

Distribution and Determinants of *Dermatophagoides* Mites Sensitization of Allergic Rhinitis and Allergic Asthma in China

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Keywords

Allergic rhinitis · Allergic asthma ·
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Abstract

Background: The implementation of allergen immunotherapy (AIT) requires extensive knowledge of allergen distribution in the region to identify high-risk regions for AIT utilization. However, the geographical distribution patterns of the major *Dermatophagoides* allergens in China remain unclear despite the increasing prevalence of these allergens. **Methods:** We performed comprehensive database searches of articles demonstrating the distribution patterns of *Dermatophagoides*-sensitized allergic rhinitis (AR) and allergic asthma (AA) in China, published between 1990 and 2017. **Results:** We retrieved 163 articles encompassing 114,302 allergen-positive cases to generate the distribution maps. The rate of sensitization to *Dermatophagoides pteronyssinus*

(*D. pteronyssinus*) and *Dermatophagoides farinae* (*D. farinae*) was similar in patients with AR (75.1 vs. 75.2%, $p > 0.05$) but not in those with AA (78.5 vs. 77.7%, $p = 0.041$). Patients with AR and AA shared similar regional distribution patterns of both *D. pteronyssinus* and *D. farinae* sensitization, which were highest in the southern and central parts of China and lowest in the northern regions, especially in the Northwest. The overall rate of sensitization to *D. pteronyssinus* and *D. farinae* was significantly higher in patients with AA ($p < 0.001$). Additionally, the annual mean temperature and humidity were the 2 major determinants of *D. pteronyssinus* and *D. farinae* sensitization in AR and of *D. pteronyssinus* sensitization in AA, whereas the annual mean temperature was the sole determinant for *D. farinae* sensitization in AA. **Conclusion:** These findings may inform clinicians of the strategies for the prevention of *Dermatophagoides* sensitization and may be of benefit to the future clinical management of allergic diseases associated with sensitization to *Dermatophagoides* mites.

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Introduction

Allergic rhinitis (AR) and allergic asthma (AA) are prevalent upper and lower airway diseases with a different but progressively increasing incidence worldwide and represent a major public health concern [1–3]. To date, assessment of the prevalence of allergen sensitization in mainland China has been conducted in separate regional studies and in either AR or AA; thus, there is a lack of standardization, and a compilation of the data is highly desired. Hitherto, allergen immunotherapy (AIT) is potentially the only curative treatment against allergic airway diseases and has been recommended by the latest guidelines in both the USA and China [4, 5]. However, AIT utilization in China remains low partly because the effective implementation of AIT often requires an extensive knowledge on regional allergen distribution, which is largely heterogeneous throughout China.

A previous study found that the major source of perennial aeroallergens of AR and AA both in adults and children were *Dermatophagoides* mites [6] (online suppl. Fig. S1; for all online suppl. material, see www.karger.com/doi/10.1159/000499409), and *Dermatophagoides* frequently contributed to exacerbation of AR and AA [7–9]. Meanwhile, the only approved AIT formulation in China is the *Dermatophagoides* preparation. However, there remains a lack of systematic reviews delineating the nationwide distribution pattern and determinants pertaining to *Dermatophagoides* allergens in patients with AR and AA in China, which hampers the effective implementation of AIT based on the high-risk localities. We hypothesized that there are “hot spots” of *Dermatophagoides* associated with environmental factors, which would be areas of interest for implementing and boosting AIT utilization, increasing success rates by ensuring its clinical utilization. To this end, we aimed to comprehensively investigate the geographical distribution patterns associated with 2 major *Dermatophagoides* allergens in China, *Dermatophagoides pteronyssinus* (*D. pteronyssinus*) and *Dermatophagoides farinae* (*D. farinae*).

Materials and Methods

Literature Search and Data Retrieval

Cited evidence was mainly derived from the Chinese and English literature. We searched PubMed (from January 1990 to December 2017), Chinese Biomedical Database (from January 1990 to December 2017), China National Knowledge Infrastructure (CNKI) (from January 1990 to December 2017), and the

Chinese literature included in China Technology Core Journals of 2013. For AR, the search strategy included for English: (“Rhinitis” OR “Allergic Rhinitis”) AND (“Allergen” OR “Skin prick test”), and for Chinese: “Bian Ying Xing Bi Yan” (变应性鼻炎) or “Guo Min Xing Bi Yan” (过敏性鼻炎) and “Pi Fu Dian Ci Shi Yan” (皮肤点刺试验) or “Guo Min Yuan Jian Ce” (过敏原检测) or “Bian Ying Yuan Jian Ce” (变应原检测). For AA, the search strategy included for English: (“Allergic Asthma” OR “Bronchial asthma” OR “Asthma”) AND (“Allergen” OR “Skin prick test”), and for Chinese: “Guo Min Xing Xiao Chuan” (过敏性哮喘) or “Zhi Qi Guan Xiao Chuan” (支气管哮喘) or “Xiao Chuan” (哮喘) and “Pi Fu Dian Ci Shi Yan” (皮肤点刺试验) or “Guo Min Yuan Jian Ce” (过敏原检测) or “Bian Ying Yuan Jian Ce” (变应原检测). The titles, abstracts, and full texts were reviewed by 2 independent researchers who then screened the articles according to the inclusion and exclusion criteria. A third reviewer was consulted if there was any disagreement between the 2 researchers. We retrieved 163 articles that reported the rates of sensitization to *D. pteronyssinus* and *D. farinae* from all geographical regions of China, including 114,302 patients with AR or AA. The search methodology and the results are outlined in Figure 1.

In this study, the inclusion criteria included papers presenting a clear positive rate or sufficient data to calculate a positive rate in patients who underwent a skin prick test (SPT), or a positive rate of *D. pteronyssinus* and *D. farinae* in patients with AR or AA, respectively. We excluded the literature that did not present a clear outcome, or presented a mixture of several diseases as the outcomes, papers only presenting the total positive rate of *Dermatophagoides* sensitization, and papers in which the positive rates of *D. pteronyssinus* and *D. farinae* were not detected with SPT.

Sources of Geographical Data

The average temperature and humidity within the last decade and the altitude for different geographical regions were provided by the Earth Science Data Sharing Platform (<http://www.geodata.cn>). The population density was calculated based on the data derived from the 6th National Population Census (<http://www.stats.gov.cn/ztc/zdtjgz/zgrkpc/dlcrkpc/>), the Census and Statistics Department of Hong Kong Special Administrative Region (<https://www.censtatd.gov.hk/home.html>), and Directorate-General of Budget Accounting and Statistics, Executive Yuan (Taiwan) (<https://www.dgbas.gov.tw>).

Statistical Analysis

All data were analyzed using SPSS version 16.0 (SPSS Inc., USA). Categorical data were presented as frequencies and percentages. The rate of sensitization to *D. pteronyssinus* and *D. farinae* in AR or AA in all provinces and regions was compared by the χ^2 test. Correlation between the rate of sensitization to *D. pteronyssinus* and *D. farinae* in patients with AR or AA and the average temperature and the humidity within the past decade, the altitude, and the population density was performed with Spearman’s correlation analysis model. The geographical determinants of *Dermatophagoides* sensitization for AR or AA were calculated by multiple linear regression analysis. The cutoff values of geographical conditions to predict a *Dermatophagoides* sensitization of >70% in AR and AA were evaluated using the receiver operating characteristic (ROC) curve.

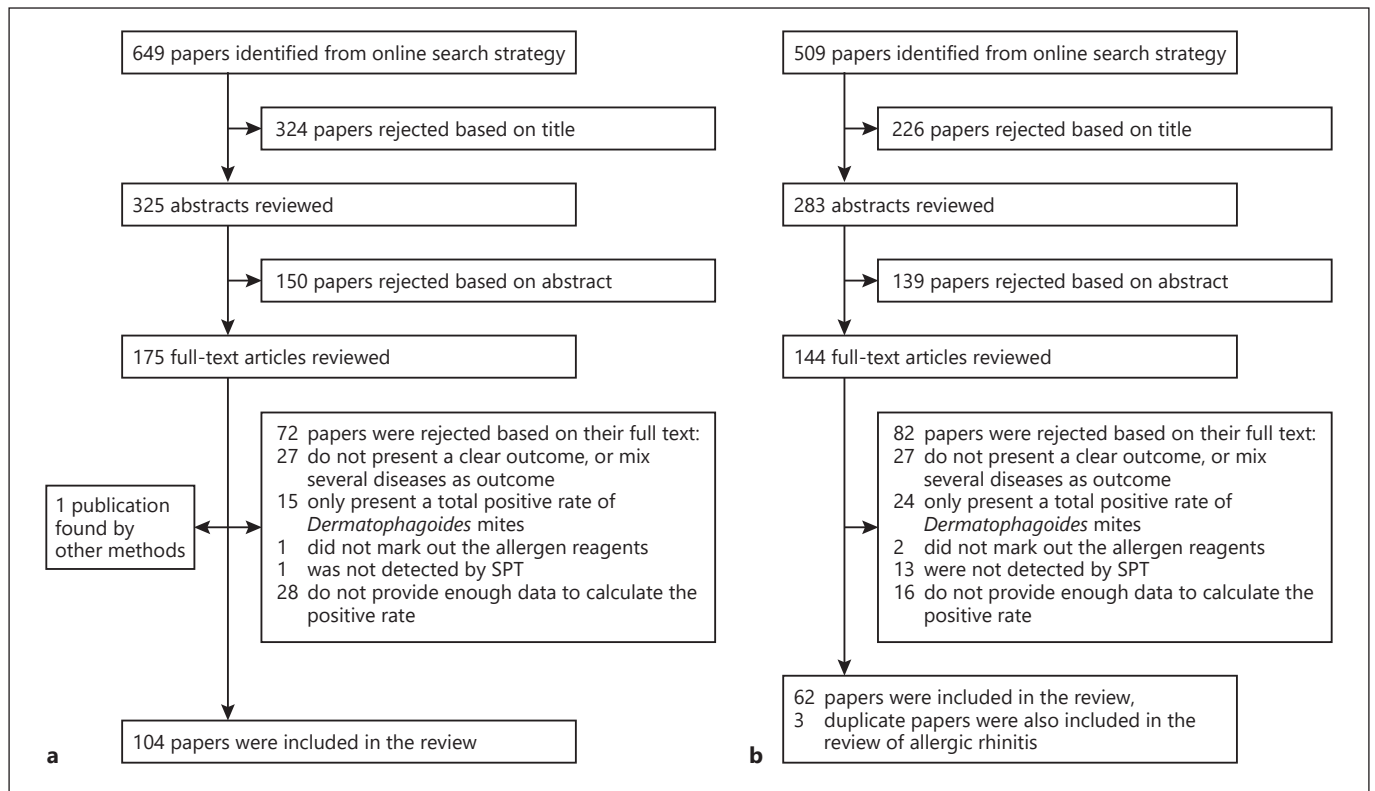


Fig. 1. Outlines of the search methodology with results for allergic rhinitis (a) and allergic asthma (b).

Results

We retrieved 163 articles that reported the rates of sensitization to *D. pteronyssinus* and *D. farinae* from all geographical regions of China, including 114,302 patients with AR or AA. Of these, 104 articles studied AR, and the included cases were distributed over 29 provinces, municipalities, and autonomous regions. There were 93,786 cases of SPT-positive AR, of which 52,049 were male (55.5%) and 41,737 were female (44.5%). On the other hand, there were 62 articles (3 articles were duplicates as they also had data on AR) on AA distributed across 21 provinces, municipalities, and autonomous regions. There were 32,504 AA cases included, of which 18,740 cases were male (57.7%) and 13,764 were female (42.4%), and 20,516 SPT-positive AA cases were identified.

Distribution of Dermatophagoides Sensitization in Patients with AR across China

In patients with AR, the rate of sensitization to *D. pteronyssinus* and *D. farinae* was 75.1 and 75.2%, respectively ($p = 0.677$), showing a high prevalence of *Derma-*

trophagoides mite sensitization in China. In terms of regional distribution, both *D. pteronyssinus* and *D. farinae* were highly clustered in the eastern, southern, and central regions of China (>80% sensitization rate), with provinces such as Hunan, Anhui, Hainan, and Guangxi having very high sensitization rates (>90%) for either *D. pteronyssinus*, *D. farinae*, or both. On the other hand, the northern parts of China, especially the Northwest, had a fairly low rate of *Dermatophagoides* sensitization, with provinces such as Xinjiang and Inner Mongolia having sensitization rates of <30% (Table 1). The rates of sensitization to *D. pteronyssinus* and *D. farinae* in AR were highly correlated with each other ($r = 0.971$, $p < 0.001$) (Fig. 2).

Distribution of Dermatophagoides Sensitization in Patients with AA across China

In AA patients, the rate of sensitization was slightly higher for *D. farinae* (78.5%) than for *D. pteronyssinus* (77.7%, $p = 0.041$). Distribution of both *D. pteronyssinus* and *D. farinae* sensitization in AA patients exhibited a pattern in which the rates of allergen sensitization descended progressively from the eastern, southern, and

Table 1. Distribution of *D. pteronyssinus* and *D. farinae* sensitization in Chinese allergic rhinitis patients (sorted by regions and administrative regions)

Regions	SPT positive cases for at least 1 allergen	Sensitization rate of <i>D. pteronyssinus</i> , %	Sensitization rate of <i>D. farinae</i> , %	Province	SPT positive cases for at least 1 allergen	<i>D. pteronyssinus</i> -positive individual	Sensitization rate of <i>D. pteronyssinus</i> , %	<i>D. farinae</i> -positive individual	Sensitization rate of <i>D. farinae</i> , %	χ^2	p value
East China	43,668	81.3	80.1	Jiangsu	12,997	10,195	78.4	10,052	77.3	4.6	0.033
				Shandong	1,905	1,353	71.0	1,385	72.7	1.3	0.249
				Anhui	848	776	91.5	760	89.6	1.8	0.184
				Shanghai	11,744	9,561	81.4	9,738	82.9	9.1	0.003
				Zhejiang	4,004	3,362	84.0	3,441	85.9	6.1	0.014
				Fujian	7,367	6,395	86.8	6,366	86.4	0.5	0.483
				Jiangxi	4,490	3,632	80.9	2,976	66.3	246.5	<0.001
				Taiwan	313	214	68.4	246	78.6	8.4	0.004
South China	14,164	87.7	87.7	Guangdong	10,525	9,219	87.6	9,048	86.0	12.1	0.001
				Guangxi	2,953	2,616	88.6	2,741	92.8	31.4	<0.001
				Hainan	686	588	85.7	638	93.0	19.2	<0.001
North China	7,770	50.8	51.1	Beijing	2,263	1,162	51.3	1,132	50.0	0.8	0.372
				Hebei	776	516	66.5	478	61.6	4.0	0.044
				Shanxi	469	191	40.7	185	39.4	0.2	0.689
				Tianjin	3,292	1,923	58.4	1,965	59.7	1.1	0.293
				Inner Mongolia	970	158	16.3	209	21.5	8.7	0.003
Central China	10,102	85.4	89.0	Hubei	6,419	5,334	83.1	5,651	88.0	63.4	<0.001
				Hunan	2,276	2,141	94.1	2,128	93.5	0.7	0.391
				Henan	1,407	1,154	82.0	1,208	85.9	7.7	0.006
Northeast	4,854	59.2	64.7	Liaoning	4,692	2,774	59.1	3,026	64.5	28.7	<0.001
				Jilin	162	101	62.3	113	69.8	2.0	0.159
Northwest	6,012	32.2	33.2	Gansu	746	299	40.1	313	42.0	0.5	0.461
				Shan'xi	166	80	48.2	88	53.0	0.8	0.380
				Ningxia	1,346	661	49.1	688	51.1	1.1	0.298
				Xinjiang	3,754	893	23.8	909	24.2	0.2	0.665
Southwest	7,216	70.7	69.2	Sichuan	231	190	82.3	186	80.5	0.2	0.633
				Yunnan	2,135	1,470	68.9	1,436	67.3	1.2	0.264
				Chongqing	4,721	3,343	70.8	3,274	69.3	2.4	0.121
				Guizhou	129	97	75.2	97	75.2	<0.1	1.000

central parts of China (>80% sensitization rate) to the northern parts of China. Guizhou, Jiangsu, Hubei, Hainan, Guangdong, and Guangxi showed very high positive rates (>90%) for either *D. pteronyssinus*, *D. farinae*, or both, while the lowest sensitization rate was found in Xinjiang (Table 2). Additionally, sensitization rates of *D. pteronyssinus* and *D. farinae* also highly correlated with each other in AA ($r = 0.866$, $p < 0.001$) (Fig. 2).

Comparison of Dermatophagoides Sensitization between AR and AA Patients

From the collated analysis, *Dermatophagoides* sensitization patterns were comparable for both AR and AA (Fig. 2). The rates of sensitization to *D. pteronyssinus* and *D. farinae* were significantly higher in patients with AA than in those with AR (*D. pteronyssinus*, 77.1 vs. 75.1%; *D. farinae*, 78.5 vs. 75.2%, all $p < 0.001$). Interestingly, the sensitization rate of *D. pteronyssinus* was higher in patients with AA than in

those with AR in all regions of China with the exception of the northeastern region. The sensitization rate of *D. farinae* was also higher in AA patients in most regions of China, including the East, North, Southwest, and Northwest of China. But the distribution of *D. farinae* sensitization in AR and AA patients was similar in southern, central, and northeastern regions (Table 3).

Correlation between Geographical Conditions and Dermatophagoides Sensitization in AR and AA Patients

In both patients with AR and AA, the sensitization rate of both *D. pteronyssinus* and *D. farinae* correlated positively with the temperature (AR: $r = 0.675$ and 0.660 ; AA: $r = 0.504$ and 0.491 for *D. pteronyssinus* and *D. farinae*, all $p < 0.001$), humidity (AR: $r = 0.677$ and 0.698 ; AA: $r = 0.844$ and 0.391 for *D. pteronyssinus* and *D. farinae*, all $p < 0.05$), and population density (AR: $r = 0.258$ and 0.276 for

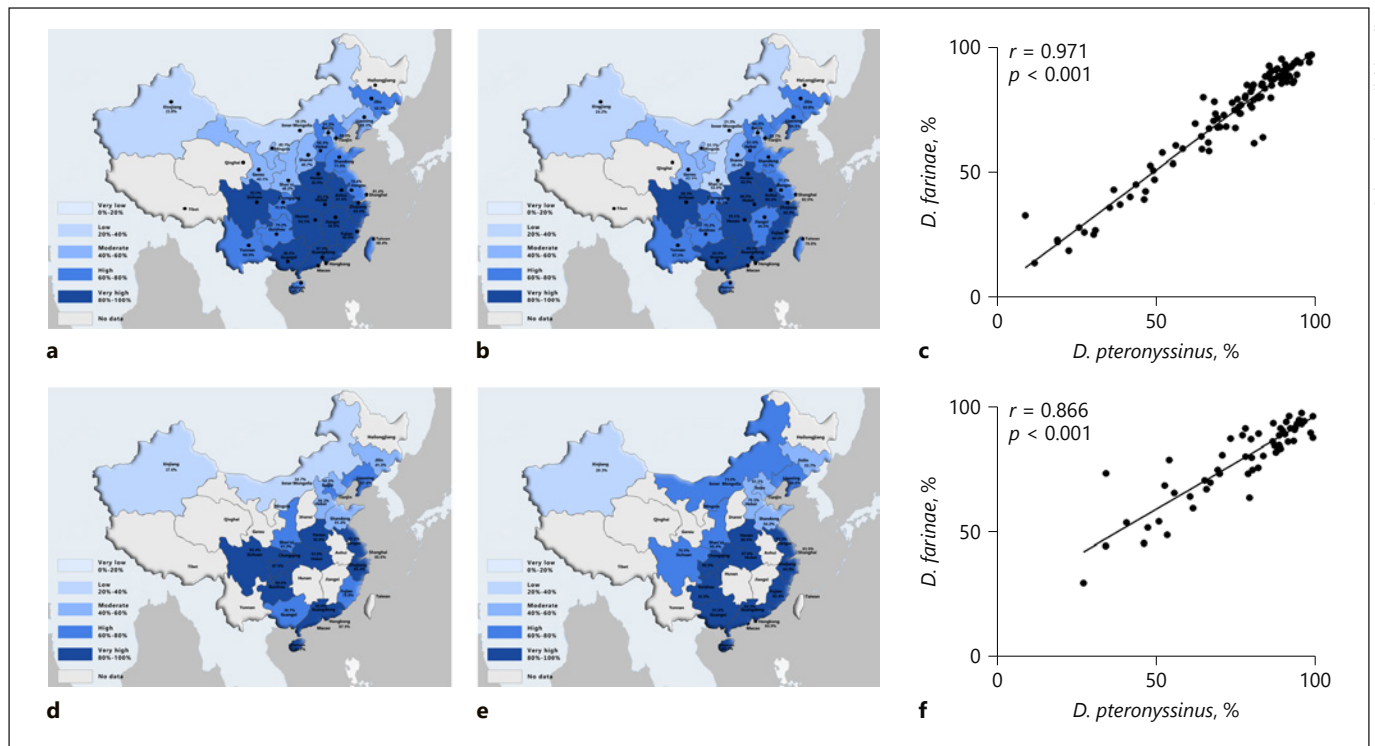


Fig. 2. Allergen distribution map of allergic rhinitis (AR) and allergic asthma (AA). The regional distribution of both *D. pteronyssinus* and *D. farinae* sensitization in AR (a, b) and AA (d, e) patients was similar with the highest sensitization rates in eastern,

southern, and central China, while they were substantially lower in the northern parts of China. The sensitization rates of *D. pteronyssinus* and *D. farinae* allergen in AR and AA patients were highly correlated (c, f).

D. pteronyssinus and *D. farinae*; AA: $r = 0.269$ for *D. pteronyssinus*, all $p < 0.05$) but negatively with the altitude (AR: $r = -0.598$ and -0.609 for *D. pteronyssinus* and *D. farinae*; AA: $r = -0.310$ for *D. pteronyssinus* only, all $p < 0.05$) (Fig. 3, 4). In multiple linear regression analysis, the temperature (positive correlation), humidity (positive correlation), and altitude (negative correlation) were the major determinants of *Dermatophagoides* sensitization for AR (*D. pteronyssinus*: $R^2 = 0.758$, $p < 0.001$ and *D. farinae*: $R^2 = 0.759$, $p < 0.001$, respectively). In AA, however, temperature (positive correlation) and humidity (positive correlation) were the major determinants of *D. pteronyssinus* sensitization ($R^2 = 0.494$, $p < 0.001$), and temperature was the sole determinant of *D. farinae* sensitization ($R^2 = 0.282$, $p < 0.001$) (Fig. 3, 4), possibly due to the higher complexity and variability of disease presentation.

Geographical Conditions for Estimating

Dermatophagoides Sensitization >70% in AR and AA

Considering the major geographical determinants of *Dermatophagoides* sensitization patterns may inform clinicians of the strategies for prevention and manage-

ment of *Dermatophagoides* sensitization. We used ROC curves and set a practical cutoff of >70% sensitization rates. The optimal cutoff point was calculated based on the maximal Youden index (sensitivity + specificity – 1). The temperature and humidity can be used to estimate the conditions under which the sensitization rates will increase >70% in AR (*D. pteronyssinus*, area under the curve [AUC] = 0.916 and 0.965; *D. farinae*, AUC = 0.857 and 0.866 for the annual mean temperature and humidity, respectively) and in AA (*D. pteronyssinus*, AUC = 0.898 and 0.842 for the annual mean temperature and humidity, respectively) with high accuracy. Only annual mean temperature was able to predict *D. farinae* sensitization >70% in AA (AUC = 0.853) (Table 4, Fig. 5).

Discussion

The incidence of AR and AA in most countries has recently increased dramatically worldwide [10, 11]. Large-scale epidemiological surveys have found that in coun-

Table 2. Distribution of *D. pteronyssinus* and *D. farinae* sensitization in Chinese asthmatic patients (sorted by regions and administrative regions)

Regions	SPT positive cases for at least 1 allergen	Sensitization rate of <i>D. pteronyssinus</i> , %	Sensitization rate of <i>D. farinae</i> , %	Province	SPT positive cases for at least 1 allergen	<i>D. pteronyssinus</i> -positive individual	Sensitization rate of <i>D. pteronyssinus</i> , %	<i>D. farinae</i> -positive individual	Sensitization rate of <i>D. farinae</i> , %	χ^2	<i>p</i> value
East China	4,378	86.2	86.6	Jiangsu	1,166	1,075	92.2	1,111	95.3	9.5	0.002
				Shandong	72	27	51.4	39	54.2	0.1	0.738
				Shanghai	1,233	1,048	85.0	1,035	83.9	0.5	0.470
				Zhejiang	1,662	1,420	85.4	1,411	84.9	0.2	0.661
				Fujian	245	193	78.8	197	80.4	0.2	0.654
South China	4,439	89.8	87.8	Guangdong	1,475	1,328	90.0	1,276	86.5	8.9	0.003
				Guangxi	155	122	78.7	142	91.6	10.2	0.001
				Hainan	2,388	2,121	90.7	2,079	88.9	4.1	0.042
				Hong Kong	471	414	87.9	400	84.9	1.8	0.183
North China	2,413	59.2	68.8	Beijing	1,371	829	60.5	837	61.1	0.1	0.754
				Hebei	970	575	59.3	769	79.3	91.2	<0.001
				Inner Mongolia	72	25	34.7	53	73.6	21.9	<0.001
Central China	580	90.0	88.1	Hubei	475	435	91.6	417	87.8	3.7	0.055
				Henan	105	87	82.9	94	89.5	2.0	0.161
Northeast	2,378	61.4	66.1	Liaoning	1,817	1,229	67.6	1,270	69.9	2.2	0.142
				Jilin	561	231	41.2	301	53.7	17.5	<0.001
Northwest	2,620	60.5	59.7	Shan'xi	2,562	1,570	61.3	1,548	60.4	0.4	0.529
				Xinjiang	58	16	27.6	17	29.3	<0.1	0.837
Southwest	3,708	85.8	87.8	Sichuan	2,023	1,687	83.4	1,609	79.5	10.0	0.002
				Chongqing	1,486	1,304	87.8	1,315	88.5	0.4	0.533
				Guizhou	199	189	95.0	186	93.5	0.4	0.519

Table 3. Comparison of the sensitization rate of *Dermatophagoides* mites between AR and AA (sorted by regions and administrative regions)

Regions	<i>Dermatophagoides</i> mites	Sensitization rate, %			
		AR	AA	χ^2	<i>p</i> value
East China	<i>D. pteronyssinus</i>	81.3	86.2	64.3	<0.001
	<i>D. farinae</i>	80.1	86.6	110.1	<0.001
North China	<i>D. pteronyssinus</i>	50.8	59.2	51.9	<0.001
	<i>D. farinae</i>	51.1	68.8	231.9	<0.001
Central China	<i>D. pteronyssinus</i>	85.4	90.0	9.4	0.002
	<i>D. farinae</i>	89.0	88.1	0.4	0.527
South China	<i>D. pteronyssinus</i>	87.7	89.8	13.8	<0.001
	<i>D. farinae</i>	87.7	87.8	<0.1	0.924
Southwest	<i>D. pteronyssinus</i>	70.9	85.8	303.8	<0.001
	<i>D. farinae</i>	69.2	83.9	275.5	<0.001
Northwest	<i>D. pteronyssinus</i>	32.2	60.5	608.7	<0.001
	<i>D. farinae</i>	33.2	59.7	528.6	<0.001
Northeast	<i>D. pteronyssinus</i>	59.2	61.4	3.1	0.077
	<i>D. farinae</i>	64.7	66.1	1.4	0.242
Total	<i>D. pteronyssinus</i>	75.1	77.7	509.8	<0.001
	<i>D. farinae</i>	75.2	78.5	514.1	<0.001

AR, allergic rhinitis; AA, allergic asthma.

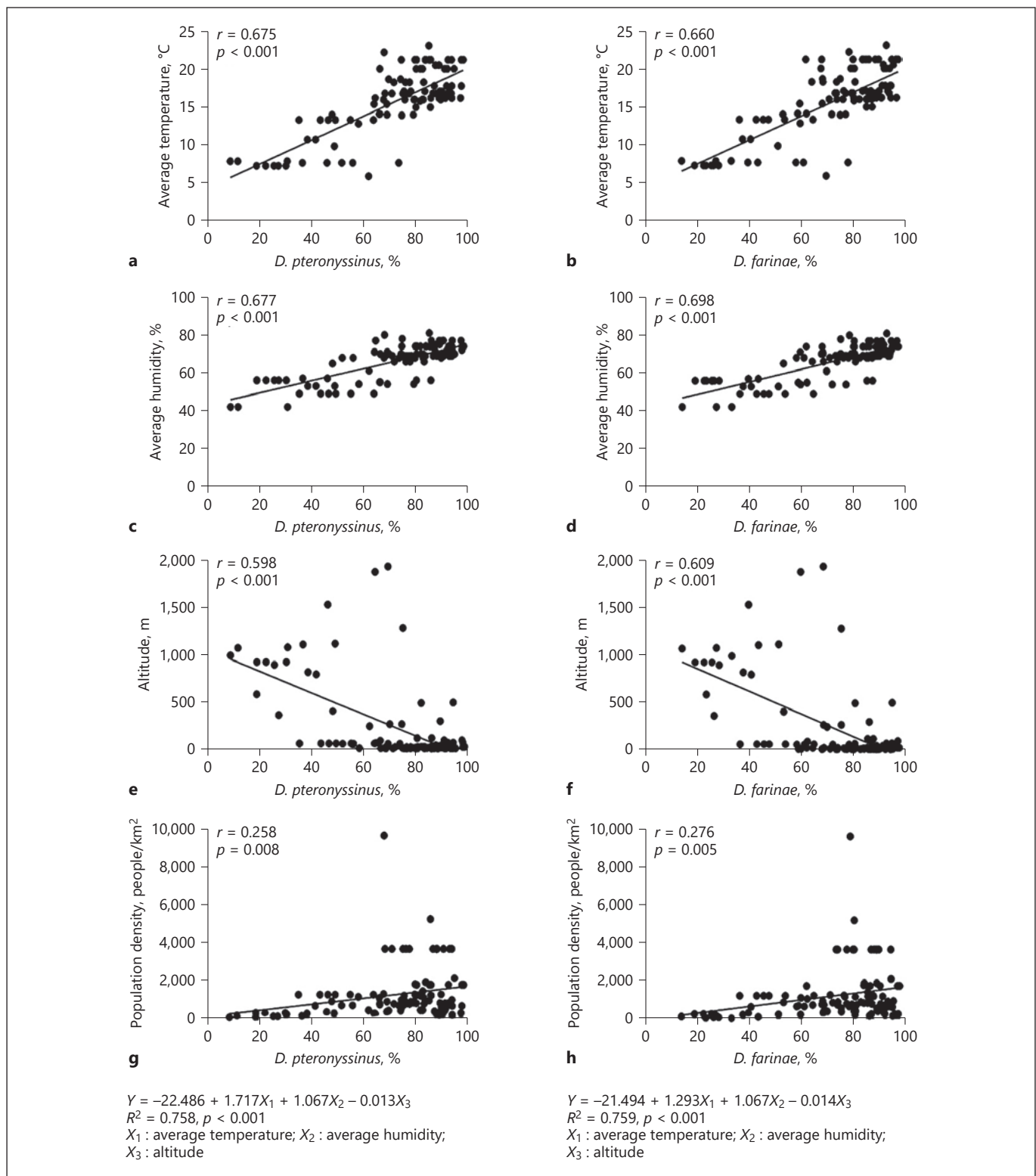


Fig. 3. Correlation between geographical conditions and *D. pteronyssinus* or *D. farinae* sensitization in Chinese allergic rhinitis (AR) patients. The sensitization rate of *D. pteronyssinus* correlated positively with temperature (a), humidity (c), and population density (g) and significantly but negatively with altitude (e) in AR patients. The sensitization rate of *D. farinae* also correlated positively with temperature, humidity, and population density but negatively with altitude in AR patients (b, d, f, h).

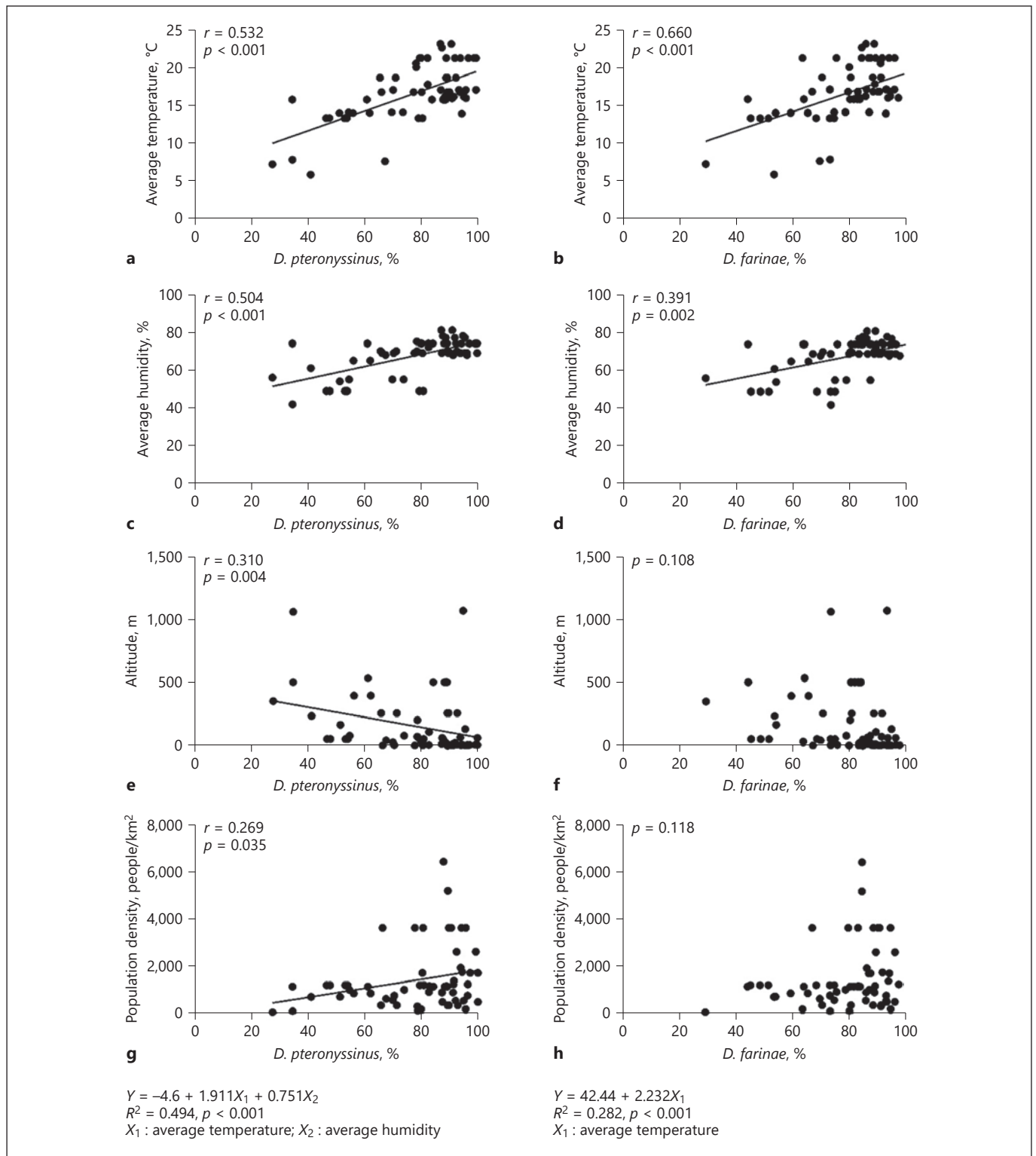


Fig. 4. Correlation between geographical conditions and *D. pteronyssinus* or *D. farinae* sensitization in Chinese allergic asthma (AA) patients. The sensitization rate of *D. pteronyssinus* correlated positively with temperature (a), humidity (c), and popula-

tion density (g) and significantly but negatively with altitude (e) in AA patients. The sensitization rate of *D. farinae* only correlated positively with temperature and humidity in AA patients (b, d, f, h).

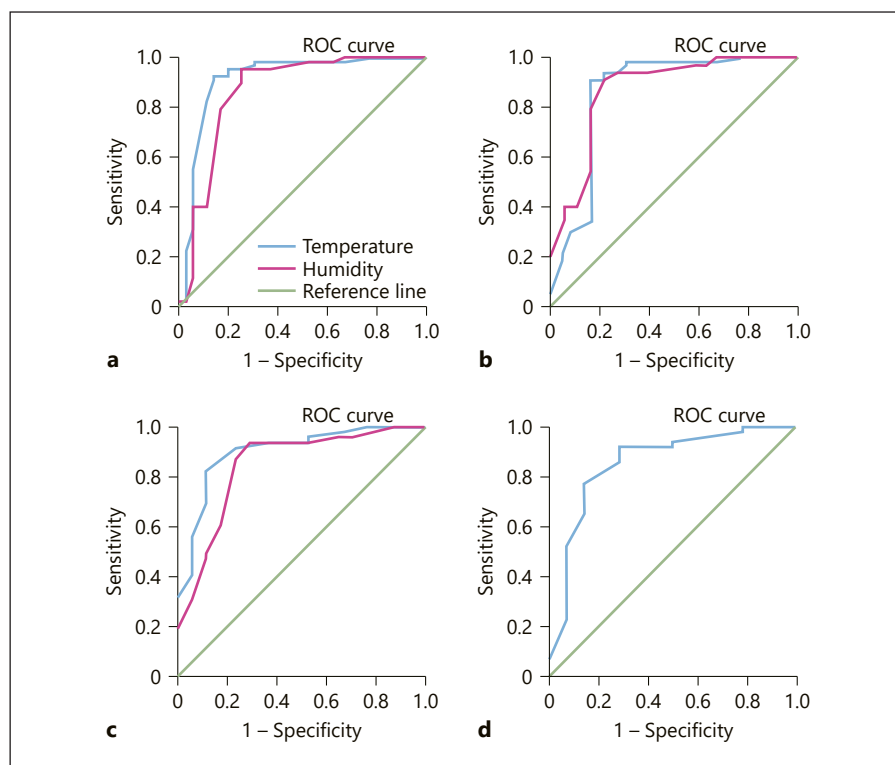


Fig. 5. ROC curve to predict the optimal cutoffs for geographical conditions to estimate a *Dermatophagoides* sensitization of >70% in allergic rhinitis (AR) and allergic asthma (AA) patients. The optimal cutoff points were calculated based on the maximal Youden index (sensitivity + specificity – 1). **a** The curve predicts *D. pteronyssinus* sensitization of >70% in AR. **b** The curve predicts *D. farinae* sensitization of >70% in AR. **c** The curve predicts *D. pteronyssinus* sensitization of >70% in AA. **d** The curve predicts *D. farinae* sensitization of >70% in AA.

Table 4. The cutoff value of geographical conditions estimated for *Dermatophagoides* sensitization >70% in AR and AA

Diseases	<i>Dermatophagoides</i> allergens	Geographical conditions	Cutoff	AUC	95% CI	Sensitivity, %	Specificity, %
AR	<i>D. pteronyssinus</i>	Temperature	15.7°C	0.916	0.846–0.987	92.6	86.1
		Humidity	65.5%	0.865	0.777–0.953	95.6	75.0
	<i>D. farinae</i>	Temperature	15.7°C	0.857	0.761–0.952	91.2	83.3
		Humidity	67.0%	0.866	0.785–0.947	91.2	77.8
AA	<i>D. pteronyssinus</i>	Temperature	16.0°C	0.898	0.808–0.988	82.2	88.2
		Humidity	66.5%	0.842	0.723–0.962	93.3	70.6
	<i>D. farinae</i>	Temperature	16.0°C	0.853	0.725–0.981	77.1	85.7

AR, allergic rhinitis; AA, allergic asthma; AUC, area under the receiver operating characteristics curve; CI, confidence interval.

tries and regions with a high incidence of AR, the incidence of AA was also correspondingly high or higher [12–14]. The most common cause of these 2 allergic airway diseases could be attributed to allergen sensitization. Therefore, our study focused on allergen-sensitized AR and AA to provide a reference for their management in different regions of China. To ensure the accuracy in collating and analyzing the studies, our inclusion criteria denoted that only studies should be included that provided

sufficient data to calculate the positive rate of patients who underwent SPTs. In addition, most articles published from most regions of China utilized 3 SPTs which are widely accepted (ALK-Abelló A/S, Denmark; Allergopharma, Germany; and Zhejiang Wolvo Bio-Pharmaceutical, China), which helped improve the precision in our pooled analysis.

While the prevalence of allergic airway diseases is rising in China, there were marked geographical differences

es in the rates of the increase, which was clustered in industrialized and urbanized regions. The determinants underlying these variations, however, are still largely unclear and may not follow the pattern of other regions. This is because China has a vast territory, with a large northern and southern latitude span that includes regions with varying topography and climate [15]. Evidence suggests that there are major differences in terms of allergen distribution across different regions, cultures, and climate conditions [16]. As the regional distribution of *Dermatophagoides* mites allergens in upper and lower airway diseases has not been reported previously, this poses a challenge to clinicians treating airway allergic diseases, particularly with regard to the accuracy and efficacy of AIT. Thus, a comprehensive geographical distribution study would help in the initial rectification of such issues.

Our analysis revealed a high *Dermatophagoides* sensitization rate for AR and AA, especially in the highly populated and coastal regions of eastern, southern, and central China. Previous literature reports have documented the marked heterogeneity of allergen sensitization patterns in different geographical regions, which rendered the implementation of allergen-specific AIT in the Chinese population challenging. Therefore, our comprehensive analysis of sensitization patterns of *Dermatophagoides* may indicate the geographical “hot spots” for implementing the appropriate AIT with greater success rates. Considering the major determinants of *Dermatophagoides* sensitization patterns may inform clinicians of the strategies for prevention and management of *Dermatophagoides* sensitization. Fluctuations in these factors due to climatic shifts can be further accounted for to redelineate the *Dermatophagoides* for real-time changes in AIT implementation. For instance, using the ROC curves and setting a practical cutoff of >70% sensitization rates, the temperature and humidity can be used to monitor for the conditions where sensitization rates will increase in densely populated cities, where AR and AA are highly prevalent.

The significant correlation between *D. pteronyssinus* and *D. farinae* sensitization reaffirmed that they share a certain homology [17], where the cross-reactivity may allow for a single-species-based formulation with a greater likelihood of success against the 2 major *Dermatophagoides* allergens in China. This nationwide study may be beneficial from the public health standpoint, where our findings will help develop strategies targeting at reducing indoor humidity for mitigating the risk of *Dermatophagoides* infestation (i.e., installa-

tion of dehumidifiers). Greater efforts are needed to mitigate *Dermatophagoides* sensitization in the “hot spots” within China. Our findings also call for clinicians’ vigilance to the identification of *D. pteronyssinus* or *D. farinae* sensitization or both based on regional climatic characteristics, which would help initiate AIT with the regionally prevalent *Dermatophagoides* species.

Several caveats should be taken into account when interpreting our findings. First, because we have undertaken a retrospective study, the standard of testing reagents and criteria for evaluating the testing results among different medical institutions might have led to detection bias. Second, *Dermatophagoides* sensitization patterns were likely to vary between pediatric and adult allergic patients [18–20]. However, in this study, we have not been able to distinguish between them. Further studies are required because of the lack of data in some geographical regions.

Notwithstanding the limitations highlighted, we have identified the geographical distribution patterns of *D. pteronyssinus* and *D. farinae* sensitization in China. Such data will equip clinicians with the knowledge to devise strategies for regional prevention, as well as for the administration of suitable treatments against *Dermatophagoides* sensitization and personalized treatments. In addition, the geographical determinants may also be applied in improving the public health management which can inform the sensitized population on the high-risk areas and conditions in China for better prevention of allergic diseases and exacerbation.

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Statement of Ethics

This study was performed after approval by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-Sen University.

Disclosure Statement

The authors report no conflicts of interest associated with this work.

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Author Contributions

Zhuang-Gui Chen, Ya-Ting Li, Wei-Hao Wang, and Kai-Sen Tan designed the study and participated in the drafting of the manuscript. Rui Zheng and Li-Fen Yang participated in the data collection and revisions of the draft. Qin-Tai Yang, Hai-Yu Hong, and Wei-Jie Guan designed the study, drafted the manuscript, and participated in the critical revisions of the draft. All authors contributed toward data analysis, drafting, and critically revising the paper and agree to be accountable for all aspects of the work.

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