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Respiratory Health Effects of Air Pollution and Climate Parameters in the Population of Drobeta Turnu-Severin, Romania

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1. Introduction

Air pollution represents a problem for the population's health in Drobeta Turnu-Severin, south-west Romania since 1970, when heavy industry started developing fast. Political openings to the western world created opportunities for great investments and development of industry. The impact of air pollution on health became a major concern, especially when a Heavy Water Plant was built on the northern side of the city. Some acute accidents occurred in this Plant and, in order to prevent them, an efficient and modern monitoring system and special protection perimeters were created. Severe accidents disappeared and the values of H_2S (hydrogen sulphide) were kept at very low levels. The population's reaction to the air pollution risk decreased in time. Instead, there were air pollution sources that emitted for a long period of time particulate matter (PM) at very high levels, and gases. A Paper Plant and numerous Power Plants necessary to sustain the heavy industry became significant sources of air pollution. Coal and oil were the main fuels used. The local authorities decided at that time to pay attention to particles and gases, carefully monitoring their levels in the air. Thus, very high levels of deposited particles and sulphates and not so high levels of total suspended particles (TSP) were registered; the maximal TSP concentration admitted daily being 150 µg/m^3. After 1989, when the Revolution changed the economical system, a great part of the heavy industry was diminished, the industrial sources of air pollution became weaker, and the capacity of monitoring pollution decreased slowly but continuously. A good monitoring system was preserved at the Heavy Water Plant, and an alternative monitoring system was created, to investigate air pollution in the city (Environmental Protection Agency). Unfortunately, there were not created any conditions to establish the levels of PM_{10} (with mass median aerodynamic diameter - MMAD less than 10 µm), coarse particles or $PM_{10\text{-}2.5}$ (MMAD between 10 and 2.5 µm) and fine particles (MMAD of 2.5 µm) [Monn, 2001] yet. Observations of photochemical oxidants were performed only in special situations. Stationary air pollution sources diminished in importance, and traffic became a major one. Second hand cars released high concentrations of gases and particles. However, stationary points fixed near the industries or inside the city remained the main sites to monitor the air pollution in Drobeta Turnu-Severin.

The impact of air pollution on human health, especially on respiratory or cardiovascular systems, is well known. Many studies found significant association between air pollution and health effects (Abbey et al., 1999; Linn et al. 2000; Kelly et al., 2003). Particles proved to have a very complex structure (association between particles and gases was found) and they were measured in various ways. In literature, values between 30% and 90% are given for the share of PM_{10} (aerodynamic diameter less than 10 μm) in TSP (Total Suspended Particles) (Chen & Mao, 1998; Fang et al., 1999). Air pollution with gases was considered as having a direct effect on health or was considered as an associated and confounding factor of air pollution with particles. This complexity and ubiquity of particles made them a major concern on human health.

The HEAPS (Health Effect of Air Pollution on Susceptible Population) study performed in Europe (Health Effect of Air Pollution on Susceptible Population [HEAPS], 2003) and the CESAR approach in Central Eastern Europe (Leonardi et al., 2002) offered and extended an accurate analysis of the effects of air pollution on health.

Respiratory diseases tend to increase in incidence and prevalence, but it was difficult to establish a relationship with air pollution due to the multi-factorial aetiology (Zielinski et al., 1997). People with chronic respiratory diseases especially Chronic Pulmonary Obstructive Diseases (COPD), Chronic Bronchitis (Chronic Bronchitis) and Asthma proved to be a susceptible sub-population exposed to air pollution (Dennis et al., 1996; Lindgren et al., 2009; Kurmi et al., 2010). Many studies analysed the existence of a connection between air pollution exposure and the aggravating or triggering of these chronic respiratory diseases in population (Wong et al., 1999). The young and the elderly were considered an especially vulnerable population (Ritz et al., 2009; Simoni et al., 2003).

Climate factors (temperature, humidity, and wind velocity or wind direction) also have an impact on chronic respiratory diseases. Variations of air temperature and humidity were demonstrated to be associated with asthma (Weiland et al., 2004). Acute accidents of air pollution happened in specific conditions of climate (Choukiker, 2005). Seasonality was demonstrated to be an important confounding factor on the relation air pollution – health. Increased variation of climate factors has a well-known direct influence on human health and on air pollution levels and variation to the same extent. Numerous present day studies demonstrate the variation of climate factors, the tendency of global warming, and its effects on human health and not only (Kowats et al., 1999; Van Vjingaarden & Vincent, 2004).

Keeping in mind all additional factors that determine or aggravate respiratory pathology makes us more aware of the complexity of the relation between air pollution and health.

In the study performed, we aimed at examining long- and short-term respiratory health effects of air pollution with particles and gases in a vulnerable population group, and its modification due to climate parameters (air temperature and air humidity). Their changes in time were studied using a longitudinal retrospective inquiry and two time-series analyses of data, obtained in two successive periods and in the same area.

2. Material and methods

In order to assess the long and short-term effects of air pollution on chronic respiratory diseases and its modification by climate parameters we used the following material and methods.

2.1 Description of population and area under study

Drobeta Turnu-Severin is a historic and industrial city situated in south-western Romania, on the north side of the Danube. Its population is about 100,000 inhabitants (Romanian Statistical Yearbook, 2006). This city used to be highly industrialized between 1970 and 1995, with an economical decrease afterwards. Heavy industry, a large carriage manufacturer, a paper plant, and numerous power plants polluted the environment intensively. The climate is temperate with Mediterranean influences. On the south-western side of the city there is a great accumulation lake built over the Danube and used by the Iron Gates Hydropower Plant. This accumulation lake changes the climate factors of the neighbouring area.

2.2 Material

The material consisted in studies on health, air pollution, and meteorological data.

2.2.1 Health data

Health data were provided by the County Hospital Drobeta Turnu-Severin. As we performed this study using two successive study periods, we used different data. In the first study period (1.01.1990-31.12.1997), we used incidence (number of new cases per 100,000 inhabitants) of COPD (ICD-10, J 44.0, 1, 8), of chronic bronchitis (ICD-10, J 41.0, 1, 8), and of asthma (ICD-10, J 45.0, 1, 8), counted in year of study and age groups, in the exposed population from Drobeta Turnu-Severin (study group), and 2 control groups from other urban and rural areas in Mehedinti County, representing the non-exposed population. Choosing diagnosed patients, we took into consideration the main definition of the three clinical endpoints.

In the second (1.01.2000-31.12.2003) study period, daily hospital admissions according to sex and age groups were recorded in the exposed area of Drobeta Turnu-Severin. During these two study periods, acute infectious respiratory disease cases were provided and used as a confounding factor.

2.2.2 Air pollution data

Air pollution data were provided by the Public Health Direction Mehedinti and comprised the maximum, minimum, and average daily concentration (μg/m^3 air) of total suspended particles (TSP) for the two study-periods. The Environmental Protection Agency (EPA) Drobeta Turnu-Severin provided daily concentrations of SO2 and NO2 only for the period 23.01.2001 - 31.08.2002, included in the second study period. These pollutants were measured at 4 fixed sampling sites inside the city, 1 point being situated in a well known polluted area (near the Paper Plant). The measurements are based on the gravimetric method for TSP and automatic monitoring stations for SO_2 and NO_2.

2.2.3 Meteorological data

Meteorological data were provided by the Romanian Regional Meteorological Centre Craiova, Oltenia and comprised daily maximum, minimum, and average air temperature (Celsius degrees), relative air humidity (%), wind velocity (m/s) and wind direction. The meteorological station is situated in the western part of Drobeta Turnu-Severin. For the analysis of the second study period, we calculated the absolute humidity that gives the amount of water in air, using the relative humidity and the air temperature (Stull, 2000).

2.3 Methods

A statistical analysis of all data gathered in the two study periods was performed.

2.3.1 First study period

A case-control study was performed for the relative risk of air pollution with particles (TSP) on respiratory health. For that purpose, three groups were considered: one population-group exposed to air pollution, and two control groups of non-exposed population, in other urban areas and the rural area of the region. Meteorological factors were considered as confounding factors. Spearman correlation was used to calculate associations of air pollution with TSP - meteorological factors and meteorological factors - respiratory health. Relative risk was measured considering the ratio of the exposed population with a specific chronic respiratory disease to the non-exposed population with a specific chronic respiratory disease. We considered relative risk taking into account an important confounding factor: different age and density distribution of population between urban and rural areas. Spearman's rank correlation coefficient assesses how well an arbitrary monotonic function can describe the relationship between two variables, without making any other assumption about the particular nature of the relationship between variables. The analysis based on rank correlations is insufficient, however, for days having zero hospital admissions due to respiratory ailments.

2.3.2 Second study period

Two time-series analyses were performed in the second study period in order to establish the short-term impact of air pollutants on health, one for TSP and the other considering gases: NO_2 and SO_2.

In the first time-series analysis, the Poisson regression, a method that belongs to the group of generalized linear models (GLM, Freeware R) was used to assess the risk. Missing TSP data were imputed by means of a special Kalman filter, which acts as a low pass for periods longer than 100 days. Absolute humidity was used, although relative humidity was recorded. The values of the current day and the values of the previous day (time lag effect) of the environmental factors were used considering a possible lagged influence on the hospital admissions. The adverse effect of TSP may be possibly modified by air temperature and/or air humidity. In the first time-series analysis, we used 2 approaches.

In the first approach, models of the following type were examined:

$$\ln(\mu_i) \approx \beta_o + \beta_1 dow_i + \beta_2 TSP_i + \beta_3 absHum_i + \beta_4 Tave_i\ ,\ i = 1, 2, \ldots, n\ , \tag{1}$$

with μ_i - the expected number of patients in day i, dow_i - the day of the week and $absHum_i$ the absolute humidity.

In the second modelling approach, the annual variation was included. The variable "day" was introduced to represent the Julian day number and modelled with a spline (s):

$$\ln(\mu_i) \approx \beta_o + \beta_1 dow_i + \beta_2 TSP_i + \beta_3 absHum_i + \beta_4 Tave_i + s(day) \tag{2}$$

Hospital admission data and risk factors follow seasonal variation. Generalized additive models (GAM – Hastie & Tibshirani, 1987) and generalized linear models with natural splines were applied. All models were compared by the criterion AIC and explained deviance (the fraction of the deviance in the data explained by the model).

In the second time-series analysis, we applied the additive models and the "Air Pollution and Health: a European Approach – 2" protocol (APHEA-2) (Atkinson et al., 2001). First, a core model without pollutants was built and, in the second stage, the core model was extended by air pollutants. Seasonal patterns and a dummy variable for the day of the week were always included and daily of mean, minimum and maximum air temperature and relative humidity as meteorological confounders were used as in the second study. Time delayed effects were moved up to seven days. Non-linear effects were modelled by thin plate regression splines with automatic smoothness selection by the mgcv-software-package (Wood, 2006). In the extended model, a PDLMs (Zanobetti et al., 2003) with a polynomial degree of three and a maximal lag effect of 10 were used for evaluation of the association and only for interpolated time-series. A threshold analysis was done for all significant effects of values greater than the threshold value, and all the concentration values below the threshold were set to zero. The modifying effect of air humidity for all observed adverse significant effects, including an interaction term (the product of the lagged effect of absolute humidity with the pollutant effect) in the model was investigated.

3. Results obtained

3.1 First period study results

3.1.1 Descriptive statistics

Chronic respiratory diseases (COPD, chronic bronchitis - CB and asthma) incidence **in the exposed population** (who live in Drobeta Turnu-Severin) was the following (Table 1), with a not so high mean of incidence for the entire first study period.

We registered an increased incidence of COPD in the third, fourth, and seventh years of the first study period, respectively in 1993 (330 cases/$\%_{000}$ inhabitants), 1992 and 1996. Chronic bronchitis incidence was increased in the years 1993 (253 cases/$\%_{000}$ inhabitants) and 1996, and asthma incidence was increased in the same years, and 1997 (with the highest value – 74 cases/$\%_{000}$ inhabitants).

Respiratory diseases	Years of first study								Mean
	1	2	3	4	5	6	7	8	
COPD	61	74	**155**	**330**	181	172	**263**	173	176
CB	43	49	116	**253**	140	114	**185**	81	122
Asthma	10	16	30	**53**	36	46	**59**	**74**	40

Table 1. Distribution of chronic respiratory diseases (COPD, CB and asthma) incidence (cases/$\%_{000}$ inhabitants) in the exposed population (Drobeta Turnu-Severin) during the first study period

Distribution of chronic respiratory diseases incidence according to age groups proved to be very different, with the highest values in the age group 15-64 years for COPD and CB, and in the age's group 1-14 years for asthma (Table 2).

Chronic respiratory diseases (COPD, chronic bronchitis - CB and asthma) incidence **in the 1st control group** (other urban areas) can be seen in Table 3.

Age group distribution of incidence in the 1st control group (other urban areas) can be seen in Table 4.

Respiratory diseases	Incidences on age groups (years)		
	1-14	15-64	>65
COPD	165	**720**	524
CB	6	**532**	445
Asthma	**159**	130	35

Table 2. Distribution of chronic respiratory diseases (COPD, CB and asthma) incidence (cases/$\%_{000}$ inhabitants) in the exposed population (Drobeta Turnu-Severin) depending on age groups, in the first study period

Respiratory diseases	Years of first study								Mean
	1	2	3	4	5	6	7	8	
COPD	188	75	71	14	286	70	299	101	138
CB	122	75	64	14	56	40	257	37	83
Asthma	66	0	7	0	230	30	42	62	54

Table 3. Distribution of chronic respiratory diseases (COPD, CB and asthma) incidences (cases/$\%_{000}$ inhabitants) in the 1st control group (other urban areas) during the first study period

Respiratory diseases	Incidence according to age groups (years)		
	1-14	15-64	>65
COPD	253	351	498
CB	37	168	460
Asthma	216	183	38

Table 4. Distribution of chronic respiratory diseases (COPD, CB and asthma) incidence (cases/$\%_{000}$ inhabitants) in the 1st control group (other urban areas) depending on age group, in the first study period

Chronic respiratory diseases (COPD, chronic bronchitis - CB and asthma) incidence **in the 2nd control group** (rural areas) can be seen in Table 5.

Respiratory diseases	Years of first study								Mean
	1	2	3	4	5	6	7	8	
COPD	139	198	154	116	123	261	174	143	164
CB	92	185	123	78	92	202	134	107	126
Asthma	22	12	21	20	22	29	27	32	23

Table 5. Distribution of chronic respiratory diseases (COPD, CB and asthma) incidence (cases/$\%_{000}$ inhabitants) in the 2nd control group (rural areas) during the first study period

Age groups distribution of incidences in the 2nd control group (rural areas) can be seen in Table 6.

Respiratory diseases	Incidences on age groups (years)		
	1-14	15-64	>65
COPD	63	798	452
CB	37	616	360
Asthma	25	119	42

Table 6. Distribution of chronic respiratory diseases (COPD, CB, and asthma) incidence (cases/$\%_{000}$ inhabitants) in the 2nd control group (rural areas) depending on age group, in the first study period

We noticed large variation of chronic respiratory diseases incidence depending on the area and age group.
In the first study period (1.01.1990-31.12.1997) we registered the following levels of **air pollution with TSP** considering the mean, the maximum and minimum values, measured yearly and for the entire first study period (Table 7).

TSP	Years of first study								Mean	Median	SD
	1	2	3	4	5	6	7	8			
M	189	104	71	129	137	161	174	110	**134**	133	39
Max	440	270	120	80	330	360	330	270	275	300	121
Min	50	40	30	2	40	20	60	30	34	35	17

Table 7. Yearly distribution of TSP values (μg/m^3 air) in the first study period

Season	Years of first study								Mean	Median	Standard deviation
	1	2	3	4	5	6	7	8			
Winter	175	167	71	80	168	161	165	164	143	**164**	42
Spring	171	141	70	105	101	143	162	096	123	123	35
Summer	194	93	-	131	132	167	174	93	123	131	61
Autumn	217	88	-	163	138	176	203	96	135	**150**	71

Table 8. Seasonal distribution of TSP values (μg/m^3 air) in the first study period

The annual means and entire study mean exceeds the maximum admitted concentration in United States for TSP (75 μg/m^3 air) or maximum admitted concentration for PM10 in Europe (40 μg/m^3 air).
Air pollution with particles (TSP) was also analysed depending on season, for each year and for entire first study period (Table 8).
The season means and medians calculated in each year of the first study and for the total study period indicate frequent surpassing of the annual maximum admitted concentration

for TSP and even daily maximum admitted concentration of TSP (150 µg/m^3 air) in winter and autumn. A possible explanation of increased air pollution in these seasons could be the use of heat sources based on burning fuel.
Climate factors measured yearly and for the entire first study period (Table 9) revealed high relative humidity in the area (over 70%), temperature higher than 10 Celsius degrees and low wind velocity (1.97 m/s). Wind direction was North/North-West.

Climate factors	Years of first study								Mean
	1	2	3	4	5	6	7	8	
T (^{o}C)	12.50	10.65	12.50	11.78	12.92	11.53	11.46	11.24	**11.82**
Hu (%)	75.66	80.58	72.50	74.25	75.50	74.33	74.25	71.00	**74.75**
w.v (m/s)	2.00	1.96	2.19	2.22	1.95	1.81	1.85	1.85	**1.97**

Table 9. Yearly mean values of climate factors in the first study period

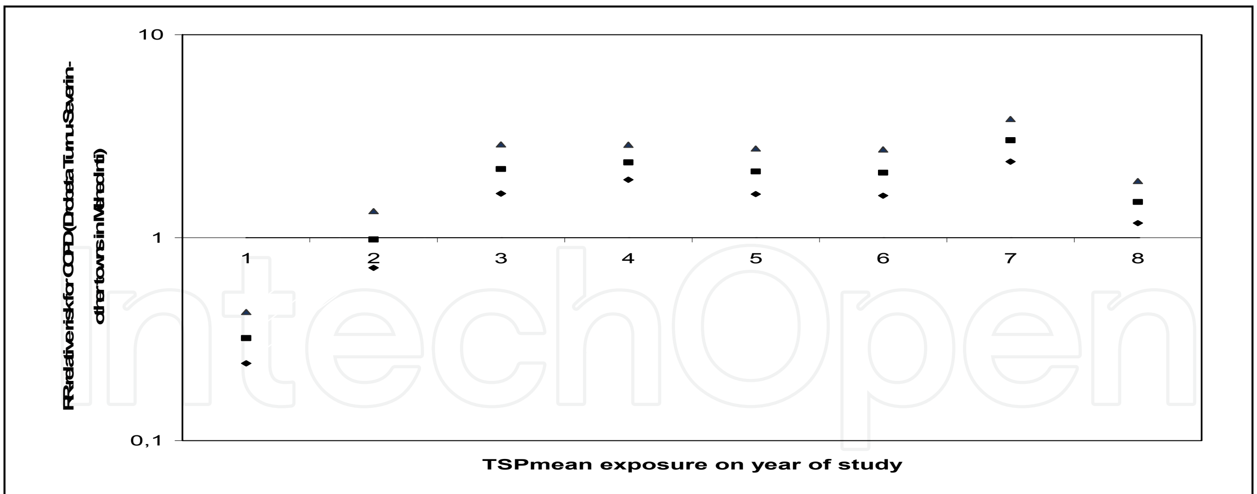
The seasonal evolution of climate factors (Table 10) indicates that the highest value of temperature was registered in summer (21.63 ^{0}C) and the lowest in winter (3.03 ^{0}C), the highest relative humidity in autumn (82.29%) and the lowest in summer (68.83%), the highest wind velocity in winter (2.22 m/s) and the lowest in autumn (1.65 m/s). We noticed that in winter there was low temperature, high relative humidity (78.24%) and increased wind velocity. The investigated area is situated near the Danube and not far from an accumulation lake built on the Danube: the Iron Gates Hydropower plant, fact that explains increased air humidity in all seasons (over 65%).

Climate factors	Seasons				Mean
	Winter	Spring	Summer	Autumn	
T (^{o}C)	**3.03**	16.59	**21.63**	6.20	11.82
Hu (%)	**78.24**	70.49	**68.83**	**82.29**	**74.75**
w.v (m/s)	**2.22**	2.06	**2.03**	1.65	1.97

Table 10. Seasonal mean values of climate factors in the first study period

3.1.2 Relative risk

A significant relative risk of TSP was found for COPD in exposed population in comparison with the 1st control group (other urban areas) and the 2nd control group (rural areas, see Figure 1).
The relative risk of TSP on chronic respiratory diseases in the exposed population measured in comparison with the non-exposed populations (1st and 2nd control groups) presented as main confounding factors different age group distribution and density of population between urban and rural areas. We excluded the differences between the two control groups comparing them. We considered the registered differences when we measured the relative risk for exposed population considering the 2nd control group (rural area). The registered values for the measured relative risk of TSP on chronic respiratory diseases (COPD, CB, asthma) can be seen in Tables 11 and 12.



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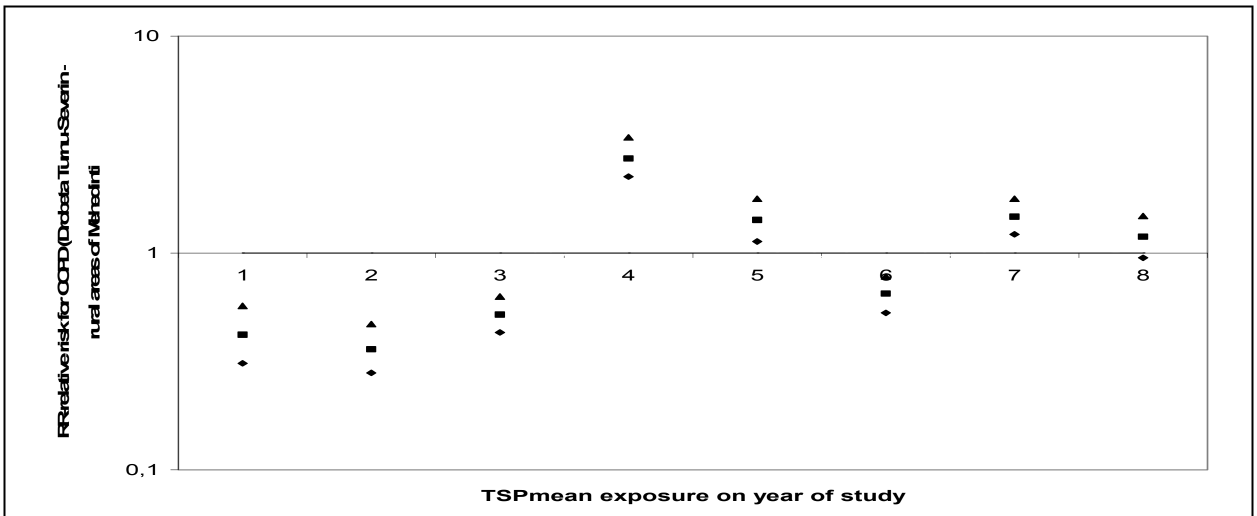

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Fig. 1. Relative risk (RR) values for COPD in the population exposed to TSP related to the 1st control group - other urban areas (A) and the 2nd control group - rural area (B)

Chronic respiratory diseases	Relative risk according to age group		
	1-14 years	15-64 years	> 65 years
COPD (RR) CI	0.65 0.53-0.79	**2.05** 1.8-2.32	**1.05** 0.93-1.18
CB (RR) CI	0.16 0.07-0.37	**3.16** 2.66-3.76	0.96 0.85-1.09
Asthma (RR) CI	0.73 0.6-0.9	0.71 0.56-0.88	0.92 0.58-1.45

Confidence interval Nurminen-Miettinen

Table 11. Relative risk of TSP on chronic respiratory diseases considering age groups and 1st control group (other urban areas)

There is an observable increase in the relative risk of TSP on **chronic bronchitis** in the age group **15-64 years** and on **COPD** in the age groups **16-64 years** and **over 65 years**, and in the exposed population as compared to non-exposed population from other urban areas.

Chronic respiratory diseases	Relative risk according to age groups		
	1-14 years	15-64 years	> 65 years
COPD (RR) CI	0.65 0.64-0.66	**2.08** 2.02-2.12	**2.94** 2.94-2.95
CB (RR) CI	0.15 0.1-0.23	**3.18** 3.03-3.44	0.96 0.96-0.97
Asthma (RR) CI	0.73 0.73-0.74	0.71 0.69-0.72	0.89 0.75-1.04

Confidence interval Nurminen-Miettinen

Table 12. Relative risk of TSP on chronic respiratory diseases considering age group and 2nd control group (rural areas) with exclusion of confounding factors between urban and rural areas

Comparing the exposed with the non-exposed population from rural areas, after excluding the differences urban – rural, we noticed the same increased risk of TSP on **chronic bronchitis** in the age group **15-64 years** and on **COPD** in the age groups over **65 years** and **15-64 years.**

3.1.3 Spearman correlation of variables

We applied the following Spearman correlations: chronic respiratory diseases - air pollution with TSP, air pollution with TSP - climate factors, and chronic respiratory diseases – climate factors. Significant results were obtained only for the Spearman correlation asthma – relative air humidity (Table 13).

		Asthma incidence 15-64 years
Relative air humidity (%)	rho	**- 0850****
CI	p value	0.007

**Correlation is significant at 0.01 level (2-tailed)

Table 13. Spearman correlation (rho) asthma incidence – relative air humidity

This result indicates a protective effect of elevated air humidity on asthma, especially in the age group 15-64 years.

3.2 Second period study results

3.2.1 Descriptive statistics

Descriptive analysis performed in the second study period (1.01.2000-31.12.2003) can be seen in Table 14. The values for all variables were available for 1461 days, but for TSP only for 820 days. The patients were classified according to sex.

	Minimum	First quartile	Average	Median	Third quartile	Maximum	Standard Error
COPDm (cases)	0	0	0.91	1	1	7	1.17
COPDf	0	0	0.43	0	1	4	0.70
CBm	0	0	0.21	0	0	4	0.48
CBf	0	0	0.16	0	0	3	0.41
Asthma m	0	0	0.24	0	0	4	0.52
Asthma f	0	0	0.46	0	1	5	0.80
TSP (µg/m^{3}air)	18	75	111.42	105	142	289	47.39
T min	-14	1	7.78	8.2	14.7	25.8	8.22
Tave (^{0}C)	-9.2	5.1	12.78	12.8	20.8	31.7	9.42
Tmax	-6	9.6	18.61	19.4	27.6	42.6	10.9
Rel. hu (%)	29	58	67.96	68	79	100	14.55
w.v. (m/s)	0	3	5.64	5	8	16	3.18

m-male, f-female

Table 14. Descriptive analysis in the second study period

We realised that the day of the week (dow) is an important confounding factor (Figure 2).

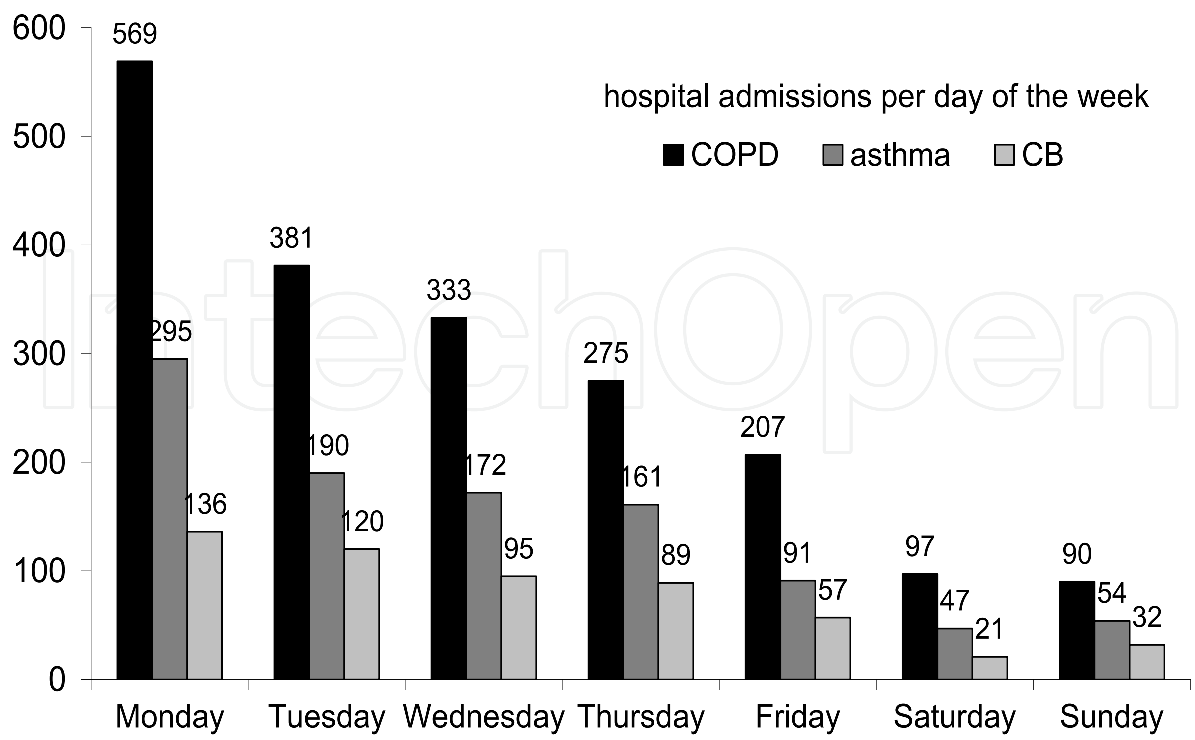

Fig. 2. Number of patients with chronic respiratory diseases for each day of the week

The number of patients is maximal on Monday and minimal on Sunday. One explanation could be the admission of patients on Monday and the discharge from hospital on Friday. The average period of hospitalisation of a patient is 5 days.

3.2.2 Risk evaluation - first time-series analysis results

COPD (Chronic Obstructive Pulmonary Diseases)

In the **first approach** (Table 15), a protective effect of absolute humidity on COPD (abs Hum coeff. = - 0.0347) was noticed. The protective effect of air humidity was modified by TSP (abs Hum: TSP = - 0.0011). The relative risk of this modification was rather small with low statistical significance (RR = exp(0.001) ~1.001, p=0.008).

Variable 1	Coefficient	s.e.	P value
Intercept	1.1870	0.0640	<0.0001
Tuesday	-0.4496	0.0670	<0.0001
Wednesday	-0.5425	0.0693	<0.0001
Thursday	-0.7590	0.0743	<0.0001
Friday	-0.9780	0.0803	<0.0001
Saturday	-1.7410	0.1084	<0.0001
Sunday	-1.8440	0.1134	<0.0001
absHum	**-0.0347**	0.0088	<0.0001
absHum:TSP	0.0011	0.0006	0.0833

Table 15. Results of the first model approach for COPD

This change of the humidity effect suggested a high influence of the season on respiratory diseases (especially COPD), the annual trend, and temperature being involved.

The second approach

The yearly variation and the effect of temperature were modelled with a spline. The absolute humidity has a significant adverse effect on the age group 18-44 years. A positive difference between absolute humidity of the current and preceding day increases the risk in three age groups (Table 16).

The absolute humidity varies direct proportionally with the number of admitted patients in the hospital. A significant influence of TSP was not observed. The spline function of seasonality has local minima in summer and local maxima in winter. If the function becomes 0, there is no influence on the expected number of hospital admissions. The function has positive values in winter and this indicates an increased risk on hospital admissions, the negative one is in summer and the risk is reduced.

Variable 1	Coefficient	s.e.	P value	RR
Intercept	-2.9672	0.2133	<0.0001	-
Tuesday	-0.4002	0.0480	<0.0001	0.6702
Wednesday	-0.5390	0.0500	<0.0001	0.5833
Thursday	-0.7336	0.0533	<0.0001	0.4802
Friday	-1.0021	0.0588	<0.0001	0.3671
Saturday	-1.7597	0.0795	<0.0001	0.1721
Sunday	-1.8520	0.0821	<0.0001	0.1569
absHum 18-44	**0.0600**	0.0229	0.0088	**1.0619**
Dif absHum 18-44	**0.1352**	0.0682	0.0473	**1.1448**
Dif absHum 45-64	**0.0645**	0.0221	0.0035	**1.0667**
Dif absHum 65-74	**0.0653**	0.0262	0.0126	**1.0678**

Table 16. Results of the second model approach for COPD

Chronic Bronchitis

In the **first approach,** we did not find a significant effect of TSP on chronic bronchitis. The absolute humidity has a protective effect at very high value (more than 6g/m^3 air).
In the **second approach,** we found a TSP risk on chronic bronchitis and a protective effect of absolute humidity on the same disease (Table 17).

Variable 1	Coefficient	s.e.	P value	RR
Intercept	-1.3895	0.1754	<0.0001	-
Tuesday	-0.1534	0.0643	0.0170	0.8578
Wednesday	-0.3731	0.0684	<0.0001	0.6886
Thursday	-0.4016	0.0698	<0.0001	0.6692
Friday	-0.8759	0.0806	<0.0001	0.4165
Saturday	-1.8801	0.1196	<0.0001	0.1526
Sunday	-1.4482	0.1002	<0.0001	0.2350
TSP lag 1 18-44	**0.0071**	0.0015	<0.0001	**1.0071**
absHum	**-0.0648**	0.0171	<0.0001	**0.9372**

Table 17. Results of second model approach for chronic bronchitis

Asthma

In the **first approach** (Table 18), TSP had an adverse effect on asthma.

Variable 1	Coefficient	s.e.	P value
Intercept	0.3169	0.1053	0.0026
Tuesday	-0.3226	0.0911	0.0004
Wednesday	-0.5215	0.0972	<0.0001
Thursday	-0.5972	0.0993	<0.0001
Friday	-1.1167	0.1194	<0.0001
Saturday	-1.7127	0.1507	<0.0001
Sunday	-1.7060	0.1507	<0.0001
TSP	**0.0167**	0.00836	0.0453
absHum:TSP	**-0.0022**	0.00073	0.0023

Table 18. Results of first model approach for asthma

Variable 1	Coefficient	s.e.	P value	RR
Intercept	-1.9800	0.1986	<0.0001	-
Tuesday	-0.4420	0.0562	<0.0001	0.6427
Wednesday	-0.5402	0.0578	<0.0001	0.5826
Thursday	-0.6037	0.0592	<0.0001	0.5468
Friday	-1.1739	0.0722	<0.0001	0.3092
Saturday	-1.8348	0.0945	<0.0001	0.1596
Sunday	-1.6989	0.0890	<0.0001	0.1829
TSP lag 1 0-17	**0.0068**	0.0014	<0.0001	1.0068
absHum 45-65	**-0.0341**	0.0149	0.0222	0.9665
absHum >66	**-0.0463**	0.0227	0.0412	0.9548

Table 19. Results of second model approach for asthma

Absolute humidity modified this effect and was protective. The relative risk of this modification was exp(-0.0022) ~0.008, for a fixed TSP value and a rise of 1 g water/m^3.
In the **second approach,** TSP has an adverse effect on asthma in age group 0-17 years. Absolute humidity has a protective effect on asthma in older people (Table 19).

3.2.3 Descriptive statistics – considering gases

TSP**,** gases (NO_2 and SO_2)**,** number of cases of chronic respiratory diseases and climate factors were analysed during the time interval 23.01.2001 - 31.08.2002 (Table 20) in the second study period.

	Missing (%)	Cases/ year	Mean	Median	Minim	Maxim	Standard Deviation
COPD (cases)	0	511	1.4	1	0	10	1.55
CB (cases)	0	160	0.44	0	0	3	0.71
Asthma (cases)	0	282	0.77	0	0	7	1.08
TSP (µg/m^{3}air)	42	-	123.4	122	22	289	44.12
SO2 (µg/m^{3}air)	16	-	4.68	4,6	1.7	10.4	1.55
NO2 (µg/m^{3}air)	16	-	11.8	11	1	33.5	3.84
T high (^{0}C)	0	-	20.23	21.5	-4	39.5	10.08
Tmean (^{0}C)	0	-	14.06	14.9	-8.2	31.7	9.03
Tlow (^{0}C)	0	-	8.81	9.6	-13.2	25.8	8.19
Rel. hu (%)	0	-	67.76	68	29	98	13.93
AbsHum (g/m^3)	0	-	8.79	8.23	2.05	19.2	4.03

Table 20. Descriptive analysis during the interval 23.01.2001 - 31.08.2002 in the second study period

Hospital admissions showed a weekly and a seasonal cycle. The maximum of average hospital admissions occurred on Monday and the minimum on Sunday (Figure 3) during this time interval, this result being similar with the situation of the second study period. Moreover, in this time interval we studied the seasonal variation. The maximum average monthly admission was in January and the minimum in August for COPD and asthma, and September for chronic bronchitis (Figure 4).

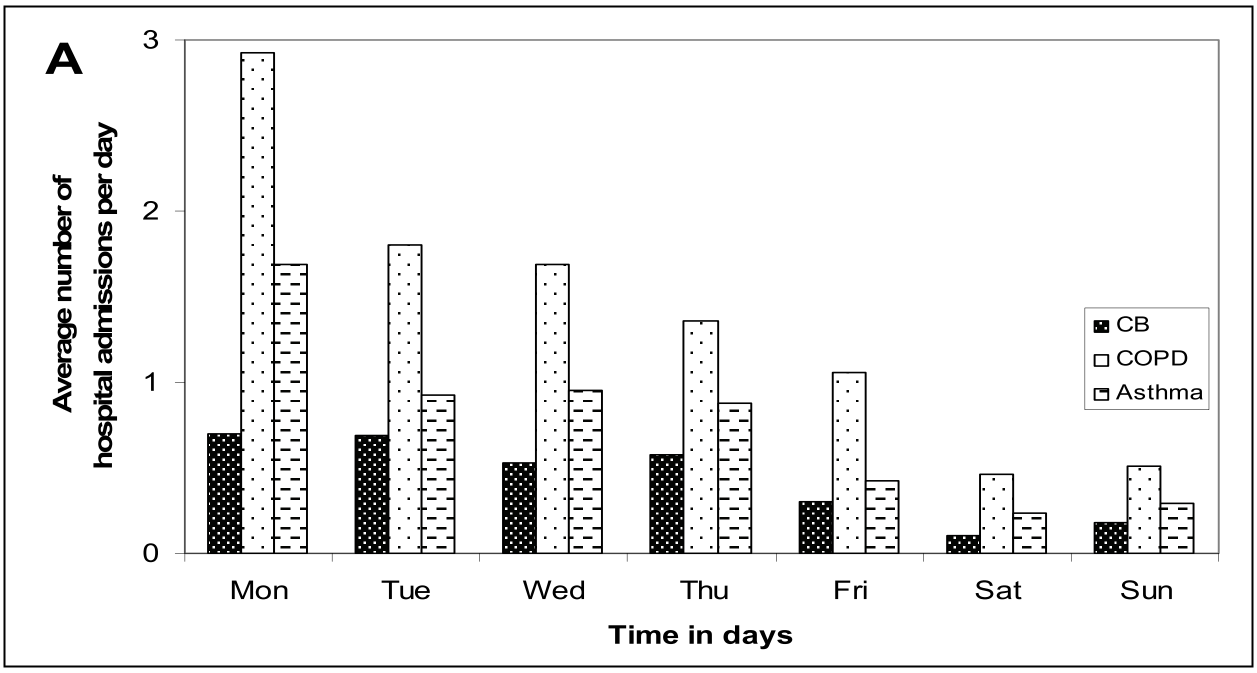

Fig. 3. The weekly cycle of daily hospital admission

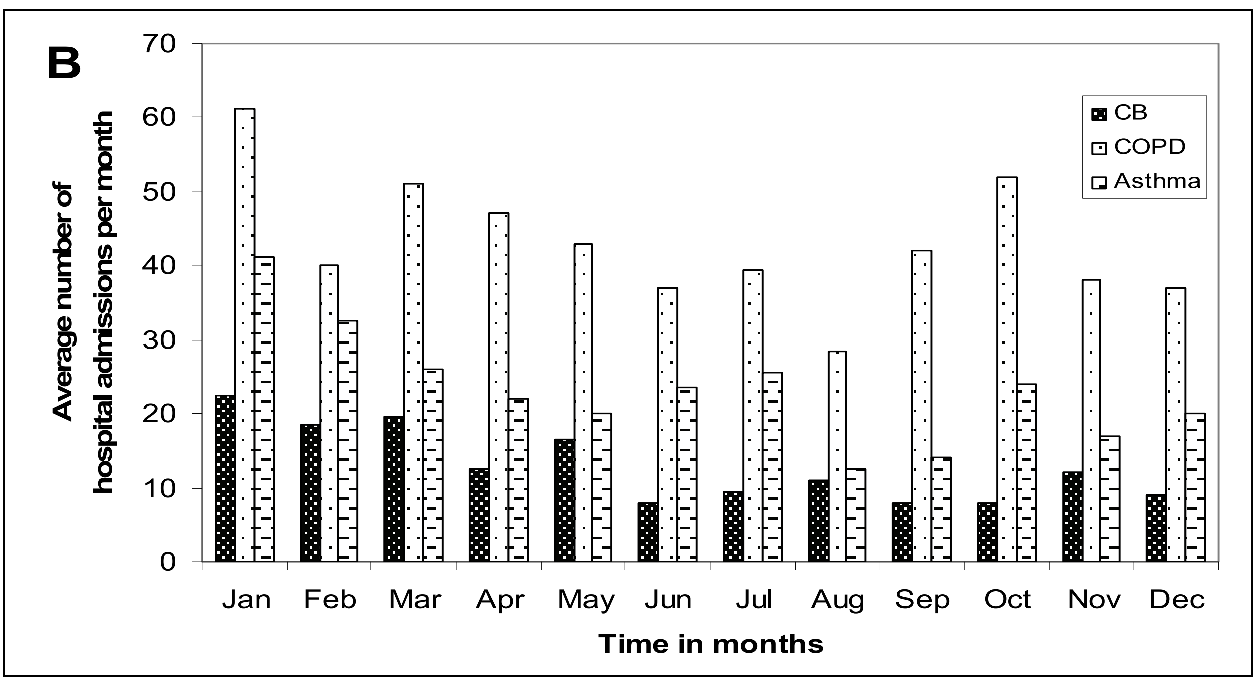

Fig. 4. The seasonal cycle of monthly hospital admission

3.2.4 Risk evaluation - second time-series analysis results considering gases

Effects of TSP on chronic bronchitis

Significant results of applying this model were found only for chronic bronchitis.
The core model for chronic bronchitis consisted of factor variables for workdays/holidays and nonlinear effects of time, of temperature with a lag of 6 days, of change of humidity over the last three days.

For the single lag model, an increase in hospital admissions for chronic bronchitis of $_{0.3}3.3_{6.4}$% with a lag of 1 day and $_{0.12}2.8_{5.7}$% with a lag of 4 day for an elevation of TSP with 10 μg/m³ air was registered (Figure 5). Displaying the estimates with confidence intervals as a triple of percentiles $_{2.5}50.0_{97.5}$ is recommended (Louis & Zeger, 2009). The effects were slightly smaller for the time-series with missing values. For PDLMs the association was significant with an increase of $_{0.01}1.6_{3.1}$% in hospital admissions for chronic bronchitis for an elevation of 10 μg/m³ TSP with a lag of three days.
A threshold analysis revealed there was no level, below which no effect of TSP was present for both lagged TSP effect levels (Figure 6).

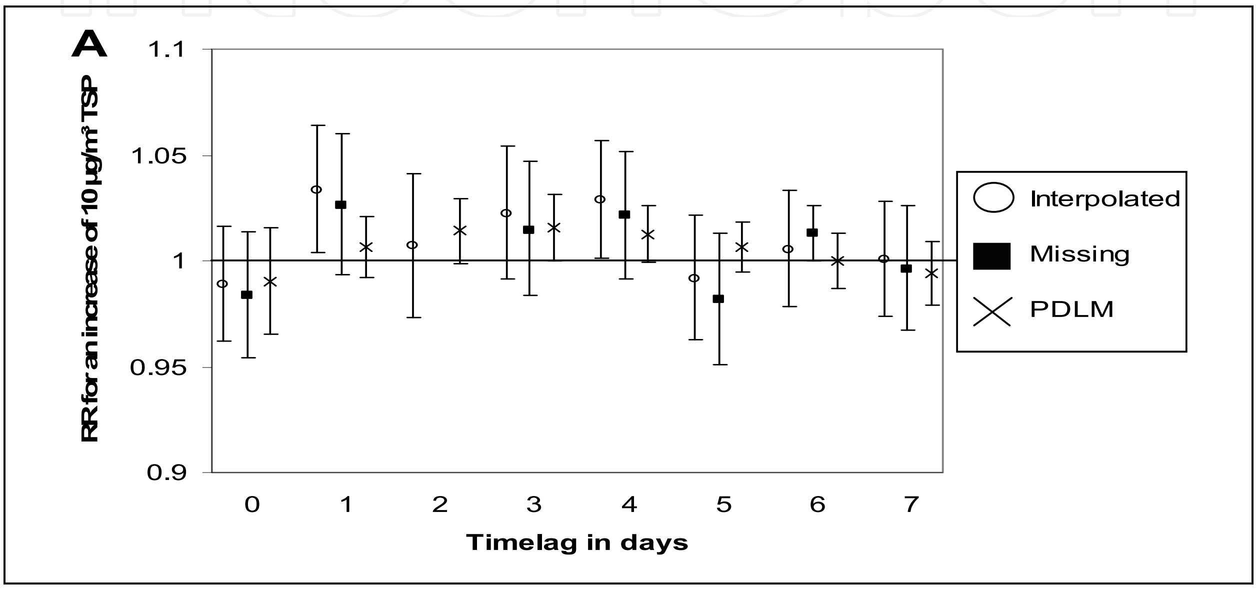

Fig. 5. Relative risk (CI 95%) for an increase of TSP with 10 μg/m³ air in single lag model with original and interpolated data and PDLMs with interpolated data

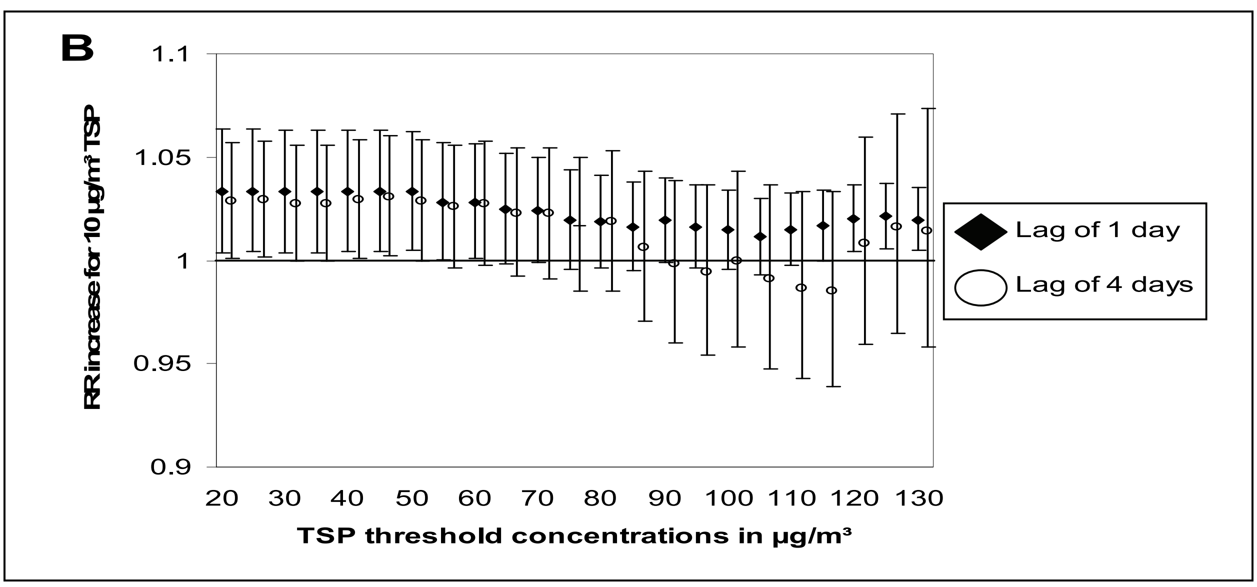

Fig. 6. Relative risk (CI 95%) for an increase of TSP with 10 μg/m³ air using the threshold of 1 day and 4 days

When we investigated subgroups depending on gender the effect was significant, the number of male hospital admissions increased to $_{1.6}4.09_{7.22}$ % with a lag of 4 days and the female hospital admissions increased to $_{0.434}4.44_{8.60}$% with a lag of one day TSP exposure (Figure 7).
The modification of the significant effects of TSP by absolute humidity was analysed adding an interaction term between the two variables (Leitte et al., 2009). For low concentration of TSP (less than 60 µg/m³), increased humidity reduces the risk of hospital admission due to chronic bronchitis (Table 21). Concentrations of TSP of more than 60 µg/m³ cancel the antagonistic effect.

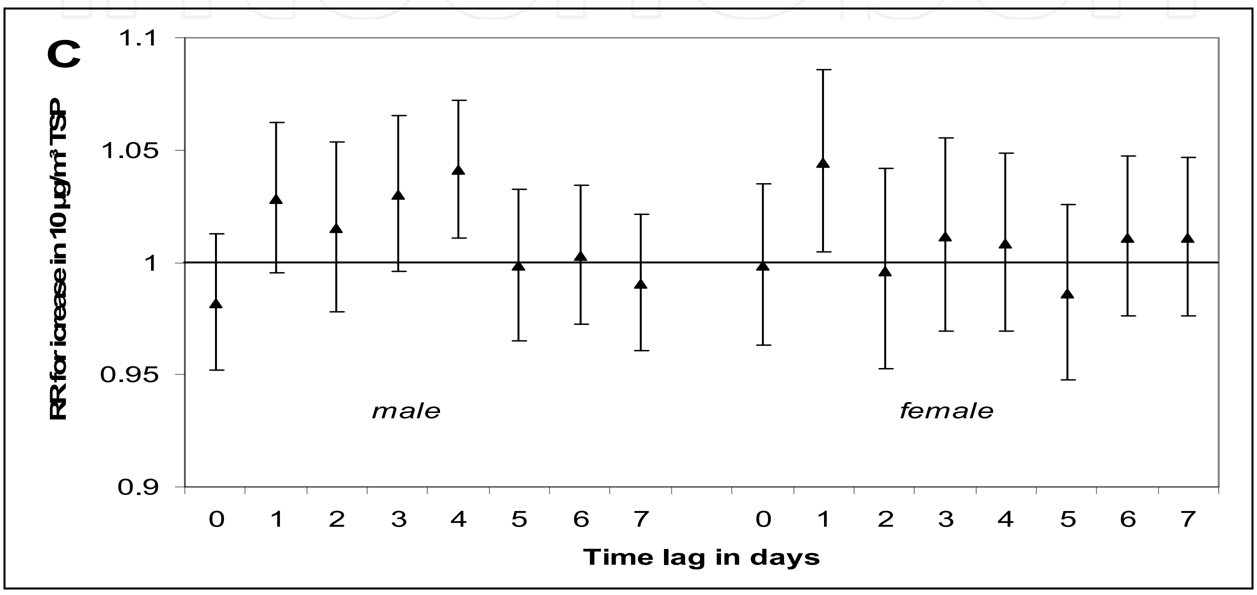

Fig. 7. Relative risk (CI 95%) for an increase of TSP with 10 µg/m³ air for gender subgroups

	Change of hospital admissions for chronic bronchitis (%)	p-value
TSP with lag of 1 day	6.97	0.002
Modification by absolute humidity, moving the average on the same and last day	-0.41	0.05
TSP with a lag of 4 days	6.02	0.009
Modification by absolute humidity with a lag of 4 days	-0.37	0.092

Table 21. Modifying effect of TSP (increment of 10 µg/m³) by absolute humidity (increment of 1 g/ m³) on hospital admissions for chronic bronchitis

Effects of SO_2 on chronic bronchitis

We observed a significant increase of 15% and 9% hospital admissions due to chronic bronchitis for an increment of 1 µg/m³ SO_2 with a delay of two or seven days when we considered a time-series with interpolated values.

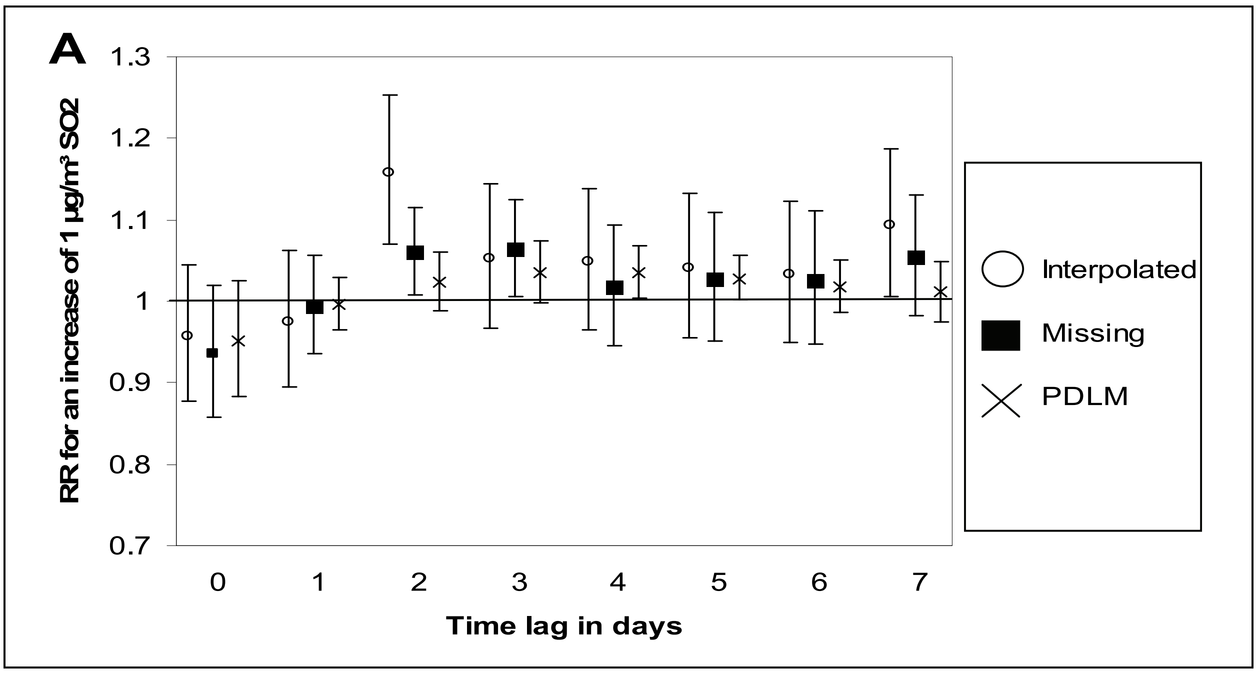

Fig. 8. Relative risk (RR – 95% CI) of an increase of 1 µg/m³ SO_2 (single lag model with interpolated, original data and PDLMs for interpolated data) for hospital admissions for chronic bronchitis and different time lags

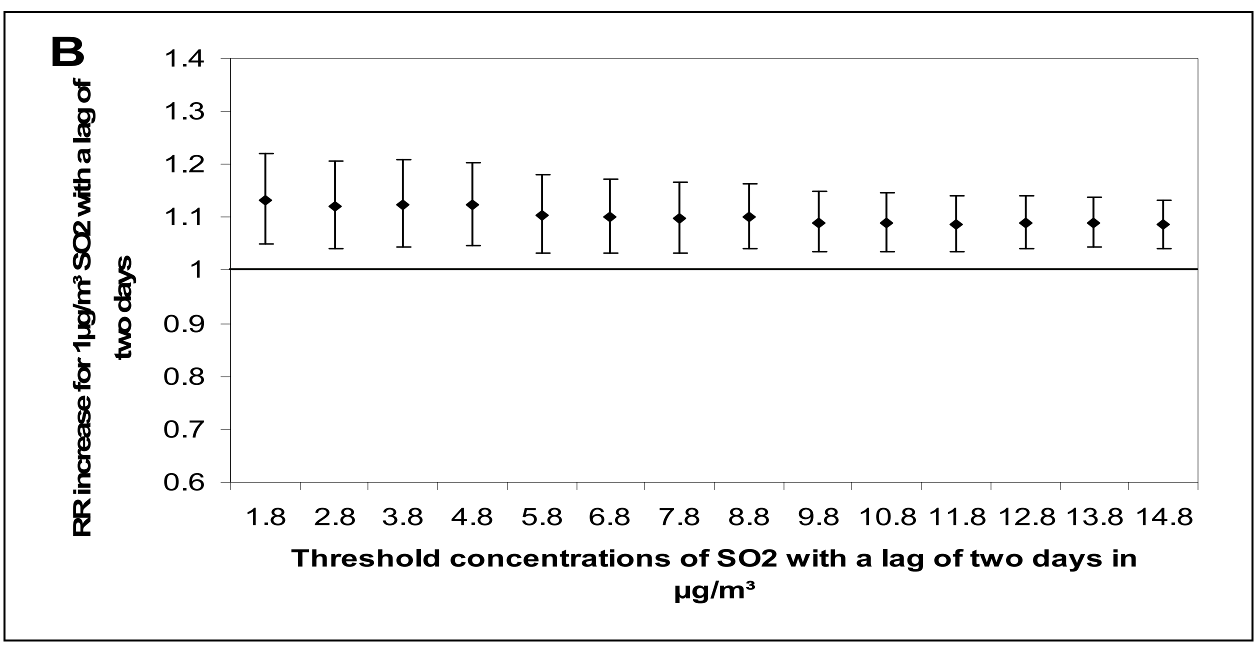

Fig. 9. Relative risk (RR – 95% CI) of an increase of 1 µg/m³ SO_2 for hospital admissions for chronic bronchitis using thresholds for a lag effect of two days

When we considered a time-series with missing values the association was reduced to a ${}_{1}6_{12}\%$ and ${}_{1}6_{13}\%$ increase of hospital admissions for chronic bronchitis for the same increment with 1 µg/m³ SO_2 with a lag of two and three days. For PDLMs an increment of 1 µg/m³ SO_2 determined an increase of ${}_{0.40}3.6_{6.81}\%$ and ${}_{0.11}2.8_{5.58}\%$ hospital admissions for chronic bronchitis (Figure 8).

There was no threshold, under which no adverse effect of SO_2 on chronic bronchitis existed (Figure 9).
All significant single pollutant effects were included in a multi pollutant model. In this model the effect of SO_2 with a delay of two days remained significant (RR=13% for a increase of 1 μg/m^3 SO_2) and the effect of TSP with a delay of four days became weakly significant (RR=2.5% for an increase of 10 μg/m^3 TSP, p=0.09). Adverse influences of TSP, SO_2, NO_2 on total respiratory admissions, COPD and asthma, and of NO_2 on chronic bronchitis were found, but without statistical significance.

4. Discussion

Air pollution with particulate matter and gases is well known in south-eastern Europe, as it is reported in numerous studies performed in this area. High levels of black smoke were found in Serbia (Milutinović et al., 2009), increasing concentrations of SO_2 were noticed in Prague (Duben, 1988). In Greece, a study that investigated the gas concentration evolution along the year indicated the powerful influence of the season on the air pollutant levels, being minimal in summer and maximal in winter (Papaioannou et al., 2010). A "Convention on Long-Range Trans-boundary Air Pollution (CLRTAP)" was opened for signature in 1979 and came into force in 1983. This Convention has now 51 parties and priority activities include review and possible revision of its most recent protocols with special focus on Eastern Europe and South Eastern Europe.
In our study, we found an increased level of air pollution with particles (134 μg/m^3 air in the first study period and 111.42 μg/m^3 air or 123.45 μg/m^3 air in the second study period) and gases (4.68 μg SO_2/m^3 air and 11.8 μg NO_2/m^3 air - in the second study period – 1 year), which surpasses the maximal admitted concentrations of TSP for the United States (75 μg/m^3 air) and the maximal admitted concentration of PM10 specified by the European Commission (40 μg/m^3 air corresponding to 57 - 133 μg/m^3 air TSP) and are lower than the maximal admitted concentration of gases (SO_2 - 20 μg/m^3 air and NO_2 – 40 μg/m^3 air) (2008/50/EC).
Climate change and climate factors influence both air pollution and human health (Mc Michael et al., 2008) and is also a largely investigated topic. Climate change was not found to have high impact on the distribution of the deposition, nor did regional air pollution (in the form of sulphate aerosols) (Alcamo et al., 2002). In our study, we also did not find an association between climatic factors and air pollutants. Variations in meteorological parameters were evident between the two periods under study: average temperature increased from 11.82^{0}C to 12.78^{0}C; average relative air humidity decreased from 74.5% to 67.96% and wind velocity from 1.97m/s to 5.64 m/s. These results are similar with other results from literature (Kovats et al., 1999; Wjingaarden & Vincent, 1995). In literature an association climate factors – respiratory health was found, especially between air temperature, humidity and asthma (Weiland et al., 2004). In our study, the first period, we identified a protective effect of air relative humidity on asthma (Spearman correlation), and in the second period of study first time-series analysis was revealed a protective effect of absolute air humidity on chronic bronchitis and asthma. Analysing the evolution of results between the two approaches of the first time-series analysis, we noticed seasonality as a powerful confounding factor, this being considered only in the second approach. The greatest confusion created by seasonality was present especially in the case of COPD (chronic obstructive pulmonary diseases) when humidity transformed itself from a

protective factor on COPD into an adverse one, between the two approaches. The seasonal influence on COPD admission in hospital was modelled by a spline function of seasonality with local minima in summer and local maxima in winter.

Respiratory health appeared as being frequently impacted by air pollution. Many epidemiological studies described the long term effects of air pollutants on the population with chronic respiratory diseases, such as the impact on symptoms investigated in Switzerland (Zemp et al., 1999), symptoms which occurred in children exposed to air pollution in the Netherlands (Brauer et al., 2002; Abbey et al., 1995), or the impact of air pollution on other chronic diseases as carcinoma (Chen & Goldberg, 2009). Respiratory health evolution was difficult to analyse between the two study periods, because of different approaches. Only a qualitative comparison between the two study periods was possible. A similar approach was considered necessary in China, where short-term effects were studied (numerous time-series analyses). Long-term effects of air pollutants on health are less studied so far (Kan et al., 2009).

Case-control studies proved to be useful for the investigation of long-term effects of air pollution on health, investigating especially the respiratory symptoms (Burr et al., 2004). Some authors analysed the study performed in South-Eastern Europe, exposing the bad management of resources in this area and the great levels of air pollution (especially sulphur dioxide) (Jedrychowski, 1995). The case-control study performed in the first period of study offered results about long-term effects of air pollution with TSP on new cases of hospitalisation for chronic respiratory diseases. A similar study on hospital attendance due to respiratory diseases as a result of air pollution effects was made in Turin, Italy (Migliareti et al., 2007). A significant result of the first study period was the impact of outdoor air pollution on COPD at different ages, in the active population and the elderly. Similar results were obtained analysing some epidemiological studies performed in developing and industrialized countries (Viegi et al., 2006).

Short-term effects of air pollution on respiratory health were frequently approached by researchers in the area, revealing the weak effect of particulate matter and the stronger effect of sulphur dioxide on respiratory health in Paris (Dab et al., 1996), the effect of fine particulate matter on cardiovascular disease and carcinoma (Laden et al., 2006), or the association of elderly population exposed to higher risk of mortality (Gouvea & Fletcher, 2000). The two time-series analyses performed in the second study period made possible an evaluation of the short-term risk of the TSP (both analysis) and SO2 and NO2 (the second analysis) on respiratory health.

The impact of air pollution with particles on chronic bronchitis was showed in literature (Herbarth et al., 2001). Although, initially, air pollution was investigated for high levels of exposure, there is also a tendency to investigate air pollution effects on low levels (Pope et al., 1995). This approach is also supported by the results of our study, we did not find a threshold under which no effects occur for TSP and sulphur dioxide. Although the study designs were different, the impact of TSP on chronic bronchitis at a specific age (15-64 years in the first study period, 18-44 years in the second study period) was evident. In our study, active population seems to be more exposed to outdoor air pollution. Similar results were found in literature, a significant number of cases of chronic bronchitis being found in adults by a study in Barcelona (Kunzli & Perez, 2007).

In the second time-series analysis of the second study period, significant results were found only for chronic bronchitis due to air pollution with TSP and gases (SO_2) using an extension

of the time delayed effect from 1 day (in the first time-series analysis) to 7 days, PDLMs for interpolated series and an interaction term in order to observe the modifying effect of absolute humidity. Seasonality as a confounding factor was always considered.
For a single lag model, the hospital admissions for chronic bronchitis increased with 3.3% for a lag of 1 day and with 2.8% for a lag of 4 days due to an increase of **TSP** by 10 $\mu g/m^3$ air (interpolated series). The effect was lower for the series with missing values and more realistic for the series with PDLMs. When we included the TSP effect on chronic bronchitis in the multi pollutant model, the relative risk remained weakly significant (RR=2.5% for an increase of 10 $\mu g/m^3$ TSP, p=0.09), only for a lag of 4 days. The **modifying effect of absolute humidity** on the effect of **TSP on chronic bronchitis** was present and statistically significant for a time lag of 2 days and TSP concentrations lower than 60 $\mu g/m^3$ air, with a decrease of 0.41% admitted cases (p=0.05) to an increase in 1 g/m^3 air absolute humidity. The differences between health effects according to sex were described in literature (Kenedy et al., 2007). In our study, the effect for hospital admissions was more delayed and slightly lower for male admissions, but these differences between sexes are not statistically significant.
The single lag model also registered an increase of chronic bronchitis with 15% for a lag of 2 days and 9% for a lag of 7 days, for an enhancing with 1 $\mu g/m^3$ air **SO_2**, considering interpolated series. When we considered the series with PDLMs the increase of chronic bronchitis admissions was lower than 3.6% and 2.8% for a lag of 2 and 3 days, respectively, of SO_2 increment with 1 $\mu g/m^3$ air. The series with PDLMs indicated more realistic results, similar with the data found in literature (Wilson et al., 2005). When we included SO_2 effect on chronic bronchitis on multi pollutant model, the relative risk remained statistically significant (RR=13% for a increase of 1 $\mu g/m^3$ SO_2), only for a lag of 2 days. In this multi pollutant model there was no correlation between SO_2 and TSP and multicolinearity should be negligible. In our study, we did not find a threshold for TSP, neither for SO_2. This result indicates the necessity of considering low levels of air pollution as a factor with possible respiratory health impact, too. Air pollution in Drobeta Turnu-Severin, Romania, represents a risk factor for respiratory health of the exposed population, especially because of high levels of SO_2 and TSP in outdoor air. Increased air humidity of this area is a protective factor for people with chronic bronchitis and asthma.

5. Conclusion

Outdoor air pollution is a reality in Drobeta Turnu-Severin Romania, beginning during the communist period and continuing after the revolution. High levels of TSP and sulphates registered in the eighth decade of the past century diminished in time, but not in a sufficient amount to avoid its impact on health. The monitoring system of air pollution has a tendency to diminish its potential. The Danube and the accumulation lake "Iron Gates" change the climate factors and the ecosystem in the area. Humidity is higher than in other areas of the region and it affects the relationship air pollution - respiratory health, acting as a protective factor on specific chronic respiratory diseases as chronic bronchitis and asthma. The different study designs (case-study for the first study – 8 years and time-series analysis for the second successive study – 4 years) indicated similar results regarding the TSP effect on chronic bronchitis in active population. A short period of time extended as procedures time-series analysis (1 year) included in the second study indicated similar results for TSP and SO_2 on chronic bronchitis, also revealing the delayed effects of 4 days or 2 days respectively for both pollutants. Air humidity appeared as modifying the effect of TSP on chronic bronchitis for a delayed effect of 2 days, revealing itself as being protective. A limitation of the study results consists regards the action of TSP and humidity on COPD. In the first study period, the long-term exposure of the population to TSP acted as a trigger factor for COPD, in active and elderly population. In the second study period, TSP and humidity seemed to have an antagonistic effect on COPD. Moreover, seasonality determined a specific evolution of this disease during the year. A powerful impact of seasonality referred to the action of TSP on asthma, the differences of results between the two approaches of the second study period, in the first time-series analysis being huge. New studies are necessary in order to clarify these aspects.

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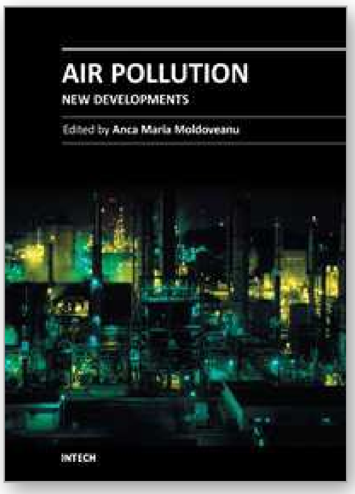

Air Pollution - New Developments
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Today, an important issue is environmental pollution, especially air pollution. Due to pollutants present in air, human health as well as animal health and vegetation may suffer. The book can be divided in two parts. The first half presents how the environmental modifications induced by air pollution can have an impact on human health by inducing modifications in different organs and systems and leading to human pathology. This part also presents how environmental modifications induced by air pollution can influence human health during pregnancy. The second half of the book presents the influence of environmental pollution on animal health and vegetation and how this impact can be assessed (the use of the micronucleus tests on TRADESCANTIA to evaluate the genotoxic effects of air pollution, the use of transplanted lichen PSEUDEVERNIA FURFURACEA for biomonitoring the presence of heavy metals, the monitoring of epiphytic lichen biodiversity to detect environmental quality and air pollution, etc). The book is recommended to professionals interested in health and environmental issues.

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