

The prevalence of PFS and prevalence and characteristics of reported food allergy; a survey of UK adults aged 18–75 incorporating a validated PFS diagnostic questionnaire

I. J. Skypala¹, S. Bull², K. Deegan³, K. Gruffydd-Jones⁴, S. Holmes⁵, I. Small⁶, P. W. Emery⁷ and S. R. Durham⁸

¹Royal Brompton & Harefield NHS Foundation Trust, London, UK, ²Old Leake Medical Centre, Boston, UK, ³Upper Norwood Group Practice, Croydon, UK,

⁴Box Surgery, Wiltshire, UK, ⁵Park Medical Practice, Somerset, UK, ⁶Peterhead Health Centre, Aberdeenshire, UK, ⁷King's College, London, UK and ⁸Imperial College, London, UK

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Summary

Background Pollen-food syndrome (PFS), a food allergy affecting pollen-sensitized individuals, is likely to be the most prevalent food allergy in adults, estimated to affect 50–90% of people allergic to birch tree pollen.

Objective A validated PFS diagnostic questionnaire (PFSDQ2) was used to determine the prevalence of PFS and also to characterize those who report reactions to foods.

Methods Five UK General practices each sent the PFSDQ2 by post to 2000 patients aged 18–75 years randomly selected from their practice database. The validated questionnaire was accompanied by an additional set of questions to ascertain the demographic of the population, the foods involved and the age of onset.

Results There were 3590 subjects who returned completed questionnaires, with an average return rate from each practice of 36% (range 22–47%). Of these, 73 were diagnosed with PFS according to the questionnaire (PFS+ve) giving a population prevalence of 2%. A further 482 subjects reported reactions to foods but did not fulfil the diagnostic criteria for PFS. The greatest prevalence of PFS was in the Croydon (SE England) urban practice (4.1%) and the lowest in the Aberdeen (Scotland) urban practice (0.8%) ($P < 0.001$). The most frequently reported trigger foods were apples, hazelnuts and kiwifruit and the majority of those with PFS first experienced symptoms below the age of 20 years. PFS+ve subjects were also more likely to be female and have a higher socio-economic status than those who did not report reactions to foods.

Conclusions The UK prevalence of PFS was 2%, although this varied according to the location of the practice population. The majority of PFS+ve subjects first reported symptoms in their teens. The reported age of onset has important implications for the diagnosis of primary and cross-reactive peanut and tree nut allergies in teenagers and young adults. The continuing rise in aeroallergen sensitization is likely to result in an increased frequency of PFS presenting in both primary and secondary care.

Keywords adults, age onset, allergy, food, pollen, prevalence, syndrome, validated questionnaire

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Correspondence:

Dr Isabel Skypala
Director of Rehabilitation and
Therapies, Royal Brompton &
Harefield NHS Trust, Sydney Street,
London SW3 6NP

E-mail: i.skypala@rbht.nhs.uk

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Introduction

Food allergy, both IgE- and non-IgE-mediated [1] is widely accepted to be prevalent in children, whereas the frequency of adult food allergy is not well established [2]. Diesner and colleagues propose that the paediatric focus of most epidemiological studies creates an

impression that food allergies do not occur in older adults [3]. A few studies have utilized the gold standard of oral food challenge to ascertain prevalence; in 1994, Young and colleagues in the United Kingdom and Janzen and colleagues in the Netherlands reported the prevalence to be 1.4% and 2.4%, respectively, [4, 5] and 10 years later, Zuberbier and colleagues reported a

rate of 3.7% in Germany [6]. A UK Department of Health review of Allergy Services [7] drew attention to the lack of published studies on adult food allergy.

The most prevalent food allergy affecting adults is observed in people with concomitant seasonal allergic rhinitis. This condition is known as oral allergy syndrome (OAS) due to the characteristic oropharyngeal symptoms sufferers experience on immediate contact with food triggers. It occurs because of epitope recognition of plant food proteins by pollen antibodies, most frequently those against Bet v 1, the major allergen in birch trees (*Betula verrucosa*), but also involves pollens from other trees, grasses and weeds [8–16]. The plant food proteins involved are usually the pathogenesis-related (PR) 10 proteins, although profilins can also be implicated. These proteins, being thermo-labile and susceptible to digestion by proteases, cannot provoke primary sensitization in the gastro-intestinal tract leading to the development of a primary food allergy [11]. The main trigger foods for OAS vary depending on the pollen involved but the most common foods reported are apples, stone fruits and tree nuts [10, 16].

There is a growing consensus that pollen-related OAS should be specifically labelled as 'pollen-food allergy' or 'pollen-food syndrome' (PFS) [15, 17, 18], because OAS is a descriptor of a set of symptoms which can be part of any food allergic response. Also, the term OAS is often used as a generic term for any cross-reactive plant food allergy, whereas there are other cross-reactive plant food allergies such as that involving the homologous allergens in natural rubber latex (*Hevea brasiliensis*) [19] and between the non-specific lipid transfer protein (nsLTP) group of allergens [20], which can provoke symptoms of far greater severity than that usually seen in PFS.

It is accepted that PFS is a common condition which may affect 50–90% of those with birch pollen allergy in Europe [21, 22]. However, a systematic review by Zuidmeer and colleagues concluded that reliance should not be placed on estimates of allergy to plant foods due to the scarcity of population-based prevalence estimates for plant food allergy determined by the diagnostic gold standard of oral food challenge [23]. Osterballe and colleagues utilized oral food challenges to demonstrate that 3.2% of adults in an unselected cohort had an allergy to fruit and vegetables [24]. We have previously reported that 66% of birch-sensitized individuals in a UK cohort were diagnosed with PFS using oral food challenge [16]. The prevalence of confirmed allergic rhinitis in the United Kingdom is approximately 26% [25], with a quarter of these cases (6.5%) being reactive to tree pollen [26], thus up to 4.3% of UK subjects could suffer from PFS.

To investigate this further, we utilized a published PFS diagnostic questionnaire [16], validated in subjects with reported springtime hayfever, to undertake a

population survey to determine the prevalence of PFS in UK adults. In this community-based study, we also assessed the prevalence of reported food allergy, the foods involved, reported symptoms, age of onset and demographic and socio-economic differences between those who reported symptoms to foods and those who did not.

Method

Study design

The study design was an anonymized questionnaire survey of adults aged 18–75 randomly selected from five primary care practices. The study was conducted according to the World Medical Association's Declaration of Helsinki. Ethical approval was obtained from the Charing Cross Research Ethics Committee in October 2008 (REC reference number: 08/H0711/79), for all sites due to take part in the study. Separate research and development approval was obtained from the Royal Brompton & Harefield NHS Trust, Lincolnshire PCT, Wiltshire PCT, Croydon PCT, Grampian Health Board and Somerset PCT. The study was also registered with the Primary Care Research Network database.

Questionnaire

The one page questionnaire (Appendix I) was composed of a PFS diagnostic tool validated in subjects with springtime hayfever by the authors in a previous study [16], which first ascertained whether the respondents had hayfever, and if so during which season(s). A subsequent question determined the presence or absence of reported reactions to food; those who answered in the affirmative were then asked to complete questions on the foods involved and symptom characteristics. Questionnaire responses were interpreted using an algorithm (Appendix II) which incorporated information on the chronology of reactions in relation to reported hayfever, the involvement of raw or cooked foods, speed of symptom onset and symptom type to assign a diagnosis of PFS.

On the reverse of the validated questionnaire (Appendix I) were some additional questions on specific trigger foods and age of onset. All respondents were then asked to complete the final questions, which included those aimed to generate demographic data on age, gender, ethnicity, educational attainment, profession and marital status. These data were also utilized to code the social class of respondents. To assess which General practice (GP) the respondents came from, subjects were then asked to state their nearest town and whether their dwelling was in a rural, semi-rural or urban setting. All subjects were then asked to report whether they ever experienced any tingling, numbness, itching or swelling

in the mouth when eating foods. The final question listed a set of conditions and asked respondents to mark which ones they believed they had currently; the conditions were asthma, eczema, food allergy, coeliac disease or wheat intolerance, lactose or milk intolerance, irritable bowel syndrome and none of these.

GP practices

The questionnaire, together with a one page patient information sheet, a supporting letter from the GP practice and a stamped-addressed envelope for the completed questionnaire to be returned, was sealed in a stamped envelope. To preserve patient confidentiality, each consignment of 2000 packed envelopes was sent to the relevant GP practice for labelling and posting. The GP practices, selected through personal contact, were in 4 different geographical areas of England and one in Scotland (see Fig. 1). One was in a rural part of the country, two in a semi-rural location and two in urban areas. The GP practices used their computerized practice database of patient records to randomly select 2000 adults. The only inclusion criterion was that all recipients of the questionnaire should be aged between 18 and 75 years. A set of address labels was then generated, affixed to each stamped, sealed envelope and posted out to the recipients. All questionnaires were posted between November 2008 and February 2009; all

completed questionnaires received by 1st May 2009 were included in the analysis.

Classification of respondents

The returned questionnaires were analysed by applying the diagnostic algorithm to the questionnaire answers to classify the respondents in the following manner:

- Report reaction to foods and have a diagnosis of PFS (RRF+ve/PFS+ve).
- Report reaction to foods but do not have PFS (RRF+ve/PFS–ve).
- Do not report reactions to foods (RRF–ve).

A sub-analysis of the responses of RRF+ve/PFS–ve subjects to questions on symptom onset and type was undertaken to assess how many of the reactions were reported to occur within 30 min of eating and characterized by at least one reported 'allergic' symptom (itch, swelling, urticaria or anaphylaxis) and therefore likely to be due to an immune-mediated food allergy.

Sample size

The sample size was calculated to achieve sufficient power to provide robust data on the prevalence of pollen-related oral allergy syndrome, using data generated from previous published studies on this subject [16, 25]. An estimated prevalence of 0.05 with a confidence interval of ± 0.01 was used in a standard sample size calculation [27]. This calculation suggested that the number of completed questionnaires required was 1825, meaning that the proposed sample size of 10 000 would ensure a sufficient return even at a very low estimated return rate of 20%.

Statistics

Differences in the response to each question on the questionnaire between different groups were tested using the *t*-test, Chi-square, Mann–Whitney or Kruskal–Wallis test. The Statistical package for the Social Sciences (SPSS version 15.0, IBM, Portsmouth, UK) computer program was used for the analysis. Profession and social class were coded independently by a Market Research Company (GfK NOP Ltd, London, UK) using the National Statistics Standard Occupational Classification 2000 (SOC2000).

Results

PFS prevalence

Of the 10 000 questionnaires dispatched, 3609 were returned, with 3590 (36%) being complete and suitable



Fig. 1. GP practices. A. Boston – Lincolnshire (rural). B. Box – Wiltshire (semi-rural). C. Croydon – Surrey (urban). D. Peterhead – Scotland (urban). E. Shepton Mallet – Somerset (semi-rural).

for analysis (Table 1). In response to Question 2 of the questionnaire, 'Have you ever had any allergic reactions to foods' (Appendix I), 3035 respondents answered 'no' and were classified as RRF-ve. Of the 555 subjects who answered in the affirmative (15.4%) (95% confidence interval (CI) 14.3–16.6%), 73 were diagnosed with PFS following the application of the PFS diagnostic algorithm, and designated as RRF+ve/PFS+ve, amounting to 2% (CI 1.6–2.5%) of all respondents. The remaining 482 subjects who answered 'yes' to question 2 were designated RRF+ve/PFS-ve. A small number of these subjects (19) met the PFS diagnostic criteria (reported rapid-onset symptoms, characteristic of PFS, to raw fruits and vegetables only), but did not report hayfever, a prerequisite for a diagnosis of PFS using the PFS diagnostic algorithm. Nearly one third (136, 28%) of the 482 RRF+ve/PFS-ve respondents listed at least one or more typical allergic symptoms (itch, swelling, anaphylaxis or urticaria) occurring within 30 min of eating. Thus, 209 (136 RRF+ve/PFS-ve and 73 RRF+ve/PFS+ve) of the 3590 respondents (5.8%) reported a clinical history consistent with an IgE-mediated food allergy.

Geographical and demographic features

There was variation between GP practices with regard to the number of subjects reporting reactions to foods; 11% of subjects from Peterhead reported reactions to foods compared with 22% of subjects from Croydon ($P < 0.001$) (Table 1). The greatest number of RRF+ve/PFS+ve subjects were also from the Croydon practice, 4.1% of whom were diagnosed with PFS, compared with 0.8% in the Peterhead practice ($P < 0.001$) (Table 1). The median age of RRF+ve/PFS+ve respondents was 46 years (Mean 44 years, range 20–64 years), and the majority (73%) were female, a significantly higher proportion than the 54% in the RRF-ve group ($P < 0.001$) but similar to the RRF+ve/PFS-ve group (69%) (ns). Other demographic differences were also

seen in ethnicity ($P < 0.001$), job classification ($P < 0.005$), profession ($P < 0.001$) and social class ($P < 0.001$) (Fig. 2) when comparing all three groups (Chi-square), although there was no difference between the RRF+ve/PFS+ve and RRF+ve/PFS-ve groups for these variables.

Reported clinical conditions

The most commonly reported atopic condition was hayfever, affecting 23% of all respondents, although this varied between practices with only 19% of the Boston (rural) cohort reporting hayfever compared to 32% in the Croydon cohort ($P < 0.001$, Chi-square). On average, 55% of those with reported hayfever had symptoms in the summer months, with respondents from Peterhead reporting the highest rate of 63%. Conversely, Peterhead had the lowest rate of spring-time symptoms, with only 21% affected, compared to 34% in the Croydon practice ($P < 0.001$, Chi-square). Asthma and eczema were reported to affect 11% and 10% of the respondents, respectively, but there were no significant differences between the GP practices in the reported prevalence of these conditions (data not shown). The rates of reported asthma and eczema were significantly different between the RRF-ve, RRF+ve/PFS-ve and RRF+ve/PFS+ve groups ($P < 0.001$, Chi-square), with those who reported reactions to foods (RRF+ve/PFS-ve and RRF+ve/PFS+ve) more likely to report asthma, eczema and hayfever than those who did not (RRF-ve) ($P < 0.001$, Chi-square) (Fig. 3). An analysis of question 17 – 'Do you ever experience any of the following sensations in your mouth when you eat a food – tingle, numb, itchy, swollen, other symptom, no symptom' (Appendix I), revealed that sensations of numbness, itch, tingle and swelling when eating were reported by 330 (9%) of the 3590 subjects who returned questionnaires, 201 of whom reported reactions to foods (60 RRF+ve/PFS+ve, 41 RRF+ve/PFS-ve) by

Table 1. Questionnaire returns for each GP practice

GP practice	No completed questionnaires returned	% of total sent	RRF-ve (%)	RRF+ve /PFS-ve (%)	RRF+ve /PFS+ve (%)
Boston	771	38.5	681 (88)	80 (10)	10 (2)
Box	822	41	676 (82)	123 (15)	23 (3)
Croydon	430	21.5	335 (78)	77 (18)	18 (4)*
Peterhead	632	31.5	559 (88)	68 (11)	5 (1)
Shepton mallet	935	46.7	784 (84)	134 (14)	17 (2)
Total	3590	35.9	3035 (85)	482 (13)	73 (2)

* $P < 0.001$.

RRF+ve/PFS+ve – report reactions to foods and have pollen-food syndrome.

RRF+ve/PFS-ve – report reactions to foods but do not have pollen-food syndrome.

RRF-ve – does not report reactions to food.

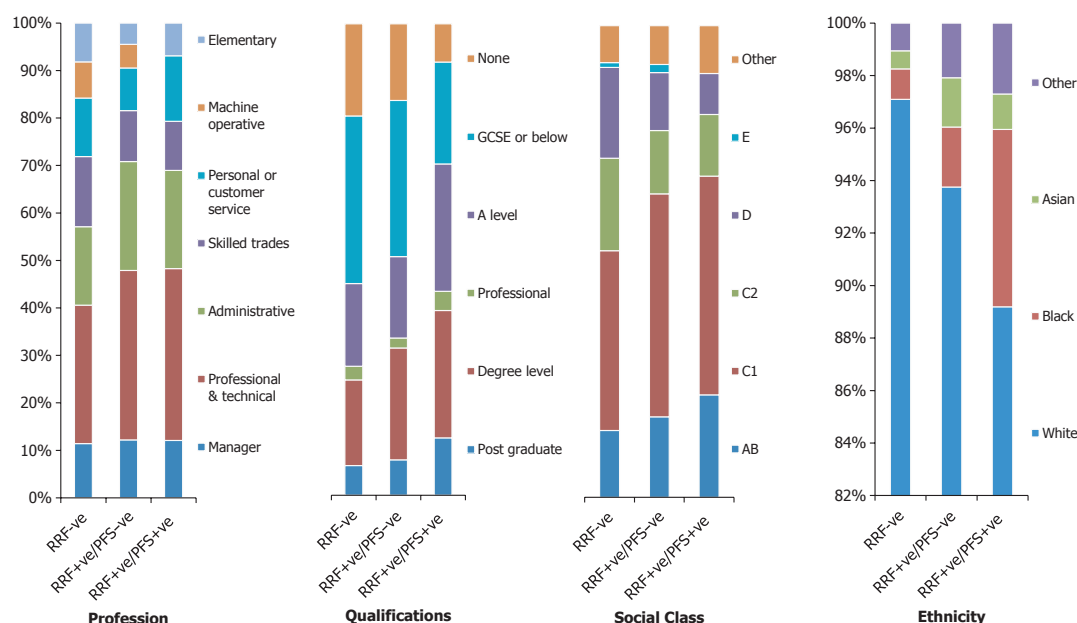


Fig. 2. Demographic features of subjects with no reported reactions to food compared to those with reported reactions to food but not diagnosed with pollen-food syndrome and those who were diagnosed with pollen-food syndrome.

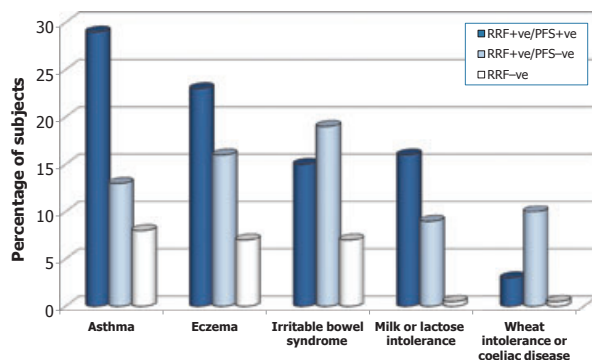


Fig. 3. Prevalence of reported conditions in the three groups of subjects.

replying in the affirmative to question 2. The remaining 129 subjects who reported sensations on eating did not answer yes to question 2, and therefore did not consider themselves to have a food allergy. This group reported experiencing oral tingling (70%), itching (31%), numbness (13%) and swelling (10%) when eating foods. They also reported a greater level of hayfever compared with the rest of the RRF-ve group, with 41% reporting hayfever compared to the RRF-ve average of 20%.

Foods

Overall wheat, crustaceans, milk, eggs and food additives were the food triggers cited most frequently by those who reported reactions to foods (RRF+ve/PFS-ve and RRF+ve/PFS+ve) (Table 2). Grouping the food triggers together into categories (milk and dairy;

Table 2. Percentage of all respondents who reported reactions to foods (RRF+ve/PFS-ve and RRF+ve/PFS+ve) reporting reactions to specific foods. Corresponding data from the study by Young *et al.* [4] in 1994 are also shown for comparison

Food	2009		1994	
	Rank*	%†	Rank*	%†
Non-citrus fruit	1	4.7	13	1
Fish/shellfish	2	4	4	2.9
Nuts	3	3.5	8	1.7
Vegetables	4	3.3	15	0.5
Wheat	5	3	14	0.9
Cow's milk	6	2.4	5	2.9
Food additives	7	1.6	2	4.9
Eggs	8	1.6	7	2.1
Citrus fruit	9	1.3	3	3.5
Curry and spices	9	1.3	—	NA
Tomatoes	10	0.9	12	1.2
Seeds	11	0.7	—	NA
Beans and lentils	12	0.5	—	NA
Soya	13	0.3	16	0.3
Chocolate	—	NA	1	6.6
Cheese	—	NA	6	2.3
Alcohol	—	NA	9	1.7
Meat	—	NA	10	1.6
Caffeine	—	NA	11	1.4

*Rank order of percentage of respondents who reported a reaction to the specified food.

†Percentage of respondents who reported a reaction to the specified food.

seafood; fruits; vegetables, herbs and spices; nuts, seeds and legumes; wheat and cereals; other; food additives) revealed that fruits accounted for nearly one quarter of

all reactions. The individual foods cited most frequently by the RRF+ve/PFS+ve group to trigger reactions were hazelnuts, apples, kiwifruit, strawberry and Brazil nuts (see Fig. 4). RRF+ve/PFS+ve subjects were also significantly more likely to report reactions to apples, apricot, cherry, grapes, kiwi, melon, peach, pear, pineapple, plum, strawberry, avocado pear, carrot, potato and tree nuts than the RRF+ve/PFS–ve group ($P < 0.001$, Chi-square) (Fig. 4). The number of foods reported by each person to provoke reactions also varied; RRF+ve/PFS+ve subjects reported an average of 4.0 foods to provoke symptoms, compared with 2.8 reported by the RRF+ve/PFS–ve group ($P < 0.001$, t -test).

Symptoms

Taking the PFS+ve and RRF+ve/PFS–ve groups together, overall the most commonly reported symptoms triggered by foods were gastro-intestinal; nausea, vomiting or diarrhoea and bloating constituted 35% of all reported symptoms. As symptom type and speed of onset were used to allocate subjects into a diagnostic grouping, the results could not be analysed for differences between the RRF+ve/PFS–ve and RRF+ve/PFS+ve respondents. However, the number of symptoms was significantly different between the groups. The majority

of RRF+ve/PFS–ve subjects reported one to two symptoms (median of 2), whereas the majority of PFS+ve subjects reported three or more symptoms (median of 3) ($P < 0.05$, Mann–Whitney U-test). An analysis of all of the reported trigger foods and symptoms of both the RRF+ve/PFS–ve and RRF+ve/PFS+ve groups revealed that rapid-onset reactions (touching the lips, biting and chewing, five minutes after eating) were associated with fish, apple, kiwi, peach, pineapple, cashew, hazelnut and chestnut ($P < 0.001$, Chi-square). Reactions after 15 min were associated with banana ($P < 0.001$, Chi-square) and after 30 min with milk ($P < 0.001$, Chi-square). No foods were associated with delayed-onset symptoms.

The data also showed an association between certain foods and symptom type. People who reported symptoms of oral tingle, itch or a scratchy sore throat were more likely to report apple, pear, peach and tree nuts as trigger foods ($P < 0.001$, Chi-square). Oral swelling was associated with pear, kiwi and codfish ($P < 0.001$, Chi-square) and urticaria with strawberries ($P < 0.001$, Chi-square). Chestnuts were associated with anaphylaxis ($P < 0.001$, Chi-square), and asthma with reactions to chestnuts, Brazil nuts, peanuts, soy, curry spices and food additives ($P < 0.001$, Chi-square). Bloating was associated with beans and lentils, egg, milk, wheat, peppers, oranges, onions, food additives, and curry spices ($P < 0.001$, Chi-square), and molluscs with nausea and vomiting ($P < 0.001$, Chi-square). For symptom severity, the mean and median scores for each subject were calculated from their individual symptom scores, and the cumulative scores of all individuals were then used to calculate differences between RRF+ve/PFS+ve and RRF+ve/PFS–ve groups. There were no significant differences in symptom severity with both groups having a median score of 2 (Mean 1.7 PFS+ve, 1.8 RRF+ve/PFS–ve).

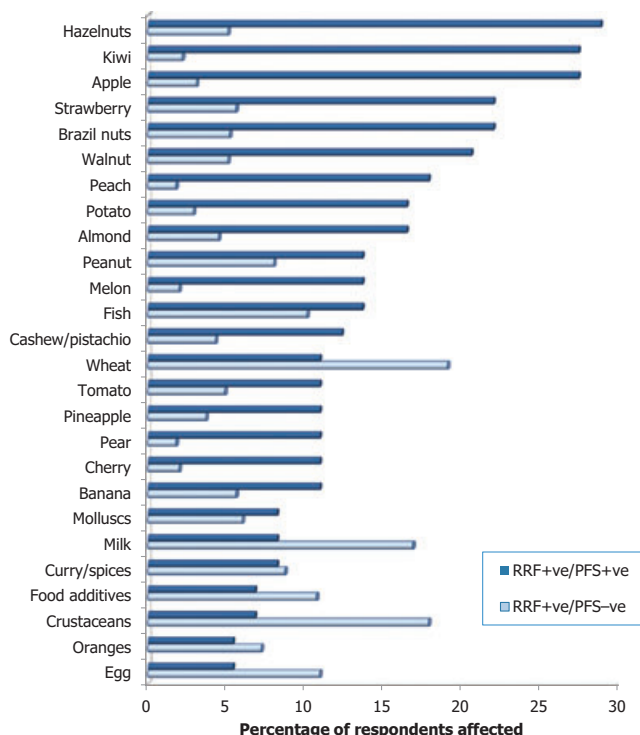


Fig. 4. Reported trigger foods affecting 5% or more of subjects diagnosed with Pollen-food syndrome compared to those reported by subjects who reported reactions to foods but were not diagnosed with pollen-food syndrome.

Age of onset of reactions to food

Of the 555 subjects who reported reactions to foods, 527 (95%) stated the age of onset. The median age of onset was 26 years (Mean 25 years, range 1–71 years), with the majority (63%) of those who reported reactions to foods becoming symptomatic at the age of 20 years or over; 59% of RRF+ve/PFS–ve subjects reported their reactions becoming symptomatic at the age of 20 years or over (Mean 25.9, SD 16.8), compared to 45% of RRF+ve/PFS+ve subjects (Mean 20.7, SD 12.6), ($P = 0.02$, t -test) (Fig. 5). There was no relationship between age and age of onset in the RRF+ve/PFS+ve group, with older respondents no less likely to have developed the condition in their youth than younger respondents. Taking both the RRF+ve/PFS+ve and RRF+ve/PFS–ve groups together, an analysis of all the trigger foods against

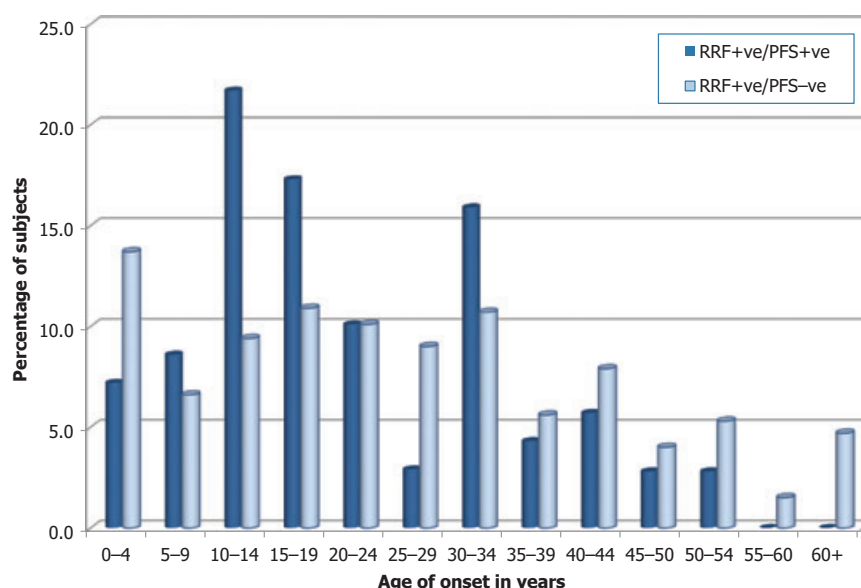


Fig. 5. The age of onset of reported reactions to food in subjects who were diagnosed with pollen-food syndrome and those who do not have pollen-food syndrome.

reported age of onset revealed chestnuts as the only food trigger associated with age of onset, being most likely to be reported in those who had childhood-onset reactions to foods ($P < 0.001$, Chi-square).

Discussion

This study is the first to provide data on the prevalence of PFS in an unselected population from the United Kingdom. The overall rate of 2% is less than half of the 4% predicted although Croydon in the London region did have a rate of 4.1%, which might be expected given the subjects were from a similar area to those who participated in the validation study [16]. Other geographical regions had lower rates of PFS, with Peterhead in Scotland recording a rate of 1%, in line with that predicted by Vieths *et al.* [22] in 2002.

The prevalence of reported hayfever in the whole study population (23%) was similar to the UK reported figure of 26% [25], lending confidence to the figures for reported hayfever. However, only 25% of those with reported spring hayfever, a marker of tree pollen allergy, were diagnosed with PFS, which suggests that in addition to geographical variations, there may be a degree of under reporting. The mild nature of the symptoms of PFS and variation in the allergenicity of different varieties of plant foods [28] may result in a failure to connect sensations on exposure to raw fruits and vegetables with an allergic response. This is supported by the fact that 41% of the RRF-ve subjects who reported sensations such as tingle or itch when eating, also reported hayfever and might therefore have been experiencing PFS symptoms. Data from our previous

study [16] showed that 6% of apparently asymptomatic subjects with spring hayfever had convincing objective signs of PFS on oral food challenge.

The validation study included only those who reported hayfever; it was therefore considered necessary that the algorithm used in this study (Appendix II) required reported hayfever as a necessary condition for the diagnosis of PFS. This might also have contributed to the lower than expected prevalence of PFS. Our data showed that 19 subjects fully met the other diagnostic criteria for PFS but did not report any hayfever. Such subjects may be sensitized to pollen but asymptomatic; Rashid *et al.* reported that 4 of 24 patients with PFS had no previous history of spring rhinitis, one of whom had a complete absence of any seasonal or non-seasonal rhinitis [29]. The PFS prevalence might also have been greater if the low response rate from subjects in the Croydon practice, possibly caused by it being a large conurbation with a transient population, had been more in line with that from other practices. However, it could also be argued that the 2% figure could be an overestimate as the respondents were self-selecting and those who perceive themselves to have a food allergy may have been more likely to return the questionnaires, leading to a built-in bias towards an overestimation of the problem. Also, the GP practices were chosen by personal contact and the sample receiving questionnaires was selected only on the basis of age, which will affect the generalizability of the sample.

Geographical differences in prevalence have not been much reported in the literature, although Kanny and colleagues showed city dwellers are more likely to report a reaction to foods [30]. Our data showed no dif-

ferences between urban and rural dwelling and the rate of reported reactions to foods or PFS. The high rate of PFS and reported reactions to food in the Croydon practice is unlikely to be due to its urban location; respondents from urban Peterhead had the lowest rate of PFS and were the least likely to report a reaction to food. The Croydon subjects reported not only the highest rate of hayfever, but the highest rate of spring hayfever and Peterhead subjects the lowest level. Reported hayfever in the springtime is traditionally linked to birch pollen sensitization, the pollen most frequently associated with PFS [22]. It could be speculated that the disparity between the two practices may be due to a greater number of days with high birch pollen counts in the South East, compared to Scotland which has the lowest number of high birch pollen days in the UK [31]. In addition, higher mean daily temperatures are associated with an increase in Bet v 1 in mountain birch sub species [32], which may be relevant due to the warmer ambient temperature of the South East.

There is a strong association between the presence of atopic disease and manifestations of food allergy in adults; Schäfer [33] and colleagues found that 73.1% of subjects reporting adverse food reactions also had allergic rhinitis. Our data confirm this finding; 230 of the RRF+ve/PFS+ve and RRF+ve/PFS−ve subjects (41%) collectively reported hayfever compared with 20% of the RRF−ve subjects. Asthma and eczema were similarly linked to the reporting of reactions to foods. The incidence of reported allergic rhinitis has trebled in the last three decades in the UK [34], which could be due to an increase in the aeroallergen sensitization rate in all age groups over a 25-year period, as reported by Linneberg et al. [35] Ziska and Beggs [36] concluded that climate change and increasing atmospheric CO₂ concentrations are likely to affect the severity and prevalence of allergic diseases linked to aeroallergen exposure in the future.

The overall rate of 15.4% of reported reactions to foods is comparable to the 19.9% UK rate cited by Young and colleagues in 1994 [4]. Our data also showed 5.8% of the whole cohort (2% RRF+ve/PFS+ve and 3.8% RRF+ve/PFS−ve) reported symptoms consistent with an IgE-mediated food allergy, similar to that reported by US subjects [37], although greater than the 3.7% directly measured prevalence rate reported by Zuberbier et al. [6]. The most common trigger foods reported by the PFS+ve subjects were similar to those reported in other European countries [10, 38, 39] and identical to those foods reported by UK subjects diagnosed with PFS by oral food challenge [16]. Overall, 41% of all reported reactions to foods were attributed to fruits and vegetables, matching data from a large pan European study [40] in which 29.5% of subjects were affected by fruits and 13.5% by vegetables. In

1994, Young et al. [3] found citrus fruits to be the most commonly cited fruits to provoke symptoms, whereas our data suggest non-citrus fruits are now the most frequent cause of reported reactions in adults (Table 2).

It remains unclear what risk factors exist for the development of food allergy in adult life. It has been suggested that age-related changes might alter the potential for the onset of food allergy in older adults, for example, vitamin D deficiency in adulthood and medications to inhibit gastric acidity may both increase the likelihood of late-onset food allergy [41]. Few prevalence studies have assessed the age of onset of reported food allergy in adults although Vierk et al. [37] found that 54% of reported reactions in adults commenced aged 20 years or older. Our data found this level to be slightly higher; 63% of all RRF+ve/PFS+ve and RRF+ve/PFS−ve subjects first realized or suspected an allergy to food when they were aged 20 years or older. However, the majority of RRF+ve/PFS+ve subjects reported their age of onset to be below the age of 20 years, despite the fact that PFS is primarily considered to manifest itself in adult life. Sensitization to tree nuts and peanuts is closely correlated with sensitization to birch and/or grass pollen [21, 22, 42, 43], especially as children get older. Thus, our data on age of onset demonstrate the necessity to consider PFS as a differential diagnosis in older children and young adults, especially in the case of reported reactions to tree nuts and peanuts.

A significantly greater proportion of women than men were diagnosed with PFS, although this trend was also true for the RRF+ve/PFS−ve group. In comparison with 2011 census data for England and Wales and data from the General Register office for Scotland [44, 45], the gender of the whole cohort was skewed towards females (50.8% of the UK population vs. 56.5% of study respondents). This may have had an effect on the number reporting reactions to foods, although a gender bias towards women has been reported by other food allergy prevalence studies [6, 30, 33]. Falcão showed that males who reported reactions to foods sought no medical advice after a food hypersensitivity episode, whereas all women in their survey reporting food reactions had a diagnosed food allergy, suggesting under-diagnosis of food allergy in males [46]. Knibb et al. [47] demonstrated that those reporting self-diagnosed food allergy and intolerance were significantly more likely to be female. DunnGalvin et al. [48] suggest this is not just due to biological sex differences. They propose that gender differences in processing information for making self-assessments for health, and differences in the general belief in one's own ability to respond to, and control, environmental demands and challenges, could also influence the perception, reporting and management of symptoms.

There was also a trend for PFS+ve subjects to have a higher educational attainment and socio-economic status. Others have reported similar findings; Zuberbier *et al.* showed the rate of IgE-mediated food allergy to be more than double in those with 12 years of education rather than 9 years [6], and Vierk *et al.* [37] found that reported reactions to food were more frequent in subjects who had an education beyond high school. It can be speculated that this skew towards higher educational attainment may be attributable to similar factors to those responsible for female predominance or it may be an expression of the advantage the better educated may have in terms of their confidence to recognize and report suspected symptoms and their access to appropriate healthcare. This study is the first to report on the association between social class and reported reactions to foods.

In summary, these data demonstrate that PFS is already a significant problem in the United Kingdom, affecting an average of 2% of the adult population, although this varied from 1.8% in Scotland to 4.1% in the South of England. We have demonstrated that the condition commonly occurs before the age of 20 years, and the foods reported to provoke symptoms

in those with PFS are consistent with other studies, with apples and tree nuts dominating. The likely continued rise in aeroallergen sensitization [35] and reported allergic rhinitis [34] could lead to an epidemic of PFS in years to come. Standardized diagnostic and management strategies, suitable for older children and adults, need to be developed, addressing issues specific to these age groups, such as the relevance of sensitization and the extent of cross-reactions between different plant species.

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Conflicts of interest

The authors declare that they have no conflicts of interest relating to this study and its publication.

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Appendix I Food allergy in adults: how prevalent is oral allergy syndrome?

CONFIDENTIAL Food Allergy in adults: how prevalent is Oral Allergy Syndrome?

Please answer questions on both sides of this questionnaire

Q1 Do you have hay fever? YES [] NO [] If YES do you get symptoms mainly in the: ☐ Spring time (February/March to May/June) ☐ Autumn (September to November) ☐ Summertime (May/June to August) ☐ Winter (November to February) ☐ All year round															
Q2 Have you ever had any allergic reactions to food? YES [] - please go to next question – Q3 (please tick one) NO [] - please turn over and go to Q9															
Q3 Which foods have you had a reaction to: (please tick any in column A or column B that apply) <table border="0"> <thead> <tr> <th>Column A</th> <th>Column B</th> </tr> </thead> <tbody> <tr> <td>☐ Fruit or vegetables</td> <td>☐ Milk, eggs, chicken</td> </tr> <tr> <td>☐ Bean sprouts, salad leaves or herbs</td> <td>☐ Fish, shellfish</td> </tr> <tr> <td>☐ Nuts including all tree nuts and peanuts</td> <td>☐ Wheat or other cereal</td> </tr> <tr> <td>☐ Peeling potatoes or other root vegetables</td> <td>☐ Other food</td> </tr> <tr> <td>☐ Beans, lentils, chickpeas or other legumes</td> <td></td> </tr> <tr> <td>☐</td> <td></td> </tr> </tbody> </table>		Column A	Column B	☐ Fruit or vegetables	☐ Milk, eggs, chicken	☐ Bean sprouts, salad leaves or herbs	☐ Fish, shellfish	☐ Nuts including all tree nuts and peanuts	☐ Wheat or other cereal	☐ Peeling potatoes or other root vegetables	☐ Other food	☐ Beans, lentils, chickpeas or other legumes		☐	
Column A	Column B														
☐ Fruit or vegetables	☐ Milk, eggs, chicken														
☐ Bean sprouts, salad leaves or herbs	☐ Fish, shellfish														
☐ Nuts including all tree nuts and peanuts	☐ Wheat or other cereal														
☐ Peeling potatoes or other root vegetables	☐ Other food														
☐ Beans, lentils, chickpeas or other legumes															
☐															
Q4 If reactions are to any food in Column A, is your reaction to: (tick one) ☐ Raw foods only ☐ Cooked foods only ☐ Both raw and cooked foods ☐ Not sure															
Q5 How quickly do the symptoms occur: (tick one) ☐ On touching lips ☐ Within 30 minutes of eating ☐ On biting or chewing ☐ 1-2 hours after eating ☐ On or up to 5 minutes after swallowing ☐ 2-4 hours after eating ☐ Within 15 minutes of eating ☐ More than 6 hours after eating															
Q6 Which of the following symptoms do you have after eating foods to which you are allergic (tick all that apply and grade each symptom from 0-3 (0 = none, 1 = mild, 2 = moderate, 3 = severe): ☐ Tingling/numbness of lips/mouth or strange mouth sensation (____) ☐ Intense itching of the lips, mouth, roof of mouth (palate) or ears (____) ☐ Scratchy/sore throat (____) ☐ Rash (nettle rash) either on touching the food (e.g. peeling potatoes) or on eating (____) ☐ Swelling of lips, tongue, mouth or throat (____) ☐ Anaphylaxis (rapid onset of flushing, with severe difficulty in breathing or collapse) (____) ☐ Asthma (____) ☐ Hay fever (____) ☐ Eczema (____) ☐ Feeling sick, vomiting, diarrhoea (____) ☐ Bloating (____) ☐ Other (____)															

PLEASE
TURN
OVER

Q7 Which foods do you have a reaction to: (please tick all relevant foods)

☐ Almonds	☐ Cod/other white fish	☐ Mussels, clams, oysters	☐ Potato
☐ Apple	☐ Courgette	☐ Mustard	☐ Prawns, lobster, crab
☐ Apricot	☐ Cucumber	☐ Onions/garlic	☐ Rocket
☐ Aubergine	☐ Curry/spices	☐ Oranges, lemon, grapefruit, etc	☐ Sesame seeds
☐ Avocado pear	☐ Egg	☐ Other cereal	☐ Soy
☐ Banana	☐ Food additive	☐ Peach/Nectarine	☐ Spinach or Swiss chard
☐ Beans or Lentils	☐ Grapes	☐ Peanut	☐ Strawberry
☐ Brazil nuts	☐ Hazelnuts	☐ Pear	☐ Sunflower seeds
☐ Carrot/Parsnip	☐ Herbs	☐ Peas	☐ Tomato
☐ Cashew/Pistachio nut	☐ Kiwi	☐ Peppers	☐ Tuna, salmon, oily fish
☐ Celery/fennel	☐ Lettuce	☐ Pineapple	☐ Walnut or pecan
☐ Cherry	☐ Mango/tropical fruit	☐ Plum	☐ Wheat
☐ Chestnut	☐ Melon		
	☐ Milk		

Q8 How old were you when your current food reactions started? _____ years

Q9 Are you ☐ male ☐ female (please tick one)

Q10 What was your age on your last birthday? _____ years

Q11 What is the name of your nearest town or city? _____

Q12 Do you live in: ☐ countryside ☐ village ☐ town ☐ city (please tick one)

Q13 Please tick the box which best describes your ethnic background: (tick one box only)

☐ White	☐ Black or Black British	☐ Chinese
☐ Mixed Race	☐ Asian or Asian British	☐ Other

Q14 We need to know about your education. Please tick all qualifications you have/working towards:

☐ School certificate, GCSE, 'O' levels, CSE, or Standard Grade	☐ A, AS, A2 levels, Higher Grade
☐ Degree	☐ Masters level qualification
☐ Doctorate	☐ Other

Q15 What is or was your occupation or profession _____
If you are still in full-time education please put student

Q16 Are you: ☐ single ☐ married/cohabiting ☐ divorced/separated ☐ widowed (please tick one)

Q17 Do you ever experience any of the following sensations in your mouth when you eat a food : (tick all that apply)

☐ Tingly	☐ Numb	☐ Itchy	☐ Swollen	☐ Other symptoms	☐ No symptoms
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Q18 Do you currently have any of the following conditions: (tick all that apply)

☐ Asthma	☐ Irritable Bowel Syndrome	☐ Eczema	☐ Food allergy
☐ Coeliac disease or wheat intolerance	☐ Lactose or milk intolerance	☐ None of these	

Thank you for completing this questionnaire. Please return in the envelope provided to:
Isabel Skypala, Director of Rehabilitation and Therapies, Royal Brompton Hospital, Sydney Street, London SW3 6NP

Appendix II Diagnostic algorithm

