

Original article

Effect of short-term exposure to air pollution and pollen on medical emergency calls: a case-crossover study in Spain

Background: A symmetric case-crossover design was used to analyse the short-term relationship between air pollution, pollen and emergency calls to medical services.

Methods: This study covered patients who made medical emergency calls in the City of Vigo (Spain) during the period 1996–1999. Morbidity data were obtained from the records of the 061 Medical Emergency Control Center, in its capacity as the body officially coordinating all medical emergencies by telephone. Air pollution data were furnished by the Vigo Municipal Air Pollution Surveillance Grid. Pollen levels were provided by the staff of the Spanish Aerobiology Network in Vigo.

Results: A rise of $10\mu\text{g}/\text{m}^3$ in ambient particulate levels led to the risk of medical emergency calls requesting attention increasing by: (i) 1.97% [95% confidence interval (95% CI): 1.83–2.11%] for circulatory causes on the same day; (ii) 1.95% (95% CI: 1.76–2.14%) for respiratory causes at 2 days and (iii) 1.34% (95% CI: 1.23–1.45%) for combined circulatory and respiratory causes on the same day. A number of pollens displayed a statistically significant relationship with emergency calls. No interaction was in evidence between pollens and air pollutants.

Conclusions: While elevations in particulate air pollution increase medical emergency calls because of cardiac or respiratory causes or both combined, elevations in pollen levels increase medical emergency calls because of respiratory causes.

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Exposure to air pollution is a potential risk factor for the development of respiratory and cardiovascular disorders (1, 2). Despite efforts to improve the quality of the air, the persistent increase in the fleet of motor vehicles poses a threat to air quality in industrialized countries (3). In urban surroundings, traffic is the main source of emission of fine particulate matter (4), with diesel exhaust emissions in particular accounting for a high percentage of total particles released into the atmosphere. Indeed, it is estimated that diesel produces 10 times more particles than unleaded gasoline (5).

Most studies addressing the relationship between short-term exposure to air pollution and respiratory or circulatory morbidity have relied on Poisson time-series regression to measure hospital admissions or emergency room visits (6, 7). Some researchers have argued that the results of time-series analyses depend, in great measure, on the model employed, something that hinders inter-study comparison (8, 9). An alternative to time-series analysis is case-crossover (CCO) methodology, which has

the advantage of controlling for intrasubject confounding variables and time trends by design rather than by modeling (10).

Although studies have used CCO methodology to study the relationship between air pollutant levels and hospital admissions or emergency room visits (11, 12), this approach has never been used before to measure a relationship of this type with telephone calls requesting emergency medical attention. Furthermore, recent studies indicate that pollen may be associated with an increase in respiratory morbidity (13), but its relationship with medical emergency calls has never been analysed, whether using Poisson time-series or CCO methodology.

Accordingly, this study sought to analyse the relationship between air pollution and pollen levels and medical emergency calls requesting attention for cardiovascular and respiratory causes, among the population of the City of Vigo (Spain) 1996–1999, using a symmetric bidirectional CCO design.

Methods

Design and settings

A symmetric bidirectional CCO design was used for the purpose of this study (9). In this type of design, only cases are sampled, and estimation of risk is based on comparing intrasubject exposures at the time of the effect ('case' period) with exposures at various points in time when the effect does not occur ('control' period).

This design has a number of advantages over the alternative methods: first, control subjects do not have to be sampled; and secondly, when making intrasubject comparisons, all possible confounders (measured and unmeasured) that remain unchanged between the control and case periods are automatically controlled for by design, as they remain constant for each subject (14). Nevertheless, to prevent estimates being biased by trend and seasonality, control periods must be sampled before and after the effect (14). In our study, we used a symmetric bidirectional CCO design with two control day, one 7 day before and the other 7 day after the event (14). This period was chosen because: (i) it was short enough to minimize selection bias; (ii) it coincided with the weekly pattern of the effect, thereby minimizing any confounding bias and (iii) it was long enough to ensure the absence of autocorrelation (14).

The designated geographic setting was the municipality of Vigo (Spain), a port city situated on the Atlantic Ocean, which has a mild climate with little year-round variation and an important industrial sector. Vigo has a population of approximately 300 000 and an automobile fleet of around 130 000 vehicles.

Vigo's population pyramid is pagoda-shaped, with its mode belonging to the age range from 25 to 30 years. Of the city's total population: 13.16% are aged > 65 years and 52.46% are female. In descending order of importance, the main reasons for hospital admission in the city area – as in most of North-west Spain – are traumas and gastrointestinal, circulatory and respiratory diseases. Data for the period 1996–1999 were analysed (this being the period for which air-pollution data were available).

Data sources

Air pollution data were furnished by the Vigo Municipal Air Pollution Surveillance Grid (*Red Municipal de Vigilancia de Contaminación Atmosférica*), which has seven semiautomatic monitoring devices deployed throughout the city. Mean 24-h (black smoke) particulate and sulphur dioxide (SO₂) values were studied. Black smoke was measured by means of the normalized smoke method, using Whatman filtrate paper no. 1, which mainly captures particulates having an aerodynamic diameter of around 4–5 µm. Sulphur dioxide was measured using the Thorina method. The population's daily exposure was estimated using the average of the readings made at the eight manual monitoring stations, in accordance with the methodology employed in the EMECAM project (15). We included the values of stations that registered a percentage of valid data for more than 75% of day across the study period. The missing values of the stations included were calculated with the aid of regression models, using the remaining monitoring stations as explanatory variables, provided, in all cases, that there was a minimum of three valid stations per pollutant.

Meteorological data were obtained from the National Meteorology Institute and the following variables were studied: temperature; atmospheric pressure and relative humidity. The number of weekly cases of influenza, based on reports submitted to the Notifiable Disease Reporting Registry (*Registro de Enfermedades de Declaración Obligatoria*), was supplied by the Epidemiology Department of the Galician Regional Health Authority (*Consellería de Sanidade de la Xunta de Galicia*). The weekly number of cases was

divided by seven to obtain an approximation of daily cases. Pollen levels were provided by the staff of the Spanish Aerobiology Network in Vigo. Using the volumetric method, data were measured at one station located in the city hall. Daily counts of allergenic pollens belonging to the families *Asteraceae*, *Betulaceae* (*alnus*, *betula*, *corylus*), *Cupresaceae*, *Chenopodiaceae*, *Ericaceae*, *Fagaceae* (*castanea*, *quercus*), *Myrtaceae*, *Oleaceae* (*fraxinus*, *olea*), *Pinaceae*, *Plantaginaceae*, *Platanaceae*, *Poaceae*, *Polygonaceae*, *Salicaceae* and *Urticaceae* were considered, as were total grass (*gramineae*) and pollen counts.

Morbidity data were obtained from the records of the 061 Medical Emergency Control Center (*Central de Emergencias Médicas 061*), in its capacity as the body officially coordinating all medical emergencies by telephone. At this control centre, the medical staff tasked with managing emergency telephone traffic, codes all incoming calls as per the International Classification of Diseases, 9th Revision (ICD-9). Medical staff members are required to undergo previous training and pass regular quality controls to ensure the reliability of the database.

Data analysis

Statistical analysis was performed using conditional logistic regression models. The baseline model was constructed, with these variables introduced in the following order, namely, temperature, humidity and atmospheric pressure – all in terms of averages for the same and preceding day (lag 01) and for 2 and 3 days previously (lag 23) – plus influenza and a binary variable that indicated whether the day was a Sunday or Public Holiday. The combination of the above variables which minimized the Akaike Information Criterion (AIC) was then chosen as the baseline model (16). A series of pollutants or pollens was added to the baseline model to assess the unipollutant or unipollen effect. Only variables that obtained a *P*-value of at least 0.2 in the unipollutant or unipollen model were included in the multipollutant or multipollen models. The estimators for the respective pollutants and pollens were calculated for the same day and for prior exposures of up to 3 day, as well as the averages for lags 01 and 23. Results were expressed as Odds ratios (OR) with their 95% confidence intervals (95% CI).

Results

A general upward trend was observed for total cardio-respiratory emergencies across the 4 years (see Table 1 and Fig. 1). Broken down by season of the year, means were higher in fall and winter for cardiovascular emergencies (daily means of 4.14 and 3.98, respectively) and in winter for respiratory emergencies (daily mean of 3.22); both decreased in summer, with means of 3.30 and 0.91 respectively. Ambient black-smoke air pollution levels tended to rise over the study period, whilst SO₂ levels, after declining from 1996 and 1997, remained fairly

Table 1. Annual emergency rate per 100 000 population

Year	Cardiovascular	Respiratory	Cardiorespiratory
1996	167	229	397
1997	225	440	665
1998	207	552	759
1999	292	654	946

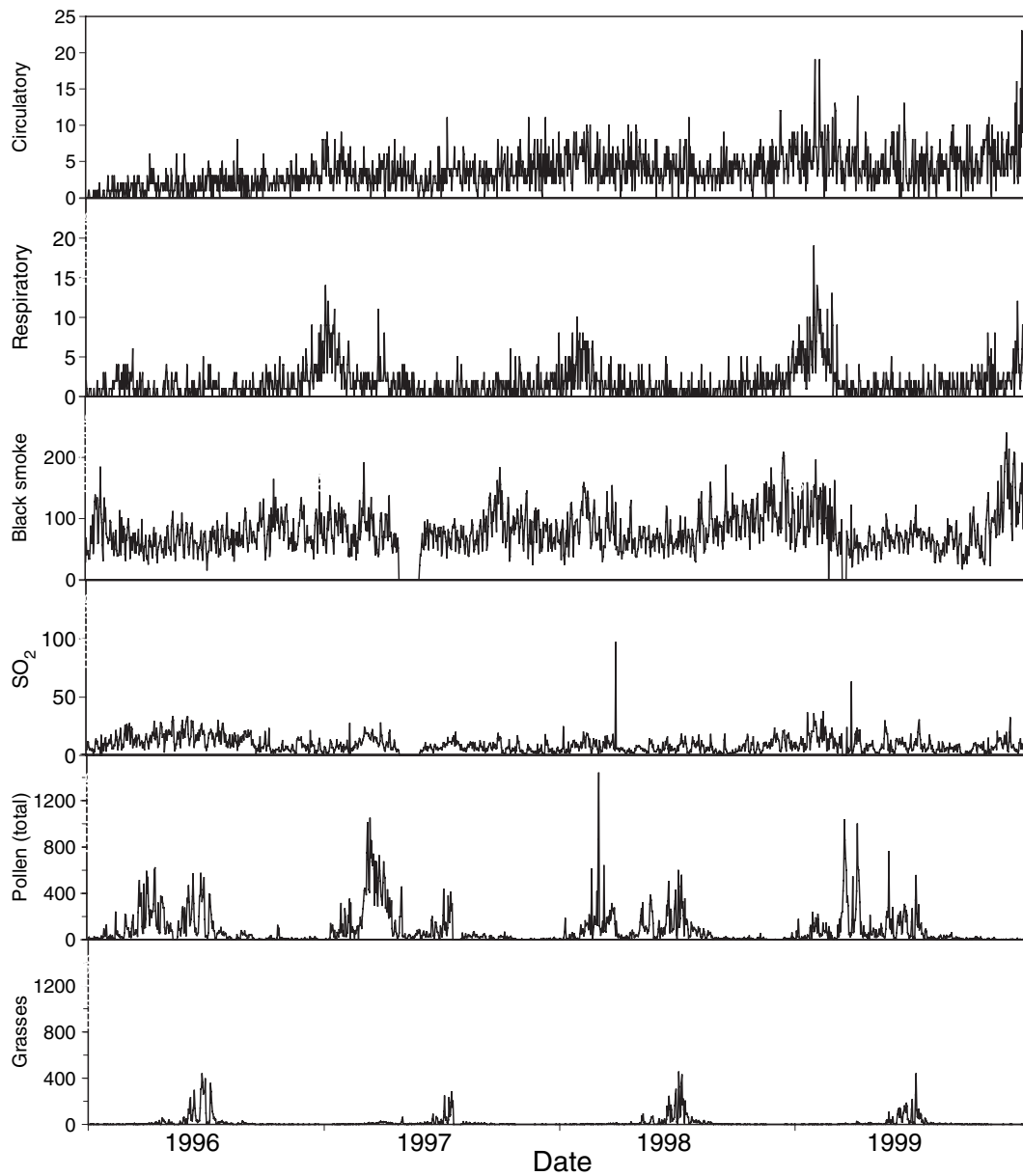


Figure 1. Daily trend in the number of medical emergency calls arising out of circulatory causes (circulatory), respiratory causes (respiratory), black smoke ($\mu\text{g}/\text{m}^3$) and SO_2 levels ($\mu\text{g}/\text{m}^3$) and total pollen and grass counts (grains/m^3).

constant (see Table 2 and Fig. 1). The mean temperature was 14.33°C , summer being the hottest season, with a mean of 19.50°C and winter being the coldest season, with a mean of 10.20°C . Mean relative humidity was 80.43% and mean atmospheric pressure was 988.23 millibars. Reported cases of influenza followed a seasonal pattern, with higher means in the months of January and February. The pollen time series registered a seasonal pattern, with the highest values in spring for total pollens and in summer for *gramineae* (see Fig. 1).

Table 3 shows the OR and their 95% CI for exposure to each pollutant with respect to medical emergency calls

Table 2. Ambient air pollution levels in the city of Vigo

Variable	Year	Mean $\pm$ SD	Median	Maximum
SO_2 ($\mu\text{g}/\text{m}^3$)	1996	12.51 ± 7.04	11.42	33.14
	1997	7.80 ± 4.85	6.79	27.71
	1998	7.65 ± 6.65	6.30	96.71
	1999	9.18 ± 7.21	7.42	62.85
Particles ($\mu\text{g}/\text{m}^3$)	1996	71.05 ± 25.87	66.85	183.95
	1997	79.81 ± 27.34	77.34	191.00
	1998	85.51 ± 33.59	78.42	208.10
	1999	80.94 ± 39.71	72.28	239.94

SD, standard deviation.

Table 3. Odds ratios (OR) and their 95% confidence interval (CI) for exposure to each pollutant with respect to medical emergency calls because of respiratory, cardiovascular and cardiorespiratory causes

	Cardiovascular OR (95% CI)	Respiratory OR (95% CI)	Cardiorespiratory OR (95% CI)
Black smoke ($\mu\text{g}/\text{m}^3$)			
Same day	1.002 (1.001–1.003)*	1.001 (0.999–1.002)	1.001 (1.000–1.002)*
1-day lag	0.999 (0.998–1.001)	1.001 (0.999–1.003)	1.000 (0.999–1.001)
2-day lag	1.000 (0.999–1.001)	1.002 (1.000–1.004)*	1.001 (1.000–1.002)
3-day lag	1.000 (0.999–1.002)	1.001 (0.999–1.002)	1.000 (0.999–1.001)
Average days 0 and 1	1.001 (0.999–1.003)	1.000 (0.999–1.004)	1.001 (1.000–1.002)
Average days 2 and 3	1.000 (0.998–1.002)	1.002 (1.000–1.004)	1.001 (0.999–1.002)
SO ₂ ($\mu\text{g}/\text{m}^3$)			
Same day	1.003 (0.997–1.009)	0.992 (0.981–1.003)	1.002 (0.996–1.007)
1-day lag	0.997 (0.991–1.003)	1.004 (0.994–1.014)	1.000 (0.995–1.006)
2-day lag	0.997 (0.991–1.003)	1.007 (0.997–1.016)	1.001 (0.995–1.002)
3-day lag	0.999 (0.993–1.005)	1.001 (0.992–1.009)	1.000 (0.995–1.005)
Average days 0 and 1	1.001 (0.994–1.008)	0.998 (0.985–1.011)	1.002 (0.885–1.010)
Average days 2 and 3	0.996 (0.989–1.004)	1.005 (0.994–1.015)	1.000 (0.994–1.006)

* $P < 0.05$.

arising out of respiratory, cardiovascular and both causes combined. For an increase of $10 \mu\text{g}/\text{m}^3$ in particulate levels, we observed a same day 1.97% (95% CI: 1.83–2.11%) increase in medical emergency calls because of circulatory causes and a 1.34% (95% CI: 1.23–1.45%) increase because of combined causes, whereas at 2 days there was a 1.95% (95% CI: 1.76–2.14%) increase in the number of calls because of respiratory causes. Sulphur dioxide registered no statistically significant effect with any of the causes of morbidity.

Pollen levels showed a relationship with respiratory but not with cardiac diseases. Table 4 shows the OR and their 95% CI for exposure to each pollen with respect to medical emergency calls because of respiratory causes.

The pollens that displayed this relationship were: grasses (same day), birch (3-day lag and average lag of 2 and 3 day), alder (2-day lag), hazel (2-day lag and average lag of 2 and 3 days) and wormseed or chenopodium (*Chenopodium ambrosioides*) (same day). A rise in pollen levels from the 95th to the 99th percentile was associated with the following percentage increases in medical emergency calls: (i) 19.62% (95% CI: 19.32–19.92%) at 2 days for alder in the case of respiratory causes; (ii) 30.56% (95% CI: 30.02–31.10%) at 3 days for birch in the case of respiratory causes, with a 24.97% (95% CI: 24.42–25.52%) average for the second and third days; (iii) 8.70% (95% CI: 5.33–12.18%) at 2 days for hazel in the case of respiratory causes, with a 7.91% (95% CI: 3.28–

Table 4. Odds ratios (OR) and their 95% confidence interval (CI) for exposure to each pollen with respect to medical emergency calls because of respiratory causes

OR (95% CI)	Lags					
	Same day	1-day lag	2-day lag	3-day lag	Average days 0 and 1	Average days 2 and 3
<i>Asteraceae</i>	1.022 (0.916–1.141)	0.982 (0.888–1.086)	1.027 (0.931–1.132)	0.948 (0.857–1.048)	1.000 (0.871–1.148)	0.980 (0.865–1.109)
<i>Alnus</i>	0.998 (0.995–1.001)	1.002 (0.999–1.005)	1.003 (1.001–1.006)*	1.000 (0.997–1.003)	1.001 (0.997–1.004)	1.003 (0.999–1.006)
<i>Betula</i>	1.003 (0.998–1.008)	1.003 (0.998–1.007)	1.003 (0.998–1.007)	1.005 (1.001–1.009)*	1.003 (0.998–1.008)	1.004 (1.000–1.009)*
<i>Corylus</i>	0.993 (0.959–1.029)	1.003 (0.973–1.033)	1.042 (1.010–1.076)*	1.013 (0.978–1.050)	0.998 (0.955–1.042)	1.052 (1.006–1.099)*
<i>Cupresaceae</i>	0.996 (0.991–1.001)	1.004 (0.999–1.008)	1.001 (0.996–1.005)	0.998 (0.993–1.003)	1.001 (0.994–1.006)	0.999 (0.993–1.005)
<i>Chenopodiaceae</i>	1.118 (1.012–1.233)*	0.959 (0.865–1.062)	0.998 (0.905–1.100)	0.970 (0.879–1.070)	1.065 (0.933–1.214)	0.973 (0.857–1.105)
<i>Ericaceae</i>	0.997 (0.980–1.013)	1.012 (0.993–1.030)	1.004 (0.986–1.022)	1.005 (0.984–1.026)	1.005 (0.984–1.026)	1.005 (0.984–1.027)
<i>Castanea</i>	1.001 (0.992–1.009)	0.993 (0.982–1.004)	0.993 (0.982–1.005)	0.993 (0.982–1.005)	0.997 (0.986–1.008)	0.991 (0.977–1.004)
<i>Quercus</i>	1.002 (0.998–1.007)	1.003 (0.998–1.007)	1.002 (0.997–1.006)	1.001 (0.998–1.005)	1.003 (0.998–1.008)	1.002 (0.997–1.006)
<i>Myrtaceae</i>	0.999 (0.986–1.012)	0.997 (0.982–1.011)	1.006 (0.993–1.019)	1.012 (0.999–1.026)	0.997 (0.980–1.014)	1.014 (0.997–1.030)
<i>Fraxinus</i>	0.986 (0.933–1.041)	1.001 (0.957–1.047)	1.000 (0.956–1.046)	1.004 (0.958–1.052)	0.991 (0.930–1.056)	1.003 (0.948–1.061)
<i>Olea</i>	1.003 (0.998–1.008)	0.999 (0.994–1.004)	0.999 (0.995–1.004)	1.001 (0.997–1.004)	1.001 (0.995–1.007)	1.000 (0.995–1.005)
<i>Pinaceae</i>	1.000 (0.999–1.001)	1.000 (0.999–1.001)	1.001 (0.999–1.001)	1.000 (0.999–1.001)	1.000 (0.999–1.002)	1.001 (0.999–1.002)
<i>Plantaginaceae</i>	1.011 (0.996–1.026)	1.008 (0.994–1.022)	0.989 (0.974–1.003)	0.999 (0.986–1.012)	1.013 (0.996–1.030)	0.992 (0.975–1.008)
<i>Platanaceae</i>	1.005 (0.998–1.012)	1.003 (0.995–1.010)	1.000 (0.993–1.007)	1.001 (0.993–1.008)	1.005 (0.997–1.013)	1.000 (0.992–1.008)
<i>Poaceae</i>	1.002 (0.999–1.003)	1.000 (0.998–1.002)	0.999 (0.996–1.001)	1.000 (0.997–1.001)	1.001 (0.999–1.004)	0.999 (0.996–1.001)
<i>Polygonaceae</i>	1.003 (0.392–2.562)	1.082 (0.428–2.738)	0.462 (0.172–1.238)	0.992 (0.349–2.821)	1.085 (0.289–4.072)	0.405 (0.098–1.674)
<i>Salicaceae</i>	1.010 (0.979–1.042)	1.007 (0.969–1.045)	1.012 (0.979–1.045)	1.009 (0.978–1.041)	1.015 (0.971–1.062)	1.018 (0.976–1.061)
<i>Urticaceae</i>	1.000 (0.997–1.002)	0.982 (0.888–1.086)	1.001 (0.999–1.003)	1.000 (0.997–1.002)	0.999 (0.996–1.002)	1.000 (0.998–1.003)
<i>Graminaeae</i>	1.002 (1.000–1.004)*	1.001 (0.999–1.003)	0.999 (0.997–1.001)	1.000 (0.998–1.002)	1.002 (0.999–1.004)	0.999 (0.997–1.002)

* $P < 0.05$.

12.75%) average for the second and third days and (iv) 24.91% (95% CI: 13.18–37.85%) and 44.99% (95% CI: 44.73–45.25%) on the same day for chenopodium and *gramineae*, respectively, in the case of respiratory causes.

Joint evaluation of air pollutants and pollen failed to reveal variations in the relationship observed. The possible interaction between pollens and air pollutants was studied but no statistically significant relationship was found.

Discussion

The results of our study indicate that particulate pollution increases medical emergency calls arising out of respiratory causes, cardiovascular causes or the two combined. Moreover, our results suggest that pollen concentrations increase telephone requests for emergency medical services in the case of respiratory causes.

The effect of air-borne particulate matter on medical emergency calls observed in our study is in line with that reported by Medina et al. (17) in Paris, but contrasts with the study by Hautemanière et al. (18) in Rouen, in which no relationship was encountered. Insofar as SO₂ is concerned, we, unlike the Paris (17) and Rouen (18) studies, observed no relationship with medical emergency calls. A possible explanation for this fact could be that over the study period, SO₂ levels in Vigo were moderate whereas black-smoke levels were very high, to the point of even surpassing those of Athens, the city with the highest levels in the APHEA study (19).

Furthermore, our findings on the relationship between particulate matter and respiratory or cardiovascular morbidity agree with those reported by numerous studies that link pollution to morbidity measured by hospital admissions (20–22). In this regard, we feel that a measure of morbidity based on emergency calls has certain advantages and drawbacks vis-à-vis an admissions-based measure. Thus, the event (call *vs* admission) depends neither on hospital admission criteria nor on patients' access to hospital, and may be more sensitive to the physiopathological changes that pollution can generate. Against this, there is a greater risk of misclassification in the diagnosis; yet in our opinion, this possible bias is minimized by the inclusion of major disease groups (respiratory, cardiovascular or both).

From a physiological standpoint, our results are coherent with the biological mechanisms put forward to explain that particulates increase respiratory disorders by exacerbating inflammatory mechanisms in the respiratory system (23). Human and animal laboratory-based studies have shown that particulate air pollutants, and diesel air pollution particles in particular, can enhance allergic inflammation and induce the development of allergic immune responses, because of the release of mediators of the allergic and inflammatory response that initiates a cascade, which can culminate in airway inflammation,

mucus secretion, serum leakage into the airways and bronchial smooth muscle contraction (24). Worldwide increases in allergic respiratory disease have been observed, mainly in urban communities (25). Diesel air pollution particles appear to have greater immunological effects in the presence of environmental allergens than they do alone (26). In the case of cardiovascular disorders, this is not entirely established and a number of mechanisms have been proposed, such as increased blood plasma viscosity (27), increased heart rate (28), alterations in heart rate variability (29) or diesel exhaust particle-induced enhancement of coagulatory disturbances (30).

The magnitude of the association between air pollution and the health outcomes observed in our study might be thought very small compared with other pollutants such as tobacco, but it should be borne in mind here that in the latter case, only smokers and, to a lesser extent, passive smokers are exposed. Nonetheless, the entire population is exposed to air pollution, so that the overall result of its effects may be considerable.

In this study, pollen levels were associated with respiratory disease as measured by medical emergency calls. We failed to locate previous studies with a CCO design. To date, only one study has been published, which analyses the causes of medical emergency calls retrospectively: in it, an increase in the number of calls because of pollinosis-related symptoms in the study period was linked to a peak in pollen concentration on these same dates (31). There have been various studies that have reported a relationship between pollen levels and other variables, such as respiratory morbidity or hospital admissions because of respiratory causes in different areas (32). Very few studies reported significant associations between pollen concentrations and/or concentration of individual pollen species and (paediatric) hospital admissions (33, 34). This might be because of geographic differences in allergen levels or the prevalence of allergies (35). Thus, the main Vigo-based pollen types with allergenic capacity used in this study may be different from those of other cities. This is the first study to address the interaction between pollen and air pollutants in terms of medical emergency calls, but no significant interaction was observed.

The mechanism of action whereby pollen exerts effects at the level of the respiratory tree is through allergic-type sensitization of the proteins present in pollens, which provokes an IgE-mediated inflammatory response with a series of physiological changes, such as an increase in eosinophils and neutrophils, exhaled nitric oxide or the number of cells in bronchoalveolar lavage, ultimately leading to clinical conditions affecting the respiratory tree (32, 36).

Several authors have demonstrated a twofold prevalence of pollen disease in urban *vs* rural environments, even though pollen levels are higher in rural areas (37). An increase in pollen disease incidence has also been observed, which has been attributed by a number of authors to diesel particles in the atmosphere (38, 39). The main mechanism

that could explain these observations is the finding that several pollen species can adsorb diesel particles, thus facilitating their entry into the bronchial tree (40).

One limitation of this study is that, given its ecological design, the cause–effect relationship must be interpreted with caution. The limitation posed by using fixed-site air pollution monitors to measure the exposure of the whole population has often been debated (41). It might be thought that important variables (such as tobacco habit or chronic diseases) have not been controlled for, but there is no reason to believe that many of the individual risk factors, such as presence of chronic diseases or smoker status, might be correlated with the daily changes in air pollution levels. Accordingly, these cannot be confounding factors in this study, as a confounding factor must be correlated with both cause and effect.

Case-crossover design has several advantages over Poisson time series, such as controlling for many confounding factors by design rather than by statistical modelling. Yet, one disadvantage of CCO vs Poisson methods is that the former are slightly more inefficient, producing slightly wider OR CI than those of the Poisson time series and so implying a lower statistical power (42). In general, however, CCO designs and Poisson time series with generalized additive models have yielded almost identical results (43–45), so that results are not believed to

depend on the type of design used. Indeed, the fact that an association was found between air pollution and medical emergency calls in this study, despite its having a lower statistical power than the Poisson models, serves to reinforce earlier studies that were undertaken with other methodologies.

In conclusion, this study reveals that there is an increased risk of telephone requests for emergency medical attention in the case of cardiac or respiratory causes in response to a rise in ambient air particulate levels, something that underscores the importance of monitoring these pollutants. A relationship was likewise observed between pollen levels and calls because of respiratory causes, although no interaction between pollen and pollution was found: studies with a larger sample size may possibly be required to study this interaction.

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