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The association between daily outpatient visits for allergic rhinitis and pollen levels in Beijing

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ABSTRACT

To investigate the effects of aerosol pollen on human health, we carried out a time-series analysis of daily general practitioner consultations for allergic rhinitis (AR) in Beijing. The objective of this study was to assess the possible effects of pollen on clinic visits for allergic rhinitis in Beijing during the pollen season. We found a strong association between the concentration of pollen in ambient air and the number of consultations for allergic rhinitis. Females had significantly more outpatient visits than males when the levels of pollen increased. Young people (20–60 years old) had had significantly more outpatient visits than older people (over 60 years old) when the levels of pollen increased. After adjusting for air pollutants, the relative risks of pollen on daily number of outpatient for AR were increased.

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1. Introduction

Allergic rhinitis (AR) is increasing in both prevalence and severity in most countries (Breton et al., 2006; D'Amato, 2002; Schatz, 2007), affecting 25% of the population worldwide (Van Hoecke et al., 2006). AR has a significant impact on the quality of life, causing multiple comorbidities and considerable costs in terms of use of healthcare resources, school or work absenteeism and loss of productivity, affecting work, home and social life. Therefore, this disease represents a major global health concern (D'Amato, 2002; D'Amato et al., 2007; Gratziou et al., 2001; Guillemin and Segala, 2008; Muehlmeier et al., 2008; Van Hoecke et al., 2006).

Pollen is the most important reported cause of seasonal AR (Boutin-Forzano et al., 2005; Cakmak et al., 2002; Ciprandi et al., 2010). High levels of pollen can therefore be a risk factor in the development of AR symptoms (Erkara et al., 2009; Guillemin and Segala, 2008).

Pollen counts are often used in epidemiological surveys but are also used clinically for differential diagnosis and timing of immunotherapy (Erkara et al., 2009; Guillemin and Segala, 2008). However, little is known about the relationship between pollen concentration and AR. Studies conducted in France, Canada, and Britain have found strong associations between severity of AR and daily Poaceae pollen counts

(Cakmak et al., 2002; Fuhrman et al., 2007; Ross et al., 1996). A study conducted in Montreal showed that there was a significant association between the number of outpatients visits for AR and pollen levels, and significant associations were found for consultation on the day of exposure, and 1, 2, 3, and 5 days after exposure to high levels of pollen (Breton et al., 2006).

Data on the prevalence of AR in China mainland are sparse (Celedon et al., 2001; Kong et al., 2009). A study conducted in 2000 showed that the self-reported prevalence of AR was 30.0% in 2978 children in Beijing, and 31.1% in 2840 children (6 and 7 years old) in Urumqi (Zhao et al., 2000). After adjustment for age and sex, the self-reported prevalence of residents for AR was 8.7% in Beijing (Zhang et al., 2009).

Most of the studies conducted on AR are focused on children (Cakmak et al., 2002; Droma et al., 2007; Kong et al., 2009; Lee et al., 2003; Zhao et al., 2010), while a small number of daily consultations precluded an evaluation of the relationship in adults (Li et al., 2009; Villeneuve et al., 2006; Zhang et al., 2009).

Within the Fifth Ring (road) of Beijing, there are 99 kinds of pollen-allergic plants in the Beijing urban area (Ouyang et al., 2007). The blooming period of pollen-allergic arbors in the Beijing urban area is concentrated in March and April, while that of pollen-allergic herbs is from July to September (Ouyang et al., 2007). No studies have addressed the health effect of aero-pollen on the frequency of AR consultation for residents in Beijing. However, there are few epidemiological and ecological studies of the adult population in Beijing, the capital of China, a city with 18.18 million population in 2008 (Statistics et al., 2009).

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Air pollutants (SO_2 , PM_{10} , NO_2 , and O_3) enable easier penetration of pollen allergens into the airways. Air pollutants can increase the release of antigens in pollen grains that leads to allergic responses, and pollutants can also absorb pollen grains and thus prolong the retention of pollen grains in the body once inhaled (D'Amato et al., 2002, 2005).

Temperature, precipitation, relative humidity, day length and wind directions all are parameters that influence pollen production and its variability in ambient air. The occurrence of high relative humidity and precipitation corresponds to a low level of pollen concentration (Breton et al., 2006).

GAM takes a non-parameter approach to integrate independent variables that have complex non-linear relations with the response variable into the model, in the form of a sum of group smooth functions (Dominici et al., 2002; Jiang et al., 2007; Mentzakis and Delfino, 2010; Ramsay et al., 2003; Tsai et al., 2010; Wood and Augustin, 2002). GAM has been used for scientific research in various fields (Ballester et al., 2010; Bayentini et al., 2010; Damalas and Megalofonou, 2010; Dominici et al., 2002; Gutierrez and Bilton, 2010; Powell et al., 2010). In the field of public health, it was mainly used to study the distribution of infectious disease (Dominici et al., 2002; Jiang et al., 2007; Mentzakis and Delfino, 2010; Ramsay et al., 2003; Tsai et al., 2010; Wood and Augustin, 2002).

The main object of this study was to estimate the short-term association between the number of daily visits of adult patients for AR and daily concentrations of aerosol pollen. Our findings should provide decision-makers with important information on the health impact of air pollution/air allergens and provide evidence for the need to reduce environmental pollution and aerosol allergens. Our study provides evidence to health services policy makers for the need to be more proactive and to insure that sufficient resources are available to provide real-time public health alerts based on pollen counts and other allergy indices so that those affected can be advised.

2. Materials and methods

2.1. General practitioner consultation data

The number of patients consulting general practitioners for AR for the period between April 1, 2009 and September 30, 2009 (the study period) was obtained from the Department of Otolaryngology-Head and Neck Surgery, Beijing Hospital, Ministry of Public Health. Beijing Hospital is a leading Class-Three, Grade A level hospital, located in the Dong Cheng district and serving a large catchment within central Beijing. The hospital is open to the general public providing large-scale comprehensive integrated health services including medical treatment, teaching and education, scientific research and disease prevention.

2.2. Study populations and definitions

The study population comprises of all outpatients examined by general practitioners of Beijing hospital, during April 1st 2009 to September 30th 2009. For this prospective study, AR patients were defined as showing symptoms of sneezing, and/or a running, itchy or blocked nose when the patient did not have a cold or flu. The further diagnosis of rhinitis was based on the evaluation of a patient's medical history, a standardized questionnaire and the relevant test (skin prick test, trying to identify the possible allergen).

For further examination of any outpatient showing the symptoms of AR, a physician or a qualified research nurse at Beijing hospital used a standardized questionnaire. The questionnaire covered demographic characteristics, family history of allergic diseases, symptoms of rhinitis, wheezing or cough, eczema and burning or itching of the eyes, smoking habits, environmental exposure factors, pet ownership.

Only one visit per individual per day was included in the tabulation of the daily visit counts. Follow-up visits that occurred within

30 days subsequent to the initial consultation were excluded, in order to avoid double counting.

This study was approved by the Ethics Review Board of the hospital and all of the AR patients gave written consent to participate in the study.

2.3. Pollen, air pollution, and meteorological data

Daily average airborne pollen concentrations (grains/1000 mm^2) were provided by the Beijing Specialized Meteorological Observatory. Sampling was performed at four stationary monitoring stations distributed in four urban districts of Beijing: Haidian District (Northwest), Chaoyang District (East and Northeast), Shijingshan District (West), and Fengtai District (South). All of the four monitoring sites were close to the main residential areas of the city. The mean values of the above four monitoring sites were used for the pollen concentrations in our study.

Air quality data were provided by the Beijing Municipal Environmental Protection Monitoring Center for daily PM_{10} , SO_2 , and NO_2 concentrations.

Daily maximum, mean and minimum temperatures, wind speed and humidity for Beijing were obtained from the Beijing Meteorological Office.

2.4. Data analysis

All data were entered twice into the database by two independent investigators and then validated. Pearson correlation coefficients among the variables were analyzed using SPSS18.0 (IBM Company, New York, USA).

The objective of the data analysis was to quantify the association between daily levels of pollen and daily number of outpatient visits for AR, while adjusting for weather and temporal factors in the multi-variable modeling. Consistent with other time-series studies (Huang et al., 2009; Peng et al., 2006), we used the generalized additive model (GAM) with penalized splines to analyze the daily counts of outpatient visits for AR, levels of pollen, and covariates (meteorological factors, time trend, and day of the week). Because the daily number of consultations for AR was small and typically followed a Poisson distribution (Dominici et al., 2002; Hajat et al., 2001), the core analysis was a GAM with log link and Poisson error that accounted for fluctuations in daily numbers of deaths. A detailed introduction of the GAM has been previously described in Dominici et al. (2002) and Hajat et al. (2001).

All analyses were conducted using R2.9.2 using the MGCV package (R Development Core Team, 2010). The results are presented as the percentage change in daily counts of outpatient visits for AR per 10 grains per 1000 mm^2 increase of pollen, or a $10 \mu\text{g}/\text{m}^3$ increase in air pollutant concentrations.

2.5. Quality control

Daily counts of AR patients were sent every month to the Institute of Geographic Sciences and Natural Resources Research, CAS, where the data were entered and analyzed.

Our statistical models were constructed following an accepted methodology that has been proved by Dominici and Hajat (Dominici et al., 2002; Hajat et al., 2001) and were checked to ensure that the model fit was satisfactory.

3. Results

3.1. Descriptive characteristics

A total number of 24,679 outpatients attended the hospital during April 1st 2009 to September 30th 2009. Of these, 1448 were diagnosed with AR.

Table 1 summarizes the distribution of the annual mean air pollutant concentrations, temperature, relative humidity and other meteorological factors of Beijing during the study period. Table 1 also summarizes the main characteristics of AR patients. The gender distribution was about 1:1. A large number of patients belonged to age group between 20 and 60.

Fig. 1 shows daily concentrations of pollen and the daily number of outpatient visits for AR during April to September. Daily aerosol pollen concentrations varied from 11 grains per 1000 mm² to 456 grains per 1000 mm². The frequencies show two peaks during the study period, one was in April and early May, and the other one was in August and September.

3.2. Statistic analysis

Correlation statistics between air pollution parameters and meteorological factors are presented in Table 2.

The results showed that pollen levels were significantly positively correlated with SO₂ and NO₂ ($p < 0.05$), but not with PM₁₀. With regard to meteorological factors, pollen levels were significantly positively associated with daily average temperature, and significantly negatively associated with the daily dew point. No significant association was found between pollen and other meteorological factors (average humidity, average air pressure, and average wind speed). Air pollutants had a significant positive correlation with each other ($p < 0.01$). PM₁₀ levels were significantly positively correlated with humidity and negatively correlated with mean air pressure, but there was no significant correlation with mean temperature. SO₂ and NO₂ concentrations were significantly positively correlated with mean air pressure and mean humidity, and they were negatively correlated with mean temperature.

3.3. GAM analysis

By controlling the influence of temperature, relative humidity, dew point and other confounding factors, relative risks (RRs) for pollen without adjustment of air pollutants were calculated using lag days of 0–3 as the hazard time for outpatient visits for AR. These analyses were designed to investigate the possibility that different health endpoints are affected by pollen levels at different time frames, because a visit to an outpatient clinic following exposure to high pollen concentrations may have a time-delay. For considering the cumulative exposure effect, the 4 day cumulative exposure effects (lag03) of pollen levels were also considered in the model. The results are shown in Table 3.

We found that associations were generally weaker for lags 1 and 2; by lag 3, the observed associations had disappeared in all the study groups (Table 3).

Table 1

Characteristics of the daily number of patients, air pollutants and meteorological factors.

		Mean	SD	Percentage				
				Min	25%	Median	75%	Max
Air allergen	Pollen	94	86	11	26	65	140	456
	PM ₁₀	113	49	18	78	106	146	292
	SO ₂	16	13	7	9	12	19	138
	NO ₂	45	11	1	40	45	53	90
Daily number of outpatients	Total	8	5	2	5	6	10	34
	Male	4	3	1	2	4	4	20
	Female	4	3	1	2	3	6	17
	D60	2	1	1	1	1	2	8
	X60	6	5	2	2	5	8	27
	Dewp	11	10	–19	5	12	19	23
Meteorological measures 24 h mean	Avet (°C)	22	6	3	18	24	26	30
	Aveh (%)	56	20	12	40	55	73	92
	Avp (hPa)	1058	665	994	1004	1008	1014	10,006

Note. n = 183. Abbreviations: PM₁₀: fine particulate matter with an aerodynamic diameter of <10 µm; SO₂: sulfur dioxide; NO₂: nitrogen dioxide; D60: over 60 year age group; X60: 20–60 year age group; Avet: average temperature; Dewp: dew point; Aveh: average humidity; Avp: average air pressure.

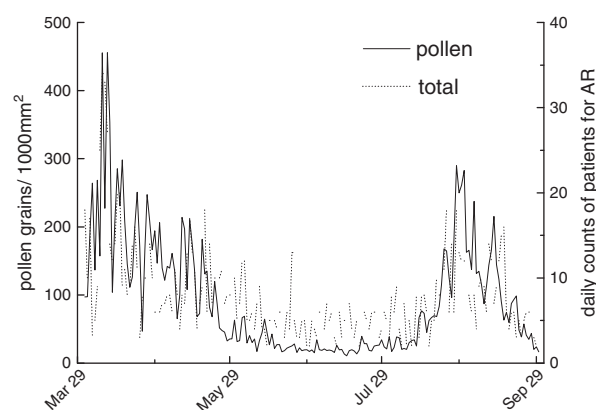


Fig. 1. Daily levels of pollen and daily numbers of outpatients for AR.

Table 3 shows the RRs of total AR patients, male patients, female patients, the 20–60 year age group, and the over 60 year age group for every 10 grains/1000 mm² increase in pollen level, without adjustments for air pollutants.

Since we found that pollutants at lag 0 day had the highest RR for outpatient visits for AR, we defined lag 0 day as the hazard time. We then used multiple-factor models to analyze the effect of multiple factors (air pollutants and pollen) on AR by controlling the influence of the weather conditions and the day of the week. The results of this analysis are shown in Table 4.

In multiple models, significant associations were found between pollen and the number of outpatient visits for AR.

4. Discussion

In this study, we have presented epidemiological evidence for an association between the number of AR outpatient visits and outdoor aerosol pollen in Beijing. When the concentration of pollen increased, the amount of outpatient visits increased. The gender and age group have the same increasing trends with the increasing of pollen concentration.

The results of this study are novel for the following reasons. 1) This was the first investigation of the short-term effects of pollen on outpatient clinic visits for AR conducted in Beijing, China. 2) All patients in our study were diagnosed by health professionals of the Department of Otolaryngology-Head and Neck Surgery of Beijing hospital, and all documentation was completed under the supervision of physicians, thereby avoiding over-estimation or under-estimation often related to self-reporting studies. 3) After controlling for long term trends, the 'day of the week' effect and other confounding factors (meteorological

Table 2

Pearson correlation coefficients for pollen, air pollutants and weather data during the study period.

	Pollen	PM ₁₀	SO ₂	NO ₂	Avet	Dew	Aveh	Avep	Wind
Pollen	1								
PM ₁₀	0.069	1							
SO ₂	0.300**	0.451**	1						
NO ₂	0.151*	0.451**	0.271**	1					
Avet	0.616**	−0.230**	−0.383**	−0.227**	1				
Dew	−0.443**	−0.170*	−0.398**	−0.209**	0.786**	1			
Aveh	−0.136	−0.075	−0.299**	−0.104	0.317**	0.817**	1		
Avep	0.087	0.031	0.087	−0.067	−0.151*	−0.083	−0.008	1	
Wind	0.117	0.023	0.213**	0.103	−0.310**	−0.598**	−0.614**	0.034	1

n = 183.

Abbreviations: PM₁₀ fine particulate matter with an aerodynamic diameter of <10 µm; SO₂ sulfur dioxide; NO₂ nitrogen dioxide; Avet: average temperature; Dewp: dew point; Aveh: average humidity; Avep: average air pressure; Wind: average wind speed.* Correlation is significant at the $p < 0.05$ level.** Correlation is significant at the $p < 0.01$ level.

factors), the non-parametric GAM was used to analyze the highly non-linear or non-monotonic exposure–response relationship between aerosol pollen and daily outpatient visits to the clinic for AR. 4). We investigated the possible interactions between levels of pollen and different types of patients with AR.

There is evidence to suggest that exposure to pollen in the outdoor environment may trigger the exacerbation of AR attacks (Frei and Gassner, 2008; Guillam and Segala, 2008; Kampe et al., 2010; Kessler et al., 2001; Mahillon et al., 2006). A study conducted in Montreal investigated the links between weather, *Ambrosia* (ragweed) pollen, and medical consultations for AR. Logistic regression showed strong correlations between pollen counts and higher medical consultations for AR on days 0, 1, 2, 3, and 5 days after elevated pollen exposure (Breton et al., 2006).

In our study in Beijing during a 6 month period, we found that the increase in pollen levels was significantly associated with hospital outpatient visits for AR. We also found that the daily amount of outpatient visits for AR had a similar time trend to that of pollen (Fig. 1). Higher levels of pollen were associated with an increased likelihood of hospital visits (with every 10 grains/1000 mm² increase in pollen level) (Table 2). The RRs for every 10 grains/1000 mm² increase in pollen level in the total number of people, males, females, 20–60 year age group and over 60 year age group were 2.619, 2.371, 2.955, 2.789, 2.078, respectively. Females had significantly more outpatient visits than males when the levels of pollen increased; Young people (20–60 years old) had had significantly more outpatient visits than older people (over 60 years old) when the levels of pollen increased; there were many causes of these, the time-activity, lifestyle, exposure time, individual difference, and so on. Further studies are needed to clarify these.

Using multiple models in our study, we found that after importing daily concentrations of PM₁₀ and NO₂ into the model, the RRs of pollen for AR were increased, but no changes were found after importing SO₂ into the model. With regard to air pollutants, no statistically significant

associations were found between air pollutants and outpatient visits for AR in multiple models (Table 3).

PM₁₀ can induce adverse effects by acting directly on the airways, by inducing inflammation of the mucous membranes, and it can also act as a carrier of other pollutants or allergens or potentiate their effects. The latter adverse effect could explain the increase in cases of sensitization to pollen allergens in urban areas (D'Amato, 2002). We found positive statistically significant associations between AR and traffic-related NO₂. Persistent exposure to NO_x may increase the prevalence of AR in children (Prieto et al., 2002) (Hwang et al., 2006). SO₂ can increase the permeability of the mucous membrane in airways, which may favor the penetration of allergens and the development of allergic reactions. SO₂ has been found to be an important predictor of consultations with general practitioners for AR (Hajat et al., 2000, 2001). The main source of air pollutant SO₂ is from coal burning for heating in the cold season. April to September is the warm season in Beijing; therefore, the levels of SO₂ in this period were low, and this may explain the marginal increase of RRs for pollen in the pollen-SO₂ double models.

This study has also a couple of limitations. We were only able to use data from one hospital in Beijing as this was an initial study looking into the methodology and the usefulness of the approach. As the catchment boundaries of hospitals in the central part of Beijing are not clearly defined it was not possible to establish population characteristics within the catchment area. Likewise, possible differences in treatment-seeking behavior including the use of Traditional Chinese Medicine (TCM) could not be included in our study. As PM_{2.5} pollution data were not available we had to limit our analysis to PM₁₀. Also, the identification and counting of different species of pollen grains are labor intensive, and therefore, only the total pollen concentration for 6 months was available for our study. Further investigations on the relationship between meteorological factors, aero-pollens, and AR are required for confirming and extending these findings.

Table 3Percentage increase (mean and 95% CI of daily outpatients for AR with 10 grains/1000 mm² increase of pollen in Beijing).

	Total			Male		Female		D60		X60	
	RR (%)	95% CI		RR (%)	95% CI	RR (%)	95% CI	RR (%)	95% CI	RR (%)	95% CI
lag0	2.619**	2.563–2.675		2.371**	2.301–2.441	2.955**	2.883–3.026	2.078**	2.021–2.135	2.789**	2.727–2.851
lag1	1.690**	1.629–1.751		0.914**	0.838–0.991	2.407**	2.333–2.481	1.225**	1.164–1.285	2.008**	1.942–2.073
lag2	0.406**	0.337–0.475		0.650**	0.564–0.736	0.244**	0.162–0.326	−0.482**	−0.549 to −0.415	0.237**	0.162–0.311
lag3	−0.204**	−0.277 to −0.132		−0.32**	−0.409 to −0.231	−0.150**	−0.237 to −0.062	−2.586**	−2.651 to −2.521	0.304**	0.224–0.384
Lag03	5.127**	5.022–5.232		4.691**	4.557–4.825	5.581**	5.452–5.710	3.205**	3.099–3.312	5.351**	5.236–5.467

**Correlation is significant at the $p < 0.01$ level.

Table 4

Association of the daily number of outpatient visits for AR and pollen/air pollutants in multiple models.

		+ PM ₁₀		+ SO ₂		+ NO ₂		+ PM ₁₀ + SO ₂ + NO ₂	
		RR (%)	95% CI	RR (%)	95% CI	RR (%)	95% CI	RR (%)	95% CI
Total	Pollen	2.649**	2.593–2.706	2.611**	2.555–2.668	2.734**	2.678–2.789	2.759**	2.702–2.815
	Sum	3.226	3.094–3.358	2.985	2.681–3.291	10.685	10.312–11.059	11.387	10.973–11.802
Male	Pollen	2.411**	2.341–2.48	2.263**	2.193–2.332	2.418**	2.349–2.487	2.314**	2.245–2.383
	Sum	3.341	3.178–3.504	7.701	7.326–8.075	10.388	9.917–10.86	13.674	14.519–9.858
Female	Pollen	2.967**	2.895–3.039	3.058**	2.987–3.13	3.171**	3.099–3.243	3.371**	3.298–3.443
	Sum	3.155	2.986–3.324	3.058	2.987–3.13	11.619	11.142–12.097	14.176	13.644–14.802
D60	Pollen	2.189**	2.133–2.245	2.104**	2.046–2.161	2.211**	2.156–2.267	2.379**	2.323–2.434
	Sum	3.787	3.661–3.914	2.104	2.046–2.161	10.996	10.627–11.366	11.63	11.151–12.108
X60	Pollen	2.806**	2.743–2.868	2.788**	2.725–2.851	3.057**	2.997–3.118	3.095**	3.033–3.157
	Sum	3.168	3.013–3.321	2.788	2.725–2.851	15.478	15.043–15.916	17.938	17.445–18.433

Sum is the RRs value of pollen plus RRs value of air pollutants.

** Correlation is significant at the $p < 0.01$ level.

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