

Non-linear short-term effects of airborne pollen levels with allergenic capacity on asthma emergency room admissions in Madrid, Spain

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Summary

Background Several time-series studies have shown positive associations between pollen levels and asthma morbidity. However, few studies have included air pollution as a potential confounder when examining this relationship, and they have only done so on a linear basis.

Objective To investigate the potential non-linear short-term effects of the types of pollen with allergenic capacity across the whole range of exposure on the daily number of asthma-related hospital emergencies in Madrid for the period 1995–1998.

Methods Data were collected on the daily number of asthma emergency room admissions and daily average levels of major types of pollen with allergenic capacity: Olea, Plantago, Poaceae and Urticaceae. We used Poisson regression with generalized additive models, controlling for trend and seasonality, meteorological variables, acute respiratory infections and air pollutants. To study the non-linear effect of pollen levels on asthma emergency room admissions, pollens were categorized into five groups defined on the basis of their respective distributions.

Results The strongest associations were registered in respect of a lag of 1 day for Urticaceae, a lag of 2 days for Plantago, and a day lag of 3 days for Poaceae. Adjustment for the different types of pollen failed to result in major changes. Non-linearities were evident for pollen levels. The greatest increase in risk vs. the reference category (minimum value – 50th percentile) was observed for the categories between the 95th and 99th percentiles, with increases of 32.0% for Plantago, 32.2% for Poaceae and 24.6% for Urticaceae, and between the 99th percentile and the maximum value, with increases of 31.3%, 78.7% and 49.8%, respectively. Olea was not related with asthma emergency room admissions.

Conclusions Pollens with allergenic capacity in Madrid are positively associated with asthma-related hospital emergencies. These associations remain stable when simultaneous adjustment is made for the four types of pollen and for air pollutants and meteorological variables. In terms of non-linear effects, Poaceae register the strongest association with asthma emergency room admissions.

Keywords air pollution, asthma emergency room admissions, non-linear effects, pollen, time-series regression

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Introduction

The increase described in various countries in the frequency and severity of asthma and allergic diseases, together with their geographical variability suggest an important role for environmental factors in the epidemiological pattern of such diseases [1–8]. Asthma is frequently linked to other allergic diseases, and approximately 40% of asthma is attributable to atopy [9]. In addition to their role in the aetiology of the disease, the concentration of aeroallergens in the environment may act as a trigger for asthma attacks in susceptible

individuals. The seasonal variability in the incidence of asthma attacks has been widely described [10, 11] and the increase in asthma-related hospital admissions in spring has been principally attributed to pollen [11], and to grass-type pollen in particular [12].

Epidemiological studies based on time-series analysis have described statistically significant associations between pollutants and asthma morbidity [13–15]. Few studies, however, incorporate information on aeroallergens, ignoring their potential effect on asthma emergency room admissions. The few studies that have investigated the short-term effects of environmental aeroallergens, suitably taking air pollutants and meteorological variables into account, have reported rather inconsistent results insofar as the aeroallergens implicated are concerned [14, 16–23]. Furthermore, while the interaction between aeroallergens and air pollutants has

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been suggested in a number of studies [12, 16, 24–26], the importance of this biological interaction at the population-based level is still unknown.

The city of Madrid shows characteristic botanical and climatic conditions. There are winter days with very low temperatures that, in the space of less than 4 weeks (pollination season from mid-May to mid-June), subsequently become extremely hot with very dry ambient conditions in summer. This phenomenon leads to a simultaneous anthesis of most of the *Plantago* and *Poaceae* pollen species. These 2 months see the release of 80% of this type of pollen for the entire year [27]. Similarly, Madrid has high concentrations of *Olea* pollen, a tree that is very abundant throughout the Mediterranean basin [28]. The peak of the pollination season for these three types of pollen accounts for 20% of all asthma crises that take place during the course of the year in Madrid.

Since the increase of asthma morbidity became an important public health issue in Madrid, the Advisory Committee to the Madrid Regional Asthma Prevention & Control Program decided to carry out a wide project to assess the short-term effects of environmental factors on asthma emergency room admissions. In this context, we firstly reported that the usual air pollution levels in Madrid lead to an increase in asthma emergency room admissions [29]. This association remained after controlling for the presence of ambient pollen [29]. The city of Madrid has a large monitoring network that collects information on more than 20 different types of pollen from trees, plants and herbs, as well as others and unknown types of pollen. Thus, in the next step we reported the basic results for the eight major types of pollen- and asthma-related emergencies in Madrid [30]. However, the effects on asthma-related morbidity of the different types of pollen with allergenic capacity has not been comprehensively described and quantified. Most studies which have evaluated the short-term effects of pollen levels on asthma-related morbidity have done so on a linear basis [14, 16–19, 21, 22]. They did not take into account the fact that the asymmetric distribution, usually displayed by the distribution of any given type of pollen, may give rise to a non-linear effect.

Accordingly, our objective in this study is to assess the potential non-linear short-term effects of the major types of pollen with allergenic capacity across the entire range of exposure, with due adjustment for air pollutants and meteorological factors, on the daily number of asthma emergency room admissions in the city of Madrid.

Materials and methods

Asthma emergency room admissions

Asthma (ICD-493) daily emergency room admissions for all ages to the Emergency Ward of the Gregorio Marañón University Hospital, a facility covering an urban catchment area of 555 153 inhabitants, were studied for the period 1995–1998.

Data on pollen, air pollution and meteorological variables

Daily pollen-level data were drawn from the Madrid Regional Health Authority Palynology Network, comprising 10 monitoring stations. Information was collected on the daily average levels of pollens having major allergenic

capacity in Madrid: *Olea*, *Plantago*, *Poaceae* and *Urticaceae* (volumetric method with Burkard samplers; Burkard Manufacturing Co. Ltd, Rickmansworth, UK). The air pollutants collected were particulates measured as the daily averages of PM₁₀, SO₂ and NO₂, average of maximum 8-h O₃ values, obtained from the automated network of the Madrid Municipal Automatic Air-Pollution Monitoring, Forecasting and Information System. Mean temperature and mean relative humidity readings were taken at the Barajas meteorological observatory, situated 8 km north-east of the city. Information was also obtained on the daily number of cases of acute respiratory infections attended at the Gregorio Marañón Hospital Emergency Ward.

Statistical analysis

Data were analysed using Poisson regression with generalized additive models (GAMs). By means of non-parametric smoothing functions, GAMs allow for flexible control of the effect of seasonal components and also for the effect of confounding factors whose relationship with asthma emergency room admissions is not linear, such as temperature, which usually plots a U- or V-shaped relationship. A cubic smoothing spline with degrees of freedom (df) approximately equal to the number of months of the study period was fitted to control for temporal trend and seasonality [31]; dummy variables were included to control for the day of the week and public holidays; and cubic smoothing splines of up to four df to control for the effects of meteorological variables (temperature and relative humidity), acute respiratory infections and air pollutants (with assessment of up to fourth-order lags). Lastly, when a core model provided the best adjustment, the pollen levels (with assessment of up to 1 week order lags) were also fitted using cubic smoothing splines of up to four df. The choice of the number of df for each non-parametric smoothing function was made on the basis of minimization of the Akaike Information Criterion, and of observed residual autocorrelation using the simple and partial autocorrelation functions [31]. The lags selected for both air pollutants and pollen levels were those used with the largest independent effect on asthma admissions reported in the GAM. The short-term effects of pollen levels were assessed using independent single pollen models, and lastly in a multiple pollen model adjusting all types of pollens simultaneously.

Due to the large number of pollens and lags tested, this paper emphasizes the consistency of associations across lags and measures and discusses only the more highly significant findings ($P < 0.01$). Analyses were carried out using the S-Plus statistical package (Insightful Corporation, Seattle, WA, USA) with more restrictive convergence parameters than usual, as recently suggested by National Morbidity Mortality, and Air Pollution Study (NMMAPS) [32] and Air Pollution and Health: a European Approach, part II (APHEA-II) [33] researchers in order to avoid biased estimates.

Results

A daily mean of 3.3 (range: 0–26) asthma emergency room admissions were registered for the period 1995–1998. A total of 50% of all crises involved children of ages 0–14 years, 25%

of whom were under the age of 5 years, and 52.4% of all emergencies were women. The temporal distribution for daily asthma emergency room admissions showed a clear seasonal pattern, with two epidemic peaks occurring in the second fortnight of May 1996 and first fortnight of June 1998 (Fig. 1). Olea, Plantago and Poaceae levels also showed a clear seasonal distribution, with peaks of high concentration in May and June. Urticaceae registered lower levels than the other pollens, and their distribution was bimodal, with increases in April and June.

All types of pollens were positively correlated (Table 1), in particular Plantago and Poaceae ($r = 0.775$). Pollen levels were slightly positively correlated with O_3 and temperature, but negatively with the remaining air pollutants and relative humidity. The environmental conditions surrounding pollination days, from 15 May to 15 June – period when asthma epidemics occurred – compared with non-pollination days are shown in Table 2. The mean number of asthma emergency room admission is almost twice during the pollination days, and also the levels of the different types of pollens with allergenic capacity are, of course, much higher. According to the period of release of pollen in the environment, levels of winter-type air pollutants (PM_{10} and SO_2) were lower during the pollination days than non-pollination days, but higher for ozone and temperature, and did not differ substantially for NO_2 and relative humidity.

The core GAM selected included a cubic smoothing spline with 72 df to control for trend and seasonality, dummy variables for days of the week and public holidays, and cubic smoothing splines with four df for temperature and two df for relative humidity and acute respiratory infections. Adjustment was made for the effect of air pollutants by using cubic smoothing splines with two df for PM_{10} (lag of 3 days) and SO_2 (lag of 3 days), three df for NO_2 (lag of 3 days), and one df for O_3 (lag of 1 day). Core model showed neither residual autocorrelation nor overdispersion.

Examination of non-linear effects is shown in Fig. 2, through the graphical representation of the non-parametric adjustment of the relationship between types of pollen with allergenic capacity and asthma-related emergencies. The best adjustment, in a GAM including all types of pollen simultaneously, was made by using cubic smoothing splines with two df for Plantago (lag of 2 days) and with three df for Poaceae (lag of 3 days), Urticaceae (lag of 1 day) and Olea (lag of 1 day). Hence, non-linearities were evident for all pollen levels risk of asthma emergency room admissions. The effect of Plantago was rather linear up to a saturation point where the risk of asthma emergency room admissions remained stable. A similar effect was described for Urticaceae, although low levels showed a lower increase in the risk of asthma than Plantago. On the contrary, upper levels of Poaceae showed the increase of highest magnitude in the

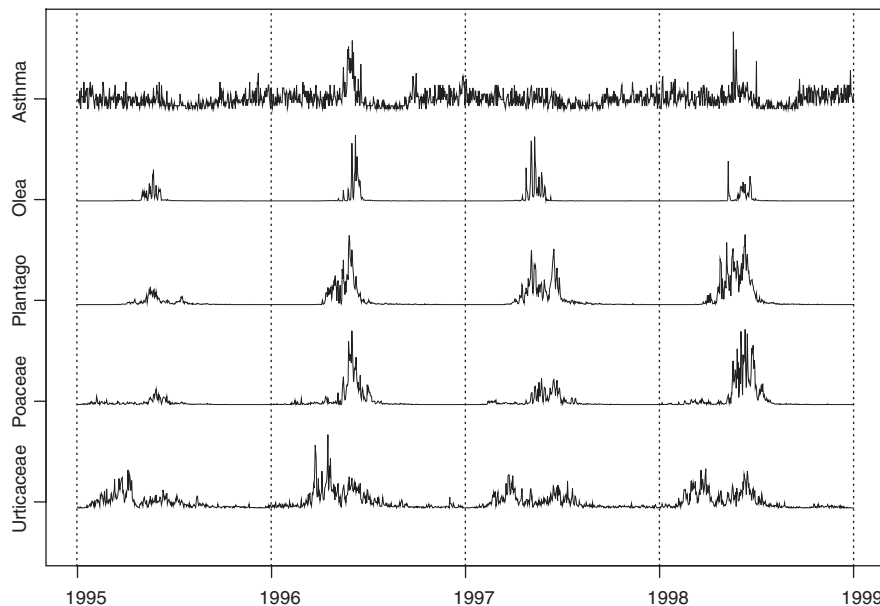


Fig. 1. Distribution of asthma emergency room admissions – all ages – and pollen levels in Madrid for the period 1995–1998.

Table 1. Percentile distribution and matrix correlation of pollen levels with allergenic capacity, in Madrid for the period 1995–1998

(n = 1461) Variables (units)	No. of days*	Percentile distribution											Matrix correlation			
		Min.	P1	P5	P10	P25	P50	P75	P90	P95	P99	Max.	Olea	Plantago	Poaceae	Urticaceae
Olea (grains/m ³)	664	0	0	0	0	0	0	0.6	6.3	37.4	148.7	321.2	1			
Plantago (grains/m ³)	873	0	0	0	0	0	0.2	2.3	15.5	27.1	50.8	72.8	0.472	1		
Poaceae (grains/m ³)	1306	0	0	0	0	0.5	2.0	6.7	28.5	59.4	158.3	237.5	0.465	0.775	1	
Urticaceae (grains/m ³)	1324	0	0	0	0.2	0.3	1.5	2.8	6.0	7.7	11.8	25.8	0.224	0.444	0.447	1

Min., minimum; Max., maximum.

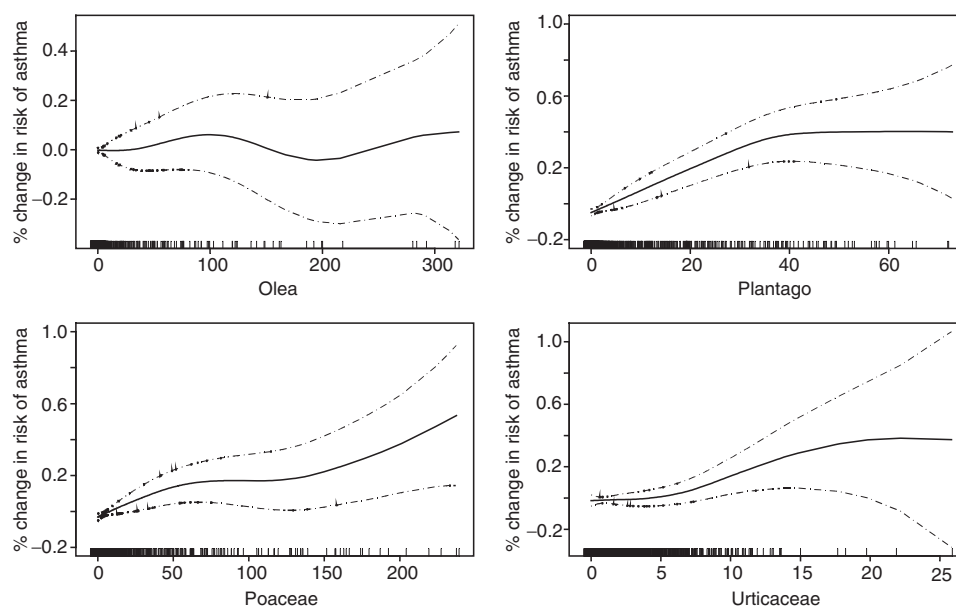
*Number of days with pollen levels > 0 grains/m³.

Table 2. Descriptive analysis of asthma emergency room admissions, pollen levels, air pollutants and meteorological variables, in Madrid for the period 1995–1998, by pollination and non-pollination period

Variables (units)	Pollination period (15 May to 15 June)						Non-pollination period (otherwise)					
	Percentiles						Percentiles					
	Mean (SD*)	Min.	P25	P50	P75	Max.	Mean (SD)	Min.	P25	P50	P75	Max.
No. of emergencies	6.0 (5.1)	0	2	4.0	8.0	26.0	3.0 (2.3)	0	1	3	4.0	16
Olea (grains/m ³)	43.2 (56.1)	0.2	4.3	22.9	57.3	321.2	2.9 (19.5)	0	0	0	0.3	313.5
Plantago (grains/m ³)	24.1 (17.3)	1.7	10.3	20.4	37.0	72.8	2.5 (7.0)	0	0	0.2	1.2	64.5
Poaceae (grains/m ³)	66.1 (56.0)	2.0	22.6	48.9	93.6	237.5	5.9 (15.7)	0	0.3	1.7	4.8	187.8
Urticaceae (grains/m ³)	4.4 (2.7)	0.5	2.3	3.8	6.3	13.0	1.9 (2.7)	0	0.3	0.8	2.5	25.8
24-h PM ₁₀ (µg/m ³)	26.2 (6.8)	11.2	21.2	24.7	30.1	45.4	32.7 (12.4)	12.7	24.2	29.5	37.6	108.6
24-h SO ₂ (µg/m ³)	13.8 (3.6)	7.3	11.1	13.4	16.8	22.7	24.5 (15.7)	5.0	12.7	19.9	32.5	121.2
24-h NO ₂ (µg/m ³)	62.1 (13.3)	36.8	51.2	61.1	69.5	98.2	67.5 (18.3)	25.8	55.4	64.9	76.5	147.5
8-h O ₃ (µg/m ³)	59.5 (16.3)	25.5	47.0	58.8	71.5	103.9	44.5 (28.8)	1.9	21.9	40.0	62.3	152.7
Mean temperature (°C)	18.9 (3.1)	11.0	16.7	18.9	21.1	26.3	14.6 (7.2)	−0.6	8.7	13.6	20.6	31.8
Relative humidity (%)	57.2 (12.7)	33.3	47.1	57.4	66.6	84.5	62.0 (16.7)	22.3	48.8	61.2	75.5	100.0

Min., minimum; Max., maximum.

*SD, standard deviation.

**Fig. 2.** Graphical representation of the non-parametric adjustment of the relationship between types of pollen with allergenic capacity and asthma emergency room admissions in Madrid for the period 1995–1998.

percentage of change in risk of asthma. Olea did not show any pattern in the increase of risk.

To quantify non-linear effects we categorized the four types of pollen into five groups, defined on the basis of their distribution shown in Table 1. The relative effect, or percentage increase in risk ($(\text{relative risk} - 1) \times 100$), was then estimated by comparing the reference category, defined as that between the minimum value and the 50th percentile, against the categories lying between the 50th and 75th percentiles, 75th and 90th percentiles, 90th and 95th percentiles, 95th and 99th percentiles, and 99th percentile and the maximum value. Results are shown in Table 3, using GAMs adjusting by a single type of pollen, also adjusting by all types of pollen jointly. Adjustment for the different types of pollen failed to result in major changes, with a slight reduction in the effect of pollen types. The highest magnitudes of risk were

registered for Poaceae in any given comparison against the reference category, with all such magnitudes proving highly significant. For Plantago and Urticaceae, the highest magnitudes of risk were solely obtained in comparisons against categories lying within the maximum levels, from the 95th percentile upwards. The increase in risk in the comparison with the category lying between the 95th and 99th percentiles was similar for Plantago, Poaceae and Urticaceae (32.0%, 32.2% and 24.6%, respectively). However, in the comparison with the category spanning the extreme levels, i.e. 99th percentile to the maximum value, the Poaceae effect (78.9%) was more than double that of Plantago (31.3%), and approximately 1.5-fold that of the Urticaceae (49.8%). These associations had small *P*-values providing a good evidence for a relationship even after a conservative Bonferroni correction.

Table 3. Percentage (%) change in risk of asthma emergency room admissions, and 95% confidence interval (95% CI)

Range of categories*	Adjusting by a single type of pollen					Adjusting by all types of pollen jointly				
	Olea % (95% CI)	Plantago % (95% CI)	Poaceae % (95% CI)	Urticaceae % (95% CI)	Olea % (95% CI)	Plantago % (95% CI)	Poaceae % (95% CI)	Urticaceae % (95% CI)		
P50-P75	-6.0 (-14.8, 3.7)	-2.7 (-12.4, 8.0)	13.6 (3.6, 23.2)	15.7 (6.3, 26.0)	-7.2 (-16.3, -2.8)	-4.8 (-14.6, 6.1)	10.6 (0.0, 22.4)	15.0 (4.1, 27.0)		
P75-P90	9.9 (-1.3, 22.4)	-2.5 (-13.4, 9.9)	22.1 (10.9, 34.5)	11.4 (1.5, 22.2)	0.5 (-12.4, 15.2)	-8.2 (-20.9, 6.7)	19.4 (5.6, 35.1)	7.9 (-4.0, 21.3)		
P90-P95	1.1 (-11.9, 16.0)	15.5 (0.4, 32.9)	52.2 (32.0, 75.4)	15.4 (0.4, 32.7)	-12.6 (-27.2, 4.9)	7.3 (-10.6, 28.7)	38.1 (14.3, 66.9)	4.4 (-11.4, 23.1)		
P95-P99	8.7 (-5.6, 25.1)	46.5 (28.0, 67.6)	50.0 (30.6, 72.1)	31.6 (14.6, 51.0)	-2.3 (-19.2, 18.2)	32.0 (7.9, 61.4)	32.2 (6.9, 63.6)	24.6 (5.8, 46.8)		
P99-Max.	-3.1 (-24.4, 24.4)	50.8 (21.6, 86.9)	96.6 (58.9, 143.2)	61.3 (24.3, 109.4)	-19.8 (-39.7, 6.6)	31.3 (-0.8, 73.8)	78.7 (34.6, 137.2)	49.8 (14.2, 96.4)		

Min., minimum; Max., maximum.

*Reference category (Min. - P50)

Discussion

The principal results yielded by this study suggest that pollens with allergenic capacity – Poaceae, Plantago and Urticaceae – are positively and statistically significantly associated with asthma-related hospital emergency room admissions in Madrid. Half of all these asthma-related emergencies correspond to children aged 0–14 years. This figure is still slightly higher in those reported by the General Practitioners to the primary-care register of asthma in our region. Although the development of allergy to pollen in Madrid could start to be important at the age of 4 years, being related to the maturation of the immune system, the crises of asthma below this age are mainly precipitated by respiratory acute infections [34].

The coincidence between the two epidemic peaks in the temporal distribution of asthma emergency room admissions (second fortnight of May 1996 and first fortnight of May 1998) and the abrupt release of Plantago and Poaceae is clearly shown in Fig. 1. However, both epidemics are different in nature. The epidemic peak of 1996 is more clearly related with pollen levels than the peak of 1998 due to the greater density of high concentrations. This would be probably related to a priming effect [35]. In 1998, although high peaks of pollen levels were reached, their distribution was continuously interrupted due to periods of rain that drag pollen mechanically to the ground. For this reason, its consequences on asthma epidemics seems to be reasonably smaller. On the contrary, in 1995, the concentrations of both types of pollen failed to reach the values of the 95th percentile, with levels lower than 50 grains/m³, below a possible threshold capable of triggering increases in the form of epidemic peaks in asthma emergency room admissions. In 1997, a peculiar situation arose, in which it rained abundantly during the period of pollenization. This could split up the distribution of Poaceae and Plantago in two shapes, and could reduce the levels of Poaceae. In the Plantago curve, maximum concentration exceeded 27 grains/m³ (95th percentile) for only 8 days of the pollenization period, separated by 30 days with concentrations below these levels. If a priming effect were essential in the mechanism of action [35], then longer uninterrupted concentrations would be needed to provoke an increase in allergic symptomatology. This would account for the absence of epidemic increases in asthma.

A number of studies based on time-series analysis have reported positive associations between grass pollen and asthma morbidity indicators, both in cases where air pollution was adjusted for [19, 20] and in those where no such adjustment was made [36]. Furthermore, other environmental aeroallergens have been linked to asthma emergency room admissions, even though with rather inconsistent results insofar as the types of pollen implicated, such as Ambrosia [16], Birch [14] or Tree [22]. This lack of consistency may be due to various causes: geographical differences in the types and levels of allergens studied [14], prevalence of atopy and bronchial hyper-reactivity [37], and clinical and pathological nature of asthma, etc. Moreover, the major types of pollen with high allergenic capacity positively associated with asthma emergency room admissions in Madrid are different from the pollens covered by others.

The lags observed in this study are in line with those described in previous studies [19, 36], suggesting that the

response to the effect of pollen may have a lag or be accumulated from 1 to 3 days. This lag is coherent with aeroallergen action mechanisms, in that the clinical consequences of pollen load tend to increase as the pollen period progresses. Moreover, asthma emergency room admissions are preceded by a period of onset of milder symptoms, probably controllable from primary care or with self-medication, and once these intensify they lead to asthma-related demand for emergency attention.

In terms of non-linear effects, Poaceae register the strongest association with asthma emergency room admissions. This non-linear association is consistent with the evidence of Poaceae being the most important cause of pollinosis in our geographical setting [27] and, in turn, being the aeroallergen to which the greatest number of asthmatics react, inasmuch as 57% of asthmatics aged 2–44 years are prick test positive [38]. Although Olea also attains substantially high ambient concentrations and the prevalence of Olea-sensitive persons is high, its release into the environment takes place at a later date than that of Plantago and Poaceae. Bearing in mind the fact that most subjects allergic to Olea pollen are also allergic to Plantago and Poaceae, by the time the former is subsequently released, most susceptible individuals have already presented with asthma and are on medication. In addition, the coincidence in time between Plantago and Poaceae gives rise to a collinearity effect, thus possibly diluting the potential effect of the abrupt release of Poaceae. The non-linear effects of Poaceae, Plantago and Urticaceae described in this study are similar to those described for grass pollen in England [20, 36], with the highest magnitudes of risk being observed for comparisons against categories lying within the maximum levels. Since the relationship between pollen levels and asthma is non-linear, there is also a low increase of risk for low levels of pollen, specially for Poaceae and Urticaceae. Low levels of pollen are present outside the pollination period, during the first and last months of every year. In this case, we could consider a more subtle relationship. Nevertheless, during the pollination period, the concentrations of pollen show a sudden increase up to extreme values, agreeing with the abrupt appearance in the atmosphere. Thus, although the relationship between concentrations of pollen and asthma admission rates is mainly driven by the pollination period, there could also be a slightly subtle relationship for susceptible asthmatics that should be deeply examined using the data at individual level in a further research.

A further aspect of special interest is the possibility that air pollution may modify the relationship between pollen and asthma [12, 16, 24–26]. While experimental evidence suggests that the effects of aeroallergens may be increased by exposure to air pollution [39–41], in this study we observed effects on asthma emergency room admissions that were independent of pollen levels and air pollutants [29, 30]. Moreover, inclusion of air pollutants as a confounding variable failed to result in any variation. These results are in line with those reported by a number of studies that have used time-series methodology [14, 17, 19–21]. Similarly, exposure to aeroallergens has also been linked to meteorological conditions. Storms [20, 36] and wet-season days [20] have been described as effect modifiers, boosting the aeroallergen–asthma relationship as a result of pollen grains rupturing. In this study, however, we observed

no such modification of effect attributable to any of the meteorological variables evaluated.

The effect of these factors can be evaluated by using analytical time-series regression models [42], controlling for trend and seasonality, daily cycles, changes in meteorological conditions, as well as the effects of air pollutants, and other related factors, such as viral epidemics. Time-series regression analyses of asthma hospital emergency room admissions offer a convenient methodology to test the hypothesis that environmental factors can provoke asthma. Yet, though the statistical method employed has been widely validated and used in this country, its suitability and the way in which potential confounding factors are controlled for have nevertheless been criticized [43]. In our particular case, asthma hospital emergency room admissions data in Madrid showed a irregular pattern. Then, seasonal control in the time-series regression model with GAM could be very sensitive picking up some of the rise in asthma admissions, certainly possible in 1998 less so in 1996.

Otherwise, we must note that GAM are very conservative at the extremes of the curve, having wide confidence intervals, as Fig. 2 shows. This is because usually there are few observations at the extremes of exposure factor, and due to a slight boundary effect inherent in all flexible methods [44]. Categorical analyses have also limitations; they generally have low statistical efficiency due to results that can only be presented in relation to a reference category and cut-off points for the categories are in most cases arbitrary and/or opportunistic [45]. However, the percentage change in risk of asthma emergency room admissions from the categorical analysis reported in Table 3 showed non-linear increases of the risks for all types of pollen, which agreed with the non-linear relationships show in Fig. 2 using GAM. This fact led us to confirm the true non-linear relationship between pollen levels and asthma emergency room admissions. However, care is needed in their interpretation and careful reporting, making it clear how variables have been modelled using GAM, because any graphical distortion can lead to misinterpretations as well as the arbitrary selection of the reference points for categories. Finally, the small magnitude of the associations means that interpretation of results must be approached with caution, given that uncontrolled variables in the regression models or the complex relationships between pollutants and/or types of pollen may confound their results.

Furthermore, the accuracy of sensor-mediated measurement of pollen exposure has been questioned. These sensors are normally positioned on the roofs of buildings, where fewer structural barriers make for enhanced pollen concentration estimates vs. readings taken at ground level [35]. Finally, in this study no information was collected on fungal and other spores, although they have also been associated with the triggering of asthma attacks [20, 21, 46]. Nevertheless, the characteristics of the Madrid climate tend to limit ambient concentration of such spores – and of *Cladosporium* in particular – to low levels compared with other geographic areas of Spain, something that is in line with the low prevalences observed among asthma sufferers of positive prick tests to *Alternaria* and *Cladosporium* [36, 47].

In conclusion, and taking into account the limitations of epidemiological time-series designs, the evidence provided by this study suggests that the major types of pollen with

allergenic capacity in Madrid are positively associated with asthma emergency room admissions. Associations remained stable when simultaneous adjustment is made for the four types of pollen with allergenic capacity and for air pollutants and meteorological variables. This relationship in the case of *Plantago* and mainly of *Poaceae* may explain the epidemic increase in this disease during the seasonal period in which these two types of pollen are abruptly released into the environment.

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