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Multivariate analysis of respiratory problems and their connection with meteorological parameters and the main biological and chemical air pollutants

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ABSTRACT

The aim of the study is to analyse the joint effect of biological (pollen) and chemical air pollutants, as well as meteorological variables, on the hospital admissions of respiratory problems for the Szeged region in Southern Hungary. The data set used covers a nine-year period (1999–2007) and is unique in the sense that it includes—besides the daily number of respiratory hospital admissions—not just the hourly mean concentrations of CO, PM_{10}, NO, NO_2, O_3 and SO_2 with meteorological variables (temperature, global solar flux, relative humidity, air pressure and wind speed), but two pollen variables (*Ambrosia* and total pollen excluding *Ambrosia*) as well. The analysis was performed using three age categories for the pollen season of *Ambrosia* and the pollen-free season. Meteorological elements and air pollutants are clustered in order to define optimum environmental conditions of high patient numbers. ANOVA was then used to determine whether cluster-related mean patient numbers differ significantly. Furthermore, two novel procedures are applied here: factor analysis including a special transformation and a time-varying multivariate linear regression that makes it possible to determine the rank of importance of the influencing variables in respiratory hospital admissions, and also compute the relative importance of the parameters affecting respiratory disorders. Both techniques revealed that *Ambrosia* pollen is an important variable that influences hospital admissions (an increase of 10 pollen grains m^{-3} can imply an increase of around 24% in patient numbers). The role of chemical and meteorological parameters is also significant, but their weights vary according to the seasons and the methods. Clearer results are obtained for the pollination season of *Ambrosia*. Here, a 10 μg m^{-3} increase in O_3 implies a patient number response from −17% to +11%. Wind speed is a surprisingly important variable, where a 1 m s^{-1} rise may result in a hospital admission reduction of up to 42–45%.

1. Introduction

Air pollution, as a major and constantly growing risk for the environment, is associated with a large rise in medical costs and is estimated to cause about 800,000 premature deaths annually worldwide (Cohen et al., 2005). The prevalence of allergic respiratory problems has also increased during the past three decades, especially in industrialised countries. This increase may be explained by changes in environmental factors (D'Amato et al., 2005). Weather conditions can also affect both the biological and chemical air pollutants. There is also evidence that air pollution increases exposure to the allergens, their concentration and/or biological allergenic activity (Just et al., 2007).

Air pollution in Hungary is one of the highest in Europe. Around 16,000 annual premature deaths attributable to exposure to ambient PM_{10} concentrations are estimated in the country (Ågren, 2010). Furthermore, airborne pollen levels are also high. The Carpathian basin, including Hungary (Fig. 1), is considered the most polluted region with airborne ragweed *(Ambrosia)* pollen in Europe (Makra et al., 2010). In Szeged, 83.7% of patients suffering from respiratory problems are sensitive to *Ambrosia* pollen (Makra et al., 2010).

The substantial increase in respiratory ailments in industrialised countries is attributable to a combination of chemical air pollutants and allergenic pollen existing in the air of big cities. Several papers have analysed separately the effects of either chemical air pollutants (Alves et al., 2010) or allergenic pollen (Díaz et al., 2007) on hospital admissions of respiratory problems; however, very few

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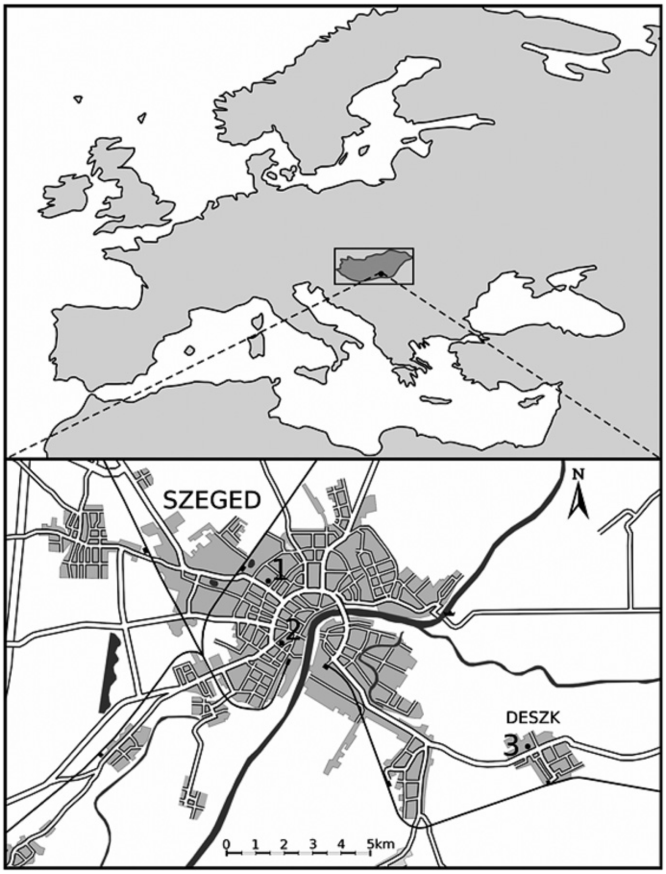

Fig. 1. Location of Europe with Hungary (upper panel) and the urban web of Szeged with the positions of the data sources (lower panel). 1: monitoring station; 2: pollen trap; 3: Thorax Surgery Hospital in Deszk.

studies have so far examined the effect of these two kinds of variables together (e.g., Andersen et al., 2007). Such papers revealed a significant effect between pollen and chemical compounds on the one hand and health for those patients admitted with respiratory complaints on the other; and this effect was higher than that found separately for the chemical air pollutants or pollen.

The purpose of this study is to analyse the joint effect of biological (pollen) and chemical air pollutants, as well as meteorological variables on the hospital admissions of respiratory-problem patients of different age groups during different seasons in the Szeged region in Southern Hungary. The data set applied is unique in the sense that includes all of the above three categories of influencing variables. This study analyses one of the largest data sets used in the literature on respiratory hospital admissions.

2. Materials and methods

2.1. Location and data

Szeged(46.25 °N; 20.10 °E) is the largest settlement in South-eastern Hungary (Fig. 1). The city is the centre of the Szeged region with 203,000 inhabitants.

Meteorological variables and chemical air pollutants were collected in a monitoring station located in the inner city area of Szeged (Fig. 1). Daily values taken were for the mean temperature (T, °C), mean global solar flux (GSF, W m^{-2}), mean relative humidity (RH, %), mean sea level air pressure (P, hPa) and mean wind speed (WS, m s^{-1}). Chemical air pollutants include the daily average mass concentrations of CO, NO, NO_2, SO_2, O_3 and PM_{10} (μg m^{-3}) (Alves et al., 2010). Two pollen variables were formed for our analysis: the pollen level of *Ambrosia*, and the total pollen count (the pollen counts of each of the 24 taxa examined) excluding the pollen of *Ambrosia*. Both pollen variables were considered for the pollen season of *Ambrosia* (July 15–October 16).

Traffic is the main source of air pollution in Szeged. An analysis of temporal and seasonal variations of air pollutants levels at one urban roadside, one urban background and one rural monitoring location (Namdeo and Bell, 2005) showed that although the rural site did not reveal it, both urban sites did show a strong diurnal variation in concentrations and did reflect a common source of air pollutants, namely exhaust emissions. Hence, representativity of traffic-origin air pollutants levels is only limited to the city excluding the rural site. A 24-h pollen sampling covers the 100 km limit of medium-range transport if the wind speed is around 1.2 m s^{-1}. Hence, pollen measurements are representative for an area of about 100 km in radius. It was found that in Szeged, long-range transport plays an important role for actual PM_{10} levels (Makra et al., 2011), while for pollen medium-range transport is more important, especially on non-rainy days (Makra et al., 2010).

The daily number of hospital admissions recorded with respiratory problems comes from the Thorax Surgery Hospital in Deszk, located about 10 km from the monitoring station in Szeged (Fig. 1, lower panel). Due to the very small number of younger patients (0–14 years) only three groups, namely adult patients (15–64 years), elderly patients (65 years of age or above), as well as all patients including the younger age group were analysed. The population consists of 133,464 hospital admissions of subjects resident in Szeged (Table 1).

The analysis was performed for the nine-year period 1999–2007 with two data sets according to the pollen season of *Ambrosia* (July 15–October 16) and to the pollen-free season (October 17–January 13). Note that Saturdays, Sundays and holidays as days without hospitalisation were excluded from the analysis. The pollen season defined by Galán et al. (2001) varies from year to year; here the longest observed pollen season during the nine-year period was considered for each year.

2.2. Methods

2.2.1. Cluster analysis

Cluster analysis is a common statistical technique for objectively grouping elements. The aim is to maximise the homogeneity of elements within the clusters and to maximise the heterogeneity among the clusters. Here a non-hierarchical cluster analysis with k-means algorithm using a Mahalanobis metric (Mahalanobis, 1936) was carried out. The data to be clustered include daily values of the 13 explanatory variables (5 meteorological elements, 6 chemical

Table 1
Parameters of daily respiratory admissions based on different age categories and seasons.

Parameter	Age categories		
	15–64 years	Over 65 years	All age groups
	Pollen season of *Ambrosia*		
Total number	81,348	13,776	95,251
Mean	83.10	11.75	95.01
Standard deviation	36.01	5.65	39.67
	Pollen-free season		
Total number	31,686	6474	38,213
Mean	59.34	12.12	71.56
Standard deviation	23.29	6.32	27.73

pollutants and 2 pollen types). The homogeneity within clusters was measured by RMSD defined as the sum of the root mean square deviations of cluster elements from the corresponding cluster centre over clusters. The RMSD value usually decreases with an increasing number of clusters. Thus, this quantity itself is not very useful for deciding the optimal number of clusters. However, the change of RMSD (CRMSD) or even the change of CMRSD (CCRMSD) versus the change of cluster numbers is much more informative (Makra et al., 2010).

2.2.2. Analysis of variance (ANOVA)

A one-way analysis of variance (ANOVA) is used to determine whether the inter group variance is significantly higher than the intra group variance of a data set. After performing ANOVA on the averages of the groups in question, a post-hoc Tukey test is applied to establish which groups differed significantly from each other (Tukey, 1985). Significant differences among mean hospital admissions corresponding to different cluster pairs may reveal an important influence of the meteorological elements, chemical air pollutants and given pollen types on the daily number of respiratory admissions.

2.2.3. Factor analysis and special transformation

Factor analysis identifies linear relationships among subsets of examined variables and this helps to reduce the dimensionality of the initial database without substantial loss of information. First, a factor analysis was applied to the initial data set consisting of 14 variables (13 explanatory variables and 1 resultant variable defined by the number of daily hospital admissions with respiratory problems) in order to transform the original variables to fewer variables. These new variables (called factors) can be viewed as latent variables explaining the joint behaviour of weather-pollutant-hospital admission variables. The optimum number of retained factors is determined by different statistical criteria (Jolliffe, 1993). The most common and widely accepted one is to specify a least percentage (80%) of the total variance in the original variables that has to be achieved (Liu, 2009). After performing the factor analysis, a special transformation of the retained factors was made to discover to what degree the above-mentioned explanatory variables affect the resultant variable, and to give a rank of their influence (Jahn and Vahle, 1968).

2.2.4. Time-varying multivariate linear regression with time lags

The task is to establish a relationship between explanatory variables and the resultant variable. As both kinds of variables exhibit annual trends, regression coefficients in the linear relationship have annual courses described by sine and cosine functions with yearly and half-yearly periods. This latter cycle was introduced to describe the asymmetries of the annual courses. The coefficients of these periodic functions were estimated using the least squares principle.

It is reasonable to allow time lags between pollutants concentrations and the number of hospital admissions. Therefore, the univariate version of the above-mentioned time-varying linear regression was carried out with each individual explanatory variable with different time lags including a zero lag. The time lags that minimise the mean square errors were regarded as optimal.

3. Results

3.1. Cluster analysis and ANOVA

A cluster analysis for the pollen season of *Ambrosia* and the pollen-free season resulted in five and four clusters, respectively (Tables 2a and 2b).

Table 2a
Cluster-related mean values of the meteorological and pollutant parameters as well as patient numbers for the pollen season of *Ambrosia* (**bold:** maximum; *italic:* minimum).

Parameter	Mean values				
Cluster	1	2	3	4	5
Total number of days	68	41	*26*	94	**137**
Frequency (%)	18.6	11.2	*7.1*	25.7	**37.4**
Temperature (°C)	23.3	16.9	20.5	**24.9**	*16.4*
Global solar flux (W m^{-2})	211.1	155.3	176.4	**223.6**	*126.7*
Relative humidity (%)	66.1	72.2	68.6	*59.3*	**75.0**
Air pressure (hPa)	1002.7	**1009.4**	*1001.7*	1005.3	1005.9
Wind speed (m s^{-1})	0.8	*0.5*	0.9	**1.1**	0.9
CO (μg m^{-3})	468.9	**700.5**	*425.1*	444.5	463.8
PM_{10} (μg m^{-3})	*36.3*	**52.8**	40.4	44.0	40.2
NO (μg·m^{-3})	10.8	**44.7**	14.1	*9.5*	15.1
NO_2 (μg m^{-3})	32.9	**48.8**	33.2	34.0	*31.8*
O_3 (μg m^{-3})	41.8	*26.2*	36.3	**58.4**	29.2
SO_2 (μg m^{-3})	*4.0*	5.5	4.9	4.9	**6.0**
Ambrosia (pollen m^{-3} day^{-1})	91.7	*43.3*	**593.2**	46.2	57.9
Total pollen excluding *Ambrosia*	**111.9**	16.8	48.7	49.9	*14.1*
Adults (15–64 years)	101.6	76.7	**114.3**	*74.5*	78.2
The elderly (≥65 years)	12.8	11.8	**13.3**	*10.5*	12.2
All age groups	114.5	88.7	**127.9**	*85.1*	90.6

The analysis of variance revealed a significant difference at least at a 95% probability level in the mean values of patient numbers among the individual clusters. The Tukey test indicated significant differences both for adults, the elderly and all age groups among the mean patient numbers of the cluster pairs. Only clusters accompanied with significantly different means were then analysed further, especially those clusters with extreme high/low patient numbers.

It was found for the pollen season of *Ambrosia* that patient numbers are the highest in cluster 3 for each age category, most probably due to the highest and medium levels of *Ambrosia* and the remaining pollen, respectively (Table 2a). Cluster 4 involving a substantial part of summer provides the lowest patient numbers. It may be accounted for by moderate or low levels of both the two pollen types and the chemical pollutants (except for O_3) promoted

Table 2b
Cluster-related mean values of the meteorological and pollutant parameters as well as patient numbers for the pollen-free season (**bold:** maximum; *italic:* minimum).

Parameter	Mean values			
Cluster	1	2	3	4
Total number of days	75	**137**	*44*	108
Frequency (%)	20.6	**37.6**	*12.1*	29.7
Temperature (°C)	**10.8**	3.2	*−2.7*	5.7
Global solar flux (W m^{-2})	**62.1**	38.9	*36.2*	44.8
Relative humidity (%)	*82.1*	87.6	**93.1**	87.1
Air pressure (hPa)	1010.6	*1004.3*	**1020.3**	1008.5
Wind speed (m s^{-1})	0.6	*0.5*	*0.5*	**1.4**
CO (μg m^{-3})	788.2	**812.4**	729.7	*652.2*
PM_{10} (μg m^{-3})	**79.2**	53.2	61.6	*52.6*
NO (μg m^{-3})	35.9	**40.6**	*28.0*	31.9
NO_2 (μg m^{-3})	**40.4**	38.0	*5.2*	36.0
O_3 (μg m^{-3})	**19.6**	15.2	16.8	*11.3*
SO_2 (μg m^{-3})	10.4	*6.6*	**15.2**	7.4
Adults (15–64 years)	61.4	59.2	*50.2*	**64.6**
The elderly (≥65 years)	11.7	11.6	*10.1*	**13.9**
All age groups	73.2	71.0	*60.3*	**78.5**

by the highest wind speed (Table 2a). As regards the pollen-free season the highest patient numbers for each age category are associated with cluster 4. This can be explained by the relatively high temperature favourable for reproducing bacteria and viruses, as well as by strong winds that encourage the inflammation in the respiratory tracts by desiccating the air. Cluster 3 having anticyclonic character exhibits the lowest patient numbers for each age category, probably due to the very low temperatures in winter time that contribute to restrict respiratory infections (Table 2b).

3.2. Optimal time lags

Although there are examples for time lags even up to 8 days (Nascimento et al., 2006), the typical delays are up to 3 days in patient response to pollution exposure (e.g. Alves et al., 2010). It is likely that the explanatory variables express their effects in the formation of the respiratory problems within 3 days (Knight et al., 1991). For instance, immediate allergic reactions of pollen can occur within 15–20 min, in certain cases 8–10 h, while all immune reactions in cells can occur 48–72 h following exposure (Petrányi, 2000). Our optimal time lag varies from zero to three days. With increasing age there is a tendency for more non-zero lags. The global solar flux has the largest number of positive time shifts from meteorological variables (typically 2–3 days) for the elderly, while the relative humidity has the largest number of non-zero delays (2–3 days) for adults. However, the role of relative humidity in positive delays is substantially smaller than the role of the global solar flux. Within the chemical pollutants, positive lags (0–3 days) are mostly associated with CO and SO_2 for both age groups, and then with NO for adults and PM_{10} for the elderly, in agreement with other studies (e.g. Orazzo et al., 2009). No time shift is typical for the pollen season of *Ambrosia* in any allergy-sufferer group.

3.3. Factor analysis and special transformation

After performing a factor analysis for adults, the elderly and all age groups for the two seasons (altogether 3 × 2 = 6 factor analyses), 7 and 6 factors were retained for the pollen season of *Ambrosia* and pollen-free season, respectively. In order to calculate the rank of importance of the explanatory variables for determining the resultant variable, loadings of the retained factors were projected onto Factor 1 (with a special transformation) (Tables 3a and 3b) (Jahn and Vahle, 1968).

As regards meteorological variables, only the wind speed and temperature display significant associations with hospital admissions for all three age groups in the pollen season of *Ambrosia*, which is confirmed by Freitas et al. (2010). The wind speed exhibits a dual character because strong winds facilitate decreasing hospital admissions by reducing the levels of the pollutants throughout the year, but they help to desiccate the air and hence encourage respiratory problems. The latter effect seems to be higher in the pollen-free season since the wind speed varies proportionally with the elderly patient numbers (Table 3b) in this period. In the pollen season of *Ambrosia*, the inverse relationship of wind speed with the number of hospital admissions suggests that the pollutant-diluting effect of the wind is predominant (Table 3a) here. In the cold pollen-free season, relatively high temperatures and strong wind speeds are associated with typical cyclonic air masses. This kind of weather can cause an increase in the number of hospital admissions of the elderly with weak immune systems, since their repeated exposition to air desiccated by winds may lead to an inflammation of the respiratory tracts (Table 3b) (Strausz, 2003).

Both for the pollen season of *Ambrosia* and pollen-free season, the total weight of the chemical pollutants is the highest for all three age groups with all variable types and is substantially higher than that of the meteorological variables. This latter finding may be due to the fact that anticyclonic weather situations, being the most frequent during the above seasons, favour enrichment of chemical

Table 3a
Special transformation. Effect of the explanatory variables on respiratory diseases as resultant variables and the rank of importance of the explanatory variables on their factor loadings transformed to Factor 1 for determining the resultant variable; pollen season of *Ambrosia* (thresholds of significance: *italic*: $x_{0.05}$ = 0.056; **bold:** $x_{0.01}$ = 0.074).

Explanatory variables	Adults (15–64 years)		The elderly (≥65 years)		All age groups	
	weight	rank	weight	rank	weight	rank
Patient number	0.914	–	−0.983	–	0.918	–
Temperature (°C)	**0.081**	10	0.021	13	0.067	10
Global solar flux (W m^{-2})	**0.168**	7	*0.134*	4	**0.146**	8
Relative humidity (%)	−0.163	8	0.057	10	**−0.152**	7
Air pressure (hPa)	−0.042	13	−0.103	7	−0.018	13
Wind speed (m s^{-1})	**−0.220**	5	**0.142**	2	**−0.228**	5
Total weight	0.675	–	0.457	–	0.611	–
CO (μg m^{-3})	**−0.255**	3	0.095	8	**−0.251**	4
PM_{10} (μg m^{-3})	**−0.314**	2	*0.119*	5	**−0.304**	2
NO (μg m^{-3})	−0.058	11	−0.032	12	−0.041	12
NO_2 (μg m^{-3})	0.047	12	*−0.134*	3	0.059	11
O_3 (μg m^{-3})	**−0.230**	4	**0.272**	1	**−0.252**	3
SO_2 (μg m^{-3})	*−0.115*	9	0.070	9	*−0.119*	9
Total weight	1.018	–	0.722	–	1.025	–
Ambrosia (pollen m^{-3} day^{-1})	**0.553**	1	*−0.117*	6	**0.520**	1
Total pollen excluding *Ambrosia*	**0.199**	6	−0.041	11	**0.177**	6
Total weight	0.752	–	0.158	–	0.697	–

Table 3b
Special transformation. Effect of the explanatory variables on respiratory diseases as resultant variables and the rank of importance of the explanatory variables on their factor loadings transformed to Factor 1 for determining the resultant variable; pollen-free season (thresholds of significance: *italic*: $x_{0.05}$ = 0.105; **bold:** $x_{0.01}$ = 0.138).

Explanatory variables	Adults (15–64 years)		The elderly (≥65 years)		All age groups	
	weight	rank	weight	rank	weight	rank
Patient number	0.993	–	0.943	–	0.992	–
Temperature (°C)	**0.168**	2	**0.165**	4	**0.188**	2
Global solar flux (W m^{-2})	0.048	8	−0.004	11	0.047	9
Relative humidity (%)	0.009	10	−0.083	9	−0.020	11
Air pressure (hPa)	*0.110*	7	*0.124*	7	0.055	7
Wind speed (m s^{-1})	0.035	9	**0.273**	2	0.022	10
Total weight	0.370	–	0.649	–	0.331	–
CO (μg m^{-3})	−0.009	11	*−0.126*	6	−0.049	8
PM_{10} (μg m^{-3})	**0.147**	3	0.092	8	**0.138**	4
NO (μg m^{-3})	*0.120*	6	**0.148**	5	0.104	5
NO_2 (μg m^{-3})	**0.175**	1	**0.186**	3	**0.197**	1
O_3 (μg m^{-3})	*−0.121*	5	**−0.351**	1	**−0.158**	3
SO_2 (μg m^{-3})	*−0.124*	4	−0.073	10	−0.091	6
Total weight	0.696	–	0.977	–	0.737	–

Table 4
Relative variance (%) of patient numbers accounted for by explanatory variables including and omitting (in parentheses) the annual cycle of patient numbers.

Patients	Pollen season of *Ambrosia*	Pollen-free season
Adults	26.8 (50.0)	17.8 (21.2)
The elderly	19.9 (23.9)	9.9 (13.9)
All age groups	26.5 (48.1)	13.8 (17.7)

Table 5
Ratio (%) of variances accounted for by explanatory variables to variance accounted for by all of the explanatory variables. Variables are indicated in an order of importance obtained via a stepwise regression. Only variables with a joint contribution just exceeding 90% of the total explained variance are shown. (in *X*: significant for $p < 0.1$, in **X**: significant for $p < 0.05$, in ***X***: significant for $p < 0.01$).

Pollen season of *Ambrosia*			Pollen-free season		
Adults	The elderly	All ages	Adults	The elderly	All ages
O_3: 15.8–31.7	**O_3: 20.1–36.7**	***O_3: 16.8–46.6***	**PM_{10}: 14.6–18.5**	*NO: 10.0–17.1*	**GSF: 8.0–12.3**
T: 1.5–10.9	T: 1.0–5.0	*T: 1.5–10.4*	*O_3: 7.9–9.0*	CO: 8.0–18.1	*O_3: 10.9–12.3*
GSF: 2.3–6.4	NO_2: 5.0–10.0	GSF: 2.2–6.0	*RH: 3.4–19.1*	SO_2: 8.0–14.1	*RH: 4.3–20.3*
NO: 3.8–6.4	WS: 5.0–6.0	NO: 3.7–6.3	T: 7.9–8.4	RH: 3.0–16.1	*CO: 4.3–11.6*
WS: 6.8–10.2	PM_{10}: 3.5–10.1	*WS: 7.1–10.1*	P: 0.2–9.6	*O_3: 13.1–16.1*	*NO_2: 12.3–13.8*
PM_{10}: 6.0–7.9	A: 2.5–4.0	PM_{10}: 6.0–8.2	*GSF: 8.4–10.7*	WS: 5.0–9.0	P: 0.1–9.4
P: 0.1–5.3	GSF: 4.5–5.0	P: 0.1–5.0	SO_2: 5.6–6.2	NO_2: 8.0–13.1	*NO: 8.0–16.7*
A: 5.7–6.4	P: 0.0–3.5	A: 4.9–6.3	*NO: 7.3–12.9*	PM_{10}: 5.0–5.1	T: 5.1–9.4
RH: 1.1–4.2	CO: 2.0–4.0	RH: 0.7–3.7	–	–	–

T = Temperature (°C); GSF = Global Solar Flux (W m^{-2}); RH = Relative humidity (%); *P* = Air pressure (hPa); WS = Wind speed (m s^{-1}); CO = Carbon-monoxide (μg m^{-3}); PM_{10} = Particulate matter smaller size than 10 μm (μg m^{-3}); NO = Nitrogen-monoxide (μg m^{-3}); NO_2 = Nitrogen-dioxide (μg m^{-3}); O_3 = Ozone (μg m^{-3}); SO_2 = Sulphur-dioxide (μg m^{-3}); *A* = *Ambrosia* (pollen m^{-3} day^{-1}).

pollutants, and so high pollutant levels have a greater effect on respiratory hospital admissions (Tables 3a and 3b).

For the pollen season of *Ambrosia*, pollen variables display the second highest weight for adults and all age groups, mainly due to the very high *Ambrosia* pollen levels (Table 3a). For adults, the first three explanatory variables that influence patient numbers the most are, in decreasing order, *Ambrosia*, PM_{10} and CO, while for all age groups they are *Ambrosia*, PM_{10} and O_3, respectively. For the elderly, there are fewer significant associations between the explanatory variables and the number of respiratory problems; furthermore, pollen variables exhibit the smallest total weight in this case. Here, influencing variables ranked highest in decreasing order are O_3, wind speed and NO_2. *Ambrosia* pollen is still significantly correlated with the number of respiratory admissions, but it is ranked only 6 (Table 3a).

For the pollen-free season, the chemical variables are ranked highest (Table 3b). The sequence of the most important influencing variables in decreasing order for adults is NO_2, temperature and PM_{10}, for the elderly it is O_3, wind speed and NO_2, while for all age groups it is NO_2, temperature and O_3 (Table 3b).

3.4. Time-varying multivariate linear regression

The ratio of variance of patient numbers accounted for by explanatory variables to variance of patient numbers is considerably larger for adults than for elderly people (Table 4). Also, the annual cycle of adult patient numbers is substantially larger (Table 4), suggesting that hospital visits of elderly people depend on pollutants and meteorological conditions to a lesser degree. This may be due to the following social factor. Some of the elderly habits tend to underestimate chronic diseases and consider them as a natural attendant of age. Hence, the elderly often do not turn to physician and seek medical treatment in time (Johnson, 2005).

Here, three questions should be raised. First, what is the order of explanatory variables in view of the strength of the influence on patient number? Second, what is the relative contribution of these variables to the variance explained by all of the variables? And third, how do the patient numbers change with a unit change in the explanatory variables? Regarding the first question, the selection of importance of explanatory variables in the formation of patient numbers was performed by the well-known stepwise regression method (Draper and Smith, 1981).

The answer to the second question is more difficult due to the multicollinearity among the explanatory variables. Namely, the sum of variances explained by individual variables is larger than the variance explained by all of the variables. Therefore, neither univariate regressions with individual explanatory variables nor the multivariate regression using all of the variables is appropriate to quantify the individual explained variances. However, elementary consideration shows that the variance percentage explained by the *i*th variable lies between $V - V_i$ and v_i, where V is the total explained variance, and v_i and V_i are the variances explained by the *i*th variable and all of the variables excluding the *i*th variable, respectively. Therefore, only the ranges of variances accounted for

Table 6
Minima and maxima of regression coefficients during the year.

Variable	Pollen season of Ambrosia						Pollen-free season					
	Minimum			Maximum			Minimum			Maximum		
	Adults	The elderly	All	Adult	The elderly	All	Adults	The elderly	All	Adults	The elderly	All
T	−3.61	−0.27	−3.96	5.28	0.01	5.83	−0.52	−0.55	−0.59	2.26	0.08	1.58
GSF	−0.03	−0.02	−0.03	0.38	0.01	0.40	−0.20	−0.02	−0.13	0.13	0.00	0.13
RH	−0.54	−0.06	−0.56	0.17	0.01	0.18	−0.77	−0.21	−0.82	0.29	0.05	0.35
P	−0.04	−0.01	−0.05	0.01	0.01	0.07	−0.03	0.00	−0.03	0.06	0.02	0.08
WS	−35.1	−2.61	−37.7	0.26	0.33	0.17	−4.11	0.00	−3.50	4.49	3.72	6.06
CO	−0.04	−0.01	−0.04	0.00	0.01	0.00	−0.01	−0.01	−0.02	0.01	0.01	0.00
PM_{10}	−0.50	−0.03	−0.55	0.14	0.03	0.18	0.00	−0.04	−0.05	0.24	0.04	0.13
NO	−1.00	−0.11	−1.07	0.25	0.01	0.23	−0.15	−0.03	−0.18	0.27	0.09	0.38
NO_2	−0.26	−0.07	−0.31	0.13	0.09	0.16	−0.42	−0.14	−0.68	0.21	0.08	0.47
O_3	−1.20	−0.16	−1.37	0.60	0.03	0.10	−0.47	−0.20	−0.70	0.24	0.02	0.00
SO_2	−1.54	−0.20	−1.75	0.63	0.18	0.99	−1.24	−0.09	−0.54	0.00	0.21	0.47
A	−0.08	−0.03	−0.11	2.78	0.24	3.05	–	–	–	–	–	–
TP	−0.02	−0.13	0.00	0.34	0.02	0.59	–	–	–	–	–	–

T = Temperature (°C); GSF = Global Solar Flux (W m^{-2}); RH = Relative humidity (%); *P* = Air pressure (hPa); WS = Wind speed (m s^{-1}); CO = Carbon-monoxide (μg m^{-3}); PM_{10} = Particulate matter smaller size than 10 μm (μg m^{-3}); NO = Nitrogen-monoxide (μg m^{-3}); NO_2 = Nitrogen-dioxide (μg m^{-3}); O_3 = Ozone (μg m^{-3}); SO_2 = Sulphur-dioxide (μg m^{-3}); *A* = *Ambrosia* (pollen m^{-3} day^{-1}); TP = Total pollen (pollen m^{-3} day^{-1}).

by explanatory variables are shown in Table 5. The most important explanatory variables that influence patient numbers in the pollen season of *Ambrosia* are O_3 and temperature for each age category. The order of the remaining variables is the same for adults and all of ages: global solar flux, NO, wind speed, PM_{10}, air pressure, and *Ambrosia*. Almost the same variables are considered to be most significant for the elderly group, but with a slightly different order. Surprisingly, *Ambrosia* is only the sixth-eighth most important explanatory variable influencing patient numbers. For the pollen-free season, O_3 is the second main factor for adults and all age groups, but is just fifth for the elderly. The order varies with the different age groups. For instance, the most significant variable is PM_{10}, NO and global solar flux for adults, the elderly and all age categories, respectively.

In addition, the order of importance of the explaining variables identified by the stepwise regression method is not the same as the order of level of the statistical significance (Table 5). The significance depends not only on the strength of the relationship, but also on data length and autocorrelations of the different variables. Significance levels were determined by a Monte-Carlo simulation experiment. Approximating the autocorrelations of an explaining variable by a first order autoregressive model fitted to observed values of this variable, a time series independent of patient numbers was generated according to the time-varying empirical probability distribution function of the underlying explaining variable. The observed values were then substituted by these simulated data and a time-varying multivariate linear regression was performed. Then the mean squared error for patient numbers obtained from this regression was calculated. These steps were repeated 1000 times, and appropriate quantiles of the empirical probability distribution function of these 1000 simulated mean squared errors yielded the critical value for checking the null-hypothesis of being this explaining variable uncorrelated with patient numbers. The procedure was applied to each explaining variable separately.

The variation of the patient numbers with unit changes in the explanatory variables exhibit annual cycles as the regression coefficients depend on dates within the year. There is evidence that confirms different effects of the explanatory variables in different periods of the year. For instance, the wind speed is inversely proportional to the patient numbers in the pollen season of *Ambrosia* due to the diluting effect of wind. In the pollen-free season, however, the wind speed is mainly in positive association with respiratory problems, especially for the elderly with weak immune systems as repeated exposition to strong winds may aid the inflammation of the respiratory tracts (Strausz, 2003). Furthermore, the optimal conditions for bacteria and viruses affecting respiratory problems are different. While, for example, Mycoplasma bacteria generating pneumonia and other respiratory inflammations favour low relative humidity (pollen season of *Ambrosia*), adenoviruses provoking upper respiratory infections and conjunctivitis are more infectious at a higher relative humidity (pollen-free season) (Strausz, 2003). The minima and maxima of regression coefficients (Table 6) tell us the boundaries of the mean patient number change with a unit change in different explanatory variables.

4. Discussion and conclusions

The analysis of hospital admissions due to respiratory disorders originating in meteorological conditions and air pollutant levels is a very important issue in public health. The present study analyses one of the largest databases on the field. Our study can be considered unique in the sense that it concurrently includes three categories of influencing variables with 5 meteorological, 6 chemical and 2 biological (pollen) parameters. Nevertheless, we know only one study (Kassomenos et al., 2008) that made an attempt to quantify the impact of different chemical pollutants together with meteorological elements on the incidence of respiratory problems. However, pollen has not been studied from this point of view.

A cluster analysis and factor analysis including a special transformation, as well as a time-varying multivariate linear regression were applied in order to examine the role of influencing variables in respiratory hospital admissions and to determine the rank of importance of these variables as well as to quantify their effects. The above two methods are novel procedures in the topic.

For the pollen season of *Ambrosia*, patient numbers are the highest in cluster 3, the most characteristic components of which are the highest and medium levels of *Ambrosia* and the remaining pollen, respectively (Table 2a).

For the pollen-free season, the highest patient numbers for each age category are associated with cluster 4, which is characterised by a high temperature, the highest wind speed and a low air pressure. These values of the meteorological parameters assume a cyclonic weather situation that facilitates the dilution of the pollutant concentrations (CO, PM_{10} and O_3 have their minimum levels of all four clusters) (Table 2b). In contrast to the low levels of the chemical air pollutants, a relatively high temperature is favourable for reproducing bacteria and viruses, while strong winds desiccating the air may encourage an inflammation in the respiratory tracts. Both effects substantially contribute to the highest patient numbers for this cluster.

In the pollen season of *Ambrosia*, a factor analysis including a special transformation revealed that the most important parameters influencing respiratory problems are, in decreasing order, *Ambrosia*, PM_{10}, CO, O_3 and wind speed for adults; furthermore, O_3, wind speed, NO_2, global solar flux and PM_{10} for the elderly, as well as *Ambrosia*, PM_{10}, O_3, CO and wind speed for all age groups. The sign of the relationship between patient numbers and the above variables is negative except for *Ambrosia* in each age group and NO_2 for the elderly group (Table 3a). Most significant variables for this season obtained with time-varying linear regression are O_3 for each age group with its negative effect on patient numbers, as well as temperature, global solar flux, NO and wind speed for both the adults and all age groups, while it is temperature, NO_2, wind speed and PM_{10} for elderly people. The sign of their effects are variable during the season (Table 5). The regression coefficients of the wind speed are rather large and this confirms the importance of this variable (Table 6). In the pollen-free season, a factor analysis including a special transformation showed the following explanatory variables to be most important: NO_2, temperature, PM_{10}, SO_2 and O_3 for adults; O_3, wind speed, NO_2, temperature and NO for elderly people; while it is NO_2, temperature, O_3, PM_{10} and NO for all age groups (Table 3b). The sign of these relationships is now positive except for O_3 and SO_2. The order of importance of explanatory variables obtained by time-varying linear regression is highly variable among age groups, but O_3 is again a key explanatory variable. The role of wind speed is essentially smaller, while relative humidity is more important compared to the pollen season of *Ambrosia*.

In the pollen season of *Ambrosia*, a statistically significant negative association was found between the daily hospital admissions for respiratory causes and CO levels for adults and all age groups, while in the pollen-free season for the elderly. CO has been associated with respiratory conditions in several studies. Freitas et al. (2010) did not find any statistically significant relationship between respiratory hospital admissions and CO, while Fusco et al. (2001) and Kassomenos et al. (2008) confirmed the positive role of CO on respiratory health effects. The impact of a long-lasting, but low-level exposure to CO on respiratory system is therefore still unclear (Tables 3a and 3b).

In the pollen season of *Ambrosia*, we found a significant negative association between the number of respiratory admissions and PM_{10} levels for all three age groups, while in the pollen-free season significant positive associations were observed between these variables for adults and all age groups (Tables 3a and 3b). Katsouyanni et al. (1996) and Fusco et al. (2001) once suggested that gaseous air pollutants, especially CO and NO_2, are more important predictors of acute hospitalisation for respiratory conditions than particulate matter. In contrast, Kassomenos et al. (2008) found that elevated PM_{10} levels indicate a dominant role among the main air pollutants. Fusco et al. (2001) and Alves et al. (2010) found that the association between particulate matter and health conditions was not significant, while others (e.g. Freitas et al., 2010) found that the number of admissions for respiratory causes rose significantly with increased exposure to particulate matter. It should be added that the health impact of particulates is complex as their biological effect can be influenced by the particle size and composition (Alves et al., 2010).

For the pollen season of *Ambrosia*, we found a significant positive association between respiratory admissions and NO_2 levels for the elderly, while for the pollen-free season significant positive associations were found between NO concentrations and respiratory admissions for adults and the elderly, as well as between NO_2 levels and admissions for all three age groups, respectively (Tables 3a and 3b). Although NO and NO_2 are thought to increase the predisposition to respiratory problems, there is still a disparity between the results of different studies concerning the association between NO_x and respiratory causes. For example, high levels of NO_2 partly indicate no significant association with respiratory admissions (Alves et al., 2010) and partly increase the susceptibility for respiratory disorders (Freitas et al., 2010). Other examples of the significant positive impact of NO_2 levels on respiratory causes are given in Fusco et al. (2001) and Kassomenos et al. (2008).

Several studies suggest that high concentrations of O_3 are harmful to human health and they reveal that there is a positive association between O_3 and respiratory hospital admissions (e.g. Kassomenos et al., 2008). In contrast, we observed a statistically significant negative effect of ozone for the three age categories in both seasons (Tables 3a and 3b). This was the most characteristic connection between the number of respiratory disorders and levels of chemical pollutants, which is corroborated by findings of Alves et al. (2010) and Freitas et al. (2010). As there is no evidence that high levels of ozone are really harmful, this association seems paradoxical. The phenomenon called Paradoxical Ozone Association, i.e. POA (Joseph, 2007) could be due to methyl nitrite from some combustion of methyl ethers or esters in engine fuels. Methyl nitrite is known to be highly toxic and closely related alkyl nitrites that are known to induce respiratory sensitivity in humans (Joseph and Weiner, 2002). Since sunlight is essential for ozone formation by photochemical oxidation, a probable explanation for POA is the existence of this nitrite pollutant that is rapidly destroyed by solar radiation. Hence, methyl nitrite is negatively correlated with O_3. Since sunlight has the opposite effect on methyl nitrite one would expect the most acute methyl nitrite effect in winter (Joseph, 2007). A negative association between O_3 levels and respiratory disorders in the summer period (pollen season of *Ambrosia*) can be explained by the fact that our monitoring station is situated at a junction with a high traffic volume (Tables 3a and 3b).

We found a significant negative association between SO_2 levels and respiratory admissions for adults in both seasons and all age groups in the pollen season of *Ambrosia* (Tables 3a and 3b). With the remaining cases, the connection is not significant. Previous findings concerning the role of SO_2 seem inconsistent. This pollutant was not significantly associated with respiratory problems by Katsouyanni et al. (1996) but other studies reported positive relationships (Kassomenos et al., 2008; Alves et al., 2010).

Ambrosia pollen levels have a significant positive association with the number of hospital admissions for all three age categories (Table 3a). Furthermore, total pollen excluding *Ambrosia* is positively associated with respiratory disorders only for adults and all age groups. Similar results can be found e.g. in Carracedo-Martínez et al. (2008). However, factor loadings associated with total pollen excluding *Ambrosia* are much smaller indicating their substantially weaker connection with hospital admissions (Table 3a).

The results obtained for the elderly differ substantially from the remaining age categories for both periods (Tables 3a and 3b) due to social factors mentioned above.

A comparison of the main results of factor analysis (Tables 3a and 3b) with stepwise regression (Table 5) and with regression coefficients (Table 6) clearly shows the difficulty of quantifying the importance of the explanatory variables due to multicollinearity among variables. The most obvious example is *Ambrosia* in its pollen season. It is the most important variable influencing patient numbers by the factor analysis for adults and all age groups, while stepwise regression treats it as only the sixth-eighth most significant parameter. However, Table 6 shows that a rise of 10 pollen grains m^{-3} in the *Ambrosia* level may imply an increase of 28–30 patient numbers (24%) except for elderly people. This is because temperature, global solar flux, relative humidity and wind speed being variables influencing the patient numbers correlate well with *Ambrosia* levels and so the stepwise regression method prefers the aforementioned variables to *Ambrosia*. Another essential circumstance is that when doing a factor analysis, the relationship between two variables is due partly to the similarity of their annual cycles and partly to the correlation between centralised (difference between data and their annual cycle) data. Moreover, a time lag between actual explanatory variables and patient numbers not introduced for factor analysis is allowed for the regression approach. Lastly, this relationship is constant in time for factor analysis, while a time-varying linear regression allows different types of relationships during the year. To sum up, time-varying regression produces a refinement of the overall picture provided by the factor analysis.

As regards O_3 (the most significant variable during the pollination season of *Ambrosia*), a 10 $\mu g\ m^{-3}$ rise results in a relative patient number change from -17% (beginning of the season) to $+11\%$ (end of the season). Temperature and wind speed, weakly significant explanatory variables, may imply a 7–8% increase at the beginning and 5% decrease at the end of the pollination season against a 1 °C temperature rise and up to a 42–45% decrease in patient numbers with a wind speed increase of 1 m s^{-1} (except for elderly people). The number of significant explanatory variables is larger for the pollen-free season. The relative contribution of the influencing variables to the total patient number varies during the year within the following ratios: -1.5% to $+1.5\%$ for global solar flux, 0% to $+8\%$ for O_3, -10% to $+5\%$ for relative humidity, -9% to $+6\%$ for NO_2 and -3% to $+6\%$ for NO for a rise of 10 W m^{-2}, 10 $\mu g\ m^{-3}$, 10%, and 10 $\mu g\ m^{-3}$ of the above-mentioned variables, respectively.

Other reasons add difficulties in determining a direct association between the explanatory variables and the number of respiratory admissions. A major concern is the different effects of specific explanatory variables on the respiratory admissions in the periods examined. A typical example is the inverse role of O_3 (see the Paradoxical Ozone Association discussed above). Other examples are temperature and relative humidity. For instance, in the pollen season of *Ambrosia*, a negative (though non-significant) association between temperature and patient numbers for elderly was found by factor analysis. For the remaining age groups here and for all three age groups in the pollen-free season this association is proportional. Inhaled cold air generates vasoconstriction in the respiratory tract mucosa and suppression of immune responses, which are responsible for an increased susceptibility to respiratory infections (Mourtzoukou and Falagas, 2007). At the same time, an increase in temperature may be associated with an increase in respiratory morbidity due to a proliferation of respiratory viruses (Omer et al., 2008). The relative humidity may display both negative and positive (in our case non-significant) associations with the patient numbers. Repeated exposition to dry air produces inflammation, obstruction and hyper-reactivity of the small respiratory tracts (Strausz, 2003). Furthermore, low temperatures with high relative humidity being favourable for viral respiratory ailments show a strong seasonality with a higher number of disorders in the cold part of the year and minor exposure in the summer (Sloan et al., 2011). At the same time, a rise in mean relative humidity together with an increase in temperature is associated with a rise in respiratory morbidity due to the proliferation of respiratory viruses (Omer et al., 2008). However, the situation is actually more complex as the temperature is governed by the global solar flux in summer, while this is not the case in winter when the temperature depends mainly on the thermal characteristics of air masses affecting the Carpathian Basin (Horváth et al., 2002).

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References

Ågren, C., 2010. Particles killing half a million. Acid News 2, 1–5. http://www.airclim.org/acidnews/2010/AN2-10.php#1. AirClim. Air Pollution & Climate Secretariat, Sweden.
Alves, C.A., Scotto, M.G., Freitas, M.C., 2010. Air pollution and emergency admissions for cardiorespiratory diseases in Lisbon (Portugal). Quimica Nova 33 (2), 337–344.
Andersen, Z.J., Wahlin, P., Raaschou-Nielsen, O., Scheike, T., Loft, S., 2007. Ambient particle source apportionment and daily hospital admissions among children and the elderly in Copenhagen. Journal of Exposure Science and Environmental Epidemiology 17 (7), 625–636.
Carracedo-Martínez, E., Sánchez, C., Taracido, M., Sáez, M., Jato, V., Figueiras, A., 2008. Effect of short-term exposure to air pollution and pollen on medical emergency calls: a case-crossover study in Spain. Allergy 63 (3), 347–353.
Cohen, A.J., Anderson, H.R., Ostro, B., Pandey, K.D., Krzyzanowski, M., Künzli, N., Gutschmidt, K., Pope, A., Romieu, I., Samet, J.M., Smith, K., 2005. The global burden of disease due to outdoor air pollution. Journal of Toxicology and Environmental Health A 68 (13–14), 1301–1307.
D'Amato, G., Liccardi, G., D'Amato, M., Holgate, S., 2005. Environmental risk factors and allergic bronchial asthma. Clinical and Experimental Allergy 35 (9), 1113–1124.
Díaz, J., Linares, C., Tobías, A., 2007. Short-term effects of pollen species on hospital admissions in the city of Madrid in terms of specific causes and age. Aerobiologia 23 (4), 231–238.
Draper, N., Smith, H., 1981. Applied Regression Analysis, second ed. John Wiley & Sons, New York.
Freitas, M.C., Pacheco, A.M.G., Verburg, T.G., Wolterbeek, H.T., 2010. Effect of particulate matter, atmospheric gases, temperature, and humidity on respiratory and circulatory diseases' trends in Lisbon, Portugal. Environmental Monitoring and Assessment 162 (1–4), 113–121.
Fusco, D., Forastiere, F., Michelozzi, P., Spadea, T., Ostro, B., Arca, M., Perucci, C.A., 2001. Air pollution and hospital admissions for respiratory conditions in Rome, Italy. European Respiratory Journal 17, 1143–1150.
Galán, C., Cariñanos, P., García-Mozo, H., Alcázar, P., Domínguez-Vilches, E., 2001. Model for forecasting Olea europaea L. airborne pollen in South-West Andalusia, Spain. International Journal of Biometeorology 45 (2), 59–63.
Horváth, Sz., Makra, L., Motika, G., 2002. An Objective Assessment of the Connection between Meteorological Elements and the Concentrations of the Main Air Pollutants at Szeged, Hungary AMS Fourth Symposium on the Urban Environment and the 12th Joint Conference on the Applications of Air Pollution Meteorology with the Air and Waste Management Association, Norfolk, USA, Proceedings, J4.3, J58–J59.
Jahn, W., Vahle, H., 1968. Die Faktoranalyse und ihre Anwendung. Verlag die Wirtschaft, Berlin, 231 pp. (in German).
Johnson, M.L. (Ed.), 2005. The Cambridge Handbook of Age and Ageing. Cambridge University Press.
Jolliffe, I.T., 1993. Principal component analysis: a beginner's guide—II. Pitfalls, myths and extensions. Weather 48, 246–253.
Joseph, P.M., 2007. Paradoxical ozone associations could be due to methyl nitrite from combustion of methyl ethers or esters in engine fuels. Environment International 33 (8), 1090–1106.
Joseph, P.M., Weiner, M.G., 2002. Visits to physicians after the oxygenation of gasoline in Philadelphia. Archives of Environmental Health 57 (2), 137–154.
Just, J., Nikasinovic, L., Laoudi, Y., Grimfeld, A., 2007. Air pollution and asthma in children. Revue Francaise d'Allergologie et d'Immunologie Clinique 47 (3), 207–213.
Kassomenos, P., Papaloukas, C., Petrakis, M., Karakitsios, S., 2008. Assessment and prediction of short term hospital admissions: the case of Athens, Greece. Atmospheric Environment 42 (30), 7078–7086.
Katsouyanni, K., Zmirou, D., Spix, C., 1996. Short-term effects of urban air pollution on health: a European approach using epidemiologic time series data. The Aphea protocol. Journal of Epidemiology and Community Health 5 (Suppl. 1), S12–S18.
Knight, A., Drouin, M.A., Yang, W.H., Alexander, M., Delcarpio, J., Arnott, W.S., 1991. Clinical-evaluation of the efficacy and safety of noberastine, a new H1 antagonist, in seasonal allergic rhinitis—a placebo-controlled, dose–response study. Journal of Allergy and Clinical Immunology 88 (6), 926–934.
Liu, P.W.G., 2009. Simulation of the daily average PM_{10} concentrations at Ta-Liao with Box-Jenkins time series models and multivariate analysis. Atmospheric Environment 43, 2104–2113.
Mahalanobis, P.C., 1936. On the generalised distance in statistics. Proceedings of the National Institute of Sciences of India 12, 49–55.
Makra, L., Sánta, T., Matyasovszky, I., Damialis, A., Karatzas, K., Bergmann, K.C., Vokou, D., 2010. Airborne pollen in three European cities: detection of atmospheric circulation pathways by applying three-dimensional clustering of backward trajectories. Journal of Geophysical Research-Atmospheres 115, D24220. doi:10.1029/2010JD014743.
Makra, L., Matyasovszky, I., Guba, Z., Karatzas, K., Anttila, P., 2011. Monitoring the long-range transport effects on urban PM_{10} levels using 3D clusters of backward trajectories. Atmospheric Environment 45 (16), 2630–2641.
Mourtzoukou, E.G., Falagas, M.E., 2007. Exposure to cold and respiratory tract infections. International Journal of Tuberculosis and Lung Disease 11 (9), 938–943.
Namdeo, A., Bell, M.C., 2005. Characteristics and health implications of fine and coarse particulates at roadside, urban background and rural sites in UK. Environment International 31, 565–573.
Nascimento, L.F.C., Pereira, L.A.A., Braga, A.L.F., Modolo, M.C.C., Carvalho, J.A., 2006. Effects of air pollution on children's health in a city in Southeastern Brazil. Revista de Saude Publica 40 (1), 77–82.
Omer, S.B., Sutanto, A., Sarwo, H., Linehan, M., Djelantik, I.G.G., Mercer, D., Moniaga, V., Moulton, L.H., Widjaya, A., Muljati, P., Gessner, B.D., Steinhoff, M.C., 2008. Climatic, temporal, and geographic characteristics of respiratory syncytial virus disease in a tropical island population. Epidemiology and Infection 136 (10), 1319–1327.
Orazzo, F., Nespoli, L., Ito, K., Tassinari, D., Giardina, D., Funis, M., Cecchi, A., Trapani, C., Forgeschi, G., Vignini, M., Nosetti, L., Pigna, S., Zanobetti, A., 2009. Air pollution, aeroallergens, and emergency room visits for acute respiratory diseases and gastroenteric disorders among young children in six Italian cities. Environmental Health Perspectives 117 (11), 1780–1785.
Petrányi, G.Y. (Ed.), 2000. Klinikai Immunológia (Clinical Immunology). Medicina Könyvkiadó, Budapest, ISBN 9789632425610 (in Hungarian).
Sloan, C., Moore, M.L., Hartert, T., 2011. Impact of pollution, climate, and sociodemographic factors on spatiotemporal dynamics of seasonal respiratory viruses. CTS-Clinical and Translational Science 4 (1), 48–54.
Strausz, J. (Ed.), 2003. Asthma Bronchiale. Mediszter GlaxoSmithKline, Budapest.
Tukey J.W., 1985. The problem of multiple comparisons (1953) (unpublished manuscript), in: The Collected Works of John W. Tukey. Vol. II: Time Series, pp. 1965–1984. Wadsworth Advanced Books & Software, Monterey, CA.