REVIEW

Prevalence of common food allergies in Europe: a systematic review and meta-analysis

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Abstract

Allergy to cow's milk, egg, wheat, soy, peanut, tree nuts, fish, and shellfish constitutes the majority of food allergy reactions, but reliable estimates of their prevalence are lacking. This systematic review aimed to provide up-to-date estimates of their prevalence in Europe. Studies published in Europe from January 1, 2000, to September 30, 2012, were identified from searches of four electronic databases. Two independent reviewers appraised the studies and extracted the estimates of interest. Data were pooled using random-effects meta-analyses. Fifty studies were included in a narrative synthesis and 42 studies in the meta-analyses. Although there were significant heterogeneity between the studies, the overall pooled estimates for all age groups of self-reported lifetime prevalence of allergy to cow's milk, egg, wheat, soy, peanut, tree nuts, fish, and shellfish were 6.0% (95% confidence interval: 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. The prevalence of food-challenge-defined allergy to cow's 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), respectively. Allergy to cow's milk and egg was more common among younger children, while allergy to peanut, tree nuts, fish, and shellfish was more common among the older ones. There were insufficient data to compare the estimates of soy and wheat allergy between the age groups. Allergy to most foods, except soy and peanut, appeared to be more common in Northern Europe. In summary, the lifetime self-reported prevalence of allergy to common foods in Europe ranged from 0.1 to 6.0%. The heterogeneity between studies was high, and participation rates varied across studies reaching as low as <20% in some studies. Standardizing the methods of assessment of food allergies and initiating strategies to increase participation will advance this evidence base.

Abbreviations

CASP, Critical Appraisal Skills Programme; CI, confidence intervals; DBPCFC, double-blind, placebo-controlled food challenge; EAACI, European Academy of Allergy and Clinical Immunology; FA, food allergy; IgE, immunoglobulin E; OFC, oral food challenge; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SPT, skin prick test.

The majority of allergic reactions to foods, particularly in children, are suggested to be caused primarily by eight foods, namely cow's milk, egg, wheat, soy, peanut, tree nuts, fish, and shellfish (1), although there is no sufficient evidence to support this in Europe. Although it has been suggested that the prevalence of adverse reactions to these foods is increasing and constituting major public health problems, including

increasing hospital utilization, increasing associated medical costs, and increasing burden of care on immediate families (1–8), reliable estimates of their prevalence in Europe are lacking.

As part of the efforts of the European Academy of Allergy and Clinical Immunology (EAACI) to develop guidelines (*EAACI Guideline for Food Allergy and Anaphylaxis*) for the management and prevention of food allergy and anaphylaxis, we undertook a systematic review to appraise the evidence on the epidemiology of food allergy; its prevention, diagnosis, and clinical management; and impact on quality of life, which will be used to inform the clinical recommendations. In our first report of the findings of this synthesis, we presented estimates of the prevalence, time trends, and risk and prognostic factors for allergy to any food (9). In the present analysis, we present the estimates of the prevalence of the above-named eight most common food allergies in Europe.

Methods

Study protocol, search strategy, and study selection

The detailed methodological approach employed in this systematic review has been presented in our first report (9). Briefly, we developed a protocol in advance on the review processes, including the search strategies, inclusion and exclusion criteria, methods of analyses and syntheses, and choice of risk of bias tools for assessing study quality. The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) at http://www.crd.york.ac.uk/prospero/ (registration number CRD42013003704) and has been published (10). We implemented a highly sensitive search strategy in four electronic databases (OVID MEDLINE, OVID EMBASE, CINAHL, and ISI Web of Science), which was devised on OVID MEDLINE and then adapted to the other databases. Experts active in the field commented on the search strategy and the list of included studies. Additional references were located by searching the references cited in the identified studies. Unpublished work and research in progress were searched through discussion with experts in the field. We made no restrictions based on language, and the literature in languages other than English was, where possible, translated.

In terms of the study design, we included systematic reviews and meta-analyses, cohort studies, case–control studies, cross-sectional studies, and routine healthcare studies, but excluded review and discussion papers, nonresearch letters and editorials, case studies and case series, animal studies, and all randomized controlled trials. As our initial search (including studies published worldwide between January 1990 and September 2012) retrieved large quantities of articles, we restricted the studies to those published in Europe between January 1, 2000, and September 30, 2012. After initial screening of the retrieved studies by two independent reviewers, the abstracts and full-text copies of potentially relevant studies were obtained and their eligibility for inclusion was independently assessed by two reviewers (BN and LH). Any discrepancies

were resolved by consensus and, if necessary, a third reviewer (AS) arbitrated.

Outcomes

The food allergy outcomes assessed in this review included cow's milk, egg, wheat, soy, peanut, tree nuts, fish, and shellfish. We included eligible studies that have assessed these outcomes based on self-report (i.e., participants or their parents reported that they have any of the outcomes or not), skin prick test (SPT) positivity, specific immunoglobulin E (IgE) positivity, open food challenge (OFC)/double-blind placebo-controlled food challenge (DBPCFC) positivity, OFC/DBPCFC positivity, or convincing clinical history (i.e., outcomes confirmed by a convincing clinical judgment by a physician without food challenge).

Assessment of risk of bias

We assessed the risk of bias in the studies using an adapted and modified relevant version of the Critical Appraisal Skills Programme (CASP) quality assessment tool (http://www.casp-uk.net/). As we described in our previous report, each component of the studies (i.e., the appropriateness of the study design for the research question, the risk of selection bias, exposure measurement, and outcome assessment) was graded and an overall grading was calculated from grading for the different study components (9). Two reviewers (BN and LH) independently assessed the risk of bias in the studies, and any discrepancies were resolved by consensus and, if necessary, a third reviewer (AS) arbitrated.

Analysis

Using a customized data extraction form, we recalculated all the frequency estimates of food allergy occurrence if adequate data were provided by authors using minimal measured events rather than extrapolated estimates. If any discrepancies were observed between our recalculated estimates and those of the authors, we preferentially reported our recalculated estimates. If inadequate data were given to enable recalculation, we reported the estimates provided by the authors. Where needed and possible, we contacted authors of primary studies for clarifications. To adjudge the precision of the prevalence estimates presented in the studies, we extracted the 95% confidence intervals (95% CI) of the estimates from the studies, and where we undertook the recalculation of the estimates, the 95% CI were computed using the Wilson score method without continuity correction (11). All the different reports from the same primary study were reported together. We performed a random-effects meta-analysis for clinically and methodologically comparable studies (comparable particularly with regard to the type of endpoint measure [point or lifetime prevalence] and assessment method [self-report, SPT, IgE, FC] reported in the studies), excluding systematic reviews, to estimate the prevalence of each specific food allergy based on the different assessment methods.

The pooled estimates were stratified by age (≤1 year, 2–5 years, 6–17 years, ≥18 years) and geographical region of Europe (i.e., East, West, South, and North). A study with overlap between the age groups was included in an age group if the age distribution was skewed to that age group. For cohort studies that gave frequency estimates at different ages for the same individuals, we used the estimates for the highest age within each age strata in computing the pooled estimates. For studies reporting more than one tree nuts, each tree nut was separately included in the pooled estimates. The heterogeneity of the estimates was computed both for the stratified analysis and for all the groups combined. Statistical analyses were undertaken using STATA 11 (Stata Corp, College Station, TX, USA).

Results

Study selection and characteristics

Our initial database searches identified 4053 articles and additional 11 studies through hand searches and expert suggestions, giving a total of 4064 articles that were screened. After removal of duplicates and taken into account the predefined exclusions based on titles and abstracts, the full texts of 109 articles were examined in more detail. For the current report, of the 109 articles, 26 were excluded for not being population based, eight for not studying any of the eight specific food allergies of interest, and 10 for being unable to be translated into English, leaving us with 65 papers (based on 50 primary studies) that were finally included in the narrative synthesis (12–80), and 42 studies were included in at least one meta-analysis. Of the 50 primary studies reviewed, 27 were cross-sectional studies, 17 cohort studies, three systematic reviews, and three case–control studies. The majority of the studies ($n = 37$) were undertaken exclusively in children, usually those <18 years of age. The majority of the studies were from Northern and Western Europe.

Of the 50 primary studies, 42 examined cow's milk allergy, 44 egg allergy, 25 wheat allergy, 17 soy allergy, 36 peanut allergy, 26 tree nut allergy, 31 fish allergy, and 15 shellfish allergy (Table 1, Tables S1 and S2). Of the 42 studies included in the meta-analysis, 35 were included for cow's milk allergy, 33 for egg allergy, 17 for wheat allergy, 11 for soy allergy, 29 for peanut allergy, 20 for tree nut allergy, 19 for fish allergy, and nine for shellfish allergy. For each specific food allergy, all of the assessment methods (self-report, SPT sensitization, specific IgE sensitization, and food challenge) were employed to measure food allergy, although self-report was most commonly used. Some studies combined symptoms plus either SPT or IgE sensitization to measure food allergy, while few studies used food challenge or convincing clinical history (Table 1). Table 1 presents the characteristics of the studies included in the review. The participation rate across studies varied widely, ranging between as low as 17.3–99.5%, while in several studies, the participation rate was not reported.

Assessment of risk of bias

We presented details of the risk of bias grading of the studies included in this systematic review in our first report (9). The overall grading indicates that almost all of the studies ($n = 48$) had a 'moderate' grading, while only one study had 'strong' grading.

Frequency of food allergy

The detailed results of the frequencies of the different food allergies are shown in Tables S1 and S2. Table S3 shows the summarized ranges of frequencies for each food allergy for the different age groups (<1, 2–5, 6–17, ≥18 years) according to the different assessment methods used to measure food allergy. Estimates in Table S3 are the lifetime prevalence for self-reported food allergy and point prevalence for all assessment methods. The pooled prevalence estimates of the specific food allergies are shown in Figs 1–8 and Figs S2–S9. There was significant heterogeneity between the studies when pooled together regardless of the assessment method used.

Cow's milk allergy
The detailed estimates of the frequency of cow's milk allergy are presented in Table S1 and range of estimates in Table S3. Across all assessment methods and age groups, the prevalence of cow's milk allergy varied across studies, the greatest variation seen in point prevalence of self-reported cow's milk allergy. The range of point prevalence of food-challenged cow's milk allergy was the same for all age groups (0.0–3.0%) (Table S3). The pooled age-stratified prevalence estimates of cow's milk allergy according to the different assessment methods are shown in Fig. 1, and the region-stratified estimates are shown in Fig. S2. The overall lifetime prevalence of self-reported cow's milk allergy was 6.0% (95% CI 5.7–6.4). The overall point prevalence of self-reported cow's milk allergy was 2.3% (95% CI 2.1–2.5), 0.3% (95% CI 0.03–0.6) for SPT positivity, 4.7 (95% CI 4.2–5.1) for specific IgE positivity, 0.6% (95% CI 0.5–0.8) for FC positivity, and 1.6% (95% CI 1.2–1.9) for FC or history of cow's milk allergy. In most cases, these estimates were usually higher in younger age groups than older ones (Fig. 1). The region-stratified estimates show that in most cases, the estimates of cow's milk allergy according to each assessment method were higher in Northern Europe than in other regions (Fig. S2).

Egg allergy
Frequency estimates of hen's egg allergy are shown in Table S1 and the range of estimates in Table S3. The ranges of the prevalence estimates of egg allergy were comparable across the age groups regardless of the assessment method used, but varied widely between studies (Table S3). The pooled age-stratified prevalence estimates of egg allergy according to the different assessment methods are shown in Fig. 2, and the region-stratified estimates are shown in Fig. S3. The overall lifetime prevalence of self-reported egg allergy was 2.5% (95% CI 2.3–2.7). The overall point prevalence of self-reported egg allergy was

Table 1 Summary of the characteristics of studies in the review: studies published January 1, 2000—September 30, 2012

Reference, country*	Study design	Number invited/eligible participants	Participation rate N (%)	Age of subjects	Method of outcome assessment	Measure (s) of occurrence
Burney et al. (12), Woods et al. (13), Europe, United States of America, Australia, New Zealand	Cross-sectional study	Not indicated	4522	20–44 years old	Self-reported, sIgE	Point and lifetime prevalence
Caffarelli et al. (14), Italy	Cross-sectional study	900	625 (69.4)	5–14 years old	Self-reported	Point and lifetime prevalence
Chafen et al. (15), worldwide	Systematic review	1216 studies	72 studies included	All age groups	Self-reported, physician diagnosis, SPT, sIgE, OFC, DBPCFC	Point, period, lifetime prevalence; cumulative incidence, incidence rate
Du Toit et al. (16), United Kingdom and Israel	Cross-sectional study	10 786	8826 (81.8)	4–18 years old	Self-reported, clinical history, OFC	Point prevalence
Dubakiene et al. (17), Lithuania	Cohort study	Not indicated	1558	6–12 months old	Self-reported, SPT, sIgE, DBPCFC	Point prevalence
Eggesbø et al. (18–20), Norway	Cohort study	4973	3754 (75.5)	2.5 years old	Self-reported, physician diagnosis, SPT, sIgE, OFC, DBPCFC	Point prevalence, cumulative incidence
Eller et al. (21), Kjaer et al. (22), Jøhnke et al. (23), Denmark	Cohort study	1095	562 (51.3)	6 years old	Self-reported, SPT, sIgE, OFC, DBPCFC	Point prevalence, cumulative incidence
Falcaõ et al. (24), Portugal	Cross-sectional study	1565	659 (42.1)	>39 years old	Self-reported	Point prevalence
Fox et al. (26), United Kingdom	Case–control study	Not indicated	133 cases and 310 controls	<4 years old	SPT, sIgE, DBPCFC	Point prevalence
Frongia et al. (27), Italy	Cross-sectional study	Not indicated	2284	11–20 years old	Self-reported	Point prevalence
Gelincik et al. (28), Turkey	Cross-sectional study	17 064	11 816 (69.2)	≥18 years old	Self-reported, SPT, sIgE, DBPCFC	Point and lifetime prevalence
Grundy et al. (29), United Kingdom	Cohort study	2858	1273 (44.5)	3–4 years old	Self-report, SPT, OFC	Point prevalence
Hourihane et al. (31), United Kingdom	Cross-sectional study	5072	1125 (22.2)	4–5 years old	SPT, sIgE, DBPCFC	Point prevalence
Host et al. (30), Denmark	Cohort study	1758	1749 (99.5)	15 years old	SPT, sIgE, OFC, DBPCFC	Point prevalence
Isolauri et al. (32), Finland	Cross-sectional study	Not indicated	400	7, 27, 47, 67 years old	Self-reported, sIgE	Lifetime prevalence and point prevalence
Johansson et al. (33), Sweden and Norway	Cross-sectional study	Not indicated	Sweden 1002, Norway 500	Adults	sIgE	Point prevalence
Julge et al. (34), Vasar et al. (35), Estonia	Cohort study	455	298 (65.5)	5 years old	SPT, sIgE	Point prevalence
Krause et al. (37), Greenland	Cross-sectional study	1213	1068 (88.1)	5–18 years old	sIgE	Point prevalence

Table 1 (Continued)

Reference, country*	Study design	Number invited/eligible participants	Participation rate N (%)	Age of subjects	Method of outcome assessment	Measure (s) of occurrence
Kristinsdottir et al. (38), Iceland	Cohort study	Not indicated	1341	1 year old	Self-reported, SPT, specific sIgE, DBPCFC	Point prevalence
Kucosmanoglu et al. (39), Turkey	Cross-sectional study	1415	1015 (71.7)	8–18 months old	SPT	Point prevalence
Kurulaaratchy et al. (40) Arshad et al. (41), Tariq et al. (42), United Kingdom	Cohort study	1536	1456 (94.8)	4 years old	SPT	Point prevalence, cumulative incidence
Kvenshagen et al. (43), Norway	Cohort study	Not indicated	609	2 years old	Self-reported, SPT, sIgE, OFC, DBPCFC	Point prevalence
Majkowska-Wojciechowska et al. (44), Poland	Cross-sectional study	Not indicated	2148	7–10 years old	Self-reported	Lifetime prevalence
Marklund et al. (45), Sweden	Cross-sectional study	2064	1488 (72.1)	13–21 years old	Self-reported	Point prevalence
Matricardi et al. (46), Germany	Cross-sectional study	7609	1314 (17.3)	2–10 years old	sIgE	Point prevalence
Mossakowska et al. (47), Poland	Cross-sectional study	Not indicated	301	>100 years old	Self-reported	Point prevalence
Nicolaou et al. (48), United Kingdom	Cohort study	1085	1029 (94.8)	8 years old	Self-reported, SPT, sIgE, OFC, DBPCFC	Point and lifetime prevalence
Niggemann et al. (49), Germany	Cross-sectional study	26 787	13 100 (48.9)	0–17 years old	sIgE	Point prevalence
Orhan et al. (50), Turkey	Cross-sectional study	3500	2739 (78.2)	6–9 years old	Self-reported, SPT, OFC, DBPCFC	Lifetime and point prevalence
Östblom et al. (51,52,53) and Almqvist et al. (54), Sweden	Cohort study	Not indicated	4089	4–8 years old	Self-reported, sIgE	Point and period prevalence
Osterballe et al. (55), Denmark	Cross-sectional study	1094	843 (77.1)	Mean age 22 years	Self-reported, SPT, OFC, DBPCFC	Point prevalence
Osterballe et al. (56), Denmark	Cohort study	Not indicated	1834	Children and adults	Self-reported, physician diagnosis, SPT, sIgE, OFC, DBPCFC	Point prevalence
Penard-Morand et al. (57), France	Cross-sectional study	9615	7781 (80.9)	9–11 years old	Self-reported, SPT	Point prevalence
Pereira et al. (58), United Kingdom	Cross-sectional study	3144	1532 (48.7)	11 and 15 years old	Self-reported, physician diagnosis, SPT, OFC, DBPCFC	Point prevalence
Pyrhönen et al. (59,60), Finland	Cohort study	5973	3899 (65.3)	0–4 years old	Self-reported, physician diagnosis, SPT, sIgE, OFC	Lifetime prevalence, cumulative incidence
Pyziak and Kamer (61), Poland	Cross-sectional study	Not indicated	83	6–17 years old	Self-reported, sIgE, SPT, OFC	Point prevalence
Rance et al. (62), France	Cross-sectional study	3500	2716 (77.6)	Mean age 8.9 years	Self-reported	Point and lifetime prevalence

Table 1 (Continued)

Reference, country*	Study design	Number invited/eligible participants	Participation rate N (%)	Age of subjects	Method of outcome assessment	Measure (s) of occurrence
Roberts et al. (63) and Lack et al. (64), United Kingdom	Cohort study	13 971	12 090 (86.5)	0–7 years old	Self-reported, SPT, DBPCFC	Point prevalence
Rona et al. (65), worldwide	Systematic review	Not indicated	Number of studies included in review not indicated	All age groups	Self-reported, physician diagnosis, SPT, sIgE, OFC, DBPCFC	Point, period, lifetime prevalence, cumulative incidence and incidence rate
Ronchetti et al. (66), Italy	Cross-sectional study	Not indicated	380	9 and 13 years old	SPT	Point prevalence
Sandin et al. (67), Sweden and Estonia	Case–control study	All 985 Sweden 645, Estonia 340	All 770 (78.2) Sweden 483 (74.9), Estonia 287 (84.4)	10–11 years old	Self-report, sIgE	Point prevalence
Schnabel et al. (68), Germany	Cohort study	3097	1082 (34.9)	6 years old	Self-reported, sIgE	Point prevalence
Schäfer et al. (69), Germany	Nested case–control study	2539	1537 (60.5)	25–74 years old	Self-reported, SPT	Point prevalence, lifetime prevalence
Soost et al. (70) and Zuberbier et al. (71), Germany; Roehr et al.	Cross-sectional study	13 300	All: 4093 (30.8) Age 0–17 years: 739 Age 18–79 years: 3227	0–79 years old	Self-reported, physician diagnosis, SPT, sIgE, OFC, SBPCFC, DBPCFC	Point and lifetime prevalence
Steinke et al. (73), Europe	Cross-sectional study	Not indicated	40 426	<18 years old	Self-reported	Point prevalence
Venter et al. (74), United Kingdom	Cohort study	5283	3382 (64.0)	3–4 years old	Physician diagnosis, SPT, sIgE, OFC, DBPCFC	Point prevalence
Venter et al. (75); Dean et al. (76); Venter et al. (77), United Kingdom	Cohort study	1096	969 (88.4)	3 years old	Self-report, SPT, OFC, DBPCFC	Point and period prevalence, cumulative incidence
Venter et al. (78), United Kingdom	Cross-sectional study	1440	798 (55.4)	6 years old	Self-report, SPT, OFC, DBPCFC	Point prevalence
Von Hertzen et al. (79), Finland and Russia	Cross-sectional study	Finland: children 546 mothers 546	Finland: children 413 (75.6) mothers 409 (74.9)	7–16 years children	SPT	Point prevalence
Zuidmeer et al. (80), World-wide	Systematic review	396 studies	33 studies included	All age groups	Self-reported, physician diagnosis, SPT, sIgE, OFC, DBPCFC	Point, period, and lifetime prevalence

CI, confidence interval; DBPCFC, double-blind placebo-controlled food challenge; OFC, oral food challenge; sIgE, specific immunoglobulin E; SPT, skin prick test; SR, self-reported.
*All studies were graded as at moderate overall risk of bias, except Caffarelli et al. (14), which was graded strong.
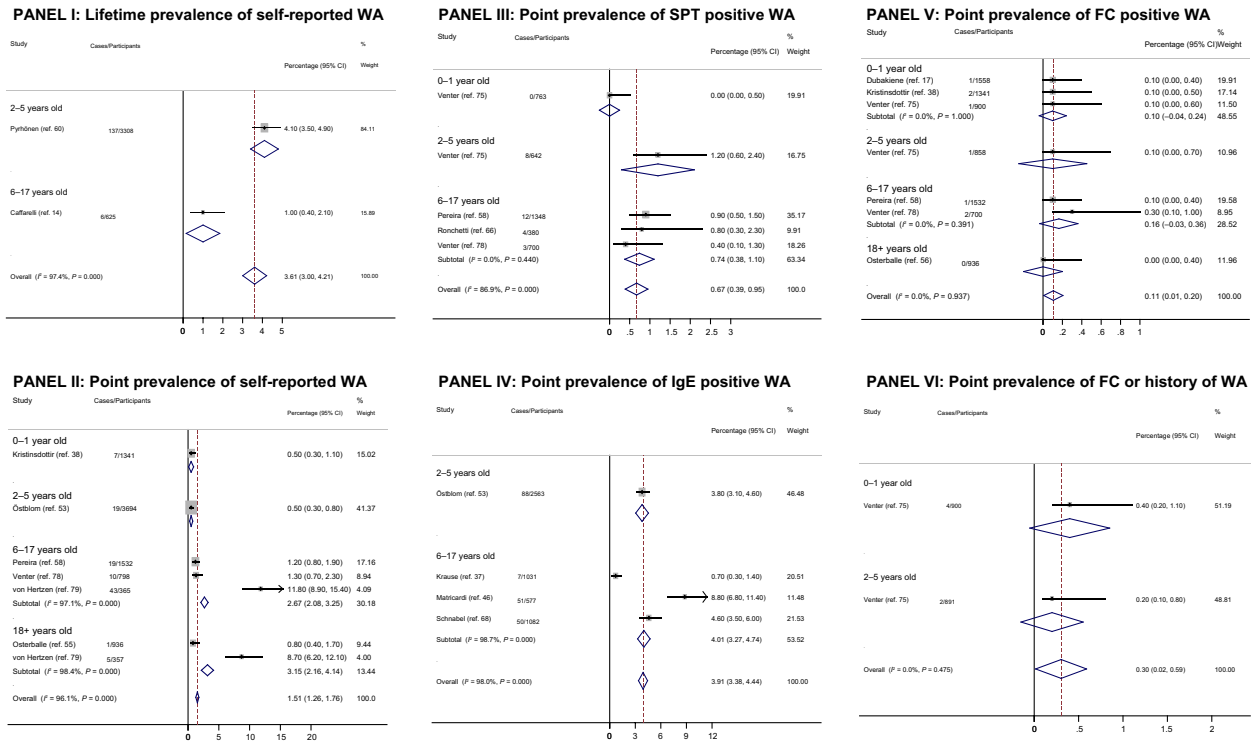
Figure 1 Age-stratified pooled prevalence of cow's milk allergy (CMA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI, and boxes represent the size of the study.
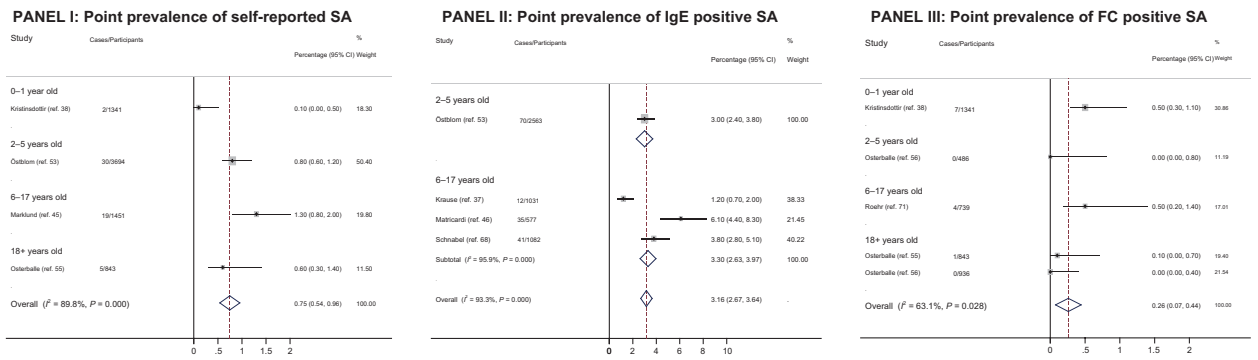

Figure 2 Age-stratified pooled prevalence of egg allergy (EA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI, and boxes represent the size of the study.

Figure 3 Age-stratified pooled prevalence of wheat allergy (WA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI, and boxes represent the size of the study.

Figure 4 Age-stratified pooled prevalence of soy allergy (SA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI, and boxes represent the size of the study.

1.5% (95% CI 1.3–1.6), 0.8% (95% CI 0.6–0.9) for SPT positivity, 3.6 (95% CI 3.2–4.0) for specific IgE positivity, 0.2% (95% CI 0.2–0.3) for FC positivity, and 1.0% (95% CI 0.8–1.3) for FC or history of egg allergy. The estimates were usually higher in younger age groups than older ones (Fig. 2), while the region-stratified estimates were highest in Northern Europe (Fig. S3).

Wheat allergy
Frequency estimates of wheat allergy are shown in Table S1 and the range of estimates in Table S3. The ranges of the

prevalence estimates of wheat allergy were also comparable across the age groups regardless of the assessment method used, but varied between studies (Table S3). The overall pooled estimate of wheat allergy was 3.6% (95% CI 3.0–4.2) for lifetime self-reported prevalence, 1.5% (95% CI 1.3–1.8) for point self-reported prevalence, 0.7% (95% CI 0.4–1.0) for SPT positivity, 3.9 (95% CI 3.4–4.4) for specific IgE positivity, 0.1% (95% CI 0.01–0.2) for food challenge positivity, and 0.3% (95% CI 0.02–0.6) for food challenge or history of wheat allergy. Although in most cases, the estimates appeared higher in older age groups than younger ones, the
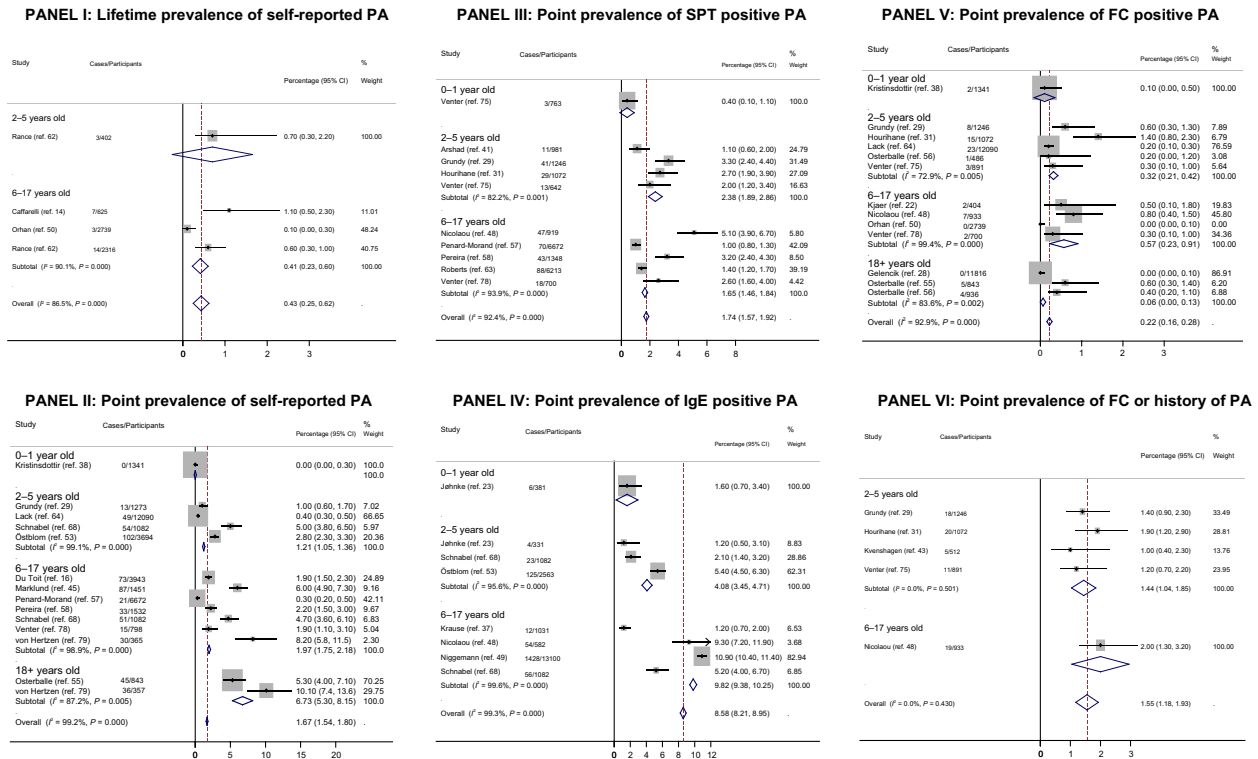
Figure 5 Age-stratified pooled prevalence of peanut allergy (PA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI, and boxes represent the size of the study.

data were insufficient to compare between age groups as in many cases only one study was available for a particular age group (Fig. 3). The region-stratified estimates were higher in Northern Europe for lifetime and point self-reported prevalence, but higher in Southern Europe for point prevalence of SPT positivity and in Western Europe for specific IgE positivity, FC positivity, and FC or history of wheat allergy (Fig. S4).

Soy allergy
Frequency estimates of soy allergy are shown in Table S1 and the range of estimates in Table S3. For each assessment method, the ranges of the prevalence estimates of soy allergy were comparable across the age groups and between studies, although some notable variations between studies were seen for specific IgE positivity (Table S3). Only one study each was eligible for pooling for lifetime self-reported prevalence and SPT positivity and no study for FC or history of soy allergy; hence, no pooled estimates were presented for these assessment methods. The overall pooled point prevalence of self-reported soy allergy was 1.5% (95% CI 1.2–1.8), 3.2% (95% CI 2.7–3.6) for specific IgE positivity, and 0.3% (95% CI 0.1–0.4) for FC positivity. Although estimates appeared higher in younger children than the older age groups, there were insufficient data to compare the pooled estimates between age groups as in most cases only one study was available for a particular age group (Fig. 4). The region-stratified estimates showed that all studies on point self-

reported prevalence of soy allergy were undertaken only in Northern Europe, while others were undertaken only in Northern and Western Europe. The point prevalence of specific IgE positivity and FC positivity was higher in Western than in Northern Europe (Fig. S5).

Peanut allergy
Frequency estimates of peanut allergy are shown in Table S2 and the range of estimates in Table S3. For each assessment method, the ranges of prevalence estimates of peanut allergy were comparable across age groups, but there were variations between studies particularly with regard to specific IgE positivity (Table S3). The overall lifetime prevalence of self-reported peanut allergy was 0.4% (95% CI 0.3–0.6), 1.7% (95% CI 1.5–1.8) for point self-reported prevalence, 1.7% (95% CI 1.6–1.9) for SPT positivity, 8.6% (95% CI 8.2–9.0) for specific IgE positivity, 0.2% (95% CI for 0.2–0.3) for FC positivity, and 1.6% (95% CI 1.2–1.9) for FC or history of peanut allergy. In most cases, the estimates were higher in older age groups than in younger children (Fig. 5), while the region-stratified estimates were mostly higher in Western Europe than in other regions (Fig. S6).

Tree nut allergy
Frequency estimates of tree nut allergy are shown in Table S2 and the range of estimates in Table S3. Generally, the ranges of prevalence estimates for each assessment method of tree nut allergy were comparable across age groups, except
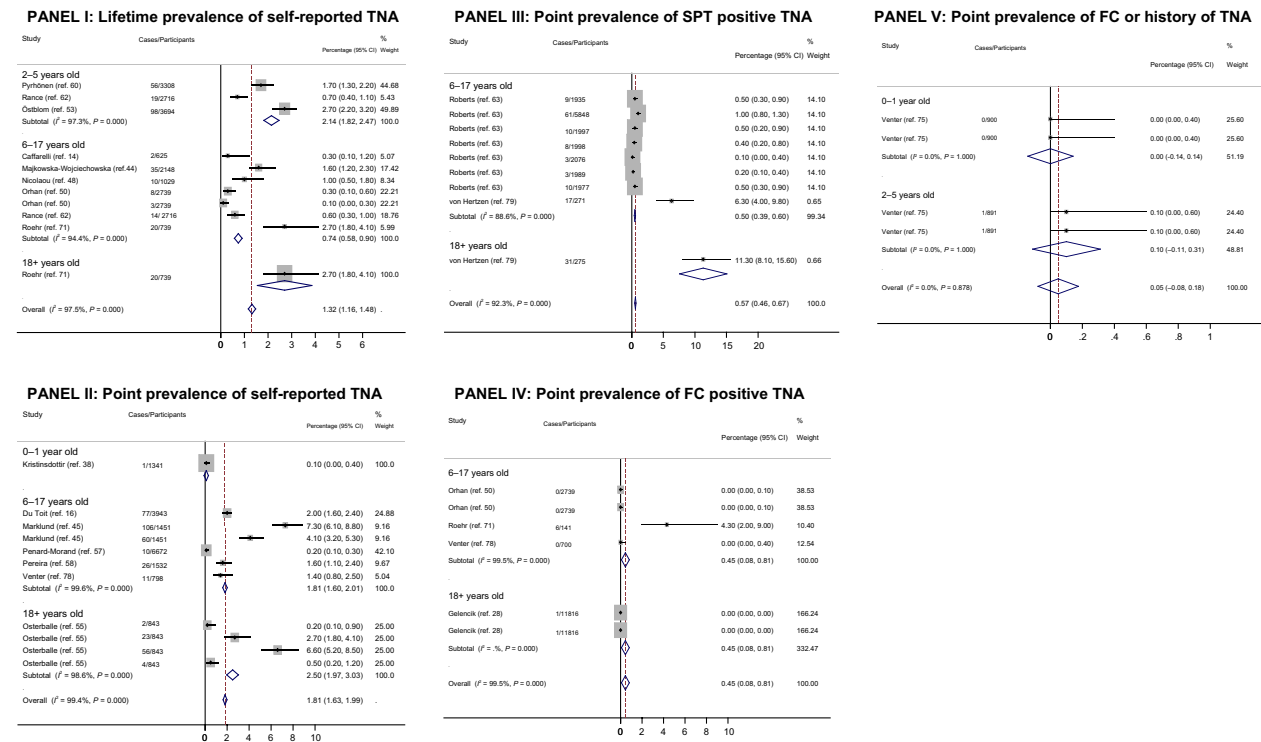
Figure 6 Age-stratified pooled prevalence of tree nut allergy (TNA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI, and boxes represent the size of the study.

for SPT positivity where the estimates appeared much higher in the older age groups. There were no studies on specific IgE assessment of tree nut allergy among children of age 17 years and younger. Variations between studies were particularly seen with regard to point self-reported prevalence, specific IgE positivity, and SPT positivity (Table S3). Only one study was eligible for pooling with regard to assessment of tree nut allergy based on specific IgE positivity; hence, no pooled estimates were presented for specific IgE positivity. The overall lifetime prevalence of self-reported tree nut allergy was 1.3% (95% CI 1.2–1.5), 1.8% (95% CI 1.6–2.0) for point self-reported prevalence, 0.6% (95% CI 0.5–0.7) for SPT positivity, 0.5% (95% CI for 0.08–0.8) for FC positivity, and 0.1% (95% CI 0.1–0.2) for FC or history of tree nut allergy. The estimates were higher in older age groups than in younger children (Fig. 6), while the region-stratified estimates were mostly higher in Northern Europe than in other regions (Fig. S7).

Fish allergy
Frequency estimates of fish allergy are shown in Table S2 and the range of estimates in Table S3. The ranges of prevalence estimates for each assessment method of fish allergy were comparable across age groups, and wide variations were seen between studies based on lifetime and point self-reported prevalence of fish allergy (Table S3). The overall lifetime prevalence of self-reported fish allergy was 2.2% (95% CI 1.8–2.5), 0.6% (95% CI 0.5–0.7) for point self-reported prevalence, 0.6% (95% CI 0.5–0.8) for SPT positivity, 0.7%

(95% CI for 0.4–0.9) for specific IgE positivity, 0.1% (95% CI 0.02–0.2) for FC positivity, and 0.1% (95% CI 0.01–0.2) for FC or history of fish allergy. The estimates were higher in younger age groups with regard to lifetime self-reported prevalence and specific IgE positivity, but higher in older age groups based on other assessment methods (Fig. 7). The region-stratified estimates were highest in Northern Europe (Fig. S8).

Shellfish allergy
Frequency estimates of shellfish allergy are shown in Table S2 and the range of estimates in Table S3. There were no studies on lifetime self-reported prevalence of shellfish allergy among children ≤5 years, on specific IgE positivity among children of age 17 years and younger, and on FC or history among all age groups. The ranges of prevalence estimates for each assessment method of shellfish allergy were comparable across age groups, and wide variations were seen between studies based on point prevalence of self-reported shellfish allergy (Table S3). In pooling, there were no eligible studies on SPT positivity, specific IgE positivity, and FC or history; hence, pooled estimates are not presented for these assessment methods. The overall lifetime prevalence of self-reported shellfish allergy was 1.3% (95% CI 0.9–1.7), 0.7% (95% CI 0.6–0.8) for point self-reported prevalence, and 0.1% (95% CI 0.06–0.3) for FC positivity. The estimates were higher in older age groups than in younger age groups (Fig. 8). All studies on lifetime self-reported prevalence of shellfish allergy were undertaken in Western Europe, while
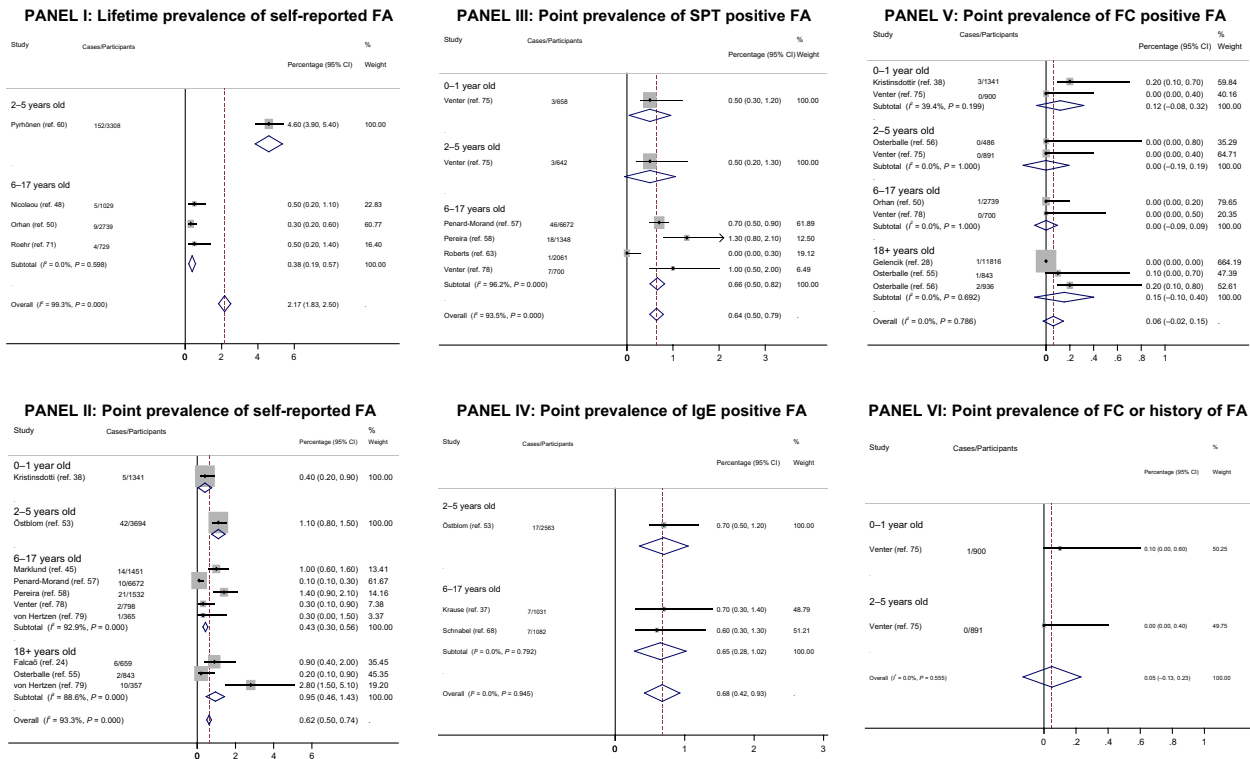
Figure 7 Age-stratified pooled prevalence of fish allergy (FA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI, and boxes represent the size of the study.

Figure 8 Age-stratified pooled prevalence of shellfish allergy (SFA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI, and boxes represent the size of the study.
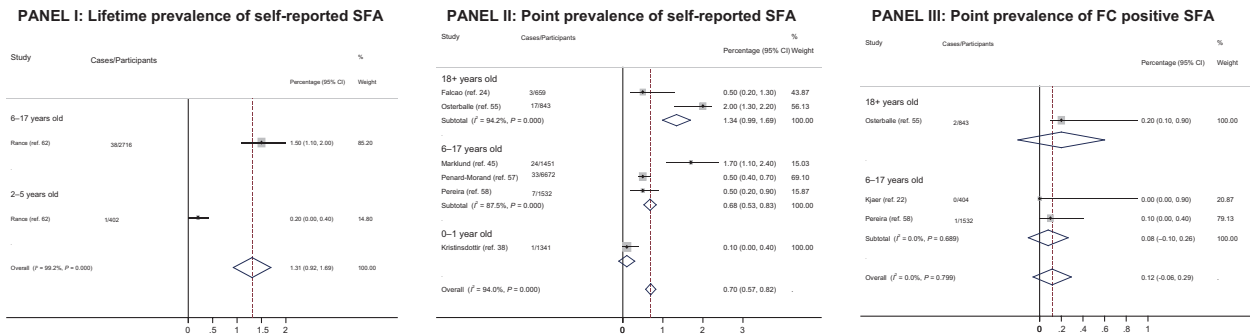
studies on point prevalence of self-reported shellfish allergy and FC positivity were undertaken only in Western and Northern Europe. While the pooled estimates for self-reported point prevalence of shellfish allergy were higher in Northern Europe, the estimates were comparable between the two regions with regard to FC positivity (Fig. S9).

Discussion

Statement of main findings

This synthesis of studies provides the most comprehensive and up-to-date estimates of the frequency of the eight most common specific food allergies across different age groups and geographical regions in Europe. Overall, most studies were graded as at 'moderate' risk of bias, taking into account appropriateness of the study design, potential for selection bias, and exposure and outcome assessment methods used. Most of the studies were undertaken among children, usually those <18 years of age. Only a few studies were undertaken in Eastern and Southern Europe compared with studies from Western and Northern Europe.

The overall pooled lifetime self-reported prevalence was highest for cow's milk allergy (6.0%) and lowest for soy allergy (0.3%). The point self-reported prevalence was also highest for cow's milk allergy (2.3%) but lowest for fish allergy (0.6%).

Based on objectively verified FC, the prevalence was also highest for cow's milk allergy (0.6%) and lowest for wheat and shellfish allergies, both each having 0.1% prevalence. Generally, the prevalence of cow's milk allergy and egg allergy was higher in younger age groups than older age groups, while the prevalence of peanut allergy, tree nut allergy, fish allergy, and shellfish allergy was higher in the older age groups than in the younger age groups. There were insufficient data to compare the estimates of soy and wheat allergy between the age groups as in most cases only one study was available for particular age group. The prevalence of cow's milk allergy, egg allergy, wheat allergy, tree nut allergy, fish allergy, and shellfish allergy was in general higher in Northern Europe than in other regions, while the prevalence of soy allergy and peanut allergy was higher in Western Europe than in other regions.

Strengths and limitations

In addition to the rigorous steps undertaken to produce the current synthesis, other strengths of the review include a comprehensive literature search that covered the major electronic databases, although we cannot rule out the possibility that our search terms might have missed some relevant articles, no language restriction, and systematic and painstaking screening and appraisal of the primary studies included. We, however, limited the period of the review to studies published only in Europe between 2000 and 2012 due to the large quantity of studies found at the initial search; this will limit the generalizability of findings beyond the period in focus and outside Europe. We observed significant heterogeneity between the studies, which might indicate important differences between studies in terms of study design and methods used to measure food allergy, particularly FC and SPT methodologies. There were also wide variations in participation rates across studies, ranging between 17.3 and 99.5%, while in several studies, neither the participation rates were reported nor there were adequate information provided to allow for recalculation, thus indicating potential selection bias in several of the studies. These methodological limitations will influence the estimates of the frequency of food allergies reported from this pooled analysis, and most likely, the pooled estimates are underestimates of the actual frequencies. We therefore recommend that caution should be exercised in interpreting these results. Unexpectedly, the point prevalence estimates of peanut and tree nut allergies were greater than their lifetime prevalence estimates. Although one reason for this discrepancy is that the estimates of lifetime and point prevalence came from different studies, a more plausible explanation is that this underscores the need for consistent study designs and reporting of results in future studies.

To our knowledge, this is the first study that provides comprehensive estimates of the prevalence of the most common specific food allergies across the different geographical regions of Europe and well-defined age groups. The observed regional differences in the estimates of the different food allergies may indicate the importance of spatial distributions of the diseases; hence, spatial distributions of food allergies should be considered in future studies. The observed regional differences may also reflect the variations and nonstandardized methods

applied in the assessment of food allergies across the different European settings. Very few studies were undertaken in Eastern and Southern Europe, possibly a true reflection of fewer studies undertaken in these settings in this evidence base or that most studies are published in local journals and not indexed in the databases included in our search. Clearly, more studies are required from these regions to establish the putative frequency of food allergies.

A further strength of this study is that we were able to analyze all possible methods that have been used to measure food allergy, including self-report, SPT, specific IgE sensitization, FC, and the various combination of these measures, particularly FC or convincing clinical history. However, because of the wide variations in the definition of food allergies based on each of these methods, particularly, the cutoff points used to define IgE or SPT sensitization to food allergens across the studies, comparison of estimates across studies is challenging. As indicated in our previous report (9), we were interested in estimating the frequency of IgE-mediated and non-IgE-mediated phenotypes of food allergy, but this was not feasible as most studies failed to make clear the different phenotypes of food allergy studied. The methodological grading of most of the studies was moderate, and as we also noted earlier (9), there is an opportunity to improve the methodological quality of studies across all regions. In particular, more systematic application of established standard methods for the assessment of food allergy across populations would improve the measurement of food allergies and allow for better comparison between studies.

Comparison of our findings with previous studies

Only three previous systematic reviews (15,65,80) have examined the prevalence of food allergies; however, comparison of our findings is primarily made with regard to two of these studies (65,80) as the third study (15) presented estimates already given in one of the studies (65). Rona et al. (65) presented range of estimates that are to a great extent comparable with the ranges of estimates we have reported in this study. It was not, however, clear whether the self-reported estimates in that study were lifetime prevalence or point prevalence. In the study by Zuidmeer et al. (80), the pooled self-reported prevalence of wheat allergy among adults was 0.4% and 2.1% for point prevalence of specific IgE sensitization, although it was not also clear whether the self-reported estimates were lifetime or point prevalence. The point prevalence of self-reported wheat allergy in the present study among adults was 1.5%, whereas we did not find any eligible studies for pooling among adults based on specific IgE sensitization to wheat. Among children, Zuidmeer et al. presented pooled self-reported prevalence of tree nut allergy of 0.5%, soy allergy of 0.3%, and SPT positivity to wheat of 0.4%. In our study, the corresponding point prevalence of self-reported tree nut allergy among children was up to 1.8%, 4.2% for soy allergy, and 3.9% for SPT positivity to wheat, much greater estimates than the estimates given by Zuidmeer et al. (80). Similar to our observation, the prevalence of tree nuts compared with other allergies was higher among adults than in children in the study by Zuidmeer

et al. (80), possibly indicating difference in timing of introduction of these foods. Some of the discrepancies between our estimates and those of the previous reviews could be explained by the fact that the previous reviews included studies from all parts of the world, whereas our study was limited only to Europe. In addition, the previous reviews included studies from 1990, whereas the earliest studies in our review were those published in 2000.

Conclusions

The current study has provided so far the most comprehensive and up-to-date estimates of the eight most common food allergies across different age groups and regions in Europe. Overall, at least one in 20 children is believed by parents to have had one or more food allergy in their lifetime. Dairy products are the most foods commonly implicated by parents. There was, however, up to a 15-fold difference between self-reported and challenge-verified prevalence of food allergy, with these differences being most marked for wheat, peanut, egg, shellfish, and least for tree nuts. This discrepancy, particularly for milk, soy, and wheat, may in part be due to non-IgE-mediated food allergy. The prevalence of food allergy varied by age groups and European regions. Further studies will improve this evidence base by employing standardized methodology for the assessment of food allergies, IgE and non-IgE mediated, across populations and initiating strategies that will increase participation rates across studies.

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Author contributions

AS, AM, and GR conceived this review. It was undertaken by BN and LH, with the support of SSP. BN, LH, and AS led the drafting of the manuscript, and all authors critically commented on the drafts of the manuscript.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Supporting Information

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

Table S1. Summary of evidence on the frequency of allergy to cow's milk, hen's egg, wheat, and soy in Europe: studies published 1 January 2000 – 30 September 2012.

Table S2. Summary of evidence on the frequency of allergy to peanut, tree nut, fish, shellfish in Europe: studies published 1 January 2000 – 30 September 2012.

Table S3. Summary of range of estimates of lifetime and point prevalence of each specific food allergy in Europe by different methods of assessment: estimates from studies published between 1 January 2000 and 30 September 2012.

Figure S1. PRISMA flow diagram for studies on the epidemiology of food allergy in Europe, 2000–2012.

Figure S2. Region-stratified pooled prevalence of cow's milk allergy (CMA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI and boxes represent the size of the study.

Figure S3. Region-stratified pooled prevalence of egg allergy (EA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI and boxes represent the size of the study.

Figure S4. Region-stratified pooled prevalence of wheat allergy (WA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI and boxes represent the size of the study.

Figure S5. Region-stratified pooled prevalence of soy allergy (SA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI and boxes represent the size of the study.

Figure S6. Region-stratified pooled prevalence of peanut allergy (PA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI and boxes represent the size of the study.

Figure S7. Region-stratified pooled prevalence of tree nut allergy (TNA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI and boxes represent the size of the study.

Figure S8. Region-stratified pooled prevalence of fish allergy (FA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI and boxes represent the size of the study.

Figure S9. Region-stratified pooled prevalence of shellfish allergy (SFA) in studies published in Europe between January 2000 and September 2012. Markers represent percentages and 95% CI and boxes represent the size of the study.

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Appendix 1
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