Open access • Journal Article • DOI:10.1111/ALL.12341

The prevalence and distribution of food sensitization in European adults

Peter Burney, James Potts, Ischa Kummeling, E. N. C. Mills ...+22 more authors

Institutions: National Institutes of Health, Boston Children's Hospital, Vilnius University, Hospital Clínico San Carlos ...+9 more institutions

Published on: 01 Mar 2014 - Allergy (John Wiley & Sons, Ltd)

Topics: Food allergy

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

EAACI

Allergy

ORIGINAL ARTICLE EPIDEMIOLOGY AND GENETICS

The prevalence and distribution of food sensitization in European adults

P. G. J. Burney[1], J. Potts[1], I. Kummeling[1], E. N. C. Mills[2], M. Clausen[3], R. Dubakiene[4], L. Barreales[5], C. Fernandez-Perez[5], M. Fernandez-Rivas[6], T.-M. Le[7], A. C. Knulst[7], M. L. Kowalski[8], J. Lidholm[9], B. K. Ballmer-Weber[10], C. Braun-Fahlander[11,12], T. Mustakov[13], T. Kralimarkova[13], T. Popov[13], A. Sakellariou[14], N. G. Papadopoulos[14], S. A. Versteeg[15], L. Zuidmeer[15], J. H. Akkerdaas[15], K. Hoffmann-Sommergruber[16] & R. van Ree[15]

[1]Department of Respiratory Epidemiology and Public Health, National Heart and Lung Institute, Imperial College London, London; [2]Institute of Inflammation and Repair, Manchester Institute of Biotechnology, Manchester, UK; [3]Children's Hospital Iceland, Landspitali, University Hospital, Reykjavik, Iceland; [4]Clinics of Chest, Allergology and Radiology, Medical faculty, Vilnius University, Vilnius, Lithuania; [5]Clinical Epidemiology Unit, Preventive Medicine Department, Hospital Clinico San Carlos, IdISSC, Madrid; [6]Allergy Department, Hospital Clinico San Carlos, IdISSC, Madrid, Spain; [7]Department of Dermatology/Allergology, University Medical Center Utrecht, Utrecht, the Netherlands; [8]Department of Immunology, Rheumatology and Allergy, Faculty of Medicine, Medical University of Lodz, Lodz, Poland; [9]Thermo Fisher Scientific, Uppsala, Sweden; [10]Allergy Unit, Department of Dermatology, University Hospital of Zurich, Zurich; [11]Swiss Tropical and Public Health Institute, Basel; [12]University of Basel, Basel, Switzerland; [13]Clinical Centre of Allergology of the Alexandrovska Hospital, Medical University, Sofia, Bulgaria; [14]Allergy Department, 2nd Pediatric Clinic, University of Athens, Athens, Greece; [15]Department of Experimental Immunology and Department of Otorhinolaryngology, Academic Medical Center, Amsterdam, the Netherlands; [16]Department of Pathophysiology and Allergy Research, Medical University of Vienna, Vienna, Austria

To cite this article: Burney PGJ, Potts J, Kummeling I, Mills ENC, Clausen M, Dubakiene R, Barreales L, Fernandez-Perez C, Fernandez-Rivas M, Le T-M, Knulst AC, Kowalski ML, Lidholm J, Ballmer-Weber BK, Braun-Fahlander C, Mustakov T, Kralimarkova T, Popov T, Sakellariou A, Papadopoulos NG, Versteeg SA, Zuidmeer L, Akkerdaas JH, Hoffmann-Sommergruber K, van Ree R. The prevalence and distribution of food sensitization in European adults. *Allergy* 2014; **69**: 365–371.

Keywords
adults; Europe; food hypersensitivity; microarray analysis; prevalence.

Correspondence
Prof. P. Burney, Emmanuel Kaye Building, 1 Manresa Road, London SW3 6LR, UK.
Tel.: +44 (0)207 352 8121
Fax: +44 (0)207 351 8322
E-mail: p.burney@imperial.ac.uk

Accepted for publication 31 October 2013

DOI:10.1111/all.12341

Edited by: Antonella Muraro

Abstract

Background: Complaints of 'food allergy' are increasing. Standardized surveys of IgE sensitization to foods are still uncommon and multicountry surveys are rare. We have assessed IgE sensitization to food-associated allergens in different regions of Europe using a common protocol.

Methods: Participants from general populations aged 20–54 years in eight European centres (Zurich, Madrid, Utrecht, Lodz, Sophia, Athens, Reykjavik and Vilnius) were asked whether they had allergic symptoms associated with specific foods. Weighted samples of those with and without allergic symptoms then completed a longer questionnaire and donated serum for IgE analysis by ImmunoCAP for 24 foods, 6 aeroallergens and, by allergen microarray, for 48 individual food proteins.

Results: The prevalence of IgE sensitization to foods ranged from 23.6% to 6.6%. The least common IgE sensitizations were to fish (0.2%), milk (0.8%) and egg (0.9%), and the most common were to hazelnut (9.3%), peach (7.9%) and apple (6.5%). The order of prevalence of IgE sensitization against different foods was similar in each centre and correlated with the prevalence of the pollen-associated allergens Bet v 1 and Bet v 2 ($r = 0.86$). IgE sensitization to plant allergen components unrelated to pollen allergens was more evenly distributed and independent of pollen IgE sensitization ($r = -0.10$). The most common foods containing allergens not cross-reacting with pollens were sesame, shrimp and hazelnut.

Discussion: IgE sensitization to foods is common, but varies widely and is predominantly related to IgE sensitization to pollen allergens. IgE sensitization to food allergens not cross-reacting with pollens is rare and more evenly distributed.

Symptoms of food allergy are common, and hospital admissions for food allergy have been increasing in England (1, 2) and elsewhere (3, 4). Studies of food allergy using the gold standard test, the double-blind, placebo-controlled food challenge, are difficult to undertake in the general population, and few studies have attempted this (5–7). Studies based on the symptoms have been undertaken, and some have used standard questionnaires to enable comparisons to be made between geographical areas (8–11). Studies of IgE sensitization to foods provide more objective evidence for one determinant of food allergy, but variation in methods has made comparisons difficult (12, 13).

The European Community Respiratory Health Survey reported that IgE sensitization to food allergens among young adults appeared to be determined by place of residence, but that the relative prevalence of IgE sensitization to different foods was similar between different sites. It also reported that the prevalence of food sensitization correlated with the geometric mean total IgE for an area, but not IgE sensitization to common aeroallergens (14).

In this study, we report the prevalence of sensitization to foods among adults living in eight locations in Europe, selected to cover different geographical areas and extend the earlier study by examining specific allergens associated with food using customized allergen microarrays from the EuroPrevall allergen library (15).

Methods

Sample

The methods used in the study have been reported elsewhere (16), and the overall design is shown in Figure S1. Eight centres were selected representing the Northern Maritime (Reykjavik), Northern (Vilnius), Central (Lodz), Balkan (Sofia), Alpine (Zurich), Mediterranean (Athens, Madrid) and Atlantic seaboard (Utrecht) regions of Europe. In each of these centres, a representative sample of 20- to 54-year-old adults was drawn from local population registers, except in Athens where random digit dialling was used.

Screening survey

From these samples, initial information was collected on allergic symptoms related to food including the type of food, the symptoms experienced and the frequency with which the symptoms had occurred. From those responding to this initial screening survey (Stage I), we selected those who reported allergic symptoms associated with any of the foods that were to be tested and, in addition, a random sample of those not reporting these symptoms. We estimated the response rate to this initial survey, where possible. The foods identified in the screening survey together with the characteristics of the complaint were summarized and potential cases of food allergy were identified. From the responses, we defined 'cases', the potentially food-allergic participants, as those with allergic symptoms in relation to any of the relevant foods. We took up to 240 cases and a random sample of 240 controls from the noncases, but oversampled these where there were fewer than 240 cases (as was the case in all centres) to increase the power of the study. We planned for 240 cases and 240 controls to have 90% power across all centres to identify an odds ratio of 2 at the 5% level of probability where the exposure of interest was present in 15% of the population. If the total number of cases and controls in the final sample was less than 100, we excluded the centre from further study.

Follow-up survey and serology

These groups were invited for further study including a more extensive questionnaire and a serum sample (Stage II). All the sera were analysed in a single laboratory using the ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden). First the sera were tested for groups of food allergens, and if these groups were positive (sIgE ≥ 0.35 kU_A/L), the individual foods in the group were analysed separately (16). We also tested for aeroallergens (house dust mite, cat, and timothy grass, birch, *Parietaria* and mugwort pollens) and for total serum IgE. All sera that tested positive for at least one of the foods were further tested for specific food allergens using an allergen microarray assay (17).

Analysis

The population prevalence of IgE sensitization was estimated as the prevalence of those with a specific IgE response to a particular food among 'cases' and 'controls' weighted back to the general population according to the sampling fraction by which these had been selected for further study. We similarly estimated the population prevalence of IgE sensitization to any aeroallergen and the geometric mean total serum IgE. The relative prevalence of IgE sensitization was estimated according to the food and the place using logistic regression, and the proportion of the total deviance in the model explained by these two variables was estimated. The distribution of IgE sensitization to different foods was plotted by food and place together with the modelled estimates, and we estimated the percentage of the deviance explained by the different parts of this model. Finally, we plotted the prevalence of IgE sensitization to any of the selected foods against the prevalence of IgE sensitization to any of the aeroallergens and the geometric mean total IgE.

For analysis of the microarray data (15), we classified the allergens into 1) plant food or latex allergens homologous with pollen allergens involved in cross-reactive responses (either PR-10 allergens or profilin), 2) 'true' plant food allergens not associated with cross-reactive responses and 3) animal-derived food allergens. (Table S1 for details) No samples were positive for the wheat (Tri a 19.0101, Tri a Gliadin) or goat (Cap h casein) allergens, and these were not considered further.

Ethical approval was given by the appropriate ethical review board in each participating centre. Response to the initial questionnaire was taken to imply consent to the questionnaire study. For the clinical studies, written informed consent was provided by all participants.

Results

Table 1 gives information on the responders to Stage I of the survey. There were only minor differences between the centres in mean age (average 37 years) or proportion of females (55%). Overall 21% reported ever having trouble associated with eating a particular food, but this varied widely from 37% in Zurich to less than 2% in Vilnius and less than 3% in Sofia. The prevalence of doctor-diagnosed food allergy was much lower at 4.4% overall with substantial variation from less than 1% in Vilnius and Sofia to over 7.5% in Zurich and Madrid. The prevalence of participants reporting reactions to priority foods ranged from less than 1% in Vilnius to almost 19% in Madrid, and the proportion of these stating that they would be willing to participate further in the study ranged from 100% in Reykjavik, Sofia and Vilnius to 34% in Athens.

Table 2 gives the numbers responding to Stage I and the numbers seen in Stage II. Response rates could not be calculated for Athens as random digit dialling and quota sampling were used at that site. In Athens and Vilnius, the total number recruited to Stage II was less than 100 in each case, and they were excluded from further consideration. Table S2 compares the age and sex of the cases and controls seen at Stage II with those seen at Stage I. Differences between the stages are minimal.

Table 3 gives the estimated prevalence of IgE sensitization to different foods in the different centres. Overall the highest prevalence was for hazelnut (9.3%), peach (7.9%), apple (6.6%), celery (6.2%) and carrot (6.0%), and the lowest prevalence was for egg (0.86%), milk (0.82%) and fish (0.22%). Using these data, we tested a model that predicts the prevalence of IgE sensitization to a specific food in a specific location from the average IgE sensitization to all allergens in a single location and the average IgE sensitization to a different allergen across all locations. The results are illustrated in Fig. 1, and the detailed results are given in Tables S3 and S4. Figure 1 shows predicted prevalence of IgE sensitization to different foods in each centre as lines and the measured values as symbols. The foods are arranged from least prevalent on the left to most prevalent on the right. There is a good fit between the model estimates and the observed prevalence, and the relative prevalence of IgE sensitization against the different foods is well preserved between the different sites, with the prevalence in Reykjavik being universally low for all foods and Zurich being universally high. The principle exception is in Madrid and Utrecht. Madrid has a lower prevalence than predicted by the model for the highly prevalent allergens, and Utrecht, by contrast, has a higher prevalence than predicted for these allergens. From the regression coefficients given in Table S3, we can estimate that the prevalence of IgE sensitization to peach is approximately 37% (95% confidence limit: 5% to 68%) lower than that to hazelnut and that IgE sensitization to foods is approximately 73% (95% confidence limit: 64% to 81%) lower in Lodz than in Zurich. Approximately 86% of the variation in prevalence, expressed as 'deviance' in the model, is explained by the two variables 'food' and 'place' (Table S4).

Table 1 Characteristics of responders to Stage I by centre. Number (% of total population) unless otherwise stated

	Zurich	Madrid	Athens	Utrecht	Lodz	Vilnius	Sofia	Reykjavik	ALL
Responders	2250	943	1979	3865	1499	2598	2118	2114	17 366
Mean age (s.d.)	38.0 (8.8)	37.4 (9.2)	37.3 (9.4)	36.5 (9.0)	38.6 (10.8)	36.7 (9.4)	37.6 (10.1)	39.4 (9.6)	37.2 (9.7)
Sex (% female)	53.7	56.8	51.5	58.4	55.2	51.1	56.4	52.7	54.6
Any trouble associated with foods (%)	817 (36.8)	315 (33.7)	306 (15.5)	970 (25.1)	430 (28.7)	43 (1.7)	61 (2.9)	689 (33.1)	3631 (21.0)
Foods reported									
At least one priority food* (% as a proportion of all responders)	375 (16.7)	177 (18.8)	116 (5.9)	414 (10.2)	212 (14.1)	12 (0.5)	23 (1.1)	298 (14.1)	1627 (9.2)
'Cases'† (% reporting reactions to at least one priority food)	350 (93)	174 (98)	40 (34)	246 (63)	176 (83)	12 (100)	23 (100)	298 (100)	1319
Doctor-diagnosed food allergy (% of responders)	170 (7.8)	78 (8.4)	88 (4.5)	225 (5.9)	71 (4.8)	14 (0.5)	17 (0.8)	91 (4.4)	754 (4.4)

*Hen's egg, cow's milk, fish, shrimp, peanut, hazelnut, apple, peach, celery, kiwi, mustard, sesame, soy, walnut, wheat, buckwheat, carrot, tomato, banana, lentils, sunflower seeds, melon, corn, poppy seed.

†People with a history of problems with any priority food who agreed to be contacted again.

Table 2 Numbers seen in Stage I and Stage II of the study with response to Stage I

Centre	Initial Sample	Stage I	Response to Stage I, %	Cases identified at Stage I (agreed to be contacted)	Stage II Cases	Stage II Controls	Stage II Total
Zurich	4001	2250	56.2	375 (350)	191	294	485
Madrid	4494	943	21.0	177 (174)	80	230	310
Utrecht	6583	3865	58.7	414 (246)	154	322	476
Athens	n/a	1979	n/a	116 (40)	20	48	68
Lodz	2988	1499	50.2	212 (176)	111	268	379
Sofia	2965	2118	71.43	23 (23)	2	111	113
Vilnius	3939	2598	66.0	12 (12)	5	40	45
Reykjavik	3299	2114	64.1	298 (298)	192	287	479
Total	28 269	17 366	54.9*	1627 (1319)	719	1642	2335

*Percentage excludes Athens, which used random digit dialling and quota sampling.

Table 3 Weighted prevalence of food IgE sensitization by food and centre

FOOD	Zurich	Madrid	Utrecht	Lodz	Sofia	Rey-kjavik	ALL
Hazelnut	17.79	6.00	11.95	6.54	6.27	1.27	9.26
Peach	13.43	11.29	9.74	5.77	3.58	2.31	7.93
Apple	10.75	8.94	8.15	4.83	3.58	1.56	6.53
Carrot	10.18	9.53	5.69	4.51	6.27	1.34	5.96
Celery	11.66	8.24	6.86	4.51	4.48	1.27	6.25
Kiwi	9.35	10.35	4.67	4.88	1.79	2.38	5.20
Tomato	8.07	9.29	3.85	4.33	5.38	1.71	4.91
Wheat	8.55	10.47	3.03	4.14	4.48	0.67	4.50
Sesame	7.61	10.24	3.24	4.26	4.48	1.27	4.50
Shrimp	6.89	5.29	3.94	4.93	6.27	2.76	4.79
Banana	5.90	8.94	2.27	4.83	2.69	2.16	3.79
Corn	6.41	8.00	1.93	2.72	3.58	1.19	3.38
Sunflower	5.81	8.24	1.86	3.49	2.69	0.75	3.17
Poppy	5.44	7.77	1.38	3.12	3.58	0.97	3.03
Melon	6.55	7.88	1.79	3.05	2.69	0.15	3.10
Buckwheat	6.18	7.06	0.89	3.05	3.58	0.74	2.90
Walnut	5.59	7.65	1.86	3.57	2.69	0.07	2.98
Lentils	5.07	6.71	1.24	2.87	4.48	0.74	2.88
Peanut	5.04	7.18	1.58	3.12	1.79	0.45	2.65
Soya	4.61	6.47	1.45	2.35	1.79	0.15	2.33
Mustard	3.59	2.71	0.41	1.71	2.69	0.37	1.60
Egg	1.31	0.59	0.69	1.07	0.90	0.67	0.86
Milk	0.74	1.65	0.84	0.69	0.00	1.20	0.82
Fish	0.17	1.18	0.20	0.00	0.00	0.22	0.22
ANY FOOD	23.63	19.53	17.65	13.99	12.54	6.55	15.81

Table S5 gives the prevalence of IgE sensitization to foods, aeroallergens and specific food allergens classified as cross-reacting pollen allergens (PR-10 and profilin), 'true' plant food allergens and specific animal food allergens, and Table 4 gives a correlation matrix for the prevalence rates. This shows strong associations between IgE sensitization to birch pollen PR-10 and profilin allergens (Bet v 1 and Bet v 2) and Bet v 1 and Bet v 2 homologues in food ($r = 0.94$), any pollen ($r = 0.92$), any aeroallergen ($r = 0.89$) and any food allergen ($r = 0.86$), respectively. Associations were weaker with other airborne allergens ($r = 0.65$), total IgE ($r = 0.41$), any animal food ($r = 0.45$) or animal food allergen ($r = 0.37$), and any 'true' plant food allergen ($r = -0.10$).

Figure 2 (Table S6) gives the prevalence of IgE sensitization to the 'true' food allergens that do not cross-react with pollen allergens. Overall, the most common IgE sensitizations in this class were to sesame (1.53%), shrimp (1.46%), hazelnut (0.92%), tomato (0.52%) and peach (0.40%). The prevalence of IgE sensitization against 'true' food allergens in peanut was 0.14%. There was no evidence of any relative difference between centres in the prevalence of IgE sensitization to the different allergens in this group.

Discussion

The population prevalence of specific IgE to any of the foods studied ranged from 24% in Zurich to 7% in Reykjavik, and the relative prevalence of IgE sensitization to different foods was broadly similar between the sites.

Response rates overall were quite low in common with many recent population-based surveys, but the age–sex composition of the Stage I and Stage II samples is similar (Table S2), and by estimating the prevalence of IgE sensitization after weighting for the symptomatic and asymptomatic samples separately, we have probably accounted for much of the response bias. In those centres where the total number responding was less than 100, we have not tried to estimate the prevalence. A minimal sample size for estimating a reliable prevalence is arbitrary, but we have followed the common convention of not estimating a prevalence from less than a hundred observations.

Our results are similar to those of the European Community Respiratory Health Survey (ECRHS) in showing that the relative prevalence of IgE sensitization to different foods is very consistent between different sites in Europe, but differs in finding a strong association with IgE sensitization to other allergens and a weaker association with the geometric mean total IgE (14). Analysis of data from the protein chip helps to explain and, in an important respect, modify the interpretation of these findings.

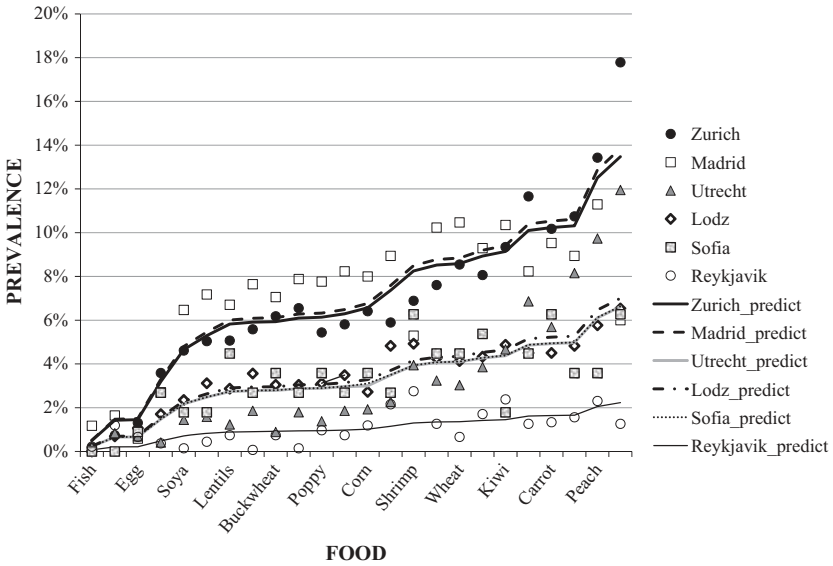

Figure 1 Observed and predicted values for the prevalence of food IgE sensitization in 20- to 54-year-olds (Vilnius and Athens removed).

Table 4 Correlation matrix for IgE sensitization against different groups of allergen

	Birch PR-10/profilin (MICROARRAY)*	Any Food	Any aeroallergen	Any animal food	Any Plant food	Food PR-10/ profilin (microarray)†	'True' Plant food Ag (microarray)‡	Any animal food (microarray)§	Any pollen¶	Other airborne**
Any food	0.86									
Any aeroallergen	0.89	0.93	–							
Any animal food	0.45	0.77	0.51	–						
Any plant food	0.84	0.999	0.92	0.78	–					
Food Pr-10/profilin (microarray)†	0.94	0.91	0.95	0.48	0.90	–				
'True' plant food antigen (microarray)‡	−0.10	0.34	0.04	0.76	0.37	0.06	–			
Any animal food antigen (microarray)§	0.37	0.18	0.49	0.24	0.15	0.35	−0.76	–		
Any pollen¶	0.92	0.94	0.93	0.57	0.95	0.96	0.18	0.26	–	
Other airborne**	0.65	0.57	0.81	0.07	0.55	0.70	−0.38	0.81	0.55	–
Total IgE	0.41	0.70	0.72	0.50	0.70	0.49	0.19	0.45	0.58	0.59

*Bet v 1 or Bet v 2.

†Plant food allergens cross-reacting with pollens [either PR-10 allergens (Api g 1.01, Ara h 8, Cor a 1.0401, Dau c1.0103, Dau c1.0201, Gly m 4, Mal d 1, Pru p 1) or profilin (Cor a 2, Dau c 4, Hel a 2, Hev b 8, Mal d 4, Tri a 12)].

‡'true' plant food allergens (Act d 1, Ara h 1, Ara h 2/Ara h 6, Ara h 3.01/Ara h 3.02, Cor a 8, Cor a 9, Cor a 11, Gly m 5, Hel a 3, Jug r 2, Jug r 4, Lyc e 3, Mal d 2, Mal d 3, Pru p 3, Ses i 1, Ses i 2, Ses i 3, Sin a 1, Tri a 19.0101, Tri a Gliadin).

§Animal-associated food allergens (Bos d 4, Bos d 5, Bos d 8, Cap h Casein, Cyp c 1, Gad m 1, Gal d 1, Gal d 2, Gal d 3, Gal d 5, Pen a 1);

¶Grass, birch, Parietaria and mugwort pollens.

**Cat or mite.

The maintenance of the relative prevalence of IgE sensitization to each food from one site to another suggests that exposure to the different foods is not the rate-limiting step in determining IgE sensitization to any particular food. The microarray data show that IgE sensitization to whole food extracts is strongly associated with IgE sensitization to pollen allergens (Bet v 1 and Bet v 2), and this is partly because most plant-based foods contain allergens that cross-react with pollens, and most animal-derived foods (milk, egg and fish) are rare sensitizers in this age group. Although we cannot exclude co-sensitization, the most likely explanation for the pattern is cross-reactivity to different allergens, which are themselves distributed unevenly across Europe. The microarray data show that the 'true' plant allergens are not similarly distributed. The model presented in Fig. 1 and Tables S2 and S3 tests how well we can predict the prevalence of

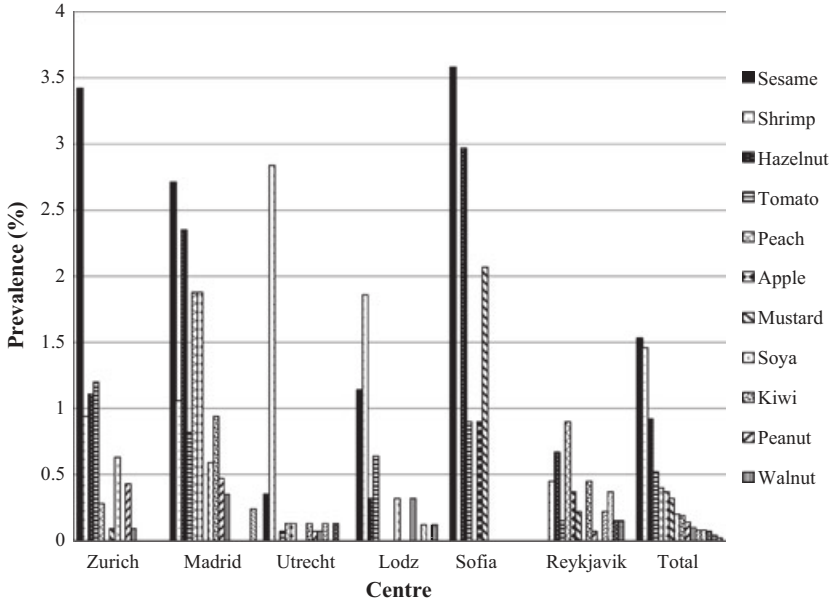

Figure 2 Distribution of IgE sensitization to 'true' food allergens by food and location.

IgE sensitization to a specific food in a specific location from the average prevalence of IgE sensitization to any other random food in that location and the mean prevalence of IgE sensitization to the specific food across all locations. The predicted prevalence (represented by the lines in the Figure) is close to the observed prevalence (represented by the symbols), and 86% of the variation is explained by these two variables. The only systematic deviation from the model is seen in relation to the IgE sensitization to celery, carrot, apple, peach and hazelnut, which is more common than predicted in Utrecht and less common than predicted in Madrid. This fits with the relatively low prevalence of IgE sensitization to the birch pollen allergens Bet v 1 and Bet v 2 in Madrid (6%) compared with Zurich (16%) and Utrecht (11%).

IgE sensitization to 'true' food allergens not cross-reacting with pollens is relatively rare. Of the allergens tested in this group, the commonest targets of IgE antibodies were sesame, shrimp and hazelnut allergens. Fish, egg and milk were again the least prevalent sensitizers even within this group. IgE sensitization to this group of allergens seems differently distributed with low prevalence in Utrecht (with the exception of the shrimp allergen Pen a 1) and a high prevalence in Sofia. We were again unable to detect any variation in the relative prevalence of IgE sensitization to these allergens, but this could be due to small numbers.

Prevalence of IgE sensitization varies considerably between sites, confirming that some of the variation in prevalence previously reported is likely to be due to true differences between populations. The sites in the study were selected to represent variation across Europe, but were never intended to be representative of the European population, and given the wide variation seen, considerable caution needs to be exercised in estimating the overall prevalence of IgE sensitization to foods across Europe as a whole.

This is the most extensive analysis of IgE sensitization to food allergens to date that includes information on individual allergens. Although this study deals solely with IgE sensitization and only a proportion of those sensitized will develop food-associated symptoms (18), IgE sensitization and the persistence of IgE to foods are an essential first step in developing IgE-related clinical food allergy. The prevalence of IgE sensitization to foods in different regions of Europe is strongly associated with the prevalence of IgE to aeroallergens. As reported earlier (14), IgE sensitization against egg, fish and milk was rare. IgE sensitization to all allergens was distributed in approximately the same ratio in the different sites, although we are unable to determine whether this extends to the 'true' food allergens. Among the 'true' food allergens included in the study, the most commonly identified IgE sensitizations were to sesame, shrimp and hazelnut. The rarest were again hen's egg, cow's milk and fish. IgE sensitization to non-cross-reacting peanut allergens was relatively rare at around 14/10 000. More information is required to understand this pattern more fully and to understand the relation of these findings to the distribution of clinically manifest food allergy.

Acknowledgments

The authors wish to thank all the volunteers taking part in the EuroPrevall surveys. The authors are grateful to Sonia Vazquez Cortés, Manuel Enrique Fuentes, Sara Cano Escudero, Emilio Cervera, Isabel Viudez, Carmen Martinez, Sigridur Kristin Sverrisdottir, Katrin Inga Geirsdottir, Stephanie Christensen and Bettina Töndury for help with the study. We also thank Asa Marknell DeWitt, Caroline Pettersson and Hakan Molander (Thermo Fisher, Uppsala) for their work developing custom food mix IgE tests and to Marianne Brill,

PhD, and Christian Harwanegg, PhD then of VBC Genomics, Vienna, AUSTRIA and currently of Phadia Multiplexing Diagnostics GmbH, Vienna, Austria, for preparing the allergen microarrays used in this study.

Funding

This work was funded by the European Union through EuroPrevall (FP6-FOOD-CT-2005-514000). James Potts was supported by the United Kingdom Department of Health Policy Research Programme. Clare Mills was supported by the Competitive Strategic Grant to Institute for Food Research from the Biotechnology and Biological Sciences Research Council (UK).

Author contributions

PB, ENCM and RvR were responsible for the initial design of the study; IK coordinated the study; JP was responsible for the analysis; JL and KH-S provided expertise and reagents relating to the assays; SAV, JHA and RvR undertook the laboratory assays; and all other authors were responsible for developing the initial protocol and implementing the study in their local area. All authors commented on the earlier drafts of this paper and approved the final draft.

Conflicts of interest

JL is a paid employee of Thermo Fisher. No other authors have any potential conflict of interests in relation to the findings in this paper.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Design of study and participation.

Table S1. Classification of food allergens used in microarray.

Table S2. Comparison of age and gender between postal survey and clinical visit.

Table S3. Relative prevalence of sensitisation to different foods and in different places assuming a simple model of where sensitisation can be explained by the overall prevalence of sensitisation to the food and overall prevalence of food sensitisation in each centre.

Table S4. The fit of different models of food sensitisation by food and centre.

Table S5. Weighted prevalence of IgE-sensitisation to classes of allergen by centre (Adults).

Table S6. Numbers (weighted prevalence, %) of IgE-sensitisation to 'true' food allergens and significance (P) of heterogeneity in relative prevalence between sites.

References

1. Grundy J, Matthews S, Bateman B, Dean T, Arshad SH. Rising prevalence of allergy to peanut in children: data from 2 sequential cohorts. *J Allergy Clin Immunol* 2002;**11**: 784–789.
2. Gupta R, Sheikh A, Strachan D, Anderson HR. Increasing hospital admissions for systemic allergic disorders in England: analysis of national admissions data. *BMJ* 2003;**327**:1142–1143.
3. Sicherer S, Munoz Furlong A, Godbold J, Sampson H. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. *J Allergy Clin Immunol* 2010;**125**:1322–1326.
4. Hu Y, Chen J, Li H. Comparison of food allergy prevalence among Chinese infants in Chongqing, 2009 versus 1999. *Pediatr Int* 2010;**52**:820–824.
5. Young E, Patel S, Stoneham M, Rona R, Wilkinson JD. The prevalence of reaction to food additives in a survey population. *J R Coll Physicians Lond* 1987;**21**:241–247.
6. Young E, Stoneham MD, Petruckevitch A, Barton J, Rona R. A population study of food intolerance. *Lancet* 1994;**343**:1127–1130.
7. Jansen JJ, Kardinaal AF, Huijbers G, Vlieg-Boerstra BJ, Martens BP, Ockhuizen T. Prevalence of food allergy and intolerance in the adult Dutch population. *J Allergy Clin Immunol* 1994;**93**:446–456.
8. Rona RJ, Chinn S. Parents' perceptions of food intolerance in primary school children. *BMJ* 1987;**294**:863–866.
9. Price CE, Rona RJ, Chinn S. Height of primary school children and parents' perceptions of food intolerance. *BMJ* 1988;**296**:1696–1699.
10. Price CE, Rona RJ, Chinn S. Associations of excessive irritability with common illnesses and food intolerance. *Paediatr Perinat Epidemiol* 1990;**4**:156.
11. Woods RK, Abramson M, Bailey M, Walters EH. International prevalences of reported food allergies and intolerances. Comparisons arising from the European Community Respiratory Health Survey (ECRHS) 1991-1994. *Eur J Clin Nutr* 2001;**55**:298–304.
12. Rona R, Keil T, Summers C, Gislason D, Zuidmeer L, Sodergren E et al. The prevalence of food allergy: a meta-analysis. *J Allergy Clin Immunol* 2007;**120**:638–646.
13. Zuidmeer L, Goldhahn K, Rona R, Gislason D, Madsen C, Summers C et al. The prevalence of plant food allergies: a systematic review. *J Allergy Clin Immunol* 2008;**121**:1210–1218.
14. Burney P, Summers C, Chinn S, Hooper R, van Ree R, Lidholm J. Prevalence and distribution of sensitization to foods in the European Community Respiratory Health Survey: a EuroPrevall analysis. *Allergy* 2010;**65**:1182–1188.
15. Hoffmann-Sommergruber K, Mills EN, Vieths S. Coordinated and standardized production, purification and characterization of natural and recombinant food allergens to establish a food allergen library. *Mol Nutr Food Res* 2008;**52**(Suppl 2): S159–S165.
16. Kummeling I, Mills ENC, Clausen M, Dubakiene R, Pérez CF, Fernández-Rivas M et al. The EuroPrevall surveys on the prevalence of food allergies in children and adults: background and study methodology. *Allergy* 2009;**64**:1493–1497.
17. Hiller R, Laffer S, Harwanegg C, Huber M, Schmidt WM, Twardosz A et al. Microarrayed allergen molecules: diagnostic gatekeepers for allergy treatment. *FASEB Journal* 2002;**16**:414–416.
18. Osterballe M, Hansen TK, Mortz CG, Bindslev-Jensen C. The clinical relevance of sensitization to pollen-related fruits and vegetables in unselected pollen-sensitized adults. *Allergy* 2005;**60**:218–225.