT, the highest prevalence estimates of more than 4% were found for hazelnut. Two studies from the UK and one from Germany reported positive wheat challenge tests in children with a prevalence as high as 0.5%. In adults, the prevalence of sensitization to wheat (assessed by IgE) was >3% in several studies. In adults and adolescents, the highest prevalence estimates of allergy to soy were found in three Swedish studies (sensitization assessed by IgE as high as almost 3%). Studies from all other countries showed prevalences well below 1% regardless of method used or age group. Meta-analyses showed significant heterogeneity between studies regardless of food item or age group. In adults, there was significant heterogeneity (P<0.001) among the seven studies regarding perception of allergy caused by fruits (summary prevalence estimate, 1.22%; 95% CI: 0.82%-1.63%), vegetables (six studies: 0.98%; 95% CI: 0.52%-1.45%), and wheat (five studies: 0.40%; 95% CI: 0.21%-0.59%), as well as for sensitization against wheat (assessed by IgE in five studies: 2.08%; 95% CI: 0.87%-3.29%). Similarly, among studies in children, the heterogeneity was significant (P<0.001) for perception of allergy caused by tree nuts (five studies: 0.52%; 95% CI: 0.20%-0.85%) or soy (seven studies: 0.34%; 95% CI: 0.12%-0.56%), whereas the heterogeneity was of a lower level but still significant (P=5.016) among the five studies assessing sensitization against wheat by SPT (0.43%; 95% CI: 0.16%-0.70%).

TABLE B-4 Continued

Limitations	Few studies used OFC or DBPCOFC to determine food allergy. Meta-analysis was done only when five or more studies were available, so, due to the lack of studies using OFC or DBPCOFC, meta-analysis was done only for studies that determined food allergy by SPT, sIgE, or self-report. The authors could not rule out that studies were missed, particularly from non-European or non-American journals. The comparison of prevalence estimates from different studies is hampered by using different types of prevalence. A limitation of the interpretation of findings on allergic sensitization may be that positive IgE or SPT results to plant-derived foods can be a result of cross-reactivity to pollen. Consequently, the prevalence of food allergy may rise or fall with the presence of the sensitizing pollen in the study area, which depends on the season and climate and may vary from year to year. Fairly low AMSTAR rating.
AMSTAR rating	
An a priori design?	Y
Duplicate study selection and data extraction?	Y (study selection)/ Not clear for data extraction
Comprehensive literature search?	N (searched only one database)
Status of the publication as an inclusion criterion?	N
List of studies (included and excluded) provided?	Y/N (no list of excluded studies)
Characteristics of included provided?	Y
Scientific quality of the included studies assessed and reported?	N
Scientific quality used in formulating conclusions?	N
Methods used to combine the findings appropriate?	Y
Likelihood of publication bias assessed?	N
Conflict of interest stated?	Y/N (COI of the systematic review authors was provided but not provided for included studies)

continued

TABLE B-4 Continued

Author, year	Rona et al., 2007
Aims/Key questions	To assess the prevalence of food allergy by performing a meta-analysis according to the method of assessment used.
Study eligibility criteria	Inclusion criteria: • Primary outcomes: Self-reported symptoms, specific IgE positive, specific skin prick test positive, symptoms combined with sensitization, and food challenge studies. Exclusion criteria: • Types of studies: Studies restricted to the prevalence of food allergy in groups with asthma, eczema, or allergic rhinitis and those performed in selected patients in a clinical setting. Also excluded studies using a case control design if it did not provide a prevalence estimate for the community, and duplicate publications. Excluded articles when the original community sample was enriched with a sample including patients, or the sample size was not provided.
Literature search dates or year range	January 1990 to December 2005
Number of food allergy studies included	51
Synthesis methods	Narrative text, summary tables, meta-analysis
Key findings	The studies showed marked heterogeneity regardless of type of assessment or food item considered, and in most analyses this persisted after age stratification. Self-reported prevalence of food allergy varied from 1.2% to 17% for milk, 0.2% to 7% for egg, 0% to 2% for peanuts and fish, 0% to 10% for shellfish, and 3% to 35% for any food. Prevalence of food allergy determined by OFC or DBPCOFC: • The prevalence for fish was near 0% (based on two studies). • The prevalence for milk varied from 0% to 3% (based on seven studies). A marked heterogeneity was observed for milk in preschool children, the only group for which sufficient studies were available for useful analysis. • The prevalence for egg varied from 0% to 1.7% (based on three studies). • The prevalence for any food varied from 1% to 10.8% (based on six studies). Meta-analysis results were presented graphically in this paper.

TABLE B-4 Continued

Limitations	In the overall estimate of the prevalence of food allergy related to food challenge, the authors were unable to omit positive challenges to nonallergic food hypersensitivity; thus, these estimates may give an overestimate of prevalence. Marked heterogeneity among studies.	
AMSTAR rating		
An a priori design?		Y
Duplicate study selection and data extraction?		Y
Comprehensive literature search?		Y
Status of the publication as an inclusion criterion?		N
List of studies (included and excluded) provided?		Y/N (list of excluded studies not provided)
Characteristics of included provided?		N
Scientific quality of the included studies assessed and reported?		N
Scientific quality used in formulating conclusions?		N
Methods used to combine the findings appropriate?		Y
Likelihood of publication bias assessed?		N
Conflict of interest stated?		Y/N (COI of the systematic review authors was provided but not provided for included studies)

NOTE: CDC = Centers for Disease Control and Prevention; CI = confidence interval; DBPCOFC = double-blind, placebo-controlled oral food challenge; IgE = immunoglobulin E; NHANES = National Health and Nutrition Examination Survey; NHIS = National Health Interview Survey; sIgE = food-specific serum IgE; SPT = skin prick test; UK = United Kingdom; US = United States.

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Appendix C

Risk Determinants Literature Search Strategy

Electronic literature searches of published systematic reviews (from 2010 to September 2015) and primary studies (from 2012 to September 2015) indexed in Medline, Cochrane Database of Systematic Reviews, EMBASE, and ISI Web of Science were conducted. For systematic reviews, a broad search was conducted to identify all systematic reviews with or without meta-analysis from 2010 onward related to food allergies or food sensitizations without restrictions to any interventions or exposures. For primary studies, search strategies in European Academy of Allergy & Clinical Immunology (EAACI) (de Silva et al., 2014) and Marrs et al. systematic reviews (Marrs et al., 2013) were adopted. The EAACI search strategies were developed to identify all randomized controlled trials, quasi-randomized controlled trials, controlled clinical trials, controlled before-and-after studies, interrupted time series studies, and prospective cohort studies that were primarily concerned with preventing sensitization to food(s) and/or the development of food allergy. The Marrs et al. search strategy was intended to capture any study designs describing food allergy or sensitization overall and to individual foods (milk, egg, peanut, tree nuts, fish, wheat, sesame, shellfish, and seafood) combined with search terms of factors that directly or indirectly influence microbial exposure (Marrs et al., 2013). All searches were restricted to human studies that were published in the English language from 2012 onward. Duplicate citations across databases were removed before screening. Medline searches conducted for this report for systematic reviews and individual studies are in Table C-1. Medline searches were used to develop the search strategies for the EMBASE and Web of Science databases.

Abstrackr software (abstrackr.cebm.brown.edu), Endnote, and Microsoft Excel were used to manage the search outputs, screening, and data abstraction. After a training session to ensure understanding of the inclusion and exclusion criteria, title/abstract screening was conducted independently by two reviewers using a screening form that listed the inclusion and exclusion criteria and allowed selection of reasons for exclusion. A third reviewer reconciled the discrepant title/abstract selections. Full-text articles of all accepted title/abstracts were then retrieved and screened by one reviewer based on the study eligibility criteria. Second-level screening of full text articles was conducted by two reviewers and differences reconciled by a third reviewer. Boxes C-1 and C-2 list the study inclusion and exclusion criteria, respectively. Figure C-1 illustrates the study selection flow. Summary tables for the systematic reviews and studies selected for the evidence-based review are included in Tables C2-C6.

TABLE C-1 Medline Search Strategy to Identify Relevant Literature

Search Number	Search Terms
	a. Systematic Reviews Search Strategy
1	exp food hypersensitivity/ or exp egg hypersensitivity/ or exp milk hypersensitivity/ or exp nut hypersensitivity/ or exp peanut hypersensitivity/ or exp wheat hypersensitivity/
2	(food$ adj2 (allergy$ or hypersensitivity)).mp.
3	((milk or egg$ or shellfish or fish or nut$ or peanut$ or wheat or soybean$ or seasame or seafood$) adj1 (allerg$ or hypersensitivity or sensitization)).mp.
4	(sensitization or hypersensitivity).mp.
5	(food$ or diet$).mp.
6	4 and 5 (13121)
7	1 or 2 or 3 or 6 (15068)
8	(rat or rats or cow or cows or chicken? or horse or horses or mice or mouse or bovine or animal?).ti.
9	exp animals/not humans.sh.
10	8 or 9
11	7 not 10
12	MEDLINE.tw.
13	systematic review.tw.
14	meta analysis.pt.
15	or/12-14
16	11 and 15
17	limit 16 to (English language and yr="2010 -Current")
	b. Primary Studies: EAACI Search Strategy
1	exp food hypersensitivity/ or exp egg hypersensitivity/ or exp milk hypersensitivity/ or exp nut hypersensitivity/ or exp peanut hypersensitivity/ or exp wheat hypersensitivity/
2	(food$ adj2 (allergy$ or hypersensitivity)).mp.
3	((milk or egg$ or shellfish or fish or nut$ or peanut$ or wheat or soybean$ or seasame or seafood$) adj1 (allerg$ or hypersensitivity or sensitization)).mp.
4	(sensitization or hypersensitivity).mp.
5	(food$ or diet$).mp.
6	4 and 5 (13121)
7	1 or 2 or 3 or 6 (15068)
8	(rat or rats or cow or cows or chicken? or horse or horses or mice or mouse or bovine or animal?).ti.

continued

TABLE C-1 Continued

Search Number	Search Terms
9	exp animals/ not humans.sh.
10	8 or 9
11	7 not 10
12	randomized controlled trial.pt.
13	controlled clinical trial.pt.
14	randomized.ab.
15	placebo.ab.
16	clinical trials as topic.sh.
17	randomly.ab.
18	trial.ti.
19	or/16-22
20	intervention?.ti. or (intervention? adj6 (clinician? or collaborat$ or community or complex or DESIGN$ or doctor? or educational or family doctor? or family physician? or family practitioner? or financial or GP or general practice? or hospital? or impact? or improv$ or individuali?e? or individuali?ing or interdisciplin$ or multicomponent or multi-component or multidisciplin$ or multidisciplin$ or multifacet$ or multi-facet$ or multimodal$ or multimodal$ or personali?e? or personali?ing or pharmacies or pharmacist? or pharmacy or physician? or practitioner? or prescrib$ or prescription? or primary care or professional$ or provider? or regulatory or regulatory or tailor$ or target$ or team$ or usual care)).ab.
21	(pre-intervention? or preintervention? or "pre intervention?" or postintervention? or postintervention? or "post intervention?").ti,ab.
22	(hospital$ or patient?).hw. and (study or studies or care or health$ or practitioner? or provider? or physician? or nurse? or nursing or doctor?).ti,hw.
23	demonstration project?.ti,ab.
24	(pre-post or "pre test$" or pretest$ or posttest$ or "post test$" or (pre adj5 post)).ti,ab.
25	(pre-workshop or post-workshop or (before adj3 workshop) or (after adj3 workshop)).ti,ab.
26	trial.ti. or ((study adj3 aim?) or "our study").ab.
27	(before adj10 (after or during)).ti,ab.
28	("quasi-experiment$" or quasiexperiment$ or "quasi random$" or quasirandom$ or "quasi control$" or quasicontrol$ or ((quasi$ or experimental) adj3 (method$ or study or trial or design$))).ti,ab,hw.
29	("time series" adj2 interrupt$).ti,ab,hw.

TABLE C-1 Continued

Search Number	Search Terms
30	(time points adj3 (over or multiple or three or four or five or six or seven or eight or nine or ten or eleven or twelve or month$ or hour? or day? or "more than")).ab.
31	pilot.ti.
32	Pilot projects/
33	(clinical trial or controlled clinical trial or multicenter study).pt.
34	(multicentre or multicenter or multi-centre or multi-center).ti.
35	random$.ti,ab. or controlled.ti.
36	(control adj3 (area or cohort? or compare? or condition or design or group? or intervention? or participant? or study)).ab. not (controlled clinical trial or randomized controlled trial).pt.
37	comment on.cm. or review.ti,pt. or randomized controlled trial.pt.
38	or/24-41
39	exp cohort studies/
40	cohort$.tw.
41	controlled clinical trial.pt.
42	epidemiologic methods/
43	exp case-control studies/
44	(case$ and control$).tw.
45	or/43-48
46	11 and 19
47	11 and 38
48	11 and 45
49	or/46-48
50	limit 49 to yr="2012 -Current"
51	limit 50 to "review articles"
52	50 not 51
	c. Primary Studies: Marrs et al. Search Strategy
1	Measles/ or measles.mp,
2	exp Mumps/ or mumps.mp,
3	Whooping Cough/ or whooping cough.mp,
4	exp Pneumonia/ or pneumonia.mp,
5	exp Chickenpox/ or chickenpox.mp,
6	hepatitis/ or hepatitis a/ or exp hepatitis b/

continued

TABLE C-1 Continued

Search Number	Search Terms
7	Hepatitis A/ or exp Hepatitis B/
8	hepatitis.mp,
9	exp Herpes Simplex/ or herpes simplex.mp,
10	exp Rubella/ or rubella.mp,
11	exp Helicobacter pylori/ or helicobacter pylori.mp,
12	exp Tuberculosis/ or tuberculosis.mp,
13	exp Mycobacterium bovis/
14	exp Helminthiasis/
15	helminthiasis.mp,
16	exp Helminths/
17	helminths.mp,
18	exp Necator americanus/
19	Necator americanus.mp,
20	exp Trichuris/ or trichuris.mp,
21	exp Ascaris lumbricoides/ or Ascaris lumbricoides.mp,
22	exp Schistosomiasis/ or Schistosomiasis.mp,
23	exp Enterobius/
24	enterobius vermicularis.mp,
25	exp Bacterial Infections/
26	bacterial infection*.mp,
27	or/1-26
28	hygiene/ or skin care/
29	hygiene.mp,
30	hygiene hypothesis.mp,
31	exp Anthroposophy/
32	anthroposoph*.mp,
33	Child Day Care Centers/
34	day care.mp,
35	Siblings/
36	sibling*.mp,
37	Birth Order/
38	birth order.mp,
39	nurser*.mp,

TABLE C-1 Continued

Search Number	Search Terms
40	agriculture/ or animal husbandry/
41	agriculture.mp,
42	farming.mp,
43	farms.mp,
44	farm.mp,
45	Animals, Domestic/
46	pets.mp,
47	pet.mp,
48	Cats/
49	cats.mp,
50	cat.mp,
51	Dogs/
52	dog.mp,
53	dogs.mp,
54	exp Endotoxins/
55	endotoxin*.mp,
56	exp Probiotics/
57	probiotic*.mp,
58	lactobacillus.mp,
59	exp Lactobacillus/
60	intestinal microflora.mp,
61	mycobacterium vaccae.mp,
62	Prebiotics/
63	pre-biotic*.mp,
64	prebiotic*.mp,
65	pro-biotic*.mp,
66	exp Anti-Bacterial Agents/
67	antibiotic*.mp,
68	Disinfectants/ or disinfectant.mp,
69	vaccination.mp,
70	vaccinat*.mp,
71	unpasteuri* milk.mp,
72	unpasteuri* cow* milk.mp,

continued

TABLE C-1 Continued

Search Number	Search Terms
73	pasteuri* milk.mp,
74	pasteuri* cow* milk.mp,
75	raw milk.mp,
76	raw cow* milk.mp,
77	unhomogeni* milk.mp,
78	unhomogeni* cow* milk.mp,
79	un-pasteuri* milk.mp,
80	un-homogeni* milk.mp,
81	or/28-80
82	27 or 81
83	exp food hypersensitivity/ or exp egg hypersensitivity/ or exp milk hypersensitivity/ or exp nut hypersensitivity/ or exp peanut hypersensitivity/ or exp wheat hypersensitivity/
84	(food$ adj2 (allergy$ or hypersensitivity)).mp.
85	((milk or egg$ or shellfish or fish or nut$ or peanut$ or wheat or soybean$ or seasame or seafood$) adj1 (allerg$ or hypersensitivity or sensitization)).mp,
86	(sensitization or hypersensitivity).mp,
87	(food$ or diet$).mp,
88	86 and 87
89	83 or 84 or 85 or 88
90	88 and 89
91	Cesarean Section/
92	caesarian section.mp,
93	cesarian section.mp,
94	mode of delivery.mp,
95	microbiota.mp,
95	82 or 91 or 92 or 93 or 94 or 95
96	90 and 95
97	limit 96 to “review articles”
98	96 not 97
99	limit 98 to yr=“2012 -Current”

BOX C-1
Study Inclusion Criteria

Studies that reported food allergy or sensitization outcomes, including
- Food challenge outcomes,
- Physician-diagnosed food allergy,
- Reported doctor diagnosis of food allergy,
- Food sensitization diagnosed by either skin prick testing (SPT) or elevated food-specific serum immunoglobulin E (sIgE) levels, and
- Self-reported food allergies or sensitizations.

Study designs of interest:
- Systematic reviews with or without meta-analysis
- Randomized controlled trials
- Quasi-randomized controlled trials and controlled clinical trials (defined as studies where the comparison group is not fully randomized)
- Controlled before-and-after studies (only where a clearly defined comparison group is available prospectively) and interrupted time series studies
- Prospective cohort studies
- Interrupted time series studies
- Case-control studies
- Cross-sectional studies

Determinants and prevention factors of interest:
- Preconception factors
- Lactation
- Food introduction
- Microbiome/prebiotics/probiotics
- Hygiene hypothesis related factors (parity, living environment, pets, siblings, cesarean section delivery, prenatal and postnatal antibiotics use),
- Nutrient factors: vitamin D, fatty acid profiles (e.g., omega-3), folic acid
- Maternal dietary intake during pregnancy, lactation, child, adult
- Infant breastfeeding versus formula feeding
- Genetics, epigenetics (gene-environment interactions)
- Epithelial barrier function

BOX C-2
Study Exclusion Criteria

Studies seeking to prevent potential manifestations of food allergy (e.g., atopic eczema/dermatitis or asthma) but not including an explicit diagnosis of sensitization to food or food allergy or studies investigating celiac disease were excluded, as well as management guidance documents, narrative reviews, letters to the editor, commentaries, studies that used animal or in vitro models, ecological studies, and studies of transplant patients.

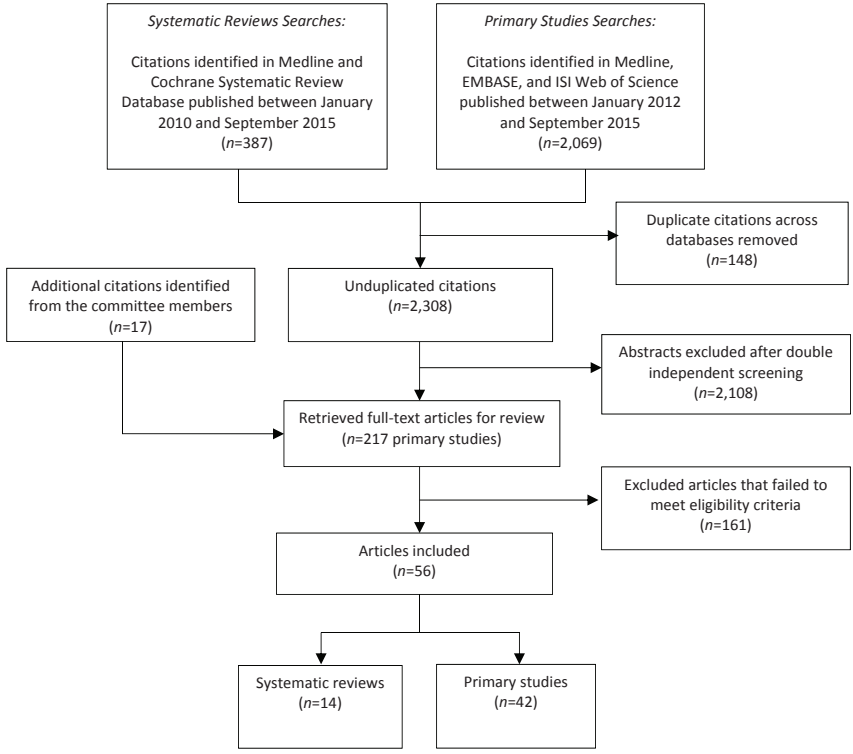

FIGURE C-1 Literature search and study selection process.

TABLE C-2a BEGINS ON THE NEXT PAGE

TABLE C-2a Microbial Exposure Hypothesis (Randomized Controlled Trials)

Author, Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Prebiotics/Probiotics				
Ivakhnenko and Nyankovskyy, 2013	Randomized controlled trial (formula feeding) + 1 BF group (nonrandomized), Ukraine	Healthy, term newborns	80 BF infants; 160 formula fed infants (80 formula enriched with the specific mixture of oligo-saccharides; 80 standard formula)	18 months

NOTE: BF = breastfed; CI = confidence interval; GI = gastrointestinal; OFC = oral food challenge.

[a] **Bold** indicates statistical significance at P<0.05. Results were reported as odds ratio (95% confidence interval) unless otherwise noted. Adjusted results were extracted in the summary table unless otherwise noted.

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
Allergic reactions to food (not defined) Allergic reactions to cow milk protein (not defined) GI symptoms of food allergy (not defined)	BF (group 1) versus formula enriched with oligosaccharides (scGOS/lcFOS; 9:1; 8 g/L) (group 2) versus standard formula (group 3)	Allergic reactions to food: **2/51 (3.92%) versus 3/62 (4.84%) versus 9/53 (16.98%); P<0.05** Allergic reactions to cow milk: **1/51 (1.96%) versus 2/62 (3.23%) versus 8/53 (15.09%); P<0.05** GI symptoms of food allergy: **1/51 (1.96%) versus 2/62 (3.23%) versus 7/53 (13.21%); P<0.05**	51 (63.7%), 62 (77.5%), and 53 (66.3%) infants in groups 1, 2, and 3, respectively, completed the study. Analysis was done in completers only. Duration and exclusivity of BF were not measured. Food allergy not confirmed by OFC.

TABLE C-2b Microbial Exposure Hypothesis (Observational Studies)

Author Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Prebiotics/Probiotics				
Loo et al., 2014	Long-term follow-up of a RCT, Singapore	Asian infants at risk for allergic disease	226	3-5 years
West et al., 2013	Long-term follow-up of an RCT, Sweden	Healthy, term infants with no prior allergic manifestations	121	8-9 years
Route of Delivery				
McGowan et al., 2015	Prospective cohort, Baltimore, Boston, New York City, St. Louis	Children from the Urban Environment and Childhood Asthma (URECA) study	516	1-5 years

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
Ever had food allergy (history of convincing symptoms of food allergy and the presence of IgE allergen) since year 3	Intervention: Cow milk formula supplemented with probiotics (BL999 and LPR) from birth to age 6 months (N=117) Control: Cow milk formula supplemented without probiotics (N=109)	RR=1.1 (0.1-17.0)	245 infants were randomized; 220 (87%) completed 5-year follow-up. The analysis was done in 226 children (number of dropouts by groups was not reported).
IgE-associated food allergy	Intervention: Infant cereals with addition of probiotics (LF19 1×10^8 CFU per serving) from 4 to age 13 months (N=59) Control: Infant cereals without addition of probiotics (N=62)	1.05 (0.14-7.73)	171/179 randomized infants completed the trial; 121 children in the long-term follow-up. More children in the placebo group received antibiotics during intervention than probiotic group (32.3% versus 16.9%, P=0.05). Unadjusted analysis.
Food allergy (N=51) or sensitization (N=286): sIgE to milk, egg, peanut; clinical history	(1) Caesarean section (food allergy versus not allergic) (2) Caesarean section (food sensitized versus not sensitized)	(1) 23.5% versus 31.6%; P=0.31 (2) 31.5% versus 30.9%; P=0.96	Unadjusted analysis.

continued

TABLE C-2b Continued

Author Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Peters et al., 2015	Prospective cohort, Australia	Infants from the HealthNuts study	5,276	1 year
Grimshaw et al., 2014	Prospective nested case-control study, UK	Cases: all infants with food allergy by age of 2 years from the Prevalence of Infant Food Allergy (PIFA) study Controls: age-matched controls from the PIFA study	123 (41 with food allergy; 82 controls)	1-2 years
Luccioli et al., 2014	Prospective cohort, US	Children who participated in the Infant Feeding Practices Study (IFPS) II	1,363	6 years

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
IgE-mediated food allergy = positive OFC in the presence of positive test of sensitization (SPT ≥2 mm or sIgE ≥0.35 kua/L). Separate analysis for single egg allergy (9% of the cohort), multiple food allergies predominantly peanut (3% of the cohort), and multiple food allergies predominantly egg (2% of the cohort), comparing to no allergic disease at baseline.	Caesarean section versus vaginal birth	Single egg allergy: 1.02 (0.81-1.29) Multiple food allergies - peanut: 1.24 (0.86-1.78) Multiple food allergies - egg: 0.93 (0.56-1.60)	5,142 infants underwent SPT to egg, peanut, or sesame and 1,089 infants were eligible for hospital assessment, of whom 908 participated in OFC.
Food allergy determined by SPT, physical exam, clinical history, sIgE, DBPCOFC	Birth by caesarean section (cases versus controls)	31.7% versus 24.4%; P=0.255	Unadjusted analysis except for pet ownership.
Physician-diagnosed food allergy as reported by parent	Caesarean section versus vaginal birth	1.37 (0.84-2.21)	

continued

TABLE C-2b Continued

Author Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Depner et al., 2013	Prospective cohort, Austria, Finland, France, Germany, Switzerland	Children from the Protection against Allergy-Study in Rural Environments (PASTURE) birth cohort	686	Birth to 1 year
Pele et al., 2013	Prospective cohort, France	Respondents to the 2-year follow-up FFQ of the PELAGIE mother–child cohort study	1,487	2 years
Pyrhonen et al., 2013	Retrospective cohort study, Finland	Children identified from the South Karelian Allergy Research Project (SKARP), a population-based study comprising all children of a given age range and living in the same province.	3,181	1-4 years

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
sIgE to food allergens (hen egg, cow milk, peanut, hazlenut, carrot, wheat flour)	Caesarean section	1.18 (0.69-2.03)	793 (378 farm and 415 nonfarm) children were included in the analyses, of whom 686 were included in IgE to food allergens model.
Mother-reported food allergy in children (N=136): 37 had a medical diagnosis of cow milk allergy, 41 had a medical diagnosis of food allergy, and 22 of both, while 36 children had no doctor's diagnosis	Cesarean section (yes versus no)	8.7% versus 9.1%; P=0.10	Nonrespondents (N=1,496) were younger at the birth of the child, less educated, and more likely to smoke. These factors were considered as covariates in the paper. Unadjusted analysis results only.
Physician-diagnosed allergic manifestations: positive specific IgE test, SPT, open food challenge (did not specify which foods)	Caesarean section	1.15 (0.80-1.63)	Large nonresponse rate.

continued

TABLE C-2b Continued

Author Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Dowhower Karpa et al., 2012	Retrospective case-control study, US	Cases: children visiting an allergy specialty clinic for a food allergy–related concern who were also born at the institution's medical center. Age- and sex-matched controls: children visiting primary care practice who were also born at the institution's medical center.	99 case; 192 controls	No data
Antibiotics Use				
Grimshaw et al., 2014	Prospective nested case-control study, UK	Cases: all infants with food allergy by age of 2 years from the PIFA study Controls: age-matched controls from the PIFA study	123 (41 with food allergy; 82 controls)	1-2 years

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
ICD-9-CM coding consistent with food-related allergic reactions and a confirmed presence of food allergies documented by either a positive serum specific IgE test or positive SPT	Caesarean (cases versus controls)	32.2% versus 33.9%; P=0.79	Retrospective chart review. Possible selection bias. Unadjusted analysis results only.
Food allergy determined by SPT, physical exam, clinical history, sIgE, double-blind placebo controlled food challenge	Maternal antibiotic use (cases versus controls)	No significant associations during or after pregnancy or while breastfeeding	Unadjusted analysis except for pet ownership.

continued

TABLE C-2b Continued

Author Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Metsala et al., 2013	Prospective nested case-control study, Finland	Cases: infants who had received a special reimbursement for the cost of special infant formulas based on diagnosed cow milk allergy. Controls: randomly selected and matched for date of birth, sex, and the hospital district of birth.	16,237 case-control pairs	0-2 years
Dowhower Karpa et al., 2012	Retrospective case-control study, US	Cases: children visiting an allergy specialty clinic for a food allergy-related concern who were also born at the institution's medical center. Age-and-sex matched controls: children visiting primary care practice who were also born at the institution's medical center.	99 case; 192 controls	No data

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
Pediatric certification of cow milk allergy based on clinical exam, symptoms, elimination diet, SPT, and elevated serum-specific IgE or open challenge test	(1) Maternal use of antibiotics before pregnancy (2) Maternal use of antibiotics during pregnancy (3) Child's use of antibiotics from birth to 1 month	(1) **1.26 (1.20-1.33)** (2) **1.21 (1.14-1.28)** (3) **1.71 (1.59-1.84)**	
ICD-9-CM coding consistent with food-related allergic reactions and a confirmed presence of food allergy documented by either a positive serum specific IgE test or positive SPT	(1) Neonatal antibiotics (cases versus controls) (2) Peripartum antibiotics (cases versus controls)	(1) 16.2% versus 12.5%; P=0.39 (2) 28.3% versus 28.1%; P=1.0	Retrospective chart review. Possible selection bias. Unadjusted analysis results only.

continued

TABLE C-2b Continued

Author Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Exposure to Animals				
Martin et al., 2015	Prospective cohort, Australia	Infants from the HealthNuts study	4,453 (2,795 without eczema; 1,903 with eczema)	1 year
Peters et al., 2015	Prospective cohort, Australia	Infants from the HealthNuts study	5,276	1 year

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
SPT or sIgE, OFC (egg white, peanut, sesame) or parent report of recent immediate-type reaction	(1) Pet dog among infants without eczema; among infants with eczema	(1) 0.9 (0.6-1.5); 0.7 (0.5-0.9)	Same cohort as Peters et al., 2015, but different analyses and outcome definitions. [Note: cesarean section results were not extracted for this study because for this factor the analysis was unadjusted.]
	(2) Pet cat among infants without eczema; among infants with eczema	(2) 0.9 (0.5-1.6); 0.6 (0.4-0.8)	
IgE-mediated food allergy = positive OFC in the presence of positive test of sensitization (SPT ≥2 mm or sIgE ≥0.35 kua/L). Separate analysis for single egg allergy (9% of the cohort), multiple food allergies, predominantly peanut (3% of the cohort), and multiple food allergies predominantly egg (2% of the cohort), compared to no allergic disease at baseline.	(1) Dogs allowed inside the home versus no dogs	(1) Single egg allergy: 0.76 (0.56-1.05) Multiple food allergies - peanut: **0.40 (0.21-0.73)** Multiple food allergies - egg: 0.59 (0.26-1.34)	5,142 infants underwent SPT to egg, peanut or sesame and 1,089 infants were eligible for hospital assessment, of whom 908 participated in OFC.
	(2) Dogs outside only versus no dogs	(2) Single egg allergy: **1.56 (1.10-2.21)** Multiple food allergies - peanut: 0.82 (0.44-1.54) Multiple food allergies - egg: 0.39 (0.13-1.18)	
	(3) Pet cats versus no dogs	(3) Single egg allergy: 0.80 (0.57-1.12) Multiple food allergies - peanut: 0.83 (0.47-1.47) Multiple food allergies - egg: 0.86 (0.38-1.91)	

continued

TABLE C-2b Continued

Author Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Grimshaw et al., 2014	Prospective nested case-control study, UK	Cases: all infants with food allergy by age of 2 years from the PIFA study Controls: age-matched controls from the PIFA study	123 (41 with food allergy; 82 controls)	1-2 years
Stelmach et al., 2014	Prospective cohort, Poland	Children from the Polish Mother and Child Cohort Study (REPRO_PL cohort)	501	1-2 years
Depner et al., 2013	Prospective cohort, Austria, Finland, France, Germany, Switzerland	Children from the Protection against PASTURE birth cohort	686	Birth to 1 year
Goldberg et al., 2013	Prospective case-cohort study, Israel	Cases: IgE-cow milk allergy children identified from a cohort study (Katz, 2010) Controls: healthy children randomly chosen from the cohort	66 cases 156 controls	2-3 years

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
Food allergy determined by SPT, physical exam, clinical history, sIgE, DBPCOFC	Pet ownership (yes versus no)	1.275 (0.49-3.33)	
Food allergy ever diagnosed by doctor according to international guidelines	Pets at home during pregnancy (yes versus no)	**1.48 (1.02-2.16)**	Frequency of cleaning was not associated with food allergy and was dropped out from multivariate model.
sIgE to food allergens (hen egg, cow milk, peanut, hazlenut, carrot, wheat flour)	(1) Early contact with sheep, goats, hares (2) Farming	(1) 0.92 (0.75-1.13) (2) **2.11 (1.33-3.34)**	793 (378 farm and 415 nonfarm) children were included in the analyses, of whom 686 were included in IgE to food allergens model.
IgE-mediated cow milk allergy defined by a suggestive history of an immediate response, a positive SPT response, and, in most cases, a positive challenge result to cow milk protein	Pets in home (cases versus controls)	26.2% versus 30.1%; P=0.72	Unadjusted analysis.

continued

TABLE C-2b Continued

Author Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Pele et al., 2013	Prospective cohort, France	Respondents to the 2-year follow-up FFQ of the PELAGIE mother–child cohort study	1,487	2 years
Koplin et al., 2012	Prospective cohort, Australia	Infants from the HealthNuts study	4,963	1 year

NOTE: CI = confidence interval; DBPCOFC = double-blind, placebo-controlled oral food challenge; FFQ = food frequency questionnaire; IgE = immunoglobulin E; OFC = oral food challenge; RAST = radioallergosorbent test; RR = relative risk; sIgE = food-specific serum IgE; SPT = skin prick test; UK = United Kingdom; US = United States.

[a] **Bold** indicates statistical significance at P<0.05. Results were reported as odds ratio (95% confidence interval) unless otherwise noted. Adjusted results were extracted in the summary table unless otherwise noted.

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
Mother-reported food allergy in children (N=136): 37 had a medical diagnosis of cow milk allergy, 41 a medical diagnosis of food allergy, and 22 of both, while 36 children had no doctor's diagnosis	Farm animal contact (yes versus no)	8.9% versus 9.1%; P=0.88	Nonrespondents (N=1,496) were younger at the birth of the child, less educated, and more likely to smoke. These factors were considered as covariates in the paper. Unadjusted analysis results only.
IgE-mediated egg allergy: Allergic on formal egg challenge or previous history of clear reaction to egg occurring within 1 month of a positive SPT or RAST	(1) Dog outside only versus no dog (2) Dog allowed inside versus no dog (3) Cat outside only versus no cat (4) Cat allowed inside versus no cat	(1) 1.09 (0.75-1.57) (2) **0.72 (0.52-0.99)** (3) 0.93 (0.49-1.77) (4) 0.75 (0.52-1.09)	Same cohort as Peters et al., 2015 but different analyses and outcome definitions.

TABLE C-3a Allergen Avoidance Hypothesis (Randomized Controlled Trials)

Author Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Breastfeeding				
Ivakhnenko and Nyankovskyy, 2013	Randomized controlled trial (formula feeding) + 1 BF group (nonrandomized), Ukraine	Healthy, term newborns	80 BF infants; 160 formula fed infants (80 formula enriched with the specific mixture of oligosaccharides; 80 standard formula)	18 months
Infant Formula				
Lowe et al., 2011	RCT, Australia	Infants with a family history of allergic disease	620	6, 12, and 24 months

NOTE: BF = breastfed; CI = confidence interval; GI = gastrointestinal; pHWF = partially hydrolyzed whey formula.

[a] **Bold** indicates statistical significance at P<0.05. Results were reported as odds ratio (95% confidence interval) unless otherwise noted. Adjusted results were extracted in the summary table unless otherwise noted.

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
Allergic reactions to food (not defined) Allergic reactions to cow milk protein (not defined) GI symptoms of food allergy (not defined)	BF (group 1) versus formula enriched with oligosaccharides (scGOS/lcFOS; 9:1; 8 g/L) (group 2) versus standard formula (group 3)	Allergic reactions to food: **2/51 (3.92%)** versus **3/62 (4.84%)** versus **9/53 (16.98%); P<0.05** Allergic reactions to cow milk: **1/51 (1.96%)** versus **2/62 (3.23%)** versus **8/53 (15.09%); P<0.05** GI symptoms of food allergy: **1/51 (1.96%) versus 2/62 (3.23%) versus 7/53 (13.21%); P<0.05**	51 (63.7%), 62 (77.5%), and 53 (66.3%) infants in groups 1, 2, and 3, respectively, completed the study. Analysis was done in completers only. Duration and exclusivity of BF were not measured. Food allergy not confirmed by OFC.
Food reaction, SPT (milk, egg, peanut)	Soy-based formula, pHWF, or cow milk formula at cessation of breastfeeding	Positive SPT to cow milk within first 2 years: pHWF versus CMF: 0.79 (0.35-1.77) Soy formula versus CMF: 0.78 (0.32-1.92) Any food reaction: pHWF versus CMF: 0.95 (0.51-1.75) Soy formula versus CMF: 1.21 (0.67-2.19)	

TABLE C-3b Allergen Avoidance (Observational Studies)

Author, Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Maternal Intake During Pregnancy and Lactation				
Bunyavanich et al., 2014	Prospective cohort, US	Mother-child pairs in the Project Viva prebirth cohort recruited from a large multidisciplinary practice	1,277 mother–child pairs	7.9 years (mean)

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
Food allergy to peanut, milk, wheat, egg, and/or soy based on sIgE to the particular food and EpiPen prescribed. Food allergy to peanut was more specifically defined by parent report of convincing symptoms of a peanut allergic reaction (history of peanut allergy AND a cutaneous, respiratory, cardiovascular, gastrointestinal and/or anaphylactic symptom following peanut ingestion).	Maternal intake (total servings per day as measured by FFQ) during first and second trimester of: (1) peanut (2) milk (3) wheat (4) egg (5) soy Intake reported as z-scores	First trimester (1) **0.53 (0.30-0.94)** (2) 0.90 (0.50-1.62) (3) 1.26 (0.75-2.12) (4) 0.76 (0.28-2.08) (5) 0.61 (0.16-2.31) Second trimester (1) 0.88 (0.61-1.27) (2) 1.47 (0.91-2.37) (3) 1.07 (0.62-1.85) (4) 0.77 (0.28-2.15) (5) 1.18 (0.95-1.48)	All ORs are adjusted for child age, sex, breastfeeding history, parental atopy, and maternal education.

continued

TABLE C-3b Continued

Author, Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Frazier et al., 2014	Prospective cohort, US	Boys and girls (born between 1990 and 1994) participating in the Growing Up Today Study 2 (GUTS2) and their mothers. (These are children of women in the Nurse's Health Study II.)	8,205 mother–child pairs	Unclear

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
Peanut or tree nut (walnut, almond, pistachio, cashew, pecan, hazelnut, macadamia, and Brazil nut) allergy in offspring based on maternal confirmation of food allergy diagnosis, review of physical copies of laboratory results of testing (SPT, sIgE, OFC) by two board-certified pediatricians, and confirmation of food allergy in writing from the child's treating physician	Peripregnancy maternal consumption of peanuts or tree nuts: (1) <1 serving/ month (2) 1-3 servings/ month (3) 1-4 servings/ week (4) ≥5 servings/ week	Multivariable OR (1) reference group (2) 0.90 (0.55-1.48) (3) 0.65 (0.43-0.97) (4) 0.58 (0.34-0.99) P_{trend}=0.04	The dietary questionnaires were not specific for the actual dates of the pregnancy but were chosen as the one completed closest to the child's date of birth. Only 45% of the dietary questionnaires were completed during the pregnancy; 76% were within 1 year of the pregnancy. Multivariable models control for continuous maternal age, maternal history of non-nut food allergy, maternal allergic rhinitis, eczema, or asthma, and season at child's birth (spring or summer versus fall or winter).

continued

TABLE C-3b Continued

Author, Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Pele et al., 2013	Prospective cohort, France	Respondents to the 2-year follow-up FFQ of the PELAGIE mother–child cohort study	1,500 mother–child pairs	2 years

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
Mother-reported food allergy in children (N=136): 37 had a medical diagnosis of cow milk allergy, 41 a medical diagnosis of food allergy, and 22 of both, while 36 children had no doctor's diagnosis	(1) Maternal pre-pregnancy consumption of fish (<1 time/month versus 1-4 times/month)	(1) 1.27 (0.72-2.24)	Nonrespondent mothers (N=1,496) were younger at the birth of the child, less educated, and more likely to smoke than the participants (N=1,500). These factors were considered as covariates in the paper. ORs adjusted for: mother's age, maternal education, folic acid supplementation, familial history of asthma/allergy, child's sex, small-for-gestational age, infant's method of feeding, day care attendance, postnatal exposure to tobacco, and child's age at follow-up.
	(2) Maternal pre-pregnancy consumption of fish (<1 time/month versus ≥2 times/week)	(2) 1.48 (0.80-2.76)	
	(3) Maternal pre-pregnancy consumption of shellfish (<1 time/month versus ≥1 time/month) All exposures measured by FFQ	(3) **1.62 (1.11-2.37)**	

continued

TABLE C-3b Continued

Author, Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Breastfeeding				
McGowan et al., 2015	Prospective cohort, Baltimore, Boston, New York City, St. Louis	Children from the Urban Environment and Childhood Asthma (URECA) study	516	1-5 years

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
Food allergy (N=51) or sensitization (N=286): sIgE to milk, egg, peanut; clinical history	(1) Ever BF	(1) Food allergy versus no food allergy: **35/51 (68.8%) versus 193/377 (52.9%); P=0.05** Food sensitization versus no food sensitization: 161/286 (58.3%) versus 121/230 (53.8%); P=0.35	Of the 609 children initially enrolled, 516 (85%) were included. Unadjusted analysis.
	(2) BF at 3 months	(2) Food allergy versus no food allergy: 16/51 (32.7%) versus 76/377 (22.8%); P=0.18 Food sensitization versus no food sensitization: 64/286 (25.1%) versus 48/230 (23.4%); P=0.76	

continued

TABLE C-3b Continued

Author, Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Peters et al., 2015	Prospective cohort, Australia	Infants from the HealthNuts study	5,276	1 year
Grimshaw et al., 2013	Prospective nested case-control study, UK	Cases: all infants with food allergy by age of 2 years from the Prevalence of Infant Food Allergy (PIFA) study Controls: age-matched controls from the PIFA study	123 (41 with food allergy; 82 controls)	1-2 years

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
IgE-mediated food allergy = positive OFC in the presence of positive test of sensitization (SPT ≥2 mm or sIgE ≥0.35 kua/L). Separate analysis for single egg allergy (9% of the cohort), multiple food allergies predominantly peanut (3% of the cohort), and multiple food allergies predominantly egg (2% of the cohort), comparing to no allergic disease at baseline	Duration of BF (up to 12 months)	Single egg allergy: 1.02 (0.99-1.04) Multiple food allergy (predominantly peanut): 1.00 (0.96-1.05) Multiple food allergy (predominantly egg): **1.17 (1.09-1.24)**	5,142 infants underwent SPT to egg, peanut, or sesame and 1,089 infants were eligible for hospital assessment, of whom 908 participated in OFC. Multinomial logistic regression was used to determine risk factors for each class, also weighted for posterior probabilities of class membership. Three separate multivariable models were fitted for the three categories of risk factors (parental, infant, and environmental).
Food allergy determined by SPT, physical exam, clinical history, sIgE, DBPCOFC	(1) BF duration, median weeks (2) Exclusive BF, median weeks (3) % BF initiation	(1) Cases versus controls: 21.0 (3.0-30.5) versus 24.0 (7.0-31.0); P=0.295 (2) Cases versus controls: 5.0 (2.8-16.3) versus 8.5 (4.0-15.0); P=0.933 (3) Cases versus controls: 92.7% versus 96.3%; P=0.21	Only age adjusted (matching factor).

continued

TABLE C-3b Continued

Author, Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Liao et al., 2014	Prospective cohort, Taiwan	Infants ≥37 weeks from the The Prediction of Allergy in Taiwanese Children (PATCH) cohort	258 (238, 226, 217, 210, and 198 completed 6, 12, 18, 24, and 36 months of follow-ups)	6, 12, 18, 24, and 36 months

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
sIgE antibody included a mix of six common allergens: Dermatophagoides pteronyssinus (Dp), Dermatophagoides farinae (Df), egg white, cow milk, Cladosporium herbarum (Hormodendrum), and wheat. Participants were characterized as atopic or been sensitized if any of the sIgE level was greater than 0.35 IU/ml.	(1) Exclusive BF ≥4 versus <4 months	(1) Cow milk sensitization at 6, 12, 18, 24, 36 months: 1.0 (0.3, 3.3); **0.2 (0.07-0.5; 0.2 (0.07-0.5); 0.3 (0.1-0.7)**; 0.6 (0.2-1.7) Egg sensitization at 6, 12, 18, 24, 36 months: 1.3 (0.5-3.5); 1.4 (0.5-3.7); 1.6 (0.7-3.8); 1.6 (0.7-3.7); 0.7 (0.2-2.0)	Of the original 258 neonates, blood samples and questionnaires were available from 238 infants at the age of 6 months. 226, 217, 210, and 198 children completed 12, 18, 24 and 36 months of follow-ups, respectively. Unadjusted analysis only.
	(2) Partial BF	(2) Cow milk sensitization: There was a trend of reduced risk for cow milk protein sensitization as duration of partial breastfeeding was increased; the result was not statistically significant	

continued

TABLE C-3b Continued

Author, Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Luccioli et al., 2014	Prospective cohort, US	Children who participated in the Infant Feeding Practices Study (IFPS) II	1,363 (823 high-risk group)	6 years
Mailhol et al. 2014	Cross-sectional study, France	Children (0 to 18 years of age) with atopic dermatitis seen consecutively at multi-disciplinary clinics from May 2002 to December 2008	386	0 to 18 years

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
Total pFA (all children with a current physician diagnosis of food allergy at age 6 years). (N=89, 7%) New pFA (subset of children with physician diagnosis of food allergy at age 6 years but with no diagnosis before 1 year of age) (N=71, 5.2%) High-risk pFA (subset of children with pFA at age 6 years and report of any of the following atopic risk factors: family history of food allergy, family history of other atopy, or eczema before age 1 year)	Exclusive BF duration 1-3 months, ≥4 months versus 0 months (reference group)	Total pFA: Exclusive BF 1-3 month = 0.72 (0.42-1.23) Exclusive BF ≥4 months = 0.69 (0.36-1.29) New pFA: Exclusive BF 1-3 month = 0.78 (0.43-1.38) Exclusive BF ≥4 months = 0.51 (0.24-1.03) High risk pFA: Exclusive BF 1-3 month = 0.81 (0.42-1.51) Exclusive BF ≥4 months = 0.58 (0.26-1.25)	Adjusted for mother's education, race, income, child's gender, parity, type of delivery, family history of food allergy, family history of other atopy, reported eczema before age 1 year, maternal tobacco smoke, other tobacco smoke exposure in home, complementary food introduction by infant age.
SPT. Positive (histamine 10 mg/mL [Stallergenes, Antony, France]) and negative controls and fresh foods or commercial extracts in the case of food items with histamine-releasing properties were used	Exclusive BF yes versus no	1.8 (0.9-3.5)	Among the 386 evaluated children, food allergy was diagnosed in 69 children, of whom 26 children had a reaction to more than one food item. Duration of exclusive BF was not measured. Note: exclusive BF was dropped out in the final model.

continued

TABLE C-3b Continued

Author, Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Stelmach et al., 2014	Prospective cohort, Poland	Children from the Polish Mother and Child Cohort Study (REPRO_PL cohort)	501	1-2 years

NOTE: BF = breastfed; CI = confidence interval; FFQ = food frequency questionnaire; IgE = immunoglobulin E; OFC = oral food challenge; OR = odds ratio; pFA = probable food allergy; RCT = randomized controlled trial; sIgE = food-specific serum IgE; SPT = skin prick test; UK = United Kingdom; US = United States.

[a] **Bold** indicates statistical significance at P<0.05. Results were reported as odds ratio (95% confidence interval) unless otherwise noted. Adjusted results were extracted in the summary table unless otherwise noted.

Food Allergy or Sensitization Outcome Definition	Exposure	Odds Ratio[a] (95% CI) of Food Allergy	Comments
Food allergy ever diagnosed by doctor according to international guidelines	Duration of BF (up to 12 months)	**0.88 (0.82-0.95)**	A stepwise forward procedure was then used to select variables.

TABLE C-4a Dual Antigen Hypothesis (Randomized Controlled Trials)

Author, Year	Study Design, Country	Population	N	Age When Outcome Was Ascertained
Timing of Introduction of Solid Foods and Infant Feeding				
DuToit et al., 2016	RCT, UK (follow-up to primary trial [DuToit et al., 2015])	Children, median age 61.3 months, who had completed the primary trial. Half were in the peanut-avoidance group; the other half were in the peanut-consumption group.	628	72 months
Perkin et al., 2016	RCT, UK	Exclusively breastfed infants age 3 months in the general population	1,303	3 years