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APPEAL-1: A pan-European survey of patient/caregiver perceptions of peanut allergy management

Katharina Blumchen[1] | Audrey DunnGalvin[2,3] | Frans Timmermans[4] | Lynne Regent[5] | Sabine Schnadt[6] | Marcia Podestà[7] | Angel Sánchez[8] | Pascale Couratier[9] | Mary Feeney[10] | Betina Hjorth[11] | Ram Patel[12] | Tessa Lush[13] | Robert Ryan[13] | Andrea Vereda[13] | Helen R. Fisher[10] | Montserrat Fernández-Rivas[14]

[1]Division of Allergology, Pneumology and Cystic Fibrosis, Department of Children and Adolescent Medicine, University Hospital Frankfurt, Frankfurt am Main, Germany

[2]School of Applied Psychology and Department of Paediatrics and Child Health, University College Cork, Cork, Ireland

[3]Paediatrics and Child Infectious Diseases, First Moscow State Medical University, Moscow, Russia

[4]Nederlands Anafylaxis Netwerk - European Anaphylaxis Taskforce, Dordrecht, The Netherlands

[5]Anaphylaxis Campaign, Farnborough, UK

[6]Deutscher Allergie- und Asthmabund, (DAAB), Mönchengladbach, Germany

[7]Food Allergy Italia, Padua, Italy

[8]Asociación Española de Personas con Alergia a Alimentos y Látex (AEPNAA), Madrid, Spain

[9]Association Française de Prévention des Allergies (AFPRAL), Paris, France

[10]Division of Asthma, Allergy and Lung Biology, Department of Paediatric Allergy, King's College London, and Guy's and St. Thomas' NHS Foundation Trust, London, UK

[11]Astma-Allergi Danmark, Roskilde, Denmark

[12]Brainsell Ltd., London, UK

[13]Aimmune Therapeutics, London, UK

[14]Department of Allergy, Hospital Clínico San Carlos, Universidad Complutense de Madrid, IdISSC, ARADyAL, Madrid, Spain

Correspondence
Katharina Blumchen, Division of Allergology, Pneumology and Cystic Fibrosis, Department of Children and Adolescent Medicine, University Hospital Frankfurt, Theodor-Stern-Kai 7, D-60590 Frankfurt, Germany.
Email: katharina.bluemchen@kgu.de

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Aimmune Therapeutics

Abstract

Background: Peanut allergy (PA) is associated with marked quality-of-life (QoL) impairment. However, data are lacking on the experience and impact of living with PA from the perspectives of persons with PA (PwPA) and their caregivers. **A**llergy to **P**eanuts im**P**acting **E**motions **A**nd **L**ife study 1 (APPEAL-1) was a pan-European survey investigating these perspectives. This first of two articles reports clinical characteristics of PwPA and PA management practices.

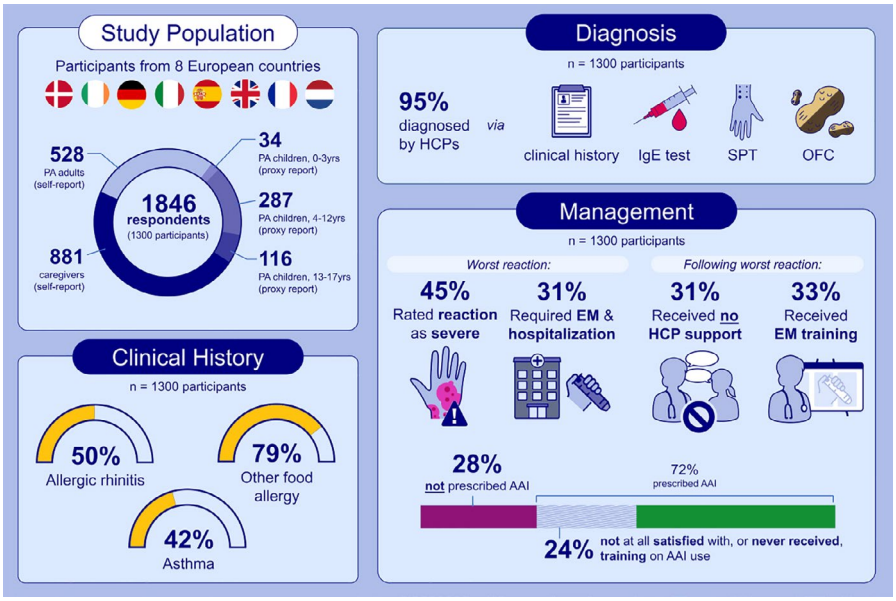
Methods: APPEAL-1 was a quantitative, online survey conducted in eight European countries, developed by eight representatives of patient advocacy groups and five healthcare professionals and researchers. Eligible participants included adults with PA and parents/caregivers of PwPA who responded by self-report and provided proxy-report for the PwPA under their care. Data were summarized using non-weighted descriptive statistics.

Results: Of 1846 completed/analysed questionnaires, 528 were from adults with PA (self-report); 437 by proxy for children with PA (34 aged 0-3 years, 287 aged 4-12 years, 116 aged 13-17 years) and 881 from parents/caregivers (self-report). Of PwPA (N = 965), 95% reported diagnosis by healthcare professionals, mostly by clinical history and peanut-specific allergy testing. Rates of allergic rhinitis, asthma and other food allergies in PwPA were 50%, 42% and 79%, respectively. Only 31% of PwPA received HCP advice/support following their worst allergic reaction, and 28% had not been prescribed an adrenaline auto-injector. Results were similar by country but varied by age group.

Conclusions: The APPEAL-1 findings contribute to greater understanding of PA impact on PwPA, caregivers and family members and the need for improved PA management across Europe.

KEYWORDS

clinical history, diagnosis, Europe, peanut allergy, quality of life



GRAPHICAL ABSTRACT

The APPEAL-1 study – pan-European quantitative investigation of the burdenof living with peanut allergy – provides essential insight on diagnosis and management of peanut allergy. Study results expand our understanding of management of peanut allergy and provide insight into diagnosis, comorbidities, and severity of symptoms. The study suggests a widespread need for improved quality of peanut allergy health management and education.

Abbreviations: AAI, adrenaline auto-injector; HCP, healthcare professional; OFC, oral food challenge; PA, peanut allergy; SPT, skin prick test.

1 | INTRODUCTION

Peanut allergy (PA) is a common and potentially life-threatening condition that imposes a significant burden of illness.[1,2] Utilizing various methods of detection and diagnosis, including self-report, prevalence estimates for PA in European countries reach up to 2.8%, with estimates higher among older age cohorts than in younger children, and in Western vs other areas of Europe.[3-5] Increases in PA prevalence have been reported in the United Kingdom (UK) and the United States, although the reasons for these trends are unclear.[6-8] Symptoms of PA typically begin between 1 and 2 years of age and persist through adulthood in ~80% of patients, in contrast to milk and egg allergies that are more likely to resolve in childhood.[1,2,9-11]

Multiple factors contribute to the burden of PA.[12,13] Compared with other food allergies, PA is associated with higher rates of severe reactions and incidence of anaphylactic events requiring emergency care in Western nations,[14-18] and is an elicitor of anaphylaxis from infancy through adolescence.[17] PA is also responsible for the highest proportion of fatal food-related anaphylaxis in most studies.[19-21] The

widespread use of peanut in a broad range of food products; inaccurate, incorrect or absent labelling; misreading of labels by persons with PA (PwPA) or caregivers; manufacturing errors; and inadvertent contamination also contribute to high rates of accidental exposure to peanut.[22] Accidental exposures have been reported to occur in ~13% of Canadian peanut-allergic children[22-24] and 48% of children and adolescents in the UK annually, among whom ~25% of the reactions were anaphylaxis.[25] In addition, up to 95% of PwPA have at least one comorbid allergic condition, such as asthma, atopic dermatitis or another food allergy.[26]

The standard of care for PA and other food allergies consists of avoidance of trigger foods and the use of rescue medication (ie adrenaline autoinjector [AAI]) in case of accidental exposure.[27-29] However, dietary avoidance itself can be a major source of anxiety, stress and impaired health-related quality of life (HRQL).[13,30,31] Research data in food-allergic and PA populations also indicate that having been prescribed an AAI, and having to use it, are independently associated with decreased HRQL related to fear and uncertainty regarding use of the device, the burden of carrying it, and the trauma of events (eg anaphylaxis) necessitating its use.[32,33] Multiple studies have shown that PA and food allergies, in general, have strong adverse impacts on the HRQL of patients, parents and caregivers.[13,30,31,34-42] However, there is a lack of multicountry, cross-sectional studies on the epidemiologic and psychological factors that provide context for, and may help explain, the impact and burden of PA.[43,44]

APPEAL (**A**llergy to **P**eanuts im**P**acting **E**motions **A**nd **L**ife) is a two-part study conducted across Europe to comprehensively evaluate the burden and psychosocial impact of living with PA. APPEAL-1 is a quantitative, cross-sectional, online survey study conducted in eight European countries to comprehensively assess multiple interactive domains of the experiences of PwPA, including adults and children, as well as parent/nonparent caregivers, hereafter referred to in this report as "caregivers." Major survey components include demographic factors, clinical characteristics and history, and experiences with healthcare professionals (HCPs); the day-to-day experience of living and coping with PA; and impacts of PA on psychosocial parameters and quality of life. While other studies have assessed HRQL in patients with food allergies across European countries,[38,39] to our knowledge, APPEAL is the first such study focused on the PA population that evaluates a comparably broad spectrum of factors involved in the burden of PA. Other distinctive features of APPEAL-1 include a large multinational cohort of patients with PA across Europe; perspectives of peanut-allergic individuals (adults and children) as well as caregivers; and analysis by age groups and country. In this first of two articles describing the results of APPEAL-1, we report data collected directly from PwPA and caregivers focusing on clinical history, diagnosis and management of PA. A tandem article reporting the psychosocial and HRQL results of APPEAL-1 is also published in this issue of *Allergy*.[45]

2 | METHODOLOGY

APPEAL-1 was conducted in Denmark, France, Germany, Ireland, Italy, the Netherlands, Spain and the UK. It consisted of a 30-minute online survey initially written in English, translated/back-translated into 6 other languages (Danish, Dutch, French, German, Italian and Spanish) and adapted to national specifications, such as the types of HCPs involved in PA diagnosis and management. The questionnaire and study protocol were developed by the APPEAL advisory board, which was comprised of representatives of eight patient advocacy groups (PAGs; one from each of the eight countries represented in the study) and a specialist panel that included five HCPs and research specialists. Ethical approval was obtained from the Freiburg Ethics Commission International (Universitätsklinikum Freiburg; https://www.uniklinik-freiburg.de/ethics-commission.html).

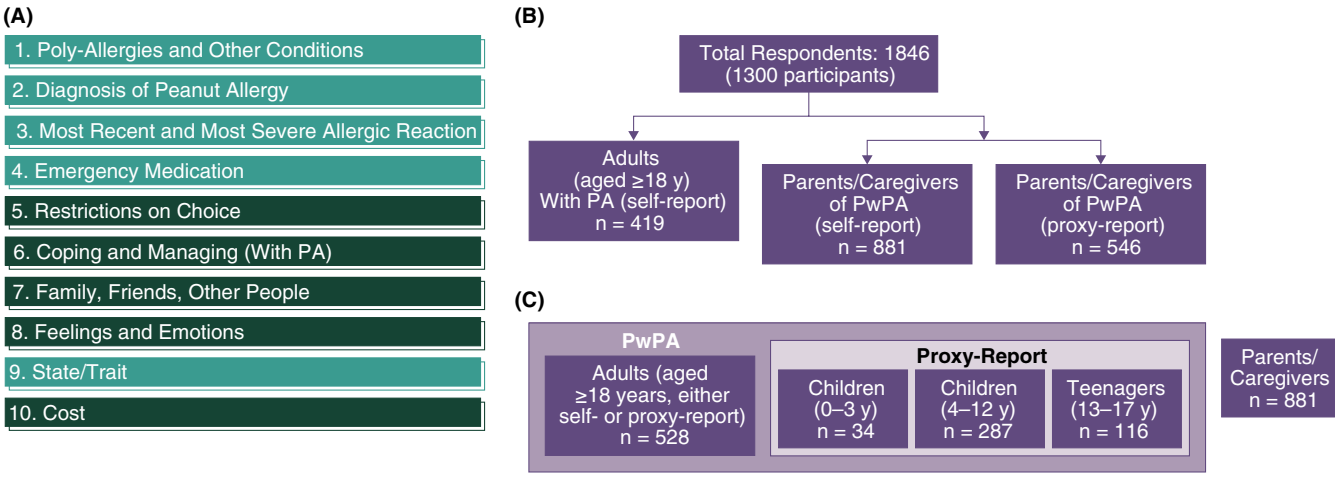


FIGURE 1 APPEAL-1 questionnaire structure and respondent groupings. A, Question categories. B, Flow chart shows the number of subjects surveyed and number of responses from each population. C, Number of respondents from each age group (self- or proxy-reported). PA, peanut allergy; PwPA, people with peanut allergy

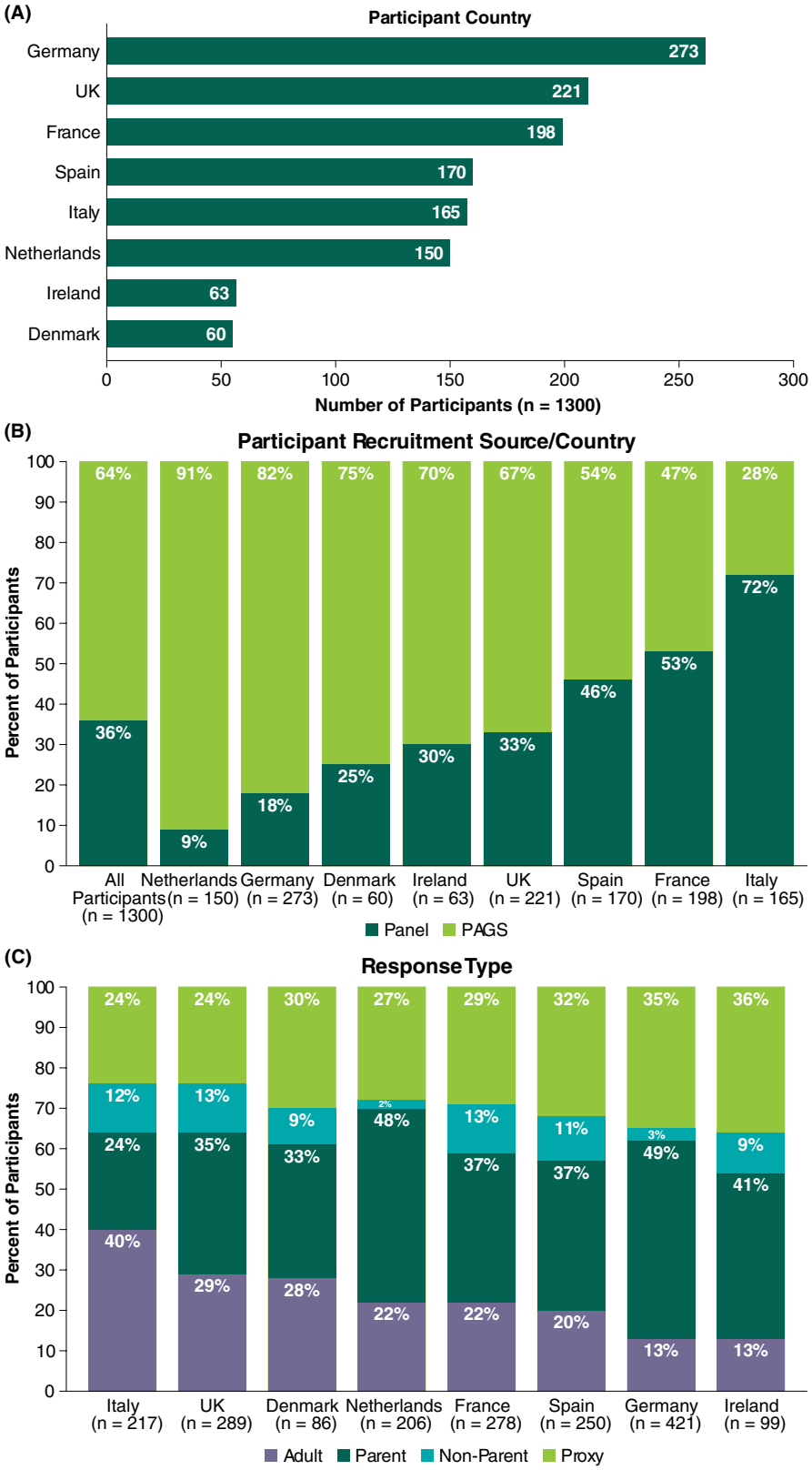


FIGURE 2 Respondents by country (A), recruitment source (B), and type (C) (adult with PA self-report; parent/caregiver of PwPA self-report; parent/nonparent caregiver proxy-report for person with PA aged < 18 y under their care). PAGs, patient advocacy groups; UK, United Kingdom

2.1 | Study population

APPEAL-1 participants were recruited through the PAGs or by a professional recruitment service for research studies. The PAGs operated independently of each other, using varied methods for recruitment, such as announcements on websites or direct email contact to registered individuals who had previously given consent to be contacted for research purposes. The recruitment service contacted individuals in its database who had expressed willingness to participate in online studies and had an interest in allergy and/or

health issues. Individuals recruited through the recruitment service received compensation for participating; the individuals recruited via the PAGs did not.

Eligible participants included adults (aged ≥ 18 years) diagnosed with PA who responded for themselves (self-report) and adult caregivers of PwPA (adult or child) who responded regarding the impact of PA on themselves (self-report) (Figure 1). The caregivers were also invited to answer a survey on behalf of the PwPA under their care (proxy-report) (Figure 1). Thus, the total number of potential responses was higher than the total number of participants. All participants had to be residents of one of the eight countries and willing and able to provide informed consent. Potential participants were emailed a link to the survey that described its purpose and procedures; persons interested in participating were asked to check a consent box before participating. The two exclusion criteria for the recruitment service were participation in a market research study of PA during the previous 2 months and PAG membership.

TABLE 1 Demographic and other allergic associations in PwPA

Characteristics	Respondent type				
	Total (either self-report or proxy-report) (n = 1300)	Adults (≥18 y; either self-report or proxy-report) (n = 610)	Children (0-3 y) (n = 61)	Children (4-12 y) (n = 442)	Teenagers (13-17 (n = 187)
Mean age, years (SD)	21.8 (17.2)	35.9 (15.4)	2.3 (0.8)	8.0 (2.5)	14.9 (1.4)
Sex, n (%)					
Female	53	67	31	43	44
Male	47	33	69	57	56
Diagnosed with PA only,[a]%	28	24	39	33	28
Diagnosed with other food allergies,[b]%					
Celery	7	10	3	4	6
Cow milk and dairy products	18	19	23	14	24
Egg (hen's)	21	15	31	24	26
Fish	7	9	10	5	8
Fruit	14	18	7	9	15
Meat or poultry	2	2	0	2	2
Mustard	5	5	2	4	6
Peach	10	15	7	5	7
Seeds (eg poppy, sunflower)	9	12	0	7	5
Sesame	11	12	2	10	14
Shellfish/crustacean/molluscs	13	17	3	9	13
Soya beans/other legumes	18	16	13	21	22
Sulphites	3	4	0	1	3
Tree nuts	54	55	43	54	53
Wheat/gluten	8	11	5	4	11
Comorbid conditions,[b]%					
Allergic rhinitis (hay fever)	40	50	21	36	48
Asthma/breathing disorder	43	42	32	44	57
Diabetes type 1	1	3	0	<0.5	0
Diabetes type 2	2	3	0	0	2
Eating disorders	4	6	3	2	3
Gastrointestinal disorder	12	20	9	6	9
Heart disease	1	1	3	<0.5	2
Mood disorders/depression	4	10	0	1	3
Skin disorders/eczema	40	34	35	44	41
None	19	16	32	22	13

(Continues)

2.2 | Questionnaire development and scoring

Questionnaire topics used for the survey were developed by the APPEAL advisory board, with the primary goal of identifying unmet research needs regarding the burden and impact of PA on patients and caregivers. The initial questionnaire draft was further developed through an interactive process, including online pilot testing with revisions made according to respondent feedback. For most survey questions, a 5-point response scale was used (in general, "1" indicated lowest impact and "5" highest). The sequence of questionnaire topics moved from clinical characteristics and practical issues of PA management to psychosocial impacts and ended with cost (Figure 1). The scoring system was developed with reference to standard survey methods to achieve the balance between sensitivity and ease of comprehension and choice for respondents.[46,47]

TABLE 1 (Continued)

Denmark (n = 60)	France (n = 198)	Germany (n = 273)	Italy (n = 165)	Ireland (n = 63)	Netherlands (n = 150)	Spain (n = 170)	UK (n = 221)
26.5 (21.6)	23.2 (17.6)	15.5 (16.5)	28.0 (16.1)	17.9 (13.2)	20.3 (15.3)	21.0 (16.6)	25.3 (17.3)
55	58	47	58	52	57	54	52
45	42	53	42	48	43	46	48
33	24	34	13	24	27	15	47
10	13	7	6	3	9	2	4
27	15	13	30	13	24	21	12
20	21	14	25	32	19	26	18
10	11	3	7	8	7	10	5
10	18	8	14	10	21	18	10
3	5	0	2	2	1	2	1
3	13	1	7	2	3	4	3
5	10	5	18	3	10	25	4
8	12	4	14	5	7	12	8
5	16	5	16	8	13	7	14
18	18	4	19	11	9	22	9
18	27	23	17	10	23	16	7
0	3	1	11	0	3	2	1
42	63	41	53	51	70	62	48
5	11	5	16	13	9	6	6
60	35	33	48	41	49	38	42
47	34	39	40	57	59	38	46
0	3	1	3	0	2	1	0
2	2	1	5	2	0	0	3
2	8	3	13	3	1	2	0
7	17	6	23	8	15	14	8
0	2	1	1	2	1	1	0
2	6	5	5	8	4	4	7
45	34	35	29	48	53	38	43
15	24	22	15	17	8	20	24

Abbreviations: HCP, healthcare professional; PA, peanut allergy; PwPA, persons with peanut allergy; SD, standard deviation; UK, United Kingdom.

[a]No other reported food allergies.

[b]Subjects were instructed to select all that applied from a list.

TABLE 2 Peanut allergy diagnostics in PwPA

Variable	Respondent type, by age			
	Total (either self-report or proxy-report)	Adults (≥18 y; either self-report or proxy-report)	Children (0-3 y)	Children (4-12 y)
Age at PA diagnosis by HCP, years, mean, (SD)	(n = 1236)	(n = 554)	(n = 56)	(n = 439)
	8.9	15.9	1.4	3.1
	(11.8)	(14.5)	(0.9)	(2.36)
Age at first allergic reaction to peanut, years, mean	(n = 1177)	(n = 578)	(n = 47)	(n = 387)
	9.15	15.43	1.19	3.88
	(12.3)	(14.9)	(0.6)	(2.2)
Reported PA reaction to HCP, %	(N = 1235)	(n = 610)	(n = 61)	(n = 442)
	95	91	92	99
HCP making first diagnosis, %	(n = 1236)	(n = 554)	(n = 56)	(n = 439)
Allergist (paediatric or general)	54.2	54.5	53.6	50.8
Emergency doctor	11.7	13.7	12.5	9.3
Paediatrician	16.0	6.5	23.2	28.2
Immunologist/immunology specialist	2.2	2.9	1.8	1.1
Primary care/family/GP	10.3	15.7	3.6	5.2
Nurse (allergy, other)	1.5	1.6	0.0	1.4
Other	4.2	5.1	5.4	3.9
Method of diagnosis,[a] %	(n = 1236)	(n = 554)	(n = 56)	(n = 439)
Clear clinical reaction to PA	48	50	54	46
SPT to peanut	50	53	39	44
Blood test (IgE to peanut)	53	36	68	70
OFC in hospital/clinic	12	9	9	16
Both SPT and IgE	29	22	29	32
Both SPT and OFC	7	5	4	8
Both IgE and OFC	9	5	7	12
SPT and IgE and OFC	6	4	2	7
Never diagnosed by an HCP, %	(n = 1300)	(n = 610)	(n = 61)	(n = 442)
	5	9	8	1

(Continues)

2.3 | Statistical analysis plan

There were a total of 1300 survey participants across the 8 countries (much higher than the original target of 800 participants). Given that this study was designed to be exploratory and to provide a descriptive analysis, a power calculation was not conducted. Data were summarized using descriptive statistics and presented as arithmetic means, with no weighting. Explorations of data were conducted at the pan-European level, by country, and respondent subgroups, including caregivers of PwPA reporting by proxy for PwPA, caregivers reporting for themselves, and adults with PA. Where appropriate, between-group comparisons were explored using inferential statistics (*t* tests and chi-square analysis). Since only descriptive analysis was conducted, no adjustments/corrections for multiple comparisons were performed.

3 | RESULTS

3.1 | Study participants

Between 10 November and 11 December 2017, 1300 participants (1846 total responses) from eight European countries engaged in the APPEAL-1 survey: 881 caregivers of a PwPA (720 parents and 161 nonparents), of whom 546 reported by proxy for a PwPA, and 419 adults with PA (Figure 1). The number and percentage of APPEAL participants by country were generally proportionate to the relative total populations of each country (Figure 2A). Most participants were recruited via PAGs (n = 829, 63.8%), with the remainder (n = 471, 36.2%) recruited via the recruitment service (Figure 2B). Participants also reporting by proxy for a PwPA under their care included 401 PAG participants (for a total of 1230 respondents) and

TABLE 2 (Continued)

	Country							
Teenagers (13-17 y)	Denmark	France	Germany	Italy	Ireland	Netherlands	Spain	UK
(n = 187)	(n = 50)	(n = 185)	(n = 266)	(n = 161)	(n = 54)	(n = 149)	(n = 149)	(n = 202)
4.4	13.0	9.7	6.3	13.7	5.3	6.4	10.9	8.1
(3.7)	(16.0)	(11.8)	(9.8)	(12.6)	(8.0)	(10.0)	(13.2)	(11.3)
(n = 165)	(n = 55)	(n = 179)	(n = 255)	(n = 150)	(n = 52)	(n = 143)	(n = 141)	(n = 202)
4.11	13.85	10.69	6.44	13.43	6.27	5.48	11.38	8.51
(3.7)	(16.2)	(13.2)	(10.2)	(12.1)	(8.4)	(9.6)	(13.2)	(12.8)
(n = 187)	(n = 60)	(n = 198)	(n = 273)	(n = 165)	(n = 63)	(n = 150)	(n = 170)	(n = 221)
100	83	93	97	98	86	99	99	91
(n = 187)	(n = 50)	(n = 185)	(n = 266)	(n = 161)	(n = 54)	(n = 149)	(n = 149)	(n = 202)
61.5	36	66	52	31	79	36	64	40
10.7	10	10	6	17	7	9	17	20
13.4	32	6	32	15	6	20	8	10
2.7	0	2	0	11	4	1	1	4
8.0	10	11	5	9	4	21	4	19
1.6	2	0	0	4	0	4	2	4
2.1	10	5	5	13	1	8	4	3
(n = 187)	(n = 50)	(n = 185)	(n = 266)	(n = 161)	(n = 54)	(n = 149)	(n = 169)	(n = 202)
47	62	49	52	47	31	52	46	44
60	38	57	26	65	63	44	51	67
60	56	45	69	42	74	61	43	44
16	20	14	14	7	15	21	6	9
39	28	34	16	33	46	35	25	31
13	14	8	4	5	11	14	4	7
13	14	9	11	6	13	15	4	5
11	12	8	4	5	9	12	2	4
(n = 187)	(n = 60)	(n = 198)	(n = 273)	(n = 165)	(n = 63)	(n = 150)	(n = 170)	(n = 221)
0	17	7	3	2	9	1	1	9

Abbreviations: GP, general practitioner; HCP, healthcare professional; IgE, immunoglobulin E; OFC, oral food challenge; PA, peanut allergy; PwPA, persons with peanut allergy; SD, standard deviation; SPT, skin prick test; UK, United Kingdom.

[a]Subjects were instructed to select all that applied from a list of single diagnostic methods.

145 recruitment service participants (for a total of 616 respondents). The proportions of participants recruited via the professional recruitment service varied widely by country (Figure 2B). Proportions of types of respondents (adults, children, parent/nonparent caregivers) were generally similar among countries although the proportion of adults with PA (self-report) ranged widely, from a high of 40% for Italy to a low of 13% for both Germany and Ireland (Figure 2C). The response rate from a total of 66,184 invitations via the professional recruitment service was approximately 10% (n = 616 completed surveys) and varied among countries with the highest from Italy (155 from 1269 invitations) and the lowest from the United Kingdom (92 from 30 794 invitations). Due to confidentiality constraints, the response rate could not be calculated for surveys distributed by PAGs. Only fully completed surveys were considered for analysis.

3.2 | Demographics, food allergy prevalence and comorbid conditions

Demographic and clinical characteristics of PwPA in each group (either self- or proxy-reported) are shown in Table 1. Adults with PA had a mean age of 36 years; children aged 0-3, 4-12 and 13-17 years had mean ages of 2, 8 and 15 years, respectively. Most survey participants were female; this included 75% (n = 315) of the 419 adults with PA. These characteristics were similar across age groups and countries (see Table 1).

Only 28% of all responding PwPA reported being allergic exclusively to peanut; 54% reported also being allergic to tree nuts, 21% to hen's egg, 18% to soya beans/other legumes and 18% to cow's milk. The five most common food allergies reported in addition to

TABLE 3 Peanut allergy reaction and treatment history

Variable	Respondent type, by age				
	Total (either self-report or proxy-report)	Adults (≥18 y; either self-report or proxy-report)	Children (0-3 y)	Children (4-12 y)	Teenagers (13-17 y)
Last saw HCP about PA, %	(n = 1300)	(n = 610)	(n = 61)	(n = 442)	(n = 187)
>5-y ago	13	24	0	2	7
Last 2-5 y	9	13	5	6	8
Last 1-2 y	15	17	7	14	16
Last 6-12 mo	24	24	23	23	25
<6 mo ago	38	22	66	55	43
Worst reaction with PA (all not in a clinical trial), %	(n = 1241)	(n = 576)	(n = 60)	(n = 425)	(n = 180)
>5 y ago	34	45	0	23	38
Last 2-5 y	24	18	10	33	24
Last 1-2 y	14	13	37	15	9
Last 6-12 mo	9	8	27	8	6
6 mo ago	6	5	7	6	7
Severity rating of worst allergic reaction to peanut, %	(n = 1128)	(n = 545)	(n = 48)	(n = 378)	(n = 157)
Severe	45	38	45	48	44
Moderate	43	50	40	43	45
Mild	8	8	10	7	7
Not sure	4	4	5	2	4
Healthcare for worst allergic reaction to peanut,[a]% (n = 1128)	(n = 1128)	(n = 545)	(n = 48)	(n = 378)	(n = 157)
Both hospitalization and EM	31	26	42	35	36
Hospitalization only	7	7	6	7	8
EM only	36	40	29	32	36
No, neither	23	24	23	23	18
Do not remember	3	3	0	2	2
Main symptoms for worst allergic reaction to peanut,[b] % (n = 1593)	(n = 1128)	(n = 545)	(n = 48)	(n = 378)	(n = 157)
Nausea	27	29	10	25	29
Vomiting	30	27	29	36	29
Heartburn/bloating	8	12	2	3	6
Stomach pain/cramps	24	26	2	22	26
Indigestion	5	7	2	3	3
Diarrhoea	12	15	10	10	8
Breathing difficulties/wheezing	50	54	48	43	54
Anxiety	25	23	31	26	28
Tiredness (acute or sudden)	17	13	21	22	14
Fainting/collapsing	9	13	0	5	10
Dizziness	13	17	0	8	13
Swelling (eg lips, eyes and/or tongue)	58	57	67	57	65
Itching mouth/throat tightness	50	53	35	45	55
Eczema flare/rashes	32	26	60	36	33

(Continues)

TABLE 3 (Continued)

Country							
Denmark	**France**	**Germany**	**Italy**	**Ireland**	**Netherlands**	**Spain**	**UK**
(n = 60)	(n = 198)	(n = 273)	(n = 165)	(n = 63)	(n = 150)	(n = 170)	(n = 221)
25	14	11	5	16	15	6	24
5	8	7	9	6	14	7	14
15	12	12	16	25	21	12	19
15	22	25	28	22	17	32	21
40	45	46	41	30	34	43	21
(n = 57)	(n = 188)	(n = 267)	(n = 144)	(n = 59)	(n = 148)	(n = 162)	(n = 216)
33	34	24	28	34	43	31	48
33	24	29	22	29	21	20	19
14	15	18	13	15	12	14	10
4	10	10	11	5	5	10	7
4	5	7	11	3	7	7	1
(n = 54)	(n = 170)	(n = 250)	(n = 128)	(n = 55)	(n = 137)	(n = 137)	(n = 197)
52	43	43	27	36	74	35	47
44	46	42	63	45	17	47	44
2	9	8	7	16	3	14	6
2	2	6	3	2	6	4	4
(n = 54)	(n = 170)	(n = 250)	(n = 128)	(n = 55)	(n = 137)	(n = 137)	(n = 197)
24	23	42	36	14	52	12	34
13	9	6	13	10	2	2	8
22	39	28	25	52	29	62	29
39	24	24	25	23	15	20	25
2	5	1	0	2	2	3	4
(n = 54)	(n = 170)	(n = 250)	(n = 128)	(n = 55)	(n = 137)	(n = 137)	(n = 197)
28	14	37	25	33	45	10	23
33	24	38	23	25	34	25	33
4	11	2	23	4	9	7	5
30	15	23	25	31	35	20	22
4	6	6	3	11	3	1	5
7	8	14	20	15	15	11	8
59	41	49	46	47	72	22	64
17	11	43	11	25	33	15	28
22	17	24	9	15	22	11	12
7	4	7	10	9	20	4	14
9	10	16	11	15	18	9	11
46	55	54	44	67	74	58	67
59	32	45	38	65	68	50	58
26	25	43	29	27	34	42	18

(Continues)

TABLE 3 (Continued)

Variable	Respondent type, by age				
	Total (either self-report or proxy-report)	Adults (≥18 y; either self-report or proxy-report)	Children (0-3 y)	Children (4-12 y)	Teenagers (13-17 y)
Hives	32	27	48	36	33
Itching (skin, eyes, and/or nose)	38	37	52	37	38
Advice/support offered after worst allergic reaction to peanut, % (n = 1128)[a]	(n = 1128)	(n = 545)	(n = 48)	(n = 378)	(n = 157)
None	31	33	23	28	34
Training on use of EM	33	26	50	41	32
Training in case of emergency	27	24	31	32	27
Psychological counselling	27	21	46	33	27
Information about PA associations	14	14	17	13	18
Do not remember	8	11	4	5	5

(Continues)

peanut, and their prevalence, varied depending on the age of the PwPA (Table 1).

The majority of PwPA reported having a "long-term illness which limits your daily activities" (Table 1). A total of 30% of adults with PA, and 28% of children and teenagers, reported having a long-term chronic, comorbid condition. The most common conditions in both adults and children/teenagers were allergic rhinitis, asthma/breathing disorders and skin disorders/eczema (Table 1).

3.3 | Diagnosis and clinical evaluations

The survey questions did not provide for any detailed assessment of the development of PA but did assess the diagnostic and clinical evaluation history of respondents. The majority of PwPA (95%) were reported being diagnosed with PA by HCPs, most commonly allergists, a finding fairly consistent across countries and age groups (Table 2).

The clinical evaluations used for PA diagnosis were also generally consistent across PwPA age groups and regions (Table 2). The reported methods used most frequently to confirm PA diagnosis were peanut-specific immunoglobulin E (IgE) test (53%), followed by peanut skin prick test (SPT) (50%); 29% of respondents reported that they received diagnosis confirmation with both IgE and peanut SPT (Table 2). Additionally, 6% reported their first PA diagnosis was based on the combined results of IgE, peanut SPT and oral food challenge.

Importantly, 95% of all PwPA reported having an allergic reaction to peanut. This percentage was consistent across all age groups. The mean age of PA diagnosis reported among all PwPA was 8.9 years, but variability was seen among adults (15.9 years), children aged 0-3 (1.4), children 4-12 years (3.1) and teenagers 13-17 years (4.4) (Table 2). These ages generally coincided with the mean age of first allergic reaction to peanut in each of the age groups (Table 2).

3.4 | Peanut allergic reactions, severity and inconvenience

A total of 38% of all PwPA reported (by self or proxy) that they visited an HCP in the last 6 months regarding their peanut allergy (Table 3). Among PwPA, 9% reported that their worst allergic reaction occurred within the past year, most commonly in children aged 0-3 years (27%). For close to half of PwPA (45%), their worst allergic reaction was rated as severe. Almost one-third of respondents (31%) said their worst PA reaction required hospitalization and emergency medication; percentages were higher in all younger age groups (children and teenagers, 35% to 42%) compared with adults (26%). Overall percentages were 7% for those reporting hospitalization only and 36% for emergency medication only (Table 3).

Among all PwPA who reported on their worst allergic reaction to peanut, most reported more than one symptom (87.4%); 142 (12.6%) reported only one symptom. The most common symptoms reported included swelling (eg lips, eyes and/or tongue) (58%), breathing difficulties/wheezing (50%); itching mouth/throat tightness (50%); and itching of the skin, eyes and/or nose (38%). Gastrointestinal symptoms were reported by almost one-third of respondents (vomiting 30%, nausea 27%, stomach pain/cramps 24%), and dizziness and fainting/collapsing were reported by 13% and 9% of respondents, respectively. Anxiety, reported by 25% of respondents, was always accompanied by other symptoms of a reaction (it was never the only symptom), regardless of the age of the PwPA reporting group or the region (Table 3).

Among all PwPA who reported the circumstances of their worst reaction to peanut, almost one-third (31%) said they received no support or PA management advice/support from HCPs following the reaction; only one-third (33%) said they received training on how to use emergency medication; and approximately only a quarter (27%)

TABLE 3 (Continued)

Country							
Denmark	**France**	**Germany**	**Italy**	**Ireland**	**Netherlands**	**Spain**	**UK**
37	22	33	24	45	19	31	47
44	29	42	27	44	48	34	39
(n = 54)	(n = 170)	(n = 250)	(n = 128)	(n = 55)	(n = 137)	(n = 137)	(n = 197)
39	42	24	20	51	26	21	40
19	22	42	37	25	34	35	30
11	14	39	37	16	22	37	21
31	6	50	34	4	47	26	4
4	15	15	21	15	11	12	16
3	9	4	5	5	6	8	14

Abbreviations: EM, emergency medication; HCP, healthcare professional; PA, peanut allergy; UK, United Kingdom.

[a]Subjects were instructed to pick one of the choices shown.

[b]Subjects were instructed to select all that applied.

received training on what to do in an emergency (Table 3). Also, only 14% said they received information about patient associations for food allergy and anaphylaxis prevention. Similar responses for these parameters were observed among age groups and countries (Table 3).

3.5 | Care and management

Among all PwPA, more than one-quarter (28%) reported having not been prescribed an AAI for PA reaction treatment, varying from 11% for children aged 4-12 years, 44% for adults and 22% for teenagers (Table 4). Of all those prescribed an AAI (n = 897), two-thirds (66%) had never used it, ranging from 52% in adults to 86% in younger children (aged 0-3 years) (Table 4). Among PwPA who were prescribed an AAI, the highest rate of complete satisfaction with the training they received for using it (score of 5 on a scale of 1-5) was 27%, seen in adults and in teenagers (Table 4).

Rates of AAI prescription also varied by the main symptoms of a worst allergic reaction. Among PwPA who were prescribed an AAI, the highest proportions had reported swelling (eg of the lips, eyes and/or tongue), itching of the mouth/throat tightness or difficulties breathing/wheezing during their worst allergic reaction.

3.6 | Costs of living with PA

Almost half of all respondents (46%) stated that living with PA was "more" (33%) or "much more" (13%) expensive (vs not living with PA). Percentages who reported that living with PA was "much more" expensive varied among age groups, including 20% of respondents for children aged 0-3 years, 10% of adults and 17% of respondents for teenagers (aged 13-17 years). Most respondents also described as "significant" the indirect costs of the extra time needed for planning day-to-day activities (85%) and special events (91%), with similar rates across age groups.

See Supporting information for a video of results from APPEAL-1.

4 | DISCUSSION

The purpose of the APPEAL-1 survey, carried out across eight European countries, was to investigate and evaluate the personal perceptions, experiences, burdens and impacts of living with PA. To this end, a 50-question survey assessing PwPA and caregivers' knowledge, experience and satisfaction was developed by an expert panel. In the current article, we provide demographic and clinical history data for multiple respondent groups, including children, teenagers and adults with PA. These data provide essential insight and data on PA diagnosis, comorbidities, severity of symptoms, management and other clinical factors. In a companion paper in this issue of *Allergy*, the psychosocial and quality-of-life impacts of PA are also reported.[45]

The overall demographics, PA symptoms, other food allergies and coexistence of other allergic conditions in the adult and children/teenager groups in this survey were generally consistent with other population studies on PA.[26,48] Previous studies in European and Canadian paediatric cohorts have reported a younger mean age of diagnosis (approximately 3 years),[26,49] than the overall age of diagnosis reported in APPEAL-1 (8.9 years), although similar to the ages reported for the paediatric subgroups. Therefore, the older overall mean age of diagnosis in APPEAL resulted from the older age of diagnosis reported by adults. Of note, adults may have recall bias towards older ages in reporting peanut allergy history whereas caregivers reporting by proxy may more accurately remember the more recent dates of peanut allergy diagnosis in their children.[50] The rates of children with a history

TABLE 4 Care management for PA

Variables	Respondent type, by age			
	Total (either self-report or proxy-report)	Adults (≥18 y; either self-report or proxy-report)	Children (0-3 y)	Children (4-12 y)
Prescribed an AAI?, %	(n = 1300)	(n = 610)	(n = 61)	(n = 442)
Yes	69	53	82	86
No	28	44	15	11
Other	3	3	3	3
Time since AAI last used, %	(n = 897)	(n = 325)	(n = 50)	(n = 381)
<6 mo ago	6	6	0	4
6-12 mo ago	6	9	10	4
1-2 y ago	7	10	4	6
2-5 y ago	8	9	0	6
≥5 y ago	8	14	0	3
Never	66	52	86	77
Satisfaction with training on use of AAIs (on scale of 1-5), %[a]	(n = 1330)	(n = 387)	(n = 79)	(n = 632)
1 - Completely satisfied	24	27	16	21
2	20	21	22	19
3	20	17	22	23
4	13	13	13	12
5 - Not at all satisfied	9	9	9	9
Did not receive training	15	13	19	16

(Continues)

of asthma, atopic dermatitis and/or eczema in our study (Table 1) are similar to those observed in other paediatric PA populations.[14,26,44] PwPA are often advised to avoid tree nuts, either because of an allergy to them, the potential for cross-reactivity or cross-contamination, or uncertainty over the ability of PwPA and caregivers (especially non-parent) to distinguish tree nuts from peanuts.[51] The APPEAL-1 survey showed that up to 53% of PwPA reported allergy to one or more tree nuts, which is also consistent with previous findings.[26,52] Several previous studies reported that PA was more common in male children (>60%),[26,44,51,52] while the APPEAL-1 survey population included more female children with PA (54%); however, one other multinational study also reported a slight majority of females in a randomly selected PA population.[53] Women may also be more inclined than men to participate in healthcare surveys in general.[54]

Our data on diagnostic testing also support previous findings. The APPEAL-1 survey confirms that PA is generally diagnosed early in childhood, similar to data reported in other European/multinational studies.[26,53] The survey analysis also showed that more than half of PwPA (53%) had their PA diagnosis confirmed via IgE, and 29% received both IgE and SPT, which validated the presence of PA in the survey population. Only 12% reported having an oral food challenge, which is typically used to confirm diagnosis when clinical history is ambiguous or nonexisting.[55] Approximately 10% of respondents said they had never experienced a reaction to peanut despite being diagnosed with PA. Such respondents may have been tested for PA despite their lack of reaction history, with resulting diagnosis, based on risk factors such as other allergic conditions (egg allergy or atopic eczema) or having a family member with PA.[49,56] In addition, study data show that only a minority of patients who have a positive SPT or specific IgE but no known exposure to peanut may have clinical PA.[4] Taken together, these data suggest that a clearly defined clinical history of PA is still required, as well as diagnostic testing, including detection of sensitization and oral food challenge, for PA diagnosis.[57,58]

With regard to PA management and clinical care, 28% of PwPA had never been prescribed an AAI, and approximately one-quarter (24%) of those prescribed an AAI were either not at all satisfied with their training for it or received no training. These data were similar across the countries surveyed, suggesting a widespread need in Europe for improved quality of PA health management and education concerning AAI use. This view is supported by a recent 10-year study of 10,184 cases of anaphylaxis in the European Anaphylaxis Registry, which found that only 27.1% of patients treated by an HCP received adrenaline "despite clear recommendations" indicating this therapy for anaphylaxis.[59] In addition, a study of all food-related anaphylactic deaths in the UK for the period of 1999-2006, including 48 deaths, 9 of which were related to peanut, found that only 40% of those who died had been provided AAIs, and less than half had received HCP advice on managing their food allergy.[19] Marked underuse of AAI for anaphylaxis, at variance with current anaphylaxis management guidelines, has also been reported in Germany.[60-62]

Almost half of respondents reported that PA caused additional living expense, and large majorities cited a cost of extra time for

TABLE 4 (Continued)

	Country							
Teenagers (13-17 y)	**Denmark**	**France**	**Germany**	**Italy**	**Ireland**	**Netherlands**	**Spain**	**UK**
(n = 187)	(n = 60)	(n = 198)	(n = 273)	(n = 64)	(n = 165)	(n = 150)	(n = 170)	(n = 221)
75	52	58	78	79	46	87	63	80
22	45	39	20	21	52	11	31	19
3	3	3	2	0	2	3	6	1
(n = 141)	(n = 31)	(n = 115)	(n = 212)	(n = 76)	(n = 50)	(n = 130)	(n = 107)	(n = 176)
10	3	11	4	8	4	6	3	5
5	3	4	3	17	10	3	6	8
6	10	10	3	12	4	13	6	5
12	3	9	6	8	10	8	8	8
8	3	3	3	8	18	16	6	10
60	77	63	81	47	54	53	72	64
(n = 232)	(n = 48)	(n = 174)	(n = 346)	(n = 103)	(n = 80)	(n = 180)	(n = 163)	(n = 236)
27	40	13	21	34	18	24	25	28
19	25	22	17	26	21	19	16	20
20	17	27	24	10	24	17	26	14
15	6	14	12	19	13	15	12	11
8	2	7	8	8	10	8	15	7
12	10	17	18	3	15	16	6	20

Abbreviations: AAI, adrenaline auto-injector; PA, peanut allergy; PwPA, persons with peanut allergy; UK, United Kingdom.

[a]The respondent base for this question is PwPA who have been prescribed an AAI + their parents/carers

planning of routine and special activities. A EuroPrevall study previously reported that mean annual healthcare costs (international dollars) were increased by I$927 for adults and I$1334 for children with food allergy, compared with age-matched controls, across 12 European countries for the period from 2007 to 2009.[63] It is clear that more research is necessary to understand and determine how to reduce the financial and economic burden for PwPA living in Europe.

Limitations of the APPEAL-1 survey include the use of a self-selecting sample from invitation, which may introduce selection bias, as no randomization was conducted (eg individuals who perceived/experienced greater impact of PA on themselves/their children may have been more likely to participate in this study vs those who felt less impact). The 2 recruitment methods used may also have influenced the study results since, hypothetically, PAG participants may be more likely to be motivated by emotions associated with PA and panel participants may have greater financial incentive because they received such compensation. Although 5% of PwPA had not been diagnosed with PA by an HCP and 10% had not experienced a reaction to peanut, the inclusion of such respondents who are, nonetheless, experiencing the impacts of perceived PA helps to broaden our study cohort and may better reflect the composition of the real-world population affected by PA than a more restricted cohort. As with many questionnaire surveys, there was a risk of recall bias on several questions (eg regarding "worst allergic reaction" and ages at first reaction and diagnosis). Descriptions and assessments of some parameters, such as severity of reaction, may also differ between survey respondents and HCPs. Additionally, because the survey was translated from English into 6 additional languages, there may have been some heterogeneity in interpretations of some questions and in the resulting responses across regions.

PwPA, families and caregivers faced with the diagnosis of PA encounter many challenges and much uncertainty. APPEAL-1 provides a functional basis for greater understanding of PA characteristics, management and impact on PwPA and caregivers across Europe. The results suggest that challenges facing PwPA, such as the need for sufficient education on disease management, are similar across Europe. Findings on the psychosocial and HRQL impacts of PA on the respondents in this study are described in a companion paper in this issue of *Allergy*.[45]

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CONFLICTS OF INTEREST

KB reports consulting for Aimmune Therapeutics, DBV Technologies, Bencard Allergie, HAL Allergy; speakers bureau for Aimmune Therapeutics, DBV Technologies, HAL Allergy, Nutricia,

Thermo Fisher Scientific, ALK, Allergopharma, Nestle; and conducting clinical trials for Aimmune Therapeutics, and DBV Technologies. ADG reports lecture honoraria/consultation fees from Aimmune Therapeutics and research support from National Children's Research Centre, Our Lady's Children's Hospital, Crumlin, Dublin 12, Ireland. FT is chair of the EAACI Patient Organizations Committee and member of Team APPEAL; the national patient advocacy organization has received honoraria from Aimmune Therapeutics. LR, SS, MP, AS, PC and BH are members of Team APPEAL, and their patient advocacy organizations have received honoraria from Aimmune Therapeutics. MF is a member of Team APPEAL and has received honoraria from Aimmune Therapeutics for advice; honoraria from Nutricia; research funding from NIAID, NIH, UK FSA, FARE, MRC & Asthma UK Centre, UK Department of Health through NIHR, National Peanut Board, Osem. RP reports consulting for Aimmune Therapeutics. AV and RR are employees of Aimmune Therapeutics. TL was an employee of Aimmune Therapeutics at the time of study. HRF is a member of Team APPEAL and reports honorarium from Aimmune Therapeutics. MF-R reports consultancies for Aimmune Therapeutics, DBV, Novartis, SPRIM; research funding from MINECO and ISCIII of Spanish government; speakers bureau for ALK, Allergy Therapeutics, HAL Allergy, Thermo Fisher Scientific.

ORCID

Audrey DunnGalvin https://orcid.org/0000-0002-1540-3959
Robert Ryan https://orcid.org/0000-0003-0827-3153

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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