

## An online survey of clinical practice for allergic rhinitis among the Asia-Pacific representatives

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### Abstract

**Background:** Physicians' knowledge and practice which are consistent with evidence-based guidelines can improve allergic rhinitis (AR) patients' care. Compared with western countries, the available literature about Asian doctors' perceptions and clinical practices regarding Allergic Rhinitis and its Impacts on Asthma (ARIA) guidelines is limited.

**Objective:** To collect detailed information about the practical management patterns specific for AR patients and investigate compliance with ARIA in the clinical practice of Asian physicians and elucidate the possible inadequacy in the existing ARIA guidelines.

**Methods:** An e-mail with a structured questionnaire was sent to members of the Asia-Pacific Association of Allergy, Asthma and Clinical Immunology. The questionnaire consisted of doctors' characteristics, environment of medical practice, routine clinical practice following ARIA guidelines and patients' adherence to the prescription.

**Results:** Physicians from 14 countries and regions sent valid questionnaires back, 94.12% of whom were senior doctors with more than 10 years of experience. 88.24% of doctors diagnosed AR depending on the history combined with allergy tests. 82.35% of participants employed the classification criteria by ARIA. 94.12%, 88.24% and 41.8% of respondents recommended intranasal corticosteroids, oral antihistamines and leukotriene receptor antagonists as first-line medications. 5.88% treated perennial AR by intranasal corticosteroids alone. 11.76% of clinicians recommended no allergen immunotherapy (AIT) or biologics and 58.82% of interviewees reported AR patients occasionally or sometimes agreed with the recommendation of AIT.

**Conclusion:** There was high compliance with ARIA guidelines in Asian senior physicians' actual notion and practice in the management of AR. New-generation ARIA guidelines are imperative for unmet needs.

**Key words:** Allergic rhinitis, guideline, ARIA, clinical practice, compliance

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## Introduction

As a worldwide public health issue, allergic rhinitis (AR) is a highly prevalent chronic respiratory disease that seriously affects the quality of life (QOL) of up to 40% of the global population.<sup>1</sup> Clinicians commonly encounter numerous cases of AR patients in primary care clinics or general otolaryngology clinics. AR patients account for 19% of otolaryngology clinics in mainland China and contribute 14 million outpatient visits annually in the USA.<sup>2,3</sup> Considering the chronicity and the frequent relapsing characteristics of this disorder, accurate diagnosis and proper, adequate treatment showed tremendous clinical implications for general practitioners (GPs), otorhinolaryngologists and allergists. There is increasing consensus that ensuring doctors' knowledge and medical practice consistent with clinical guidelines would lead to better therapeutic outcomes for AR patients.<sup>4</sup> The "Allergic rhinitis and its impact on asthma (ARIA)" guidelines, initially published in 2001 and updated in 2008, 2010, and 2016, were developed purposefully to standardize the diagnosis and treatment of AR globally<sup>5-7</sup> and are ranked as first among existing international guidelines for the management of AR.<sup>8</sup> However, the current medical management of AR has not always been consistent with ARIA recommendations in different countries. A Belgian nationwide survey demonstrated that 62% of otorhinolaryngologists mostly followed an ARIA

guideline-based approach in the daily management of AR patients.<sup>9</sup> In contrast, only 31% of 350 Belgian GPs were aware of ARIA and one tenth of them implemented the guideline.<sup>10</sup> Moreover, approximately two-thirds of Italian AR patients were diagnosed by GPs, who made clinical decisions independent of the ARIA guidelines,<sup>11</sup> A meta-analysis showed that only 36.1% and 16% of AR patients were treated according to ARIA recommendations by otolaryngologists and GPs, respectively.<sup>12</sup> In South America, one multicenter survey of 336 GPs reported that 26.6%, 62% and 6% of GPs in Brazil, Paraguay and Uruguay, respectively, knew the ARIA guidelines.<sup>13</sup> Compared with information for other continents, the published literature involving Asian doctors' perceptions, attitudes and clinical practices in relation to ARIA is quite limited. Sixty-six percent of otolaryngologists and 89% of GPs in Malaysia were satisfied with the management algorithm described in the ARIA guidelines and felt that no changes were required.<sup>14</sup> Among 100 generalists and 100 specialists in the Philippines, 54% of the generalists and 84% of the specialists stated that they adhered to the guidelines for AR. When asked which guideline they followed, 74% of the former and 90% of the latter cited ARIA.<sup>15</sup>

The purpose of the present research is to collect extensive and accurate information about the current real-world management patterns specific for Asian AR patients. Moreover, the study was intended to investigate the degree of adherence to ARIA guidelines in the clinical practice of physicians in the Asia-Pacific region and to identify potential unmet needs and expected goals for the next generation of ARIA guidelines.

## Methods

### Study design

An initial e-mail with the structured questionnaire was sent to the members of the Asian Pacific Association of Allergy, Asthma and Clinical Immunology (APAAACI) inviting clinicians, including family physicians, otolaryngologists, rhinologists and allergists, to complete the questionnaire. The study was carried out from April 9 to May 30, 2020. All email questionnaires were returned to the secretariat of the APAAACI and analyzed. This study protocol has not yet been submitted to any medical ethics committee for approval.

### Development of the questionnaire

The questionnaire was designed based on experts' opinions and updated ARIA guidelines [5-7]. The questionnaire consisted of three sections. The first part concerned the personal background and characteristics of the clinicians and their environment and conditions of medical practice, including their gender, age, country, specialty, years of work experience, available medical equipment and laboratory tests in the clinic, number of outpatient visits and proportion of AR patients. The middle section reflected the doctors' daily clinical practice according to ARIA guidelines, such as the available types of AR guidelines, the degree of acceptance of mobile technology, the method used to diagnose AR,

the applied classification criteria for AR, the preferred first-line medical treatment, common medications for seasonal or perennial AR, recommendations of new-generation oral antihistamines for special populations, use of AIT and so on. The final portion considered the degree of reluctance toward using intranasal corticosteroids among different patient groups and the degree of acceptance of AIT. The survey responses were presented on an ordinal scale, and some were rated on a 5-point Likert scale according to frequency (never, occasionally, sometimes, often, always).

### Statistical analysis

All statistical analyses were performed using SPSS Statistics for Windows, Version 19.0 IBM Corp, Armonk, NY, USA). Descriptive statistics were employed to evaluate the responses to each problem, which are expressed as percentages of the total clinician responses.

## Results

### Physicians' basic demographic and work characteristics

In this study, valid email responses were returned by 17 clinicians from 14 countries and regions, including China, Mongolia, Malaysia, India, the Philippines, Taiwan China, Bangladesh, Thailand, Vietnam, Korea, Indonesia, Hong Kong China, Japan, and Singapore. Thirteen of the respondents (76.47%) were male. Among the respondents, 4 and 8 doctors belonged to the 41- to 50- and 51- to 60-year age groups, respectively, and 2 and 3 doctors belonged to the 31-40 and 61 years and over age groups, respectively. Most of the clinicians surveyed (76.47%) were allergists, and 2 were rhinologists. There was only one otolaryngologist and one family physician. The vast majority of the respondents were regarded as experienced physicians. In terms of years of independent practice, 94.12% were practitioners with more than 10 years of work experience, and six had more than 30 years of working experience (Table 1). Regarding the environment and condition of practice, 47.06% (8) and 52.94% (9) of the participating doctors claimed that they usually employed nasal endoscopy and computed tomography (CT), respectively, to evaluate patients with nasal diseases in daily outpatient services. Furthermore, 100% of the respondents reported that skin prick tests (SPTs) or serum-specific IgE was available for evaluating patients with nasal diseases in outpatient clinics, and only 17.65% reported that olfactory tests were available. Moreover, 41.18% and 29.41% of the responding doctors ordinarily treated 25-50 and 50-75 outpatients every week, respectively. Finally, most of the participating doctors (52.94%) reported that AR patients accounted for more than 40% of the annual number of outpatient visits. (Table 2)

### Physicians' actual clinical practices in compliance with ARIA recommendations

Both ARIA guidelines and domestic AR guidelines were available in 11 of the participants' countries and regions, and 5 participants reported that only ARIA guidelines were available in their country or region. There were no official AR guidelines available for clinical practice in one participant's

**Table 1. Participating physicians' demographic characteristics.**

Domain	Percentage of physicians (%)	Number of physicians (n)
Gender		
Male	76.47	13
Female	23.53	4
Age groups (years old)		
31-40	11.76	2
41-50	23.53	4
51-60	47.06	8
61 and over	17.65	3
Medical specialty		
Allergists	76.47	13
Rhinologists	11.76	2
Otolaryngologist	5.88	1
Family physician	5.88	1
Time of independent practice (years)		
5-10	5.88	1
10-20	29.41	5
20-30	29.41	5
> 30	35.29	6

**Table 2. Univariate analyses of clinical variables that can influence PASI90 response response at week 4, week 12 and year 1.**

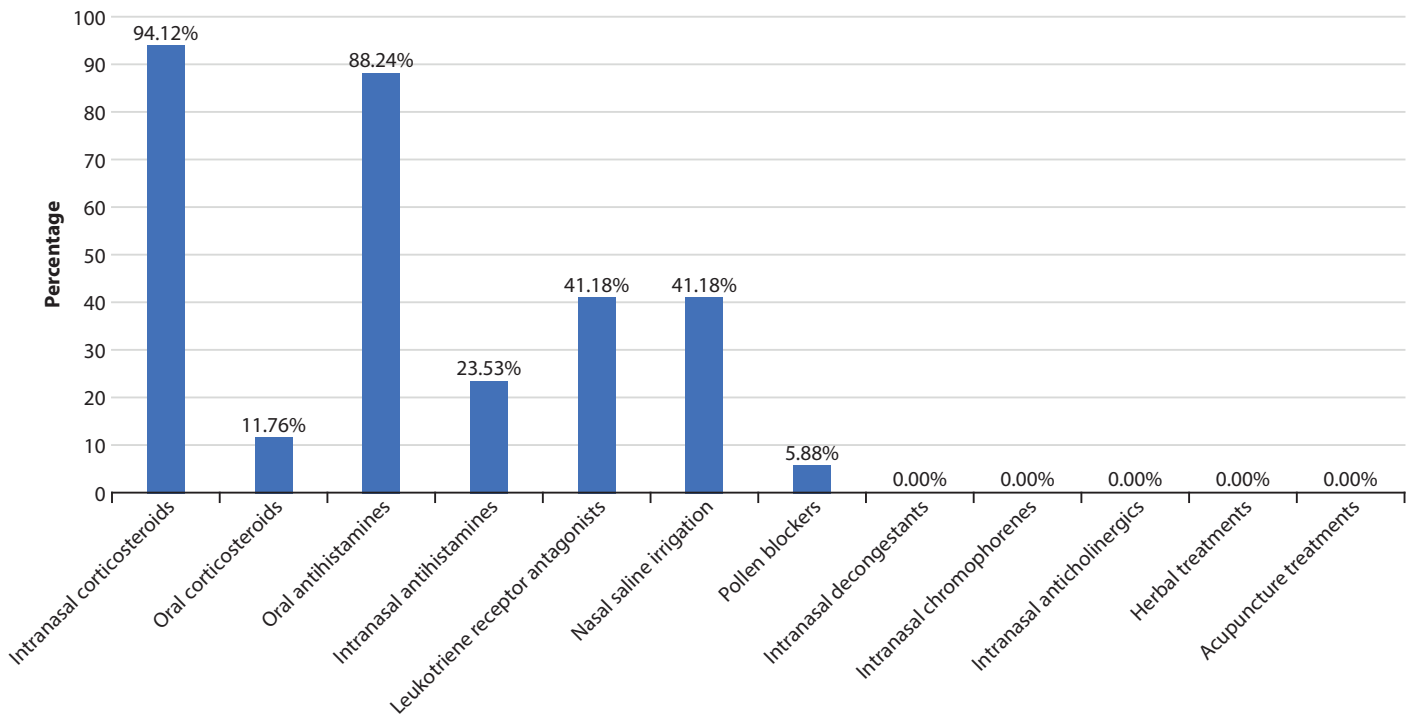
Problems and options	Percentage of physicians (%)	Number of physicians (n)
What kinds of medical instruments or equipment do you usually use to examine or evaluate patients with nasal diseases in the clinic?		
Anterior rhinoscopy	41.18	7
Nasal endoscopy	47.06	8
Sinus X-ray	52.94	9
Sinus CT scan	52.94	9
Sinus magnetic resonance imaging	11.76	2
What kinds of laboratory tests are available for evaluating patients with nasal diseases in the clinic?		
Nasal cytology with nasal secretion smear	47.06	8
SPTs or serum-specific IgE	100	17
Rhinomanometry and/or acoustic rhinometry	47.06	8
Nasal challenge test with allergens	23.53	4
Olfactory test (T&T olfactometer test, olfactory stick test, University of Pennsylvania Smell Identification Test)	17.65	3

**Table 2. (Continued)**

Problems and options	Percentage of physicians (%)	Number of physicians (n)
How many patients do you usually treat in the clinic per week?		
< 25	5.88	1
25-50	41.18	7
50-75	29.41	5
75-100	17.65	3
> 100	5.88	1
What is the approximate proportion of AR patients among all of your outpatients in a year?		
< 10%	0	0
10%-20%	11.76	2
20%-30%	17.65	3
30%-40%	17.65	3
> 40%	52.94	9

CT, computed tomography; SPTs, skin prick tests; LTRAs, leukotriene receptor antagonists; AR, allergic rhinitis

country or region. In terms of mobile technology, most of the respondents never (11.76%), occasionally (23.53%) or sometimes (29.41%) thought it could help patients better understand AR and improve their compliance and the effectiveness of medical treatment. In the clinic, 88.24% of doctors diagnosed AR based on a typical history combined with allergy tests such as SPTs or serum-specific IgE, and 11.76% diagnosed AR based only on a typical history combined with nasal endoscopy. Moreover, 64.71% of the respondents preferred to use four subtypes (mild intermittent/persistent, moderate-severe intermittent/persistent) for the classification of AR, whereas 17.65% preferred to use two subtypes (seasonal and perennial). Three of the 17 doctors diagnosed phenotypes of AR based on other classification standards (mild, moderate, severe or nasal blockage, sneezing/rhinorrhea, combined). In terms of medical treatment, 94.12%, 88.24%, 23.53% and 41.18% of the physicians often recommended intranasal corticosteroids, oral antihistamines, intranasal antihistamines and leukotriene receptor antagonists (LTRAs), respectively, to AR patients as the preferred first-line medication (**Figure 1**). Furthermore, 64.71% of the physicians treated seasonal AR with a combination of intranasal corticosteroids and oral antihistamines,



**Figure 1. Participating physicians' first-line medication recommendations for AR patients.**

and 76.47% and 5.88% treated perennial AR separately with a combination of intranasal corticosteroids and antihistamines or intranasal corticosteroids alone (Table 3). In terms of special populations, almost 90% of the clinicians always or often prescribed second-generation oral antihistamines for pediatric or geriatric patients. Finally, in terms of immunotherapy, more than four-fifths of the respondents (14/17) occasionally or sometimes prioritized the recommendation of subcutaneous or sublingual immunotherapy rather than regular medical treatment for AR patients who met the indications for AIT. In addition, 11.76% of the physicians usually recommended no AIT or monoclonal biologics for AR patients, and 5.88% recommended a combination of AIT and biologics. The percentage who recommended subcutaneous or sublingual immunotherapy was the same; both were 41.18%.

**Table 3. Participating physicians' routine prescriptions according to AR classification.**

Problems and options	Percentage of physicians (%)	Number of physicians (n)
In the clinic, how do you routinely treat seasonal AR patients?		
Intranasal corticosteroids alone	11.76	2
Oral antihistamines alone	11.76	2
Intranasal antihistamines alone	0	0
Combined intranasal corticosteroids and oral antihistamines	64.71	11
Combined intranasal corticosteroids and intranasal antihistamines	11.76	2
In the clinic, how do you routinely treat perennial AR patients?		
Intranasal corticosteroids alone	5.88	1
Antihistamines alone	0	0
LTRAs alone	5.88	1
Combined intranasal corticosteroids and antihistamines	76.47	13
Combined intranasal corticosteroids and LTRAs	11.76	2

LTRAs, leukotriene receptor antagonists; AR, allergic rhinitis

#### **Patient compliance with clinicians' medical advice**

As Table 4 shows, nearly 90% of the doctors reported that adult patients were either occasionally or sometimes or not even reluctant to use intranasal corticosteroids because of worries about the potential side effects. However, 30% of the participants indicated that the parents of pediatric AR patients always or often refuse to use intranasal corticosteroids due to concerns about their influence on children's development. Almost three-fifths of the interviewees occasionally or sometimes agreed with the recommendation of AIT for AR patients.

**Table 4. Patient adherence with physicians' recommendations.**

Problems and options	Percentage of physicians (%)	Number of physicians (n)
Are the adult patients in your clinic reluctant to use intranasal corticosteroids because they worry about the potential side effects?		
Always	0	0
Often	11.76	2
Sometimes	35.29	6
Occasionally	35.29	6
Never	17.65	3
Do the parents of pediatric AR patients refuse to use intranasal corticosteroids because they worry about their influence on children's growth and development?		
Always	5.88	1
Often	23.53	4
Sometimes	41.18	7
Occasionally	23.53	4
Never	5.88	1
Do AR patients agree with your recommendations regarding subcutaneous or sublingual immunotherapy?		
Always	5.88	1
Often	35.29	6
Sometimes	29.41	5
Occasionally	29.41	5
Never	0	0

AR, allergic rhinitis

#### **Discussion**

The online survey results in the present study afforded a good opportunity to understand of physicians' current diagnostic and therapeutic behavior with respect to AR in the Asia-Pacific region, especially in Asian countries and regions, and to determine the influence of the ARIA guidelines on physicians' concepts and practice. Overall, compared with the published data from Europe and America,<sup>9-13</sup> our study found that Asian doctors were more likely to diagnose and treat AR in compliance with ARIA recommendations in most situations in this study. However, some clinical behavior, such as patient education and drug therapy for specific subtypes of AR, needs to be improved. At the same time, more aggressive efforts should be directed towards expanding the dissemination and implementation of the existing ARIA guidelines on a larger scale and updating the recommended scheme for the next edition of the ARIA guidelines to include matters such as the indications for and application of AIT.



In this study, we found that AR patients accounted for more than 40% of the annual number of outpatient visits among more than half of the doctors surveyed. It has been reported not only that AR is the most common reason for consultation in primary care clinics<sup>16</sup> but that it accounts for one-third of all patient visits to specialist doctors' clinics.<sup>15</sup> Therefore, appropriate and reasonable clinical decision-making will significantly improve the management of AR patients. Clinical guidelines are usually developed to produce optimal health outcomes for patients and to prevent the application of improper and even harmful approaches in clinical care. Doctors' decision-making is enhanced by evidence-based guidelines, which will provide the greatest benefits for patients.<sup>17</sup> The ARIA guidelines are currently widely accepted as the foundation of health care decisions and as highly actionable practical guidelines for AR on the basis of the best available evidence. However, the present study demonstrated that there were no official AR guidelines for one Asian country or region and that only the ARIA guidelines were available in only five Asian countries and regions. However, it has been mentioned elsewhere that 25.8% of otolaryngologists followed the Korean Rhinologic Society guidelines and that 26.9% of pediatricians and 38.4% of internists followed the Korean Academy of Asthma, Allergy and Clinical Immunology guidelines;<sup>18</sup> furthermore, although 73% of ENT doctors in South Korea considered ARIA unsuitable in daily care, three-fifths of them followed the ARIA guidelines.<sup>19</sup> Subsequently, the development of clinical guidelines based on the native language as a positive complement to ARIA guidelines is necessary and imperative. Last year, the ARIA working group pointed out that mobile health had the potential to transform health service delivery globally and was a good practice that could be scaled up in the field of digitally enabled, integrated, person-centered care.<sup>20</sup> It has already been demonstrated that mobile data could provide different insights and suggest novel concepts and research question in AR, based on a pilot study in 2710 registered users from 20 countries.<sup>21</sup> Unfortunately, we found that most Asian physicians felt that mobile technology did not help patients better understand AR or improve compliance with or the effectiveness of therapy. This may be the case since mobile technology may not be readily available to many patients in the Asia-Pacific region. Nevertheless, it was encouraging that 88.24% of Asian physicians diagnosed AR based on a typical history combined with allergy tests, which is in accordance with the ARIA recommendation.<sup>5</sup> As early as 2010, Zhang concluded that only 35% ± 28% of Chinese otolaryngologists diagnosed AR based on the combination of medical history and SPTs/serum-specific IgE tests,<sup>2</sup> and in the Philippines, 92% of family physicians and 81% of specialists did not routinely use allergy tests for the diagnosis of AR in 2015.<sup>18</sup> Similar compliance with ARIA was also observed in the classification criteria for AR. More than 80% of clinicians preferred to use the subtypes recommended by ARIA, and only 17.64% adopted different subgroups from other guidelines, such as the Japanese guidelines for allergic rhinitis.

In terms of medication, the ARIA guidelines suggest that intranasal corticosteroids should be regarded as a highly effective first-line treatment for AR patients with moderate-to-severe and/or persistent symptoms and that oral antihistamines represent the first-line therapy for AR. Moreover, the 2010 revision of the ARIA guidelines suggested that clinicians should not administer any complementary and alternative medicine (CAM) for AR patients, including herbal medicine, homeopathy, acupuncture and so on.<sup>6</sup> In the present survey, 94% and 88% of physicians recommended these two kinds of medication as the preferred first-line treatment, respectively. None of the participants prescribed herbal or acupuncture treatment. Recently, Japanese scholars reported that 7.1% of children with AR and 19.2% of adults with AR had received CAM, and approximately 36.2% of adult patients thought CAM was effective.<sup>22</sup> Beyond that, a US guideline indicated that clinicians may offer acupuncture for AR patients who are interested in nonpharmacologic therapy.<sup>23</sup> Moreover, 40% of clinicians recommended LTRAs for AR patients. The US Food and Drug Administration (FDA) recently required the addition of a boxed warning about serious mental health side effects with LTRAs and advised restricted use of these substances for AR; this advice was soon introduced to the Global Strategy for Asthma Management and Prevention (GINA) update in 2021.<sup>24,25</sup> Therefore, the mechanism, efficacy, interaction and side effects of CAM and the potential risks and benefits of LTRAs need to be further discussed in future ARIA guidelines. With respect to the management of a particular subtype, the ARIA 2016 revision suggested that either a combination of intranasal corticosteroids and oral/intranasal antihistamines or intranasal corticosteroids alone should be used for the treatment of seasonal AR patients and that intranasal corticosteroids alone, rather than a combination of intranasal corticosteroids and oral antihistamines, should be recommended for the treatment of perennial AR patients.<sup>7</sup> It is interesting that two extreme situations involving adherence to ARIA guidelines were observed in the current investigation. Almost 80% of the physicians treated seasonal AR with a combination of intranasal corticosteroids and antihistamines, whereas only 5.88% treated perennial AR with intranasal corticosteroids alone, which is obviously contrary to the ARIA recommendation. The reason for the latter was probably the participants' clinical habits and the influence of their peers' clinical practices, given that senior doctors comprised the majority of the subjects interviewed in this research. Furthermore, cost issues maybe a big factor in the choice of antihistamines over intranasal corticosteroids since many Asian patients have access to generic medications which are more affordable than intranasal steroids. Almost 90% of the participants always or often prescribed second-generation oral antihistamines for pediatric or geriatric AR patients, which was in accordance with ARIA, which recommends the use of new-generation over old-generation oral antihistamines for the treatment of all AR patients and suggests that new-generation oral antihistamines be used instead of intranasal antihistamines for children

with AR. Less than one-fifth of the respondents (3/17) always or often prioritized the recommendations of AIT rather than regular medical treatment for AR patients who met the indications for AIT. Although this approach is consistent with the ARIA recommendations, which indicate that AIT should be reserved for moderate-to-severe AR patients, especially those without a good response to pharmacotherapy,<sup>6</sup> other practical guidelines suggest that factors related to the initiation of AIT include patients' acceptance of the treatment, medication requirements, and the adverse effects of medications, among others. Although AIT has an obvious economic advantage over regular pharmacological treatment, some Asian countries do not have government subsidy for AIT; thus, some patients can't afford this treatment despite the obvious indication for it.<sup>26,27</sup> In our opinion, it is worth including a more extensive discussion of the indications and opportunities for beginning AIT in the next update of the ARIA guidelines. Although more than 80% of the subjects surveyed recommended AIT for AR patients, 11.76% did not recommend AIT or biologics for AR. At the same time, only 40% of the surveyed doctors reported that AR patients always or often agreed with the recommendation about AIT. Therefore, the combination of low awareness of the value of AIT by both clinicians and patients has resulted in its underuse throughout the world. Compared with the 4.5% acceptance rate of AIT in China, 2 to 9% of AR patients in the USA accepted AIT. Similarly, a Swedish national study found that only 2.1% of AR patients accepted sublingual or subcutaneous AIT.<sup>28-30</sup> AIT is well known as the only effective therapy for AR and has the potential to alter the natural course of allergic diseases and prevent new sensitization.<sup>31</sup> Consequently, greater efforts must be made to promote and emphasize the clinical significance of AIT to both physicians and patients.

Several limitations were present in this study. First, the total sample size was inadequate, and the results cannot be considered representative of all Asian physicians' opinions and real clinical behavior. Additionally, the small sample size did not allow additional statistical analysis via data mining, and only descriptive results are presented. Second, the majority of the respondents in this study were allergists. The proportion of otolaryngologists and family physicians was significantly different from the proportion of clinical practitioners. This may not reflect the true Asia-Pacific diagnostic and management protocols for AR since many Asian countries lack allergists. Third, the online investigation made it easier for doctors from urban areas to participate in this study and may have excluded rural or remote doctors who lacked internet access. Fourth, considering the availability in clinical practice, some novel issues recommended by next-generation ARIA<sup>20</sup> were not involved in this study, such as step-up / step-down algorithm in treating AR patients based on VAS and application of fix-dose combination of antihistamine & steroid spray.

## Conclusion

Taken together, the results of this email investigation demonstrate high compliance with ARIA guidelines in Asian senior physicians' actual beliefs and practices related to the diagnosis and treatment of AR, although there were some nonideal adherence data regarding the value of mobile technology, therapy for specific subtypes of AR and the recognition of AIT by both physicians and patients. Additionally, the urgent need to update recommendations for the management of AR in the revised guidelines was mentioned. We believe that the publication of more high-quality scientific evidence regarding the management of AR is likely to lead to new ARIA guidelines that are more rigorous and practicable. The dissemination and implementation of the ARIA guidelines will be cardinal issues for their integration into real-life clinical settings, which will substantially improve the quality of health care for AR patients.

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## Conflict of interest

The authors have no conflicts of interest to declare.

## Author contributions

- Conception and design: Ming Zheng, Xiangdong Wang, Ruby Pawankar, Luo Zhang;
- Administrative support: Luo Zhang, Ruby Pawankar and Xiangdong Wang;
- Provision of study materials: Ming Zheng, Xiangdong Wang, Amir Hamzah Abdul Latiff, Ashok Shah, Duy Le Pham, Dong Young Kim, Jae Won Oh, Jiu Yao Wang, Kiat Ruxrungtham, Marysia Recto, Niken Lestari Poerbonegoro, Narantsetseg Logi, Sonomjams Munkhbayarlakh, Ting Fan Leung, Takeshi Shimizu, Wen Chin Chiang, Wasu Kamchaisatian, Ruby Pawankar and Luo Zhang;
- Collection and assembly of data: Ruby Pawankar and Luo Zhang;
- Data analysis and interpretation: Ming Zheng and Xiangdong Wang;
- Manuscript writing: Ming Zheng, Xiangdong Wang, Ruby Pawankar and Luo Zhang;
- Final approval of manuscript: all authors.

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