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ORIGINAL RESEARCH

Short-term effects of airborne pollens on asthma attacks as seen by general practitioners in the Greater Paris area, 2003-2007

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Abstract

Aims: To investigate for the first time the short-term effects of airborne pollen counts on general practitioner (GP) consultations for asthma attacks in the Greater Paris area between 2003-2007.

Methods: Counts were available for common pollens (*Betula*, *Cupressa*, *Fraxinus* and *Poaceae*). Weekly data on GP visits for asthma attacks were obtained from the French GP Sentinel Network. A quasi-Poisson regression with generalised additive models was implemented. Short-term effects of pollen counts were assessed using single and multi-pollen models after adjustment for air pollution and influenza.

Results: A mean weekly incidence rate of 25.4 cases of asthma attacks per 100,000 inhabitants was estimated during the study period. The strongest significant association between asthma attacks and pollen counts was registered for grass (*Poaceae*) in the same week of asthma attacks, with a slight reduction of the effect observed in the multi-pollen model. Adjusted relative risk for *Poaceae* was 1.54 (95% CI: 1.33-1.79) with an inter-quartile range increase of 17.6 grains/m^3 during the pollen season.

Conclusions: For the first time, a significant short-term association was observed between *Poaceae* pollen counts and consultations for asthma attacks as seen by GPs. These findings need to be confirmed by more consistent time-series and investigations on a daily basis.

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Introduction

The prevalence of respiratory and allergic disorders has increased world-wide particularly in the case of asthma.[1] The aetiology of asthma is multifactorial and includes interactions between genetic predisposition and environmental factors. Changes in environmental factors, such as climate, air pollution and airborne pollen may partly explain this increase.[2] Pollen is a well known trigger of allergies and asthma aggravation, and actually has a changing profile.[3] New sources of pollen have emerged following the use of ornamental plants in public and private places. Moreover, global climate change has been linked to an earlier onset and an extended duration of the pollen season, to an increase in pollen production, and a stronger allergenicity for some pollen types.[4] Thunderstorm asthma epidemics may be triggered by grass pollen rupture in the atmosphere and the entrapment of respirable-sized particles in the outflows of air masses at ground level.[3,4] Increasing pollution is responsible for an increase in pollen-induced respiratory allergy, including asthma, because of airway inflammatory reaction and the

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passage of pollen grains into the lower respiratory tract.[3]

Several epidemiological studies have controlled for pollen counts when investigating air pollutant effects on allergic and respiratory disease morbidity, including asthma.[5-7] Most studies have focused on the short-term impact of airborne allergenic pollens on asthma by considering hospital daily admissions or emergency room (ER) visits for asthma.[8-12] However, most well-controlled asthmatic patients who develop an exacerbation do not attend the ER but consult their general practitioner (GP). To our knowledge, no study of the effects of pollens on asthma attacks has been undertaken at the primary care level.

The present study explored the short-term effects of airborne pollens on asthma attacks requiring a GP consultation – after adjustment for air pollution, meteorological conditions and influenza – in Paris and its surrounding area, using an appropriate model, over the period 2003-2007. If the link between airborne pollen counts and asthma attacks seen by a GP were to be confirmed, the public health impact would be considerable.

Methods

Study area

The study area was chosen in order to ensure a representative sample of asthmatic patients' exposure to pollens and other air pollutants, meteorological data, and asthma exacerbations. The Greater Paris area (the city of Paris and its surrounding areas) satisfied these requirements as it provided high-quality real-time temporal surveillance of asthma attacks during the study period as well as monitoring stations which monitor pollens, air pollutants and meteorological data.

GP consultations for asthma attacks

Data on weekly counts of asthma attacks requiring a GP consultation were obtained between January 2003 and December 2007 from the 257 GPs in the French Sentinel Network (FSN) working in the Greater Paris area; 1,270 GPs have been recruited to the FSN nationally (i.e. 2% of the total number of French GPs).[13] The FSN is the national system of clinical surveillance collecting real-time data on major diseases to be used in health analysis, forecasting and redistribution.[14,15] GPs participate on a volunteer basis in the weekly surveillance of 14 health indicators, including asthma attacks, by reporting the number of cases seen in their practice and their characteristics (age, gender, smoking status, asthma status, hospitalisation and treatment).

In this study, in agreement with previous literature used by physicians in France (http://www.caducee.net/DossierSpecialises/Pneumologie/asthme.asp), an asthma attack was defined for individuals more than 3 years old as an episode of acute respiratory dyspnoea with wheeze and/or coughing, excluding exacerbation of chronic obstructive pulmonary disease (COPD) or left cardiac failure, and for children under 3 years of age as a wheezing episode, including bronchiolitis (only after the third episode). 189 asthmatic patients were seen by the FSN GPs over the four-year study period, 177 of which were fully described in terms of socio-demographic and clinical variables. All studies using FSN data are approved by the French National Commission for Data protection and the Liberties (n: 471393).

Pollen, air pollution and meteorological data

Data on pollens were collected from February to September by the French National Network of Aerobiologic monitoring (RNSA)[17] through the unique HIRST monitoring station located 5km southwest of Paris (roof of Pasteur Institute) which covers a radius of 30km corresponding to the entire study area. The four pollens studied are those with the highest allergenicity and spread in Paris and its surrounding area: *Betula* (birch); *Cupressa* (cypress); *Fraxinus* (ash); and *Poaceae* (grass). Since the data on asthma attacks were measured on a weekly basis, the daily counts of pollens grains per m^3 were averaged over each week.

Air pollution data were provided by the French Environment and Energy Management Agency (ADEME) from monitoring stations located in the study area, reflecting background pollution.[18] Monitored air pollutants were: nitrogen dioxide (NO_2) – data obtained from 19 monitoring stations; particulate matter of less than 10 µm diameter (PM_{10}) and sulphur dioxide (SO_2) – data from seven stations; and ozone (O_3) – data from 13 stations. Daily concentrations of these pollutants were averaged on a weekly basis and expressed as µg per m^3.

Meteorological data were obtained from the French Meteorological Office (Météo-France);[19] data from one station out of four were used, located 5km south of Paris (Montsouris Park) and 3km away from the pollen trap. Mean temperature (in degrees Celsius) and mean relative humidity (in %) were registered by the Paris meteorological observatory. These daily meteorological data were averaged weekly.

Statistical analysis

The mean weekly incidence rate of asthma attacks per 100,000 inhabitants in the Greater Paris area was estimated using methodology previously validated by the FSN.[16] Successively, a generalised additive model (GAM) was fitted to assess possible non-linear short-term associations between asthma attacks and pollens on a weekly basis after controlling for potential confounders, using a Poisson distribution with a log-link function.[20,21] Over-dispersion was controlled using the quasi-likelihood method. Associations between pollen and asthma attacks counts were adjusted for asthma trend and seasonality, air pollution data and meteorological variables. The potential confounding effects of public holidays and influenza were also controlled for in the model as, respectively, a dummy variable and the weekly incidence rate (per 100,000 inhabitants) obtained from the FSN.[14] To eliminate autocorrelation resulting from temporal variations of asthma counts, pollen counts, meteorological data, air pollutants and influenza, we used a locally non-parametric regression (loess) as a temporal filter.[22,23] Seasonality of asthma counts was taken into account by applying this function with a smoothing window of six months.[20] The smoothing spans of loess function applied to other temporal variables were chosen on the basis of minimisation of (1) the Akaike information criterion, and (2) the sum of partial autocorrelation function (PACF) of the residuals, and (3) on the observation of PACF plots of the residuals.

Effects of pollen counts, pollutant concentrations and meteorological factors were investigated using the same lag. They were tested at lag 0 (lag 0) – i.e. during the week of the asthma attack – and three (lag 3) and six (lag 6) days earlier to evaluate the possible delayed effect of environmental data on asthma exacerbations. The best lag was chosen on the basis of the same criteria as the span for the loess functions. The short-term effects of pollen counts were firstly assessed using independent single pollen models, and secondly using a multi-pollen model. The effect of pollen counts on the weekly number of GP consultations for asthma attacks was expressed for linear relationships as the relative risk associated with an inter-quartile range (IQR) increase in pollen counts during the pollen season and its 95% confidence interval. Due to the large number of pollens and lags tested, tests were considered to be statistically significant at the threshold of 1% (two-sided). All statistical analyses were performed using R version 2.6.2.

Results

A mean weekly incidence rate of 25.4 (range 0-307) cases of asthma attacks requiring GP consultation per 100,000 inhabitants was estimated for the Greater Paris area between 2003 and 2007.[16] The average age (standard deviation) of patients with asthma attacks was 34.7 years (23.2); 6% were under 3 years old, 18% were between 3 and 15 years old, and 76% were aged over 15 years. Sixty-nine percent were women, 20% were smokers, and 73% were known to be asthmatic. Among the remainder, 42% were under 15 years old and 14% were over 60 years old. Six percent of the patients were hospitalised after their asthma attack.

Summary statistics of pollen counts, pollutant concentrations and meteorological variables are shown in Table 1. During the studied pollen seasons, the weekly means of *Cupressa*, *Fraxinus* and *Poaceae* counts varied from 13.2 to 16.9 grains/m^3 while *Betula* reached 35 grains/m^3 (Table 1). There was a coincidence in time between peaks in the *Betula* and *Fraxinus* pollen counts and asthma incidence in April 2004 and 2006 (data not shown). A light coincidence was seen also for *Poaceae* pollen peak in late June 2003.

All types of pollens were positively and significantly correlated with each other (Table 2), in particular *Cupressa*, *Fraxinus* and *Poaceae* ($r <= 0.8$). Pollen counts were positively correlated with ozone and negatively with humidity. *Cupressa* and *Poaceae* counts were significantly negatively correlated with NO_2 and SO_2 and positively with temperature.

The GAMs included a loess function with a smoothing window equal to 6 months for the time variable to control for trend and seasonality, dummy variable for public holidays and loess functions with a smoothing span of 0.2 for temperature, humidity, NO_2, O_3, PM_{10}, SO_2 and weekly incidence rate of influenza. The best adjustment in the single pollen models was made by loess functions with a smoothing span of 0.9 for *Betula*, 0.6 for *Cupressa*, 0.7 for *Fraxinus* and 0.7 for *Betula*. Non-parametric smoothing applied to *Betula*, *Fraxinus* and

Table 1. Descriptive analysis of pollens, air pollutants, meteorological variables, Paris and surrounding area, 2003-7.

				Percentiles					
	No of weeks	Mean (SD)	Min.	P25	P50	P75	P90	P95	Max.
Pollens									
Betula (grains/m^3)*	153	35.0 (83.6)	0.1	0.3	1.3	16.6	96.0	230.9	503.9
Cupressa (grains/m^3)*	89	16.9 (40.6)	0.1	1.0	2.9	9.6	44.1	96.0	302.1
Fraxinus (grains/m^3)*	93	13.2 (31.6)	0.1	0.3	1.0	7.4	39.4	77.8	206.6
Poaceae (grains/m^3)*	164	14.1 (23.3)	0.1	0.7	3.0	18.3	45.5	72.3	121.9
Pollutants									
NO_2 (µg/m^3)	261	39.6 (11.2)	15.4	31.1	39.5	47.3	52.2	55.3	86.9
O_3 (µg/m^3)	261	38.6 (20.9)	3.7	20.4	36.9	52.9	65.0	75.3	112.3
PM_{10} (µg/m^3)	261	21.5 (6.1)	10.4	17.3	20.3	24.3	28.3	33.0	52.6
SO_2 (µg/m^3)	261	6.5 (3.9)	0.8	3.7	5.6	8.8	11.5	13.7	25.7
Meteorological variables	261								
Mean temperature (° C)	261	12.7 (6.5)	-3.4	7.3	13.1	17.7	20.8	22.4	30.3
Relative humidity (%)	261	71.6 (9.5)	44.7	65.4	71.9	79.4	83.6	85.4	91.3

* During the pollen season: when pollen counts were above 0 grain/m^3.
SD: standard deviation, min.: minimum, max.: maximum

Table 2. Spearman's correlation matrix of pollen counts with air pollutants and meteorological variables, Paris and surrounding area, 2003-7.

	Betula	*Cupressa*	*Fraxinus*	*Poaceae*
Pollens				
Betula	1.00			
Cupressa	0.31*	1.00		
Fraxinus	0.18*	0.76*	1.00	
Poaceae	0.52*	0.75*	0.77*	1.00
Pollutants				
NO_2	-0.05	-0.21*	0.10	-0.64*
O_3	0.41*	0.57*	0.31*	0.85*
SO_2	0.01	-0.18*	0.12	-0.58*
PM_{10}	0.04	0.03	0.11	0.00
Meteorological variables				
Mean temperature (° C)	0.04	0.25*	-0.05	0.80*
Relative humidity (%)	-0.41*	-0.56*	-0.34*	-0.70*

*p<0.01

Poaceae were not statistically significant in single pollen GAMs, at the threshold of 1% (p=0.0394, p=0.4115, p=0.7745 respectively). From our models, relationships between the various pollens and the number of asthma attacks requiring GP consultation were found to be linear except in the case of *Cupressa* pollens for which the relationship was non-linear. According to single pollen models, a significant increase in asthma attack counts was significantly associated with an IQR rise in *Poaceae* (RR=1.70 (95% CI=1.47-1.97)) and *Betula* counts (RR=1.07 (1.04-1.11)) (see Table 3). The association between Fraxinus and asthma attack counts was of borderline statistical significance considering a threshold of 1%.

In the multi-pollen model, the magnitude of the associations was slightly reduced for all types of pollens and became non-significant for *Betula* and *Fraxinus* (Table 3). The highest magnitude was observed for *Poaceae* with an adjusted relative risk of 1.54 (95% CI=1.33-1.79) of an asthma attack requiring GP consultation for an increase of 17.6 grains/m^3 of *Poaceae* counts, the small corresponding p-value providing good evidence of a relationship even after a Bonferroni correction.

Discussion

This time-series study carried out in a primary health care setting in the Greater Paris area enabled us to quantify the form and magnitude of the relationship between different types of pollens and asthma attacks requiring a GP consultation, after controlling for potential confounders including meteorological variables, air pollutants and influenza. The model analysing a single pollen at once (single pollen model) suggests a significant and positive linear relationship between *Betula* and *Poaceae* pollen counts and the number of asthma attacks, and a non-linear relationship for *Cupressa* pollens. Using the model including all pollens at the same time (multi-pollen model), only *Poaceae* pollen counts were highly significantly associated with an increase in asthma attacks. High correlations between *Poaceae*, *Fraxinus* and *Betula*, ranging from 0.5 to 0.8, could explain changes in the magnitude and significance of associations observed in the multi-pollen model compared to the single pollen model.

Our results are consistent with previous investigations which have reported significant positive associations between asthma morbidity outcomes and different pollen types at the secondary care level.[11,12,24-26] Tobias *et al*. have reported a significant positive association between *Poaceae* and asthma-related ER admissions in Madrid.[12] However, such findings identified a non-linear relationship on a daily basis, in contrast with our findings. Stieb *et al*. have shown a positive linear association between grass pollen and ER attendances in Saint John (Canada).[11] This association was significant only in a single pollen model and measured the effect of the grass pollen family without analysing the individual pollen components such as *Poaceae*. Lewis *et al.* have also reported a significant association between grass pollen and emergency visits for asthma in Derby (England), using another statistical modelling approach.[24]

From the analytical point of view, an added value of our study compared to the previous ones is provided by the use of generalised additive models (GAM) taking into account potential confounders and modifiers. This flexible non-parametric statistical model is widely used in time-series analysis, in particular in the investigation of air pollutant effects, since it does not require knowledge of the nature of

Table 3. Adjusted relative risks (RR) and 95% confidence intervals (CI) for GP consultations for asthma attacks for an inter-quartile range (IQR) increase in pollen counts, Paris and surrounding area, 2003-7.

		Model with one pollen			Model adjusted for all types of pollens		
	IQR (grains/m^3)	RR	IC	p value	RR	IC	p value
Betula	16.3	1.073	1.038-1.109	<0.0001	1.037	1.002-1.073	0.0396
Fraxinus	7.1	1.054	1.008-1.102	0.0195	0.987	0.944-1.032	0.5738
Poaceae	17.6	1.700	1.469-1.968	<0.0001	1.540	1.331-1.790	<0.0001

the association contrary to generalised linear models.[27,28] In the GAMs, the mean of a response variable is related to a sum of unspecified non-parametric smoothing functions applied to independent variables such as weather or pollen counts. The estimated non-parametric functions can then reveal non-linearities in the effects of these variables. In our study, the relationship between *Poaceae* pollens and the number of asthma attack cases appeared to be linear. Moreover, asthma attacks as seen by GPs were investigated in our study, which has not been previously documented. This figure includes attacks of wheezing, asthma, and breathlessness requiring medical intervention, with the exclusion of ordinary asthma consultations for treatment, check-up, follow-up; but this is a tiny fraction of all asthma attacks seen in metropolitan France,[13] where most severe asthma attacks are seen in the ER Departments of hospitals.

Our findings must be interpreted with caution due to some data limitations. From the methodological point of view, the sample of GPs providing the data on numbers of asthma exacerbations could have been biased. However, the representative nature of the FNS has been discussed at length[15] and the GPs were not particularly notified about our survey on the links between pollens and asthma attacks, which could have influenced their responses. Asthma attacks were identified on the basis of a standardised definition already used in epidemiological studies for physician assessment during a medical visit, which diminishes the risk of mis-classification of the cases. From the statistical point of view, the low incidence of asthma attacks reported by GPs did not limit the statistical power of the relationships between pollens and asthma attacks even after allowing for confounders.

Another methodological limitation of our study comes from the fact that the investigation of short-term effects of pollen counts on asthma was not made on a daily basis, since GPs only reported on a weekly basis. This constitutes a constraint on our results since the exposure of airborne allergenic pollens may induce delayed adverse effects with a lag from 0 to 3 days.[12,24,26] Moreover, the effects of variables such as "Bank Holidays" or "Sundays" or "thunderstorms" could not be explored, although some studies have suggested that they were associated with asthma outbreaks.[29] However, various lags were used, and the lag 0, the one on the same week as the asthma attacks counts, provided the best fit of the models.

Mis-classification of exposure could also have occurred. Pollen counts obtained from a unique monitoring station were considered as a proxy of individual exposure of asthma cases. Patients were not necessarily exposed to airborne pollen within the GP's office area, in particular in the holiday period. However, the RNSA has settled a representative network of monitoring stations for pollens for the Paris area.

The low average weekly incidence rate of 25.4 cases per 100,000 inhabitants could have under-estimated the relationship. Indeed, it can be expected that with a better assessment of asthma exacerbations, including also asthma attacks seen at the hospital, the relationship would have been even more significant. On the other hand, the number of weeks during which no cases (null incidence) were reported may have been overestimated due to the FSN system, which puts by default equal to zero the number of cases when not explicitly mentioned otherwise (no possibility of missing data). However, the statistical relationships and the figures we observed were robust.

Conclusion

Our study investigated for the first time the short-term effects of airborne pollens on asthma attacks presenting in GPs' clinics. A significant and linear relationship has been identified between *Poaceae* airborne pollens and asthma attacks requiring a GP consultation, with a 54% increase in the risk of asthma attacks for an IQR increase of 17.6 grains/m^3 of *Poaceae*. This relationship needs to be confirmed on a daily basis and using a more consistent time-series. If the link between airborne pollen counts and GP visits for asthma attacks is confirmed, the public health impact would be considerable. Considering that fatal asthma events can also occur in well-controlled asthmatics, and given the large number of GP consultations for asthma attacks, the impact of appropriate preventive measures during the pollen season could considerably reduce the risk of asthma attacks.[30]

Conflict of interest declaration

No conflict of interest.

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