

## The prevalence of plant food allergies: A systematic review

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**Background:** There is uncertainty regarding the prevalence of allergies to plant food.

**Objective:** To assess the prevalence of allergies to plant food according to the different subjective and objective assessment methods.

**Methods:** Our systematic search of population-based studies (since 1990) in the literature database MEDLINE focused on fruits, vegetables/legumes, tree nuts, wheat, soy, cereals, and seeds. Prevalence estimates were categorized by food item and method used (food challenges, skin prick test, serum IgE, parent/self-reported symptoms), complemented by appropriate meta-analyses.

**Results:** We included 36 studies with data from a total of over 250,000 children and adults. Only 6 studies included food challenge tests with prevalences ranging from 0.1% to 4.3% each for fruits and tree nuts, 0.1% to 1.4% for vegetables, and <1% each for wheat, soy, and sesame. The prevalence of sensitization against any specific plant food item assessed by skin prick test was usually <1%, whereas sensitization assessed by IgE against wheat ranged as high as 3.6% and against soy as high as 2.9%. For fruit and vegetables, prevalences based on perception were generally higher than those based on sensitization, but for wheat and soy in adults, sensitization was higher. Meta-analyses showed significant heterogeneity between studies regardless of food item or age group.

**Conclusion:** Population-based prevalence estimates for allergies to plant products determined by the diagnostic gold standard are scarce. There was considerable heterogeneity in the prevalence estimates of sensitization or perceived allergic reactions to plant food. (*J Allergy Clin Immunol* 2008;121:1210-8.)

**Key words:** Cereal, EuroPrevall, food allergy, food hypersensitivity, fruit, meta-analysis, nuts, prevalence, seeds, soy, vegetables, wheat

There is uncertainty regarding the prevalence of food allergy (FA), particularly to fruits, vegetables, nuts, and other edible plants. Although diagnostic studies have objectively verified allergic reactions caused by ingestion of plant food, the extent of the problem on the population level remains unclear for patients and their families, schools, the catering industry, food producers and retailers, health professionals, and policy makers.<sup>1,2</sup>

Most population-based studies have not included the diagnostic gold standard double-blind, placebo-controlled food challenge (DBPCFC) tests,<sup>3-7</sup> but have based their estimates only on perception of reactions to plant food. There has been no systematic approach of summarizing the prevalence of plant FA in the community.

Furthermore, only few studies have assessed the effect of FA on costs and quality of life for patients and their families.<sup>8-10</sup> To fill this gap, EuroPrevall, a large Europe-wide research project funded by the European Commission, was officially launched in June 2005 to evaluate the prevalence, basis, and cost of FA.<sup>11</sup> Within this integrated project, a network of collaborators are summarizing the state of the art in several disciplines, including the diagnosis focusing on IgE-mediated FA.<sup>12</sup> Our working group recently performed a meta-analysis based on food items most commonly ascribed to FA,<sup>13</sup> but with the exception of peanuts, we did not tackle plant food. Therefore, the aim of the second part of our systematic review was to summarize the prevalence of plant FA separately for fruit, vegetables, legumes, tree nuts, wheat, soy, and other edible plants.

## METHODS

### General approach

The methods are described in detail in our first report of an overall estimate of the prevalence of FA, as well as on specific allergies to cow's milk, hen's egg, peanut, fish, and shellfish.<sup>13</sup> For the current report, we defined 6 categories of plant food: fruits, vegetables/legumes, tree nuts, soy, wheat, and sesame/cereals/spices/herbs. We summarized the information in 4 separate categories of assessment: food challenge studies including both open challenge and DBPCFC, sensitization assessed by serum IgE, sensitization assessed by skin prick tests (SPT), and perception of FA.

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#### Abbreviations used

DBPCFC: Double-blind, placebo-controlled food challenge  
FA: Food allergy  
MeSH: Medical Subject Heading  
SPT: Skin prick test

## Search strategy

Following closely the guidelines from the Cochrane Handbook for Systematic Reviews,<sup>14</sup> we systematically searched the medical literature database MEDLINE (using PubMed) for the time period of January 1990 to December 2006. We defined 3 groups of Medical Subject Headings (MeSHs) and free-text terms: (1) “prevalence[MeSH]” and “incidence[MeSH]”; (2) “allergy and immunology[MeSH],” “hypersensitivity[MeSH],” “food hypersensitivity[MeSH],” “skin tests[MeSH],” “immunoglobulin E[MeSH],” and the free-text terms “challenge” and “provocation”; (3) “plants, edible [MeSH],” “vegetables[MeSH],” “cereals[MeSH],” “fruit[MeSH]” (includes “nuts”), “rutaceae[MeSH]” (includes “citrus”), “rosales[MeSH],” and 48 free-text terms using specific names for edible plant food.

## Study selection

For the current report, all titles and abstracts of identified articles were screened and the full text evaluated if appropriate. We also hand-searched their references and contacted experts in the area of FA, including the collaborating FA researchers within the European Union-funded Integrated Project EuroPrevall.<sup>11</sup>

Regarding the study design, we included only population-based cross-sectional and cohort studies. We excluded case-control studies, studies in selected patient groups with, for example, asthma or eczema, and those performed in clinical settings, because they do not provide appropriate unbiased estimates of FA prevalence in the community. Furthermore, we excluded studies that had enriched study samples with patients with allergy (for further clinical studies), or articles that did not report the sample size. Using an extraction sheet, we obtained information on relevant study characteristics, prevalence estimates, and 95% CIs of parent-reported/self-reported FA, sensitization assessed by IgE or SPT, as well as subjects with a positive food challenge test result. Each full-text article was evaluated independently by at least 3 researchers of the working group. Differences between the reviewers were discussed to find consensus.

## Analysis

If not specifically reported in the results section of the included articles, the prevalence estimates and 95% CIs for each food item were calculated by the reviewers, wherever possible, from the information presented in tables, graphs, or the text of the article. The exact 95% CIs were computed using the Wilson method<sup>15</sup> and displayed as lines on the bar, representing the corresponding prevalence estimate. We tabulated each study with information on author, year, country, age, total number of participants, and food item, but at the same time gave a graphical representation for a better comparison of the prevalence estimates for each of the 6 plant food categories. Within each category, we subclassified the prevalence estimates and 95% CIs by type of FA assessment and arranged the results per food item and, if possible, by increasing age of study participants, starting with the findings for the youngest age group. In our first report on the most commonly reported FA, we performed meta-analyses for each food item stratified into the following groups: under 5 years (infants/preschool children), 5 to 16 years (school-children/adolescents), and 17 years and older (adults). Because there were fewer studies for any specific food item on plant FAs, we stratified the meta-analyses only in 2 age categories: adults and children (up to age 17 years). At least 5 studies with prevalence estimates were available in adults for perceived allergic reactions to fruit, vegetables, and wheat, as well as for sensitization (assessed by IgE) against wheat, and in children for perceived allergic reactions to tree nuts and soy and for sensitization (assessed by SPT) against wheat.

In studies giving 1 overall estimate although both children and adults participated, we used the estimate in the most common age stratum, usually adults,<sup>6,16-18</sup> and in 1 case, children.<sup>8</sup> One study reported a prevalence of 0%,<sup>19</sup> which we increased slightly to 0.3% (assuming 1 child was positive) to be able to calculate the SE. The estimates of the meta-analyses were based on approximate 95% CI because of software restrictions. These prevalence estimates should be considered with caution given the strong heterogeneity between studies in each of the analysis. For these analyses, we used the statistical software package STATA 9.2 (Stata Corp, College Station, Tex) with random-effects meta-analytic models.

## RESULTS

Out of 396 identified references (380 hits in MEDLINE plus 16 hand search articles), we excluded 363 after screening the title/abstract or reading the full text for the following reasons: 160 articles were about plant FA but did not indicate prevalence estimates; 124 articles reported prevalences only from studies with selected participants such as workers in a food processing factory, patients attending an allergy clinic, and so forth; and 76 articles were editorials, narrative reviews, guidelines, and so forth. Three studies were excluded because they reported only a combined prevalence for fruits and vegetables.<sup>4,20,21</sup> Included for the current report were 33 publications reporting results of 36 studies with data from a total of 254,297 children and adults (ranging from 141 participants in the smallest to 92,680 in the largest study).

Twenty-seven studies originated from Europe,<sup>3-6,9,17-19,21-37</sup> 4 from the United States,<sup>16,38-40</sup> 1 from Australia/New Zealand,<sup>41</sup> 1 from all of the above,<sup>36</sup> and 1 each from Israel,<sup>42</sup> Russia,<sup>43</sup> and Asia.<sup>44</sup> Thirty investigations were cross-sectional studies, whereas 6 were cohort studies. Twenty studies examined only children and/or adolescents. The majority of prevalence estimates for allergies to plant food in the current report was based on perceived reactions. Few studies used an objective assessment (food challenge test) or determined sensitization by IgE or SPT (see this article's Table E1 in the Online Repository at [www.jacionline.org](http://www.jacionline.org)). Several studies reported prevalence estimates for the 3 main plant food groups (fruit, vegetables, and tree nuts) without specifying the food items (Table 1; see this article's Fig E1 in the Online Repository at [www.jacionline.org](http://www.jacionline.org)).

## Fruit

Challenge tests were performed in 4 studies with prevalence estimates ranging from 0.1% to 4.3%. Apart from a German study, the prevalence of sensitization (assessed by SPT) to specific fruits was well below 1%. In adults, the prevalence of perceived allergy to any fruit varied from 0.4% to 3.5% (see Fig E1), whereas in young children <3 years it ranged as high as 11.5% (Norway). This age group also showed the highest estimates of perceived reactions to specific fruits: 8.5% to apple, and 6.8% to orange and/or lemon. For adults, the prevalence of perceived allergic reactions to specific fruits was below 1% in all studies (Fig 1).

## Vegetables/legumes

In children, prevalence estimates from challenge tests and SPT were all below 0.5% for specific vegetables, whereas the only study in adults showed higher estimates. The highest prevalence for perception of allergy to vegetables was reported for Swedish children at 1.5 years of age (13.7% to tomato). In adults, the highest prevalence was found in a Dutch study (2.2% to any vegetable; Fig 2; Fig E1).

**TABLE I.** Summary of population-based prevalence estimates of allergy or sensitization to general plant food groups by diagnostic method

Diagnostic method	DBPCFC for plant food allergy	Sensitization to plant food (range of prevalence estimates)	Perceived allergy to plant food groups (range of prevalence estimates)		
			Children		
			Age 0-6 y	Age 6-18 y	Adults†
Plant food group (references)					
Fruit (3, 6, 8, 16-20, 26, 27, 41, 43)	NR	NR	2.2% to 11.5%		0.4% to 6.6%
Vegetables (3, 6, 7, 9, 16, 18, 26, 33, 41)	1.4% (all ages)	NR	0.7% to 3.3%	NR	0.5% to 2.2%
Tree nuts* (6, 8, 16-9, 21, 26, 29, 32-34, 39, 41, 42)	NR	0.02% to 0.7% (preschool children)	0.03% to 0.2%	0.2% to 2.3%	0.4% to 1.4%

NR, Not reported as a prevalence for the general plant food group; reported only for specific plant food items (see Figs 1-5).

For detailed study results, see Fig E1. For prevalence estimates of specific plant food items, see Figs 1-5.

\*For prevalence of peanut allergy, see Rona et al.<sup>13</sup> Several studies reported a prevalence for perceived allergy to nuts, but the authors did not report whether peanuts were also included.<sup>6,8,16,19,21,26,33</sup>

†Some studies included children and adults but did not report age group-specific prevalence estimates. They were included under "Adults" if the study participants were predominantly adults.

### Tree nuts

Both for challenge tests and for sensitization assessed by SPT, the highest prevalence estimates of more than 4% were found for hazelnut. The highest prevalence estimate for perceived reactions to a specific tree nut was reported in Swedish adolescents: 4.1% to almond. The prevalence of perceived reactions to any nuts ranged from 0% to 7.3% (Fig E1; some authors did not report whether this included peanut). Results for peanut allergy were included in our previously published meta-analysis of the most commonly studied food items<sup>13</sup> (Fig 3).

### Wheat

Two studies from the United Kingdom and 1 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 higher (>3% in several studies) than for perception (<1%). On the contrary, in children <15 years, perception of allergic reactions to wheat (>1%) were slightly higher than sensitization assessed by SPT (all <1%; Fig 4).

### Soy

In adults and adolescents, the highest prevalence estimates were found in 3 Swedish studies (sensitization assessed by IgE as high as almost 3%, and perception 1.3%). Studies from all other countries showed prevalences well below 1% regardless of method used or age group (Fig 5).

### Sesame, cereals, spices, and condiments

Prevalence estimates for other plant food items were most commonly published for sesame (challenge test, sensitization assessed by SPT, and perception), followed by cereals and spices/condiments (only perception; see this article's Fig E2 in the Online Repository at [www.jacionline.org](http://www.jacionline.org)).

### Meta-analyses and tests of homogeneity

For 7 plant food categories in which 5 studies or more were available, we conducted meta-analyses. In adults, there was significant heterogeneity ( $P < .001$ ) among the 7 studies regarding perception of allergy caused by fruits (summary prevalence estimate, 1.22%; 95% CI, 0.82-1.63), vegetables (6 studies: 0.98%; 0.52-1.45), and wheat (5 studies: 0.40%; 0.21-0.59), as well as

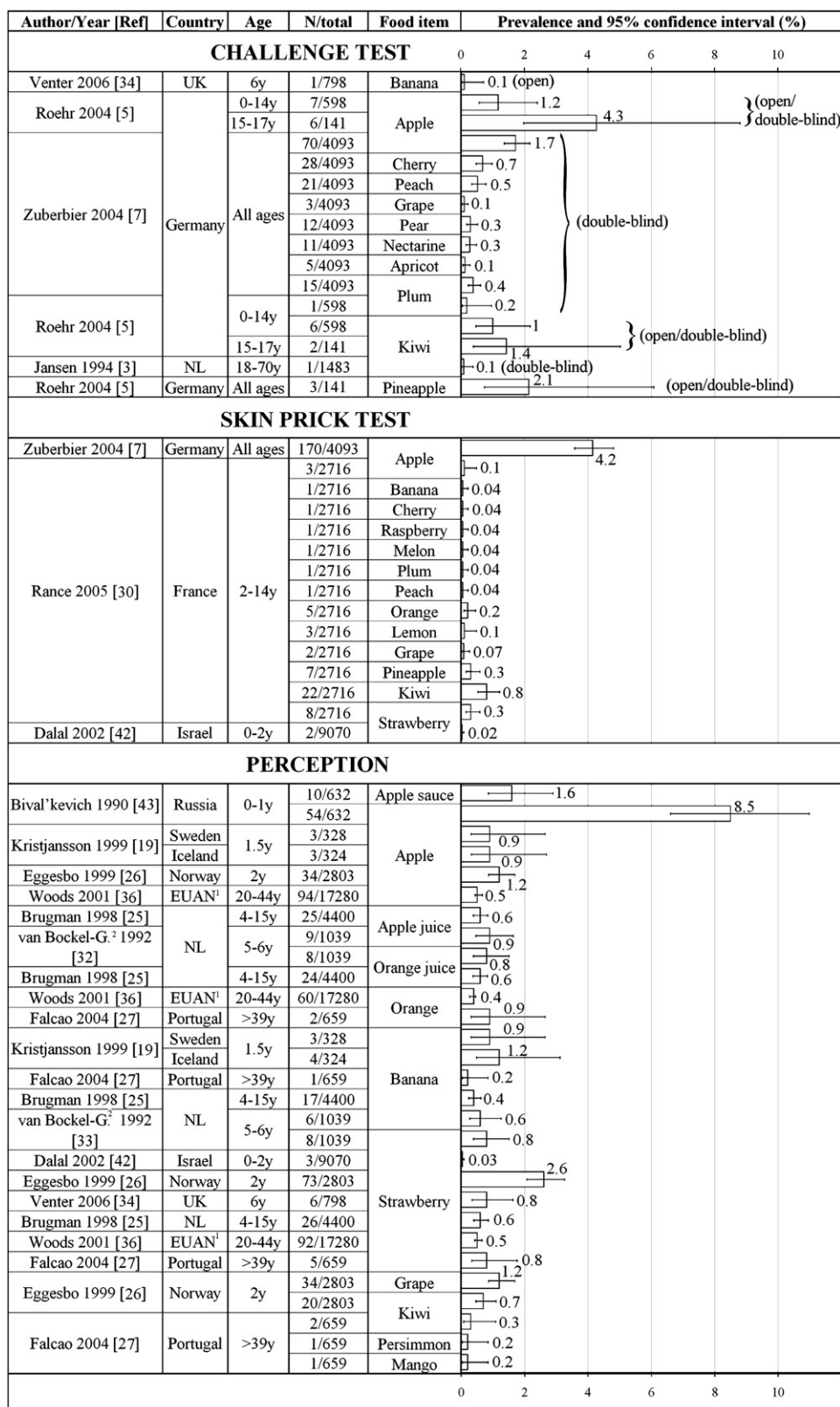
for sensitization against wheat (assessed by IgE in 5 studies: 2.08%; 0.87-3.29). Similarly, among studies in children, the heterogeneity was significant ( $P < .001$ ) for perception of allergy caused by tree nuts (5 studies: 0.52%; 0.20-0.85) or soy (7 studies: 0.34%; 0.12-0.56), whereas the heterogeneity was of a lower level but still significant ( $P = .016$ ) among the 5 studies assessing sensitization against wheat by SPT (0.43%; 0.16-0.70).

## DISCUSSION

### Principal findings

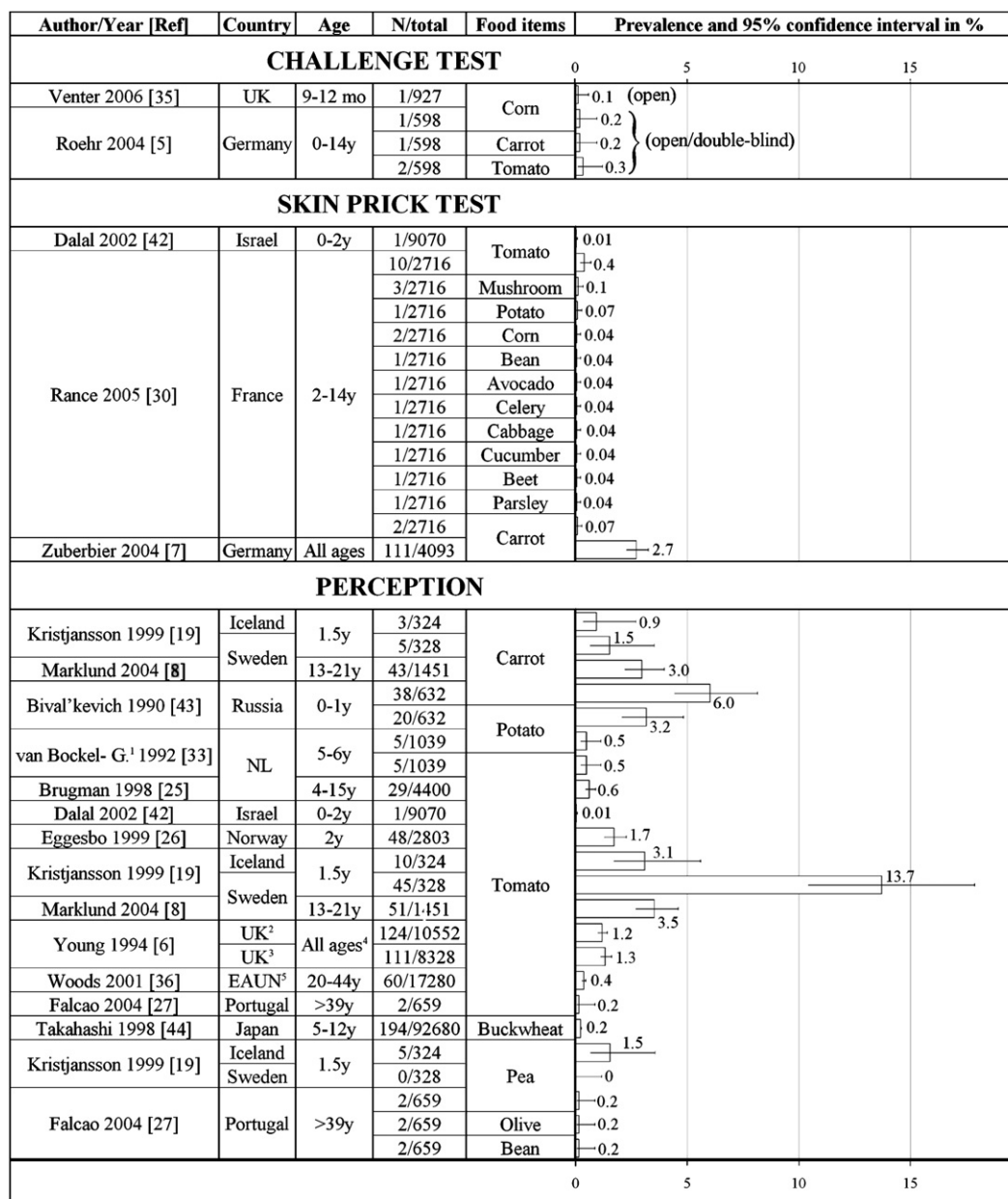
The majority of prevalence estimates for allergies to plant food was based on self-reported reactions to food. Few studies used objective assessments such as open or double-blind food challenge tests or determined sensitization to foods (by serum IgE or SPT). As in our previous meta-analyses of the most commonly reported foods,<sup>13</sup> our current findings for plant FA also showed that prevalence estimates based on self-reported assessments were well above those based on any of the objective assessments with the exception of soy and wheat. For fruits and vegetables, the self-reported prevalences were higher in children than in adolescents or adults, whereas for tree nuts, the opposite was true, possibly because of a later introduction into the diet. The difference between the higher prevalence estimates based on perception compared with sensitization was more apparent for fruits and vegetables than for the other food groups. This is probably a result of the heterogeneous nature of this food group. Nuts are often eaten separately and can be more easily identified as the possible cause of their perceived reaction than fruits and particularly vegetables, which are often eaten in mixed dishes and as such are harder to identify as the single culprit food.

Furthermore, certain foods (strawberries, citrus fruit, and tomatoes) are thought to stimulate the tissue mast cells directly to release histamine, causing symptoms that may mimic true FA while specific IgE antibodies to these foods are not elevated.<sup>45-47</sup> Indeed, the parent-reported prevalence for citrus fruits and tomato in young children was relatively high.<sup>19,26</sup> However, because this was the perception of the parents who filled out the questionnaires, this may be explained by non-IgE mediated food hypersensitivity rather than FA. Furthermore, spices in the foods can cause sensations in and around the oral cavity that can be mistaken for allergic reactions.



**FIG 1.** The prevalence of allergy to specific fruit by diagnostic method. SPT results  $\geq 3$  mm<sup>2</sup> were considered positive. N/total, Number of study participants with (reported) FA/the total number investigated. <sup>1</sup>Europe, United States, Australia, New Zealand. <sup>2</sup>van Bockel-Geelkerken. UK, United Kingdom; NL, The Netherlands.





**FIG 2.** The prevalence of allergy to specific vegetables/legumes by diagnostic method. SPT results  $\geq 3$  mm<sup>2</sup> were considered positive. N/total, Number of people with (reported) FA/the total number investigated. <sup>1</sup>van Bockel-Geelkerken. <sup>2</sup>Wycombe area. <sup>3</sup>Nationwide. <sup>4</sup>Seventy-two percent were  $\geq 20$  years. <sup>5</sup>Europe, United States, Australia, New Zealand.

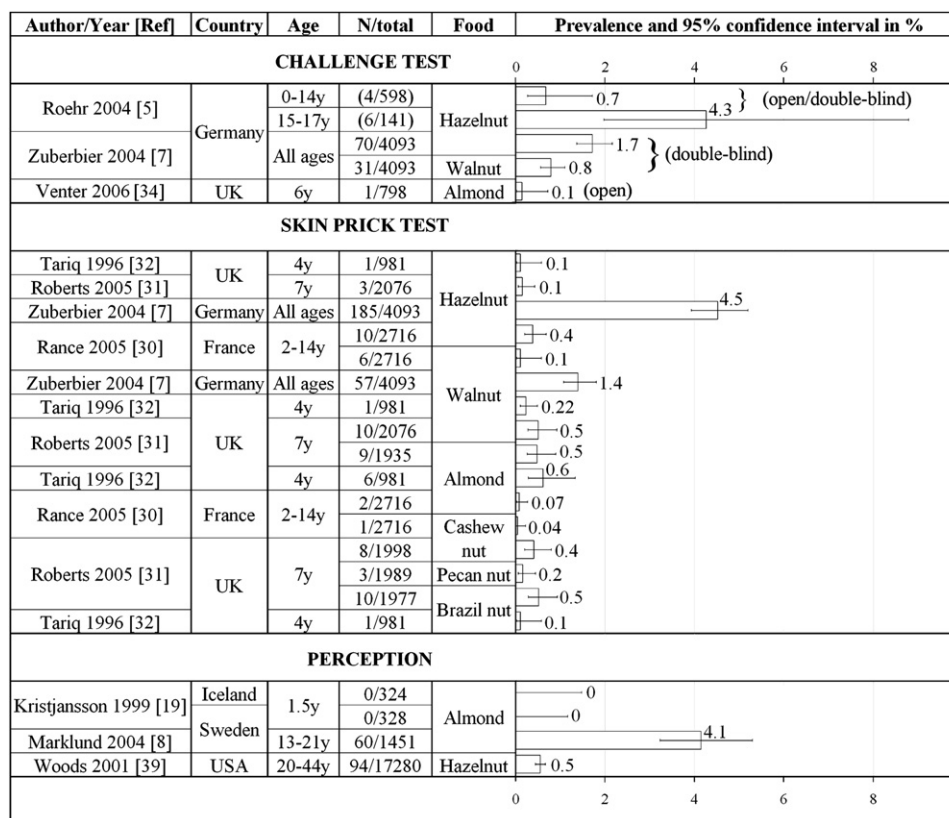
## Methods used

Although double-blind challenge tests are considered to be the diagnostic gold standard for FA, they are not always performed to secure the diagnosis. Some patients with FA do not undergo these laborious and time-consuming provocation tests if the diagnosis (for example, based on sensitization and elimination diet) is clear to the study physician. In some studies, the researchers were unable to perform food challenge tests to confirm putative IgE-mediated symptoms to many foods.<sup>3,4</sup> Furthermore, those who are not troubled by their FA symptoms are less likely to participate in food challenge assessments and may refuse a DBPCFC. Other study participants might have been excluded from challenge because they have reported a severe anaphylactic

reaction.<sup>6</sup> These factors can contribute to an underestimation or uncertainty of the reported prevalence for challenge tests.

We separated IgE assessments and SPT as indicators of sensitization. prevalence comparisons are difficult because IgE and SPT techniques are not standardized between manufacturers and may have changed over time. IgE sensitization data were only available for wheat and soy.

For plant food in general, the authors rarely reported the proportion of study participants with symptoms and concurrent sensitization against the suspected food item, or of those sensitized with FA symptoms. However, particularly if challenge tests are not available, it would be important to know whether symptomatic individuals are sensitized.



**FIG 3.** The prevalence of allergy to specific tree nuts by diagnostic method. SPT results  $\geq 3$  mm<sup>2</sup> were considered positive. N/total, Number of people with (reported) FA/the total number investigated.

Perception of FA was assessed using parent-reported or self-reported FA questionnaires, but the authors did not comment whether the instruments were validated. The subjective assessments varied from a minimum of 2 short questions to a 2-stage assessment including a screening questionnaire and an interview to confirm suspicion of FA.<sup>5,36,37</sup> Several studies determined perceived allergies to food groups, such as fruit or vegetables, but defined them differently: 1 study made a distinction between citrus fruit and noncitrus fruit,<sup>6</sup> whereas others examined perceived FA to any fruit<sup>8,16-18,21,48</sup> or focused only on specific fruits.<sup>5,19,26,27,30,36,37</sup>

Furthermore, there is a distinction between the botanical categorization of foods and the perception of the public (tomato is believed to be a vegetable; coconuts and peanuts are believed to be nuts). The prevalence for nut allergy could be overestimated when peanut (a legume)-related complaints are shared under the header of "nuts" in a questionnaire.

There was a marked variation in response rates from as low as 31.1%<sup>5</sup> to almost 100%.<sup>3</sup> Low response rates may bias (ie, overestimate) the prevalence if subjects without FA are less inclined to respond to a questionnaire than those suspecting a problem. In 2 German studies with response rates of 40% and less,<sup>5,37</sup> the prevalence estimates were significantly higher (eg, 4.2% for apple as determined by SPT, compared with 0.1% in a French study).<sup>30,37</sup>

## Limitations

A possible limitation of the current report may be the search strategy. Although we did not exclude any language in

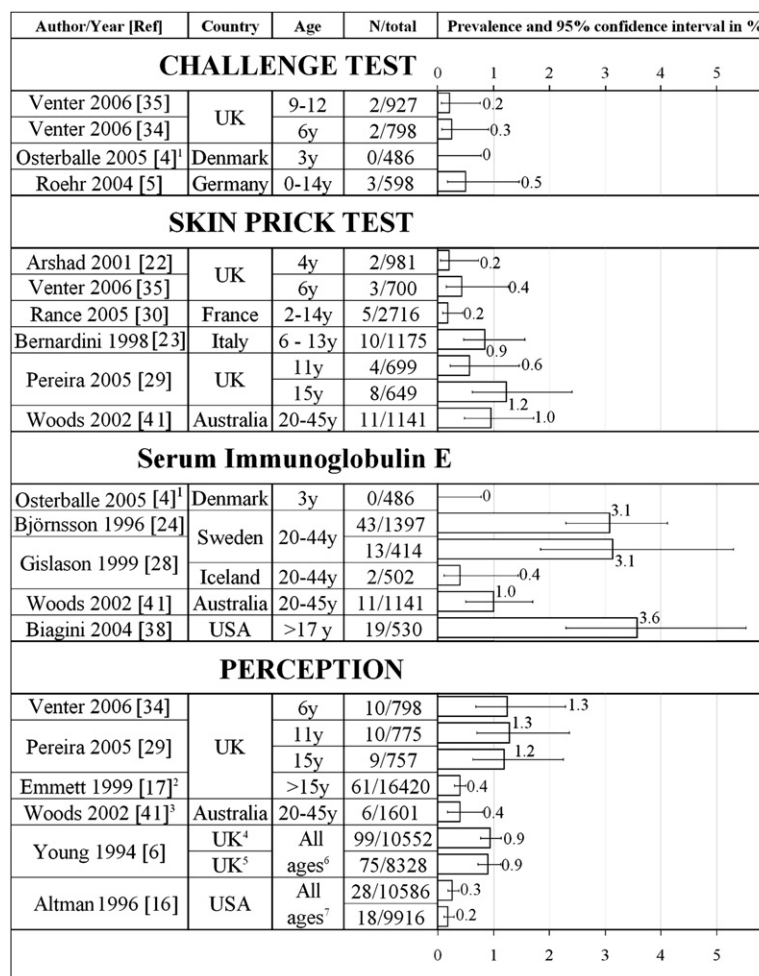
our systematic search, we cannot rule out that studies were missed, particularly from non-European or non-American journals. We were able to include only 1 study from Asia<sup>44</sup> and identified only 1 study from the African continent, which we had to exclude because a combined estimate for perception of allergic reactions to fruit and vegetables was reported.<sup>16,20,38-40</sup>

The comparison of prevalence estimates from different studies, particularly for perception of allergic reactions, is hampered by using different types of prevalence such as point or period (eg, lifetime) 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 FA 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.

## Conclusion

We found only few reported cases of confirmed allergies to plant food in population-based studies worldwide since 1990. Only 6 studies (all from Northern and Western Europe) that used the diagnostic gold standard were identified. Population-based studies of good quality to determine the true prevalence of FA are not currently available for most countries in the world. Complementing our previous review,<sup>13</sup> this analysis also indicated that we should be cautious in placing too much reliance on published prevalence estimates for allergy to plant food.



**FIG 4.** The prevalence of allergy to wheat by diagnostic method. SPT results  $\geq 3$  mm<sup>2</sup> were considered positive. N/total, Number of people with (reported) FA/the total number investigated. <sup>1</sup>Data for parents and siblings of study children not shown. <sup>2</sup>Wheat, flour, gluten. <sup>3</sup>Wheat products, bread, plain cereals. <sup>4</sup>Wycombe area. <sup>5</sup>Nationwide. <sup>6</sup>Seventy-two percent were  $\geq 20$  years. <sup>7</sup>Age distribution was not reported in this survey of US households (for 1989, N = 10586; for 1993, N = 9916).

However, a large number of studies focusing on perceived reactions suggest that subjectively assessed FA prevalence has a different dimension and may negatively affect the quality of life of patients and their families.

Standardization of questionnaires, materials used for diagnostic tests<sup>12</sup> and study methods, and a high response rate in population-based studies are important requirements for acquiring reliable prevalence estimates. In this respect, the European Union-funded Integrated Project EuroPrevall, whose pan-European cross-sectional study in adults and longitudinal study in children are based on standardized methodology and technology, will contribute to the generation of more reliable data from Europe, encompassing the clinical, socioeconomic, and quality of life effects of FA.<sup>11</sup>

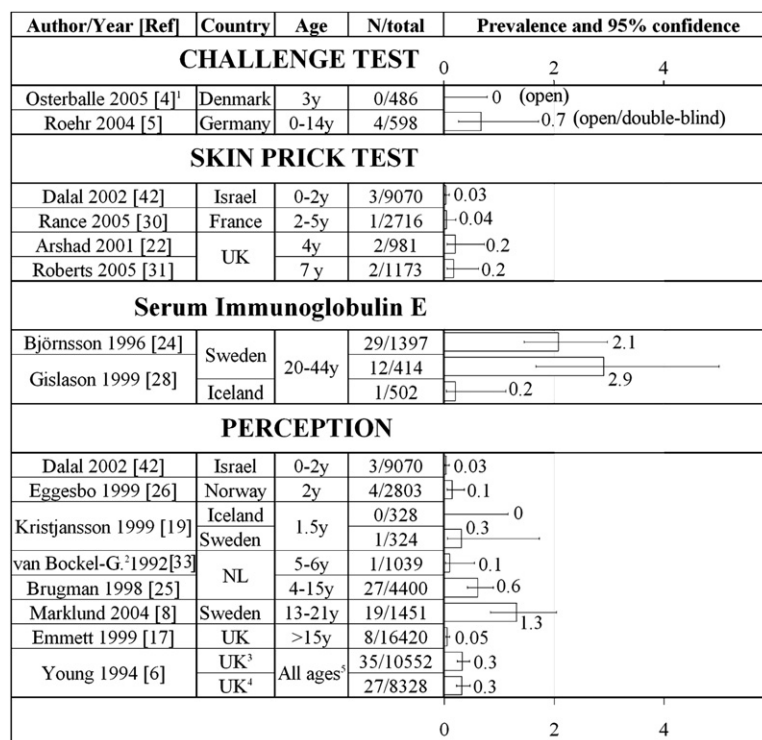
We expect that the European cross-sectional study in adults and longitudinal study in children will help solve current uncertainties on the prevalence of FA.

We thank Dr P. M. Matricardi and N. Luther and M. Kashiwabara for their translational help.

**Clinical implications: Prevalence estimates of plant FA based on self-reported symptoms should be treated with caution. Suspected allergic reactions to plant food should be confirmed with double-blind, placebo-controlled challenge tests.**

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**FIG 5.** The prevalence of allergy to soy by diagnostic method. SPT results  $\geq 3$  mm<sup>2</sup> were considered positive. *N/total*, Number of people with (reported) FA/the total number investigated. <sup>1</sup>Data for parents and siblings of study children not shown. <sup>2</sup>van Bockel-Geelkerken. <sup>3</sup>Wymcombe area. <sup>4</sup>Nationwide. <sup>5</sup>Seventy-two percent were  $\geq 20$  years.

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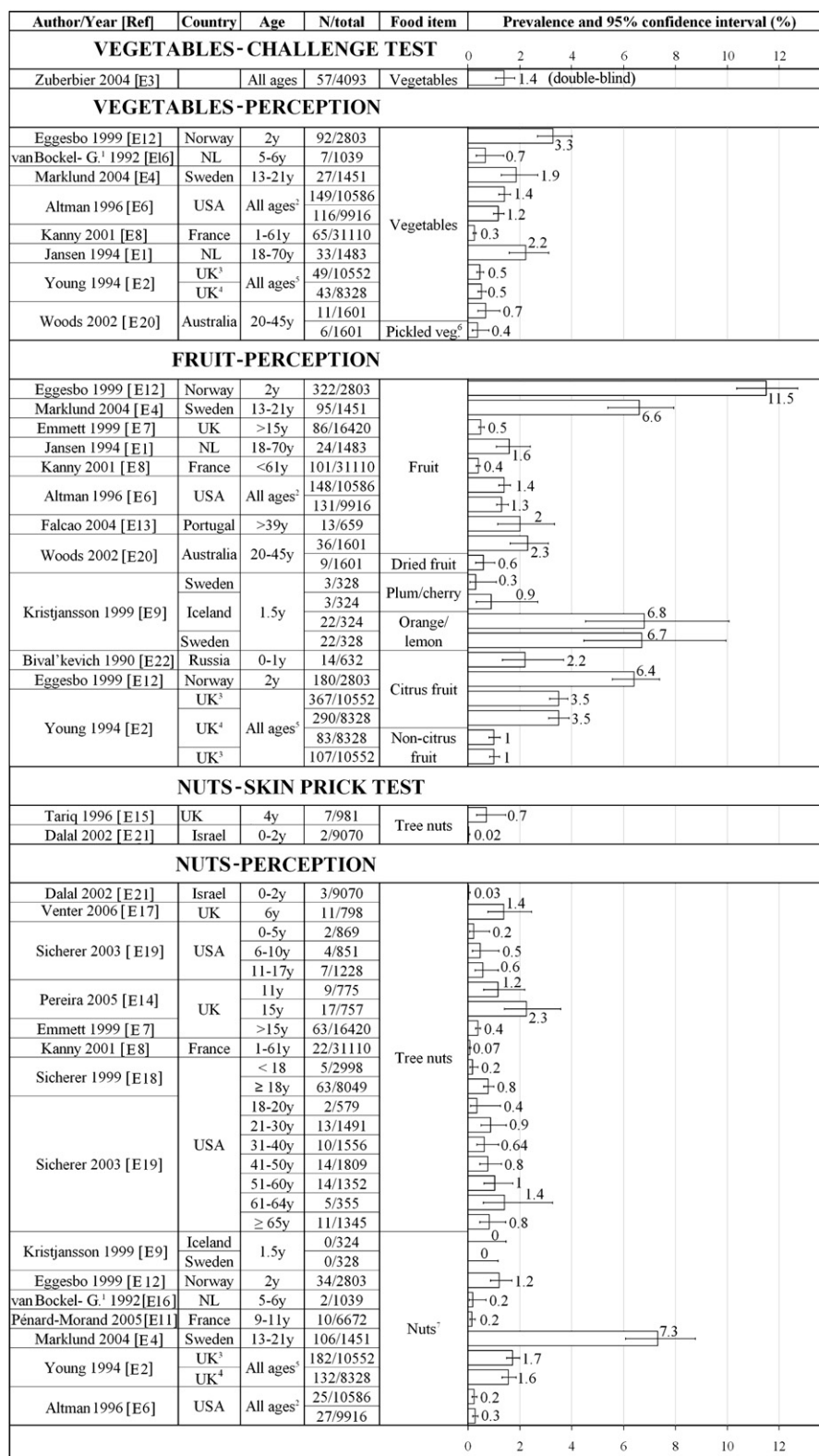
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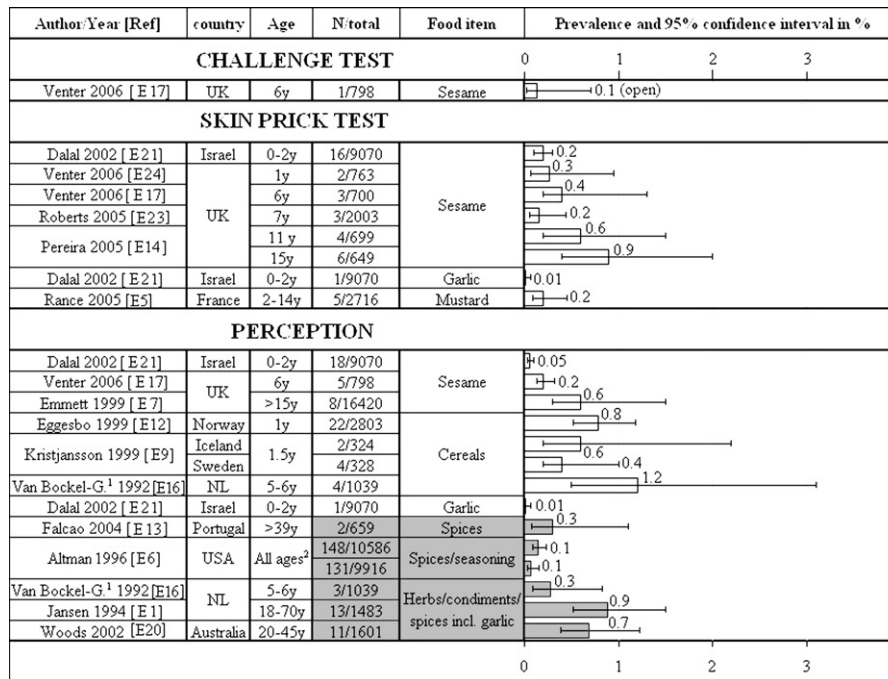
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**FIG E1.** The prevalence of allergy to the general food groups: fruits, vegetables and nuts. Indicated are the diagnostic methods used. SPT results  $\geq 3$  mm<sup>2</sup> were considered positive. Open/double-blind indicates the nature of the challenge. *N/total*, Number of people with (reported) FA/total number investigated. <sup>1</sup>van Bockel-Geelkerken. <sup>2</sup>Age distribution was not reported in this survey of US households (for 1989, N = 10,586; for 1993, N = 9916). <sup>3</sup>Wycombe area. <sup>4</sup>Nationwide. <sup>5</sup>Twenty-eight percent were  $\geq 20$  years. <sup>6</sup>Pickled vegetables. <sup>7</sup>Peanut may be included. *UK*, United Kingdom; *NL*, The Netherlands.



**FIG E2.** The prevalence of allergy to other foods. Food groups are shaded gray. Indicated are the diagnostic methods used. SPT results  $\geq 3$  mm<sup>2</sup> were considered positive. Open/double-blind indicates the nature of the challenge. N/total, Number of people with (reported) FA/the total number investigated. <sup>1</sup>van Bockel-Geelkerken. <sup>2</sup>Age distribution was not reported in this survey of US households (for 1989, N = 10,586; for 1993, N = 9916).

**TABLE E1.** Number of population-based studies included in the current report to estimate the prevalence of allergy or sensitization by type of plant food and type of assessment

	Parent-/self-reported reactions	Sensitization (assessed by serum IgE)	Sensitization (assessed by SPT)	Open or double-blind food challenge test
Fruit	18	0	3	4
Vegetables/legumes	18	1	3	3
Tree nuts	17	0	5	3
Wheat	7	6	6	4
Soy	10	4	3	2
Others (eg, sesame cereals, spices, condiments)	12	0	7	1



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