

REVIEW ARTICLE

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Analysis of factors influencing the determination of indications for allergen-specific immunotherapy

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Received 15 August 2022; Accepted 13 October 2022 Available online 1 January 2023

KEYWORDS allergen-specific immunotherapy; rhinitis; asthma; dermatitis; guidelines	Abstract <i>Objective</i> : To develop a questionnaire and a scoring system for evaluating physicians' knowl- edge of allergen immunotherapy (AIT). <i>Methods</i> : Questionnaire was designed using the Questionnaire Star tool. A total of 1024 physi- cians were assessed, and based on the score divided into accurate judgment and inaccurate judgment groups. Statistical analysis was done, and counting data were expressed as frequen- cies and percentage values. Chi-square test and multi-factor logistic analysis were used to determine influencing factors on the indications for AIT. <i>Results</i> : Physician's age, grade of the hospital, and pediatric specialty influenced the accurate judgment of AIT indication after adjustment for independent variables (P < 0.05). In all, 80.5% physicians exercised accurate assessment for allergic rhinitis. Allergic conjunctivitis was judged accurately by 47.0% physicians. Bronchial asthma was judged accurately by 71.0% physicians, and atopic dermatitis by 61.3% physicians, with a higher accuracy rate for pediatricians than non- pediatricians for all the mentioned conditions (P < 0.05). There was no significant difference in
	<i>Conclusion</i> : The results of our study demonstrated a high accuracy judgment rate among cli- nicians for rhinitis, asthma, and dermatitis, and a low accuracy rate for desensitization of healthy people with allergic conjunctivitis, food allergies, and allergen sensitization. © 2023 Codon Publications. Published by Codon Publications.

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Introduction

Allergic diseases, including atopic dermatitis (AD), allergic rhinitis, asthma, and food allergies, have become a major global public health problem,¹ and are caused by a combination of genetic background, allergen exposure, and environmental factors.² Epidemiological findings show that 358 million people worldwide suffer from asthma,³ while allergic rhinitis has affected 10-20% of global population.⁴ Allergic diseases have a negative impact on the quality of life of patients and their families, reduce their daily performance, and cause a serious socioeconomic burden.^{1,5}

Although medications used to combat allergy are safe. they are only symptomatic. Therefore, patients often require multiple medications for relief of symptoms and often a lifelong course of treatment.⁶⁻⁸ The principle of allergen immunotherapy (AIT), also known as desensitization, considers gradual exposure of patient to increasing amounts of triggering allergen over a period to allow the immune system to build natural tolerance, relieve symptoms, reduce the use of allopathic medicines, and improve patient's quality of life.⁸ Since physicians play a fundamental role in patient's adherence to the treatment,⁹ it is important to ensure that they have an adequate level of AIT knowledge. The aim of this study was to develop a specific questionnaire to assess and evaluate in a better manner the AIT-related knowledge of physicians working in all levels of hospitals and to provide recommendations for the widespread implementation of AIT.

Material and Method

We designed a questionnaire (Supplementary Table S1) that included the following information: characteristics of physicians (age, gender, years of work experience, whether the hospital is a public hospital, grade of the hospital where they work, and whether they are pediatricians), circumstances of their consultations (whether desensitization is carried out in their department, the time required to check patients with allergic diseases, and the immediate response of patients when AIT is introduced), and basic knowledge of allergen-specific immunotherapy (whether it is effective, whether there is an age limit, whether the treatment continues to be effective after it is stopped, what kind of diseases can be desensitized) and whether the factors that influence the correct judgment of desensitization are sought to provide a basis for the widespread implementation of allergen-specific immunotherapy.

The Questionnaire was designed using the Questionnaire Star tool. Of 1300 questionnaires, 1024 valid ones (one from each IP address) were collected from consenting physicians working in community, secondary, and tertiary hospitals of Shanghai, Zhejiang, Hebei, and Yunnan Provinces between September 2021 and June 2022. Secondary hospitals were defined as hospitals containing more than 100 but less than 500 beds, and tertiary hospitals are hospitals with a bed capacity exceeding 500 that are responsible for providing specialized health services.

Statistical analysis was done using SPSS 25.0. Counting data were expressed as frequencies and percentage values. Each positive answer for allergic rhinitis, conjunctivitis, bronchial asthma, and atopic dermatitis received a score of 1.

A 0 score was given for food allergy and allergenic dust mite. A score of 4 comprised accurate judgment group, and a score <4 comprised inaccurate judgment group. Chi-square test and multi-factor logistic analysis were used to determine the influencing factors; P < 0.05 was considered statistically significant.

Results

Univariate analysis for determining indications for AIT

A total of 1024 physicians (648 females, 376 males) participated in this study. Of them, 517 were pediatricians (348 general pediatricians, 92 respiratory pediatricians, and 53 internal medicine pediatricians), and 507 were adult medicine physicians (92 general internal medicine physicians, 28 adult respiratory physicians, 217 other internal medicine physicians, and 133 community physicians). Based on the results of the questionnaire, physicians were divided into two groups: accurate judgment group (n = 374), and inaccurate judgment group (n = 650).

Statistical difference was observed between the groups regarding age, years of experience, hospital grade, specialty (pediatrician or general physician), whether AIT was carried out in the department, time spent in consultation of patients with allergies, immediate patient response, knowledge of AIT effectiveness, and possible age limit (P < 0.05; Table 1).

Logistic multifactorial regression analysis and situational analysis of indications

Factors that were statistically significant for univariate analysis (age, years of experience, hospital grade, pediatrician, whether the department carried out AIT, time spent in consultation of patients with allergic diseases, immediate patient response, whether AIT was effective, and whether AIT was age-restricted) were used as independent variables in a logistic multi-factor regression analysis. Physician characteristics, such as age, grade of physician's hospital, and whether the physician was a pediatrician or a non-pediatrician, influenced the accurate determination of indications for AIT (Table 2).

Analysis of AIT indications

Most physicians (824; 80.5%) accurately assessed AIT for allergic rhinitis; 47.0% accurately assessed for allergic conjunctivitis; 727 (71.0%) accurately assessed for bronchial asthma, and 628 (61.3%) for atopic dermatitis, with a higher accuracy rate for pediatricians than for non-pediatricians (P < 0.05). There was no significant difference between pediatricians and non-pediatricians in judging AIT efficiency for food allergy and mite sensitization (P > 0.05; Table 3).

Discussion

Allergic diseases are immune system disorders characterized by sensitization and production of allergen-specific Table 1Relationship between basic physician characteristics, physician attendance, and physicians' knowledge of AIT basicswith the judgment of indications for AIT.

Research factors		Judgment of indications				Summary		P
		Inaccurate group (N, %)		Accurate group (N, %)		Ν	%	
Basic physician characte	ristics							
Gender	Male	144	38.3	232	61.7	376	36.7	0.369
	Female	230	35.5	418	64.5	648	63.3	
Age (years)	<25	100	52.4	91	47.6	191	18.7	0.000
	25-3	91	36.4	159	63.6	250	24.4	
	31-35	83	44.6	103	55.4	186	18.2	
	36-40	44	33.8	86	66.2	130	12.7	
	41-45	38	26.4	106	73.6	144	14.1	
	>45	18	14.6	105	85.4	123	12.0	
Work experience (years)	<5	99	43.0	131	57.0	230	22.5	0.000
	5-10	143	42.1	197	57.9	340	33.2	
	>10	132	29.1	322	70.9	454	44.3	
Hospital grade	Level two	95	49.2	98	50.8	193	18.8	0.000
	Level three	209	29.9	489	70.1	698	68.2	
Public hospital or not	Community hospitals	70	52.6	63	47.4	133	13.0	
	Public hospitals	358	36.5	622	63.5	980	95.7	0.982
	Private hospitals	16	36.4	28	63.6	44	4.3	
Pediatrician or not	Yes	128	24.8	389	57.2	517	50.5	0.000
	No	246	48.5	261	51.5	507	49.5	
Physician attendance								
Does the department	No	305	40.5	448	59.5	753	73.5	0.000
perform AIT	SLIT	24	22.0	85	78.0	109	10.6	
	SCIT	21	32.3	44	67.7	65	6.3	
	SCIT+SLIT	24	24.7	73	75.3	97	9.5	
Consultation time for	1-2	51	57.3	38	42.7	89	8.7	0.000
allergic patients (min)	3-5	147	37.3	247	62.7	394	38.5	
	5-10	122	34.1	236	65.9	358	35.0	
	>10	54	29.5	129	70.5	183	17.9	
Immediate response when presenting AIT to a patient	Refuse	21	42.9	28	57.1	49	4.8	0.011
	Neutral or go to a specialist clinic	246	38.6	392	61.4	638	62.3	
	Consider agreeing to	82	29.0	201	71.0	283	27.6	
	Accept	25	46.3	29	53.7	54	5.3	
Physicians' knowledge o	f AIT basics							
Whether AIT is valid?	Yes, for all patients	30	8.0	42	6.5	72	7.0	0.000
	Yes, for most patients	167	44.7	389	59.8	556	54.3	
	Yes, for some patients	131	35.0	164	25.2	295	28.8	
	No	2	0.5	3	0.5	5	0.5	
	Not sure	44	11.8	52	8.0	96	9.4	
Is there an age	Yes	110	29.4	257	39.5	367	35.8	0.004
restriction for AIT?	No	119	31.8	187	28.8	306	29.9	
	Not sure	145	38.8	206	31.7	351	34.3	
Whether AIT is valid for	Yes	79	21.1	169	26.0	248	24.2	0.206
life?	No	111	29.7	186	28.6	297	29.0	0.200
	Not sure	184	49.2	295	28.0 45.4	479	46.8	

Table 2 Multi-factor logistic regression analysis for accurate determination of indications for AIT.

Research factors	В	SE	P value	Exp (B)	95% CI
Age (years)			0.000		
<25	-1.290	0.417	0.002	0.275	0.121-0.624
25-30	-0.763	0.384	0.047	0.466	0.220-0.989
31-35	-1.277	0.350	0.000	0.279	0.140-0.553
36-40	-0.804	0.338	0.017	0.448	0.231-0.868
11-45	-0.326	0.339	0.336	0.772	0.372-1.403
Vork experience (years)			0.825		
5	0.014	0.284	0.962	1.014	0.581-1.769
j-10	0.092	0.236	0.695	0.912	0.574-1.447
lospital grade			0.003		
evel two	0.145	0.245	0.555	1.156	0.715-1.869
evel three	0.637	0.219	0.004	1.890	1.230-2.940
Pediatrician	-0.551	0.169	0.001	0.576	0.414-0.802
Whether to perform AIT			0.714		
10	-0.214	0.272	0.431	0.807	0.474-1.376
jLIT	0.049	0.348	0.889	1.050	0.531-2.076
CIT	-0.205	0.375	0.548	0.814	0.390-1.700
Reception time (min)			0.072		
-2	-0.444	0.296	0.134	0.641	0.359-1.146
3-5	0.179	0.216	0.407	1.196	0.783-1.828
j-10	-0.095	0.214	0.656	0.909	0.589-1.383
mmediate patient response			0.130		
Refuse	-0.004	0.441	0.993	0.996	0.420-2.362
leutral or referred to a specialist clinic	0.503	0.310	0.105	1.654	0.901-3.038
Consider agreeing to	0.608	0.326	0.062	1.836	0.969-3.480
s AIT valid?			0.064		
/alid for all patients	0.155	0.360	0.666	1.168	0.577-2.363
/alid for most patients	0.310	0.256	0.226	1.364	0.826-2.252
/alid for some patients	-0.167	0.263	0.525	0.846	0.506-1.416
lot valid	0.322	0.986	0.744	1.380	0.200-9.525
s there an age limit for AIT?			0.301		
/es	0.246	0.180	0.171	1.279	0.899-1.821
٩o	0.009	0.181	0.961	1.009	0.707-1.440
Constant	1.310	0.619	0.034	3.705	

immunoglobulin E (slgE).^{10,11} Desensitization, or AIT, is an allopathic treatment that involves small, repeated, and incremental doses of allergen exposure to induce immune tolerance and ultimately achieve sustained symptom relief and/or prevent progression of disease.^{1,8} However, AIT has not been universally accepted as a standard treatment for allergic conditions. One the main reasons for the lack of widespread implementation of AIT is the complex pathogenesis of allergic diseases, and the case to case variation in clinical presentation. Patients may be first examined in community hospitals, general pediatric clinics in secondary or tertiary hospitals as well as in different departments of

a hospital. Therefore, overcoming the varying perception of AIT by different physicians in different departments is a key component in improving AIT acceptance and promoting accurate graded care.

The results of our study demonstrated that the following factors influenced the accuracy of AIT-related knowledge: physician's age, hospital grade, and whether the practitioner was a pediatrician or a non-pediatrician. The accuracy rate increased from 47.6% (91/191) for physicians aged <25 years to 85.4% (105/123) for physicians aged >45 years; this could be related to the fact that younger junior physicians have less experience and less knowledge

Which diseases do you think can be treated with		ls a ped	iatrician	Summary	Р
desensitization?		Yes (N, %)	No (N, %)		
Allergic rhinitis	Not selected	63 (12.2%)	137 (27.0%)	200 (19.5%)	
	Selected (accurate judgment)	454 (87.8%)	370 (73%)	824 (80.5%)	0.000
Allergic rhinitis	Not selected	243 (47%)	300 (59.2%)	543 (53.0%)	
	Selected (accurate judgment)	274 (53%)	207 (40.8%)	481 (47.0%)	0.000
Bronchial asthma	Not selected	87 (16.8%)	210 (41.4%)	297 (29.0%)	
	Selected (accurate judgment)	430 (83.2%)	297 (58.6%)	727 (71.0%)	0.000
Atopic dermatitis	Not selected	157 (30.4%)	239 (47.1%)	396 (38.7%)	
	Selected (accurate judgment)	360 (69.6%)	268 (52.9%)	628 (61.3%)	0.000
Food allergies	Not selected (accurate judgment)	258 (49.9%)	232 (45.8%)	490 (47.9%)	
	Selected	259 (50.1%)	275 (54.2%)	534 (52.1%)	0.189
Mite sensitization	Not selected (accurate judgment)	193 (37.3%)	197 (38.9%)	390 (38.1%)	
	Selected	324 (62.7%)	310 (61.0%)	634 (61.9%)	0.652

Table 3 Judgment of indications.

of possible allergic reactions than senior and experienced physicians. Our results also reflected the fact that physicians did not learn enough about allergy at undergraduate or postgraduate level. In many hospitals, undergraduate and postgraduate rotations are often focused on the traditional major disciplines of medicine whereas allergy and immunology are often neglected because they are newer or smaller specialties.¹² Since junior doctors are the mainstay of clinical workforce, standardized curriculum can be offered to students at the end of their rotations to encourage them to participate in teaching practice in allergic diseases, thus improving the overall knowledge of young practitioners about allergic diseases.

Tertiary hospitals had the highest rate of accurate judgment (70.1%), compared to community and secondary ones, possibly because of the higher education and overall knowledge level of physicians, better training system, and availability of more resources. Higher accurate judgment in pediatricians (57.2%), compared to non-pediatricians, could be explained by the increased incidence of allergic diseases in children and adolescents.¹⁰

When individual indications were analyzed, physicians (including pediatric and non-pediatricians) had the highest accuracy rate of allergic rhinitis judgment at 80.5% (824/1024), and pediatricians had a higher accuracy rate of 87.8% (454/517) than non-pediatricians (P < 0.05). The accuracy rate for bronchial asthma was also satisfactory for general physicians and pediatricians at 71.0% (727/1024) and 83.2% (430/517), respectively, being higher than for non-pediatricians (P < 0.05). Different judgments for allergic rhinitis and asthma could be related to the varying guidelines that often recommend AIT as the first line of treatment for allergic rhinitis but not for asthma. On the other hand, accuracy for allergic conjunctivitis was only 47%, probably because of its mild symptoms and few guidelines that recommend AIT for its treatment.^{10,11,13} The rate of accurate judgment for atopic dermatitis by pediatricians was 69.6%, higher than that of non-pediatricians at 52.9% (P < 0.05). Study that retrospectively analyzed atopic dermatitis patients who had received mite allergen-specific immunotherapy for at least 3 years showed improvement in 88.4% of patients,¹⁴ indicating that AIT could be effective in some patients of persistent exogenous atopic dermatitis.¹¹

The accuracy rate for food allergy was only 47.9%, with no difference in the accuracy rate between pediatricians and non-pediatricians (P > 0.05). While some studies show that food AIT has clinical benefits during the treatment, its longterm efficacy is unclear. Owing to possible serious allergic reactions, the avoidance of allergic foods remains the primary therapy and desensitization is not advocated for food allergies.^{13,15,16} The lowest rate of accurate judgment was detected for mite allergy (38.1%). Desensitization requires potential daily use of medications, frequent medical visits, increased risk of adverse events, and higher medical costs. In addition, it is not sufficient to evaluate the efficiency of AIT only at the current endpoints of 3 or 5 years. The degree of improvement in patients' symptoms and drug scores, disease control, and quality of life should also be evaluated accordingly to assess the effectiveness of the treatment. If patient is a healthy person with allergen sensitization, the corresponding treatment endpoint cannot be assessed. Considering the pros and cons of performing AIT, it is not clinically recommended for healthy individuals.¹⁶

Conclusions

This study analyzed accurate judgments of clinicians regarding indications for AIT. We showed that age, higher grade of working hospitals, and whether the clinician was a pediatrician or a non-pediatrician were relevant influencing factors. Physicians have a high accuracy judgment rate for rhinitis, asthma, and dermatitis, and a low accuracy judgment rate for desensitization of healthy people with allergic conjunctivitis, food allergies, and allergen sensitization. Training for allergic diseases should be facilitated, especially for younger and lower hospital-level physicians, to improve guidelines treating patients with allergic diseases in clinical settings.

Author contributions

Bo Ding analyzed the data and was the major contributor in writing the manuscript. Shiwen Gao, Jun Huang, Songdi Gong, Jiahui Lin, and Guoliang Ding contributed in data collection. Qiuzhi Shen, Wentao Wang, Mei Yang, Hui Wang, and Chunmei Shen contributed in data analysis. Yanming Lu reviewed and edited the manuscript. All authors read and approved the final manuscript.

Funding

2021 Pediatric Medical Consortium (Pudong) Health Technology Project (No. PW2021A-03)

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Supplementary

Table S1 Questionnaire on willingness to carry out AIT (doctors' version). Specific AIT is currently the only allopathic treatment that can modify the natural course of allergic diseases. It induces immune tolerance to allergens and helps to relieve symptoms and/or prevent further progression of the disease (preventing allergic rhinitis from developing into asthma, and preventing the development of new allergens) and can be actively treated in the early stages of the disease.

Basic information

- 01. *Your gender is:
 - O Male
 - O Female
- 02. *How old are you?
 - O Under 25
 - O 25-30
 - O 31-35
 - O 36-40
 - O 41-45
 - O 45 or more
- 03. *How many years of work experience do you have?
 - O Shorter than 5 years
 - O 5-10 years
 - O Longer than 10 years
- 04. *The hospital where you worked is:
 - O A public hospital
 - O A private hospital
- 05. *The hospital grade is:
 - O Community hospitals
 - O Secondary hospital
 - O Tertiary hospitals
- **06.** *The province you live in is:
 - O Beijing
 - O Tianjin
 - O Hebei
 - O Shanxi
 - O Inner Mongolia Autonomous Region
 - O Liaoning
 - O Jilin
 - O Heilongjiang
 - O Shanghai
 - O Jiangsu
 - O Zhejiang
 - O Anhui
 - O Fujian
 - O Jiangxi
 - O Shandong
 - O Henan
 - O Guangdong
 - O Hainan
 - O Chongqing
 - O Sichuan
 - O Guizhou
 - O Yunnan
 - O Guangxi Zhuang Autonomous Region
 - O Shaanxi
 - O Gansu
 - O Qinghai
 - O Hubei
 - O Hunan

- 07. *Are you a pediatrician?
 - O Yes
 - O No
- 08. (1) *If yes-your department is:
 - O General pediatrics
 - O Pediatric respiratory medicine
 - O Pediatric ophthalmology
 - O Pediatric dermatology
 - O Pediatric allergy
 - O Other pediatrics

08. (2) *If not-your department is:

- O General internal medicine
- O Adult respiratory medicine
- O Adult ophthalmology
- O Adult dermatology
- O Adult allergy
- O Other adult internal medicine
- O Community doctors
- 09. *Does your department carry out AIT?
 - O No
 - O Yes, sublingual immunotherapy
 - O Yes, subcutaneous immunotherapy
 - O Both subcutaneous and sublingual immunotherapy

Patients' information

- **10.** *When you see a patient with an allergic condition, will you: (multiple choice)
 - O Direct patients to the relevant department?
 - Complete the consultation once the medication has been dispensed?
 - Test for allergens and educate on how to avoid them?
 - If positive for dust mites, AIT is introduced on a precautionary basis?
 - Communicate with guardians that disease control requires long-term cooperation between doctor and patient?
- 11. *How long does it take you to see a patient with an allergic condition?
 - O 1-2 min
 - O 3-5 min
 - O 5-10 min
 - O More than 10 min
- **12.** *When you present AIT to a patient, what is the patient's immediate response?
 - O Rejected on the spot
 - O Neutral or go to a specialist clinic
 - O Consider agreeing
 - O Accept

- 13. *Which patients do you think need to be tested for allergens? (multiple choice)
 - O Allergic rhinitis
 - O Bronchial asthma
 - O Atopic dermatitis
 - O Food allergies
 - Allergen testing rarely done, diagnosis based on medical history
- 14. *What percentage (%) of patients you see with allergic rhinitis/asthma have been tested for allergens?
- 15. *Reasons for not being tested for allergens are:
- *What method do you usually use for allergen diagnosis? (multiple choice)
 - O Skin prick test
 - O Serological allergen-specific IgE (sIgE) test
 - O Both of the above methods are used together
 - O No test, diagnose based on medical history
 - O Excitation test
 - O Other

Awareness of AIT

- **17.** *Which of the following do you consider to be indications for AIT? (multiple choice)
 - O Allergic rhinitis
 - O Allergic conjunctivitis
 - O Bronchial asthma
 - O Atopic dermatitis
 - O Food allergy
 - O Dust mite positive desensitization
- 18. *Do you think AIT is an effective treatment?
 - O Yes, effective for all patients
 - O Yes, effective for most patients
 - O Yes, effective for some patients only
 - O No
 - O Not sure
- 19. *Do you think there is an age limit for AIT?
 - O Yes
 - O No
 - O Not clear
- **20.** *How many of the major allergens in the allergen report do you think are not suitable for starting AIT?
 - 0 1
 - 0 2
 - 03
 - O More than 3
 - O Not clear
- 21. *How long do you think the AIT treatment will take?
 - The treatment can be finished when symptoms improve significantly
 - O 1 year
 - O 3-5 years
 - O Lifetime
 - O Not clear

- 22. *Do you think the effects of AIT will last a lifetime?
 - O Yes
 - O No
 - O No clear
- **23.** *Do you think AIT can be used in conjunction with drug therapy?
 - O Yes
 - O No
 - O No clear
- **24.** *Do you think AIT is possible for patients with incomplete control of asthma?
- O Yes
- O No
- O Not clear
- **25.** *Do you think AIT should be stopped when local adverse reactions occur?
 - O Yes
 - O No
 - O Not clear
- **26.** *Do you think serious life-threatening adverse reactions or deaths are likely to occur during AIT?
 - O Yes
 - O No
 - O Not clear
- **27.** *Do you think there are precautions that need to be taken for adverse reactions when providing AIT?
 - O Yes
 - O No
 - O Not clear
- **28.** *What do you think is the significance of AIT? (multiple choice)
 - O Effective control of allergy symptoms
 - O Effectively reduce the use of symptomatic medication
 - O Preventing the development of new allergens
 - O Prevents progression of rhinitis to asthma
 - O Reducing the risk of asthma attacks
 - O Modifying the course of respiratory allergic disease
 - O Reduces financial expenditure on medication
- **29.** *In your experience, is subcutaneous immunotherapy as effective as sublingual immunotherapy?
 - O Yes
 - O No
 - O Not clear

Your opinions on AIT

- 30. *What do you know about allergic diseases?
 - Allergic diseases will improve as the child grows and do not require treatment, or require symptomatic treatment only
 - Allergic diseases do not get better on their own and require medication in case of an attack
 - Allergic diseases require a combination of long-term treatment, including medication and AIT

- 31. *In your opinion, AIT is: (multiple choice)
 - O Alternative therapies to medication
 - O Complementary therapies to drug therapy
 - O Therapies that can only be used in a small number of patients
 - O Therapies that are effective
 - O Other
- **32.** *Do you think AIT should be given more attention at the conferences that you attend regularly?
 - O Yes
 - O No
- **33.** *When do you think a patient should be referred to an allergy specialist?
 - Patients who are suitable can be referred and AIT should be started as soon as possible
 - O Refer after conventional treatment has failed
 - O AIT is not considered necessary and is not referred

- **34.** *In your opinion, what are the reasons that patients do not receive AIT? (multiple choice)
 - O Concerns about safety
 - O Treatment takes too long
 - O Do not accept subcutaneous injections
 - O Inconvenience of frequent visits to hospital
 - O Concerns about the efficacy of the treatment
 - O High cost of treatment
 - O Smaller range of allergen preparations
 - Short clinic time to fully communicate the benefits of AIT
 - O Other reasons.

*Required field