Respiratory health effects of air pollution with particles and modification due to climate parameters in an exposed population: long and short term study

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Abstract — Many studies have consistently found associations between respiratory health effects and various types of airborne particles. The goal of this paper is to examine the respiratory health effects of airborne particles exposure and modification due to climate parameters using a case-control retrospective investigation and a time series analysis of data obtained in the same area (Drobeta Turnu-Severin) and two time periods: study- part 1 (1.01.1990-31.12.1997) and study- part 2 (1.01.2000-31.12.2003). We investigated the association between chronic obstructive pulmonary diseases (COPD), chronic bronchitis and asthma and total suspended particles (TSP) in Study- Part 1 (case and control data representing long-term effects) and in Study- Part 2 (daily hospital admission data as short-term effects which are analyzed with generalized additive models). In Study-Part 1, TSP was identified as a risk factor for COPD in the exposed population, with relative humidity as a protective factor against asthma. Population age's distribution and urban environment resulted as confounding factors. In Study- Part 2, adverse effects of TSP were revealed for chronic bronchitis. Seasons and days of the weeks resulted as important confounding factors. A weak adverse effect of TSP upon chronic bronchitis incidence and hospitalization (disease exacerbation) was identified, at a specific age, 15-64 years, in both study periods. As a conclusion, in the investigated area (Drobeta Turnu-Severin), the respiratory health effects of particles are substantial and modified by climate parameters and seasonality.

Keywords—climate parameters**,** respiratory health effects, risk evaluation, total suspended particles.

I. Introduction

AIR pollution with particulate matter (PM) has been found to be a major threat to human health. Health impact is caused by concentrations of PM in ambient air to PM standards, the size of the particles and spatial planning [1].

The elevated concentrations of air pollution are associated with changes in inflammation and coagulation in patients with chronic pulmonary diseases [2]. Values between 30% - 90% are given for the share of PM10 (mass median aerodynamic diameter less than 10μm) in TSP (Total Suspended Particles) [3, 4]. Over urban areas, coarse particles (PM10 and PM10–2.5) are generally less uniformly distributed than finer particles (PM2.5 and PM1) [5].

Currently, climate change has been observed, with changes in temperature and relative humidity [6, 7]. The climate influences health, such as the inverse relation of the prevalence of asthma symptoms to altitude and the annual variation in ambient temperature and relative humidity [8]. Another influence of climate is on air pollution, as can be seen in the literature. Thus, the relative humidity and dew point showed considerable variation with PM2.5, and wind speed showed inverse variation with PM2.5 [9].

Ineffective clearance of the PM from the airways could cause particle retention in lung tissues, resulting in a chronic, low-grade inflammatory response that may be pathogenetically important in both the exacerbation and the progression of lung disease [10]. Respiratory health is frequently analysed using exacerbations of chronic respiratory diseases. This allows quantifying the health effects of changing high exposure levels to airborne pollutants. COPD, chronic bronchitis and asthma are susceptible to aggravate under elevated air pollution levels [11, 12, 13].

In Europe, effects of particulate air pollution and other pollutants on respiratory health were analysed in the HEAPSS study [14]. A complex approach, exploring the association of air pollutants and human health in the Central Eastern European (CEE) region was the Central European Study of Air Quality and Respiratory Health (CESAR) [15]. Another study, completed in Serbia, indicated that current levels of ambient black smoke have an effect on health in susceptible persons [16]. People in the investigated area are estimated to be exposed to high levels of air pollution in urban areas mainly due to heavy industries and to a lack of adequate technology for emission control [17, 18].

The present study has two aims: firstly, to quantify the respiratory health risks of TSP for selected diseases in a less extensively studied region of Central Eastern Europe and,

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secondly, to analyze the implication of climate to health effects caused by air pollution. We demonstrate that environmental epidemiology has to pay increasing attention to the climate change and to climate modification of the impact of air pollution on public health.

II. Material and Methods

A. Description of study population and area

The investigated area (Drobeta Turnu-Severin), a city situated close to the river Danube, has around 100,000 inhabitants [19]. This city is a highly industrialized area with heavy industries and the largest wagon manufacturer. The main sources of air pollution are a paper plant, situated in the south-eastern zone, different power stations and other heavy industry. Less polluted areas of the region, represented by the other towns (4 towns – Baia de Arama, Strehaia, Vinju Mare, Orsova – with a total population of around 100,000 inhabitants) and a rural area with a total population around 100,000 inhabitants, were used for comparison.

The region (Mehedinti County) is a historical, well - established community, with similar socio-economic level, educational level, habits and risk behaviours (tobacco smoke). A part of the population in the exposed area resulted after migration from rural areas in the middle of the twentieth century. After 1996, migration of the population has changed with movement of population from the urban into the rural area [20]. There is a significant difference in population density and age distribution between urban and rural areas of the region. Thus, there was the following age distribution in the year 1992: 0-14 years (25% urban and 19% rural), 15-60 years (65% urban and 53% rural) and >60 years (10% urban and 28% rural) [20]. Climate conditions are specific to the temperate zone with Mediterranean influences.

B. Data

Meteorological data were provided by the Regional Meteorological Centre and comprise daily minimum, maximum and mean air temperatures in ^{0}C, relative air humidity in %, wind velocity in m/s and wind direction. In the exposed region (Drobeta Turnu-Severin), the meteorological station is located in the western part of the city. The absolute humidity gives the amount of water in air and was calculated by air temperature and relative humidity [21].

Air pollution data were provided by the Public Health Authority Mehedinti and are represented by the concentrations of TSP, which were measured gravimetrically at a paper plant near the city (a well- known source of air pollution) and in 3 inner urban sites. The paper plant presented the greatest values of air pollution. There is a protection perimeter around the paper plant and the residential area is not very close. The 3 inner urban areas overloaded also the maximal admitted concentration, and increased concentrations were found in the city centre. Atmospheric dispersion of air pollutants from specific industrial sources could be investigated through atmospheric dispersion modelling [22]. In Drobeta Turnu-Severin was observed a tendency of increase air pollution in the inner city.

Misclassification of exposure related to the use of central sites may be larger for ultrafine particles than for PM10 and PM2.5. For all that, an underestimation of health effect is possible [23]. Personal monitoring studies have generally found very poor correlations between personal exposures and outdoor concentrations. A first reason is the different type of study, and the second is that most studies have been done on healthy persons, who may be much more active and therefore generate more particles than sick persons [24]. In other study, the mean personal PM10 exposure was higher than outdoor concentrations in all seasons, and personal exposure varied less than outdoor PM10 level from one season to another [25]. Atmospheric emissions from industrial sources influence the air quality (outdoor and indoor) in a city [26]. In our study, it was difficult to establish a level of personal exposure because of its retrospective type.

Health data were provided by the County Hospital Mehedinti, which is located in the northern part of the city (Drobeta Turnu-Severin). This hospital is the only one in the city for respiratory emergencies and 100% of hospital admissions were handled by it. We considered distinctly the admission from the exposed area and the admission from the region. All investigated patients were admitted to the County Hospital and they came from the entire region. The place of residence was registered for each patient.

In two sub-studies, we considered two subsequent time periods. For identifying both health impacts of exposure, increasing short-term, and effects of long-term high exposure levels, we included data of two differently designed study parts. For Study- Part 1, we received only the incidence number of new cases reported by hospital/100,000 inhabitants. For the period 1.01.1990-31.12.1997, the incidence was analyzed on age groups, due to asthma ICD-10: J45.0, 1, 8 (International Classification of diseases – 10), chronic bronchitis (ICD-10: J41.0, 1, 8) and chronic obstructive pulmonary disease (COPD) (ICD – 10: J44.0, 1, 8). Diagnosis of the investigated diseases was realized considering the main definitions of the three clinical endpoints.

Daily hospital admissions provided in terms of gender and age groups, due to asthma, chronic bronchitis and COPD were recorded during the Study- Part 2 (1.01.2000-31.12.2003). Total respiratory admissions are computed by the sum of three clinical endpoints and a time series of infectious respiratory diseases (influenza cases) was provided and used as a confounding variable.

C. Methods

We investigated the association between incidences of chronic obstructive pulmonary disease (COPD), chronic bronchitis and asthma and the mass concentration of TSP. The relative risks (RR) were evaluated in both study periods. In Study- Part 1, the RR was calculated based on cases and controls and, therefore, is relative to the considered control group. For the daily hospital admission data in Study- Part 2,

generalized additive models were used, with control of time patterns and evaluation of weather effects. In Study- Part 2, the calculated risk is relative to days of low air pollution. Because of the different design of both parts, a direct quantitative comparison between the RR values is not possible. This is a consequence of the limited availability of data. Only a qualitative comparison is made therefore.

Study- Part 1. The method was a case-control retrospective investigation conducted in the region during the period 01.01.1990-31.12.1997.

We calculated descriptive statistics and the Spearman correlation between variables of the same categories (air pollution, meteorological factors or respiratory health). Relative risk (RR) was assessed for asthma, chronic bronchitis and COPD, by help of three control-groups (lots) of population: first lot – 100,000 inhabitants from urban and rural areas of the region, second lot – 100,000 inhabitants from other towns in the region, and third – 100,000 inhabitants from the rural area of the region. The exposed population consisted of 100,000 inhabitants from the studied area (entire population of the exposed city). The unexposed population consisted in 200,000 inhabitants (the entire population of other urban areas and rural area of the region).

Then, we counted relative risk for three age groups of population in the exposed and control areas, considering different age distribution in rural and urban as confounding factor. We also counted relative risk urban-rural, in this way taking in account unknown factors which create differences between urban and rural respiratory effects. At the end of this analysis we counted a second relative risk exposed area – the rural area of the region, extracting the relative risk urban-rural. Thus, first RR exposed city area – rural area was considered attributable risk that contain the unknown factors of urban-rural difference.

The cases number was expressed as incidence for exposed and unexposed (urban and rural) areas. We counted the incidence as:

Incidence = number of new cases of a chronic respiratory disease x 100,000/(number of population on 1st July during current year) (1)

Study- Part 2. A Poisson regression was applied as a method that belongs to the group of generalized linear models - GLM, freeware R [27]. To quantify the total amount of water inhaled during breathing, absolute humidity was used. This is the content of water vapors in the air, measured in g/m³. Missing TSP data (641 from 1461) were introduced by means of a special Kalman filter, which acts as a low pass for periods longer than 100 days [28]. In literature there are also models which can predict the concentrations of air pollutants [29]. Besides the value of the current day of an environmental factor, also the value of the previous days could have an influence on the hospital admissions of the current day (time-lag effect). In addition to the basic assumption that TSP may have a damaging effect, the effect modification by air temperature and air humidity has been studied.

In Study- Part 2, models of the following type were examined:

$$\ln(\mu_i) \approx \beta_o + \beta_1 dow_i + \beta_2 TSP_i + \beta_3 absHum_i + \beta_4 Tmean_i + s(day) \quad (2)$$

The annual variation was accounted for by a spline of the variable "*day*", numbering the days of the year. The variable "*dow"* represents the day of the week.

Both the hospital admission data and the risk factors follow seasonal fluctuations. Therefore, generalized additive models - GAM [30] and generalized linear models with natural splines were applied. A GAM is a generalized linear model [31], with linear predictors involving smooth functions of co-variates for nonlinear effects. Age and gender groups of the patients permit a classification into subgroups, and a specific sensitivity analysis was possible. All models were compared by the Akaike criteria - AIC [32] and explained deviance (R^2) criteria, which is the fraction of deviance in the data that is explained by the model.

III. Results

A. Results of Study- Part 1

The yearly mean concentration of TSP for the Study- Part 1 period (134 μg/m³ air, see Table I) surpasses the maximal concentration of TSP admitted in the United States (75 μg/m³ air) [33] and the maximum admitted concentration of PM10, specified by the European Commission (40 μg/m³ air corresponding to 57 – 133 μg/m³ TSP) [34].

Table I Descriptive parameters of TSP (μg/m³ air) in the exposed city area – Study- Part 1.

Year of study	Season				TSP mean	TSP max	TSP min
	Q1	Q2	Q3	Q4			
1990	175	171	194	217	189	440	50
1991	167	141	93	88	104	270	40
1992	71	70	na	na	71	120	30
1993	80	105	131	163	129	80	2
1994	168	101	132	138	137	330	40
1995	161	143	167	176	161	360	20
1996	165	162	174	203	174	330	60
1997	164	96	93	96	110	270	30
Mean	**143**	123	123	**135**	**134**	275	34

Q1–winter; Q2–spring; Q3–summer; Q4–autumn, na- data not available

Distribution of air pollutants by seasons (winter: January-March; spring: April-June; summer: July-September; autumn: October-December) indicates a high air pollution, with TSP in winter and autumn (143 and 135 μg/m³ air, respectively). The values of TSP in winter are not correlated (Spearman) with the values of the other three seasons and with TSPmean, therefore this result suggests an independent evolution (Table II).

Table II Spearman correlations coefficients (rho) between TSP values in the exposed city area.

		TSPm	TSP winter	TSP autumn
TSPmax	rho	**0.807(*)**	0.675	0.699
	p-value	0.015	0.066	0.054
TSPm	rho	1.000	0.548	**0.976(**)**
	p-value	.	0.160	<0.001
TSPmin	rho	0.446	**0.747(*)**	0.337
	p-value	0.268	0.033	0.414
TSP winter	rho	0.548	1.000	0.429
	p-value	0.160	.	0.289
TSP spring	rho	**0.833(*)**	0.548	**0.857(**)**
	p-value	0.010	0.160	0.007
TSPsummer	rho	**0.994(**)**	0.575	**0.970(**)**
	p-value	<0.001	0.136	<0.001
TSPautumn	rho	**0.976(**)**	0.429	1.000
	p-value	<0.001	0.289	.

**Correlation is significant at the 0.01 level (2-tailed);
*Correlation is significant at the 0.05 level (2-tailed)

Table III Climate factors (means) – Study- Part 1.

	Temperature ^{0}C	Relative Humidity (%)	Wind Velocity (m/s)
1990	12.5	75.66	2
1991	10.65	80.58	1.96
1992	12.5	72.5	2.19
1993	11.78	74.25	**2.22**
1994	12.92	75.5	1.95
1995	11.53	74.33	1.81
1996	11.46	74.25	1.85
1997	11.24	71	1.85
Q1	3.5	**78.24**	2.22
Q2	16.59	70.49	**2.6**
Q3	**21.63**	68.83	2.3
Q4	6.2	82.29	1.65
Mean	11.82	74.75	1.97

Q1–winter; Q2–spring; Q3–summer; Q4–autumn

The **climate factors** comprise a high relative air humidity in this area (>70%), a temperature (11.8^{0}C) greater than 10^{0}C, specific for temperate zones, and a small wind velocity (1.97 m/s). The highest average temperature (21.63 ^{0}C) is registered in summer (July-September), the highest relative humidity (82.29%) in autumn (October-December), and the highest wind velocity (2.22m/s) in winter (January-March) (Table III). The predominant wind direction is N/NW.

The evolution of the relative humidity registered in autumn seems to be independent on the other three seasons. The same evolution seems to happen to the lowest value of relative air humidity registered in summer, which is also independent on the other three seasons. We observed only a weak correlation between the mean of relative air humidity - relative air humidity in winter (rho=0.719, p=0.045) and the mean of relative air humidity – relative air humidity in spring (rho=0.826, p=0.011). No significant Spearman correlation was found between TSP and climate factors.

Table IV a Incidences (cases per %000 inhabitants) of COPD, chronic bronchitis (CB) and asthma, expressed annual, by age groups and in Study- Part 1 period (yearly mean), in the exposed area.

	COPD	CB	Asthma
1990	61	43	10
1991	74	49	16
1992	155	116	30
1993	330	253	53
1994	181	140	36
1995	172	114	46
1996	263	185	59
1997	173	81	74
1-14 years	165	6	159
15-64 years	720	532	130
>65 years	524	445	35
Yearly mean	**173**	**122**	**40**

Table IV b Incidences (cases per %000 inhabitants) of COPD, chronic bronchitis (CB) and asthma, expressed annual, by age groups and in the Study- Part 1 period (yearly mean), in another urban area control lot.

	COPD	CB	Asthma
1990	188	122	66
1991	75	75	0
1992	71	64	7
1993	14	14	0
1994	286	56	230
1995	70	40	30
1996	299	257	42
1997	101	37	62
1-14 years	253	37	216
15-64 years	351	168	183
>65 years	498	460	38
Yearly mean	138	83	54

Table IV c Incidences (cases per %000 inhabitants) of COPD, chronic bronchitis (CB) and asthma, expressed annual, by age groups and in Study- Part 1 period (yearly mean), in the rural area control lot.

	COPD	CB	Asthma
1990	139	92	22
1991	198	185	12
1992	154	123	21
1993	116	78	20
1994	123	92	22
1995	261	202	29
1996	174	134	27
1997	143	107	32
1-14 years	63	37	25
15-64 years	798	616	119
>65 years	452	360	42
Yearly mean	164	126	23

The greatest number of **respiratory** incidence was registered for COPD (Table IV a) with a yearly mean of 176 cases/100,000 inhabitants, followed by chronic bronchitis (122 cases/100,000 inhabitants) and asthma (40 cases/100,000 inhabitants) in the exposed city area.

In the control areas the incidence of control lots from other urban areas (Table IV b) and from the rural area (Table IV c) was registered. There is a similar means of COPD (176 and 164 cases, respectively) and of chronic bronchitis (122 and 126 cases, respectively) between exposed and rural areas. Age

distribution and density of population in control lots could be a confounding factor. There is a difference of age groups distribution between urban and rural areas. Thus, the number of people over 60 years is of 2.8 folds greater in the rural area than in the urban one, and the number of people aged 15-60 and 0-14 years is of 1.2 and 1.3 folds, respectively, greater in the urban area than in the rural one.

There are similar mean values for asthma (40 and 54 cases, respectively) between exposed and other urban areas in the region, with the same age distribution of population. In the age group 15-64 years, we observe a great number of COPD cases (720 cases) in the exposed area, in comparison with other urban areas (351 cases). The same difference is observed for chronic bronchitis in the same age group between exposed and other urban areas (Tables IV a and IV b). An increased number of asthma (mean) cases can be seen in the control urban area.

For the respiratory incidence, we found significant Spearman correlations (Table V). These results suggest an association between COPD in the exposed city area and chronic bronchitis, but no relation with asthma cases was found.

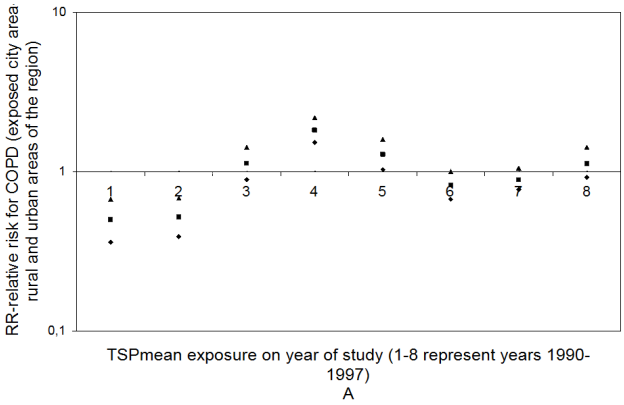
There was a powerful negative Spearman correlation between relative air humidity and asthma in the age group 15-64 years (rho=-0.850, P=0.007) in the exposed city area (Table VI). These results suggest a possible protective effect of air humidity on asthma.

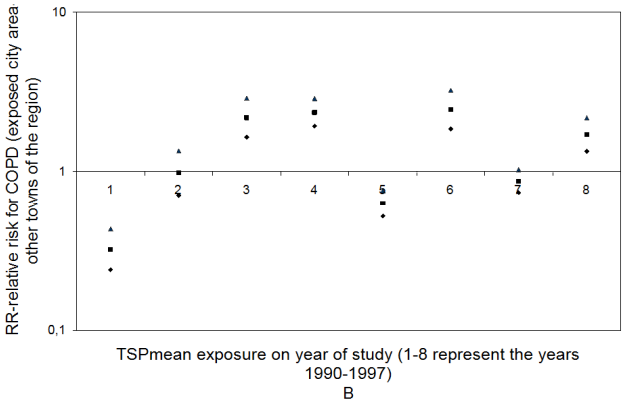
Relative risk (RR, Table VII) was significant only for COPD (Fig. 1A). When we counted RR, using the control lot from the other urban areas and from the rural area of the region, we obtained an increased relative risk (Fig. 1B) and a similar risk (Fig. 1C), respectively.

COPD in the exposed city area can be related with high concentrations of TSP registered in 1993, the highest relative risk being visible in that year and in the years 1992, 1995, 1997, when we used population from other urban areas as control lot (Fig. 1B).

TSP is not identified as a risk factor in chronic bronchitis along the first study period, although chronic bronchitis correlates with COPD. If we consider distribution on age groups, TSP has an increased risk on chronic bronchitis (CB) in age groups: 15-64 years (CB exposed city area - other towns of the region, RR = 3.16, CI 95% 2.66-3.76) and >65 years (CB exposed city area - rural areas of the region, RR = 3.46, CI 95% 3.01-3.96) (Table VIII). Other confounding factors could exist.

TSP is not identified along the first study period as a risk factor for **asthma**. If we consider the age group distribution of the population, TSP is a risk factor (RR exposed city area – rural area of the region) of asthma, in the age group 1-14 years (RR = 4.65, CI 95% 3.06-7.07) and >65, (RR=2.33, 95%CI 1.49-3.63). TSP is not a risk factor of asthma when we compare exposed area with urban control areas (Table VIII).





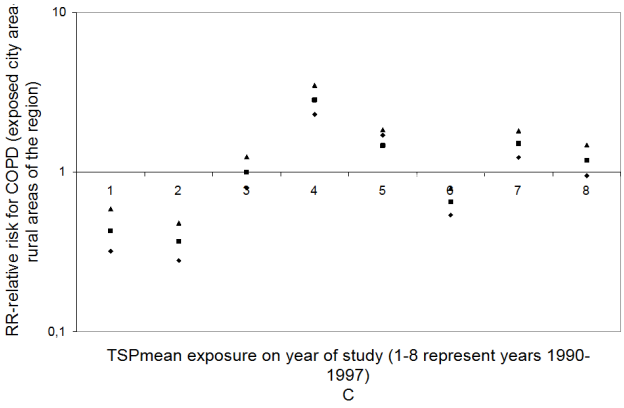


Fig. 1 Relative risk (RR, with 95% CI) for COPD in the population exposed to TSP in Drobeta Turnu-Severin, control lots: A (urban and rural except Drobeta Turnu-Severin); B (other towns of Mehedinti) and C (rural area of Mehedinti)

Table V Spearman correlations (rho) between chronic respiratory diseases (COPD, chronic bronchitis, asthma) in the exposed city area and in the region

		Chronic Bronchitis 15-64 years in exposed area	Chronic Bronchitis > 65 years in exposed area	Chronic Bronchitis 1-14 years in the region
COPD in exposed area	rho	**0.881(**)**	**0.905(**)**	**0.743(*)**
	p-value	0.004	0.002	0.035

**Correlation is significant at the 0.01 level (2-tailed);
*Correlation is significant at the 0.05 level (2-tailed)

Table VI Spearman correlation (rho) relative air humidity – asthma depending on age groups in the exposed city area

		Asthma in age group 1-14 years	Asthma in age group 15-64 years
Relative air humidity	rho	-0.513	**-0.850(**)**
	p-value	0.194	0.007
Relative air humidity in the 2nd trimester	rho	**-0.749(*)**	-0.524
	p-value	0.033	0.183

*Correlation is significant at the 0.05 level (2-tailed)
**Correlation is significant at the 0.01 level (2-tailed)

Table VII Relative risk (RR) values for COPD, chronic bronchitis and asthma due to TSP exposure (control lot – 100,000 inhabitants from the urban and rural region)

	Chronic respiratory diseases		
	COPD RR (CI)	CB RR (CI)	Asthma RR (CI)
1990	0.5 (0.32-0.67)	0.16 (0.12-0.23)	0.1 (0.05-0.19)
1991	0.52 (0.39-0.68)	0.14 (0.10-0.9)	0.57 (0.09-0.27)
1992	**1.13** (0.89-1.42)	0.38 (0.30-0.47)	0.5 (0.32-0.78)
1993	**1.82** (1.52-2.18)	0.73 (0.62-0.86)	0.72 (0.51-1.03)
1994	**1.28** (1.03-1.59)	0.48 (0.39-0.59)	0.4 (0.27-0.6)
1995	0.82 (0.67-1)	0.32 (0.25-0.39)	0.4 (0.28-0.57)
1996	0.89 (76-1.05)	0.17 (0.14-0.20)	0.18 (0.14-0.24)
1997	**1.12** (0.92-1.42)	0.36 (0.27-0.46)	0.44 (0.33-0.57)

CI- Confidence interval Nurminen-Miettinen

Table VIII Relative risk (RR) of TSP on chronic respiratory diseases considering age groups in the exposed population and in other urban and rural areas control lots

Chronic respiratory diseases	Age groups Exposed city area - other urban areas			Age groups Exposed city area - rural areas		
	1-14 years	15-64 years	>65 years	1-14 years	15-64 years	>65 years
COPD (RR)	0.65	**2.05**	**1.05**	**1.94**	0.73	**3.24**
CI	0.53-0.79	1.8-2.32	0,93-1.18	1.43-2.55	0.66-0,81	2.86-3.67
CB (RR)	0.16	**3.16**	0.96	0.11	0.7	**3.46**
CI	0.07-0.37	2.66-3.76	0.85-1,09	0.05-0.27	0.62-0.79	3.01-3.96
Asthma (RR)	0.73	0,71	0.92	**4.65**	0.89	**2.33**
CI	0.6-0.9	0.56-0.88	0.58-1,45	3.06-7.07	0.69-1.14	1.49-3.63

CI- Confidence interval Nurminen-Miettinen

Relative risk of respiratory diseases between urban and rural areas due to unknown factors was counted. Thus, there is an increased risk for COPD over the age 1-14 years (RR= 2.93, CI 95% 2.23-3.86), for CB in age group >65 years (RR=3.57, CI 95% 3.12-4.09) and asthma in age groups: 1-14 years (RR=6.32, CI 95% 4.19-9.53) and >65 years (RR=3.08, CI 95% 2.72-3.49) (Table IX).

Relative risk of respiratory diseases, exposed city area - rural area of the region, with exclusion of unknown factors (connected with urban-rural difference) indicates an increased risk on COPD (age groups 15-64 years: RR=2.08, CI 95% 2.02-2.12 and >65 years: RR=2.94, CI 95% 2.94-2.95) and on CB (age group 15-64 years: RR=3.18, CI 95% 3.03-3.44) (Table IX).

Table IX Relative risk (RR) of unknown factors (between urban and rural) in chronic respiratory diseases and RR of TSP in respiratory diseases with unknown factors (urban-rural) exclusion in the exposed population – rural areas control lot and with age group consideration

Chronic respiratory diseases	Age groups urban – rural due to unknown factors			Age groups Exposed city area - rural areas with exclusion of urban-rural due to unknown factors		
	1-14 years	15-64 years	>65 years	1-14 years	15-64 years	>65 years
COPD (RR)	**2.93**	0.35	**1.1**	0.65	**2.08**	**2.94**
CI	2.23-3.86	0.31-0.84	0,97-1.24	0.64-0.66	2.02-2,12	2.94-2.95
CB (RR)	0.46	0,22	**3.57**	0.15	**3.18**	0.96
CI	0.07-1.14	0.18-0.26	3.12-4,09	0.1-0.23	3.03-3.44	0.96-0.97
Asthma (RR)	**6.32**	**1.25**	**3.08**	0.73	0.69	0.75
CI	4.19-9.53	0.99-1.57	2.72-3.49	0.73-0.74	0.71-0.72	0.75-1.04

CI- Confidence interval Nurminen-Miettinen

If we consider relative risk between exposed areas and the control rural area with confounding factors (age group, different age groups distribution of population between control areas, different incidence of respiratory diseases between urban and rural) exclusion, we obtain approximately similar

relative risk of TSP on respiratory health with relative risk exposed population - control lot of other urban areas. Thus, results of this analysis indicate air pollution with TSP as risk factor on **COPD** (age groups 15-64 and >65 years) and on **chronic bronchitis** in the age group **15-64 years**. Along long term exposure we can observe a clear association of TSP only with COPD incidence.

B. Results of Study- part 2

In the Study- part 2 period, health variables, air pollution and meteorological factors are available for 1,461 days (Table X), except TSP values, which were measured only for 820 days. The patient numbers were classified by sex and present a weekly (maximum on Monday and minimum on Sunday) and a seasonal (maximum in January and minimum in August) variation.

Table X Descriptive statistic of all variables of the Study – Part 2 period on a daily basis

	Mean	Median	Variance	Standard Deviation
Tmin (^{0}C)	7.78	8.20	67.59	8.22
Tm (^{0}C)	12.78	12.80	88.72	9.42
Tmax (^{0}C)	18.61	19.40	118.86	10.90
TSP (g/m^3 air)	111.42	105.00	2245.85	47.39
Rel.hu (%)	67.96	68.00	211.68	14.55
wv (m/s)	5.64	5.00	10.14	3.18
COPD m (cases)	0.91	1	1.37	1.17
COPD f (cases)	0.43	0	0.48	0.70
CB m (cases)	0.21	0	0.23	0.48
CB f (cases)	0.16	0	0.17	0.41
Asthma m (cases)	0.24	0	0.27	0.52
Asthma f (cases)	0.46	0	0.65	0.80

f = female, m = male

Chronic Obstructive Pulmonary Diseases (COPD)

The values of the hospital admissions of COPD were classified into four age groups: 18-44, 45-64, 65-74 and over 75 years. The yearly variation and the effect of temperature were modelled with a spline. The absolute humidity has a significantly adverse effect in the first age group (Table XI).

Moreover, a positive difference between absolute humidity of the current and preceding day significantly elevates the risk in the three age groups. If the humidity rises, then the expected patient number increases; if it is falling, so are the expected hospital admissions. A significant influence of TSP was not found.

A spline function for seasonality is illustrated in Fig. 2, with the 95% confidence interval (broken lines). Since the first day is the 1.1.2000, the function has local minimums in summer and local maximums in winter. If the function becomes zero, then there is no influence on the expected number of hospital admissions. The positive function values indicate an increased respiratory risk for the winter time. If the function values are negative, then the risk is reduced (summer). Despite the very broad confidence interval and often small differences from zero, these findings indicate the seasonally changing effects of humidity upon respiratory health.

Table XI Significant results for COPD for the Study –Part 2

Variable one	Coefficient	s.e.	p-value	RR
absHum 18-44	**0.0600**	0.0229	0.0088	1.0619
absHum 45-64	-0.0121	0.0136	0.3721	0.9879
absHum 65-74	-0.0142	0.0143	0.3176	0.9859
absHum > 75	-0.0090	0.0166	0.5853	0.9910
Diff absHum	**0.1352**	0.0682	0.0473	1.1448
Diff absHum	**0.0645**	0.0221	0.0035	1.0667
Diff absHum	**0.0653**	0.0262	0.0126	1.0675
Diff absHum	0.0400	0.0379	0.2917	1.0408

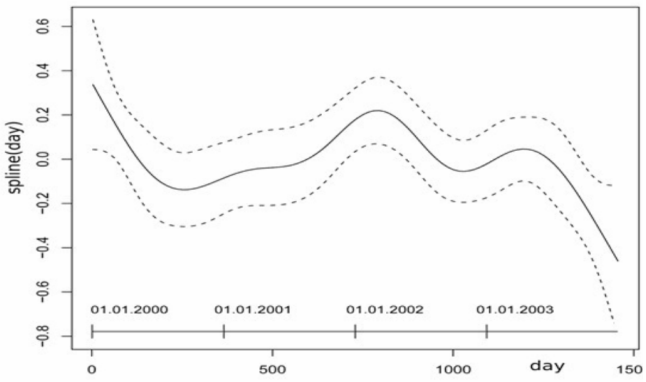


Fig. 2 The estimated spline for seasonal variation in COPD admissions

Chronic Bronchitis

For chronic bronchitis, the data are classified by the same four age groups as for COPD.

The yearly variation and the temperature are also modelled with a spline. There is a significant **protective effect of humidity**. However, a significant **elevation of risk** was observed in the group of patients aged **18–44 years**, when taking TSP values of the previous day into account (TSPlag1) (Table XII).

No threshold value for a damaging influence of TSP on the age group 18-44 years was detected. This model is however not very significant. Because of the insufficient case numbers, threshold values for health effects of TSP could not be identified.

Table XII Significant results for chronic bronchitis for the Study -Part 2

Variable one	Coefficient	s.e.	P-value	RR
TSPlag1 18-44	**0.0071**	0.0015	< 0.0001	1.0071
TSPlag1 45-64	0.0008	0.0009	0.3307	1.0008
TSPlag1 65-74	0.0013	0.0011	0.2306	1.0013
TSPlag1 > 75	0.0016	0.0014	0.2460	1.0016
absHum	**-0.0648**	0.0171	< 0.0001	0.9373

Asthma

For the analysis of the endpoint asthma, the data was stratified into four age groups: 0-17, 18-44, 45-64 and over 65 years. There is a significant negative influence of TSP on the first age group**,** but also a significant protective effect on the second. There is a significant protective effect of air humidity on asthma in the third and fourth age groups. Table XIII shows the results of the model, with splines for air temperature and yearly variation.

Table XIII Significant results for asthma for Study –Part 2

Variable	Coefficient	s.e.	p-value	RR
TSPlag1 0-17	**0.0068**	0.0014	< 0.0001	1.0068
TSPlag1 18-44	**-0.0042**	0.0011	0.0002	0.9958
TSPlag1 45-64	-0.0011	0.0007	0.1396	0.9989
TSPlag1 > 65	0.0016	0.0016	0.3145	1.0016
absHum 0-17	0.0179	0.0206	0.3848	1.0181
absHum 18-44	0.0233	0.0167	0.1614	1.0236
absHum 45-64	**-0.0341**	0.0149	0.0222	0.9665
absHum > 65	**-0.0463**	0.0227	0.0412	0.9548

IV. Discussions and Limitations

In the literature, similar studies were performed in China, where the health effects associated with both short-term and long-term exposures to air pollution. In these investigations, a time series study design was used to evaluate the health effects of short-term air pollution exposure; cross-sectional and longitudinal study design was used to evaluate the health effects of long-term air pollution exposures. Taken together, these epidemiological studies provide coherent evidence than short-term exposures to air pollution are significantly associated with excess daily morbidity, whereas long-term exposures to air pollution are associated with increased respiratory symptoms of bronchitis in adults [35].

In the study performed we also used a longitudinal study design in the Study- Part 1 period (1990-1997) and a time series study design during the period of study part 2 (2000-2003). In both study designs, the modifying effect of climate parameters on the relation between respiratory health and air pollution was considered. A limitation could be the variation of air pollution and climate factors between two periods of study.

A very recent study indicates a reduction in direct pollution of 59% between 1995 and 2007 and an avoidance of pollution, 76% greater [36]. In the study performed, the observed yearly means of TSP concentrations are 134 $\mu g/m^3$ air (period of Study- Part 1) and 111.42 $\mu g/m^3$ air (period of Study- Part 2), which indicates an air pollution reduction between the two parts of the study and a surpassing of standards. These results are similar to those in the CESAR study, which demonstrates that annual mean particulate matter concentration levels in Central and Eastern Europe exceed the limit values of the European Commission [15]. In other areas, as in China, concentrations of PM2.5 and PM10 also exceeded the WHO guideline during the Olympic period [37].

Climate parameters are also different in the two parts of the study periods: temperature mean is 11.82^0C and 12.78 ^{0}C, average relative humidity is 74.5% and 67.96% and wind velocity mean is 1.97m/s and 5.64m/s in the Study- Part 1 and Study- Part 2, respectively. During our study we observed a temperature increase of 0.96^0C, between the two study periods. Studies on temperature evolution in Europe indicated an annual increase of about 0.8^0C in the last century, with variation in time (greater in last two decades) and space (greater in mid- and high latitude) [6]. The warmest eight years have occurred since 1998 [38]. This increase in temperature in the investigated area surpasses the annual increase in Europe. In Canada, a decrease of the relative humidity was registered in 50 years (1953-2003) by an average of 6% [7]. In the investigated region, relative humidity decreases by an average of 6.54% between Study- Part 1 and Study- Part 2 periods. Temperature increase is closely related to humidity variation and therefore northern Europe becomes wetter and central-eastern Europe becomes drier [6]. Another connected aspect of this phenomenon is wind velocity that increases by 3.67 m/s between the two study periods, which suggests great variations of speed winds. In a recent study made in China, it resulted that meteorology accounted for more of the variation on PM10 concentration than source control measures [37]. Climate change in urban ecosystems of Romania presents some forms of disturbances in comparison with natural ecosystems and raises air pollution levels [39].

Respiratory health effects of air pollution were analysed during the two study periods, using the two study designs. Another limitation of our study is the difficulty to compare. Because of limited availability of data, different health indicators were used in the Studies- Part 1 and 2: annual incidence and daily exacerbations and admissions, respectively. In other study, two national datasets were linked: long- term average concentrations of PM2.5 chemical components for 2 years and relative risk of respiratory hospitalizations for old persons, associated with an increase with 10 $\mu g/m^3$ of PM2.5 on the same day [40]. Short-term exposure to air pollutants was found to be an important predictor of increased hospital admissions [41]. Therefore, it is possible to analyse, in the same study, the long- and short-term effects upon respiratory health.

Long-term exposure (over 3 years) to PM10 is significantly associated with respiratory hospital admissions in other studies, in Edinburgh and Glasgow [42]. Lung function growth was found impaired from long-term exposure to air pollutants

and improved in districts where air pollution had decreased [43]. In the Study- Part 1, TSP at high concentrations is identified as a risk factor for COPD in the exposed population. There is no correlation COPD-relative humidity. When we considered health effects on age groups and excluded confounding factors urban-rural, TSP was revealed as a risk factor on COPD in age groups 15-64 years and > 65 years and on chronic bronchitis in age group 15-64 years.

The natural course of COPD is characterized by occasional sudden worsening of symptoms, called acute exacerbations, most of which are caused by infections or air pollution [44]. In the Study- Part 2, there is no significant relation COPD-TSP. Humidity appears to be not a protective factor but an adverse one for COPD. Yet, there is evidence for the association of COPD with occupational PM10 concentration in other studies, but with a factor of 1.3 times higher than PM10 concentrations at nearby-sites [45]. The spline function of seasonality indicates an increased respiratory risk for the winter time and a decreased one for the summer time, as results in the Study- Part 2. Some studies provide evidence that the effect of PM10 on morbidity varies with season and increases during the summer [46], winter [47] or spring [48]. When the association between exposures and outcomes that vary seasonally is estimated, models must be selected carefully [49].

Individuals with chronic bronchitis may also experience a worsening of their conditions because of exposure to dust and smoke [30]. In Study- Part 1, TSP resulted as a risk factor on chronic bronchitis in the age group 15-64 years. When we considered health effect of TSP in all age groups, the risk could not be seen. In Study- Part 2, TSP has a mild adverse effect on chronic bronchitis. This weak effect of TSP on chronic bronchitis resulting in both study periods was confirmed by another study performed in the same area, in a shorter period (1 year), with decreased statistical significance [50].

Difficulties in interpretation appear for asthma. In the literature, for PM10 and PM2.5, increased odds of experiencing daily and weekly asthma symptoms are mentioned [51]. There is no risk of TSP in asthma, assessed in Study- Part 1, and there is a negative significant correlation between relative humidity and asthma, suggesting a protective effect. When we considered age groups in Study- Part 1, TSP also resulted as no risk factor on asthma. In the Study -Part 2, there is no adverse effect of TSP.

In recent studies, fluctuation in humidity and temperature appear to influence emergency daily visits for asthma in children [52]. In other studies, the risk of PM10 in asthma was increased in children [53, 54] and in the elderly [55]. A TSP risk for asthma in children and the elderly was also identified in our study, when we counted the relative risk between exposed and rural area control populations, considering age groups. Yet, this adverse effect of TSP seemed to disappear when we excluded confounding factors of the urban-rural differences in Study- Part 1. On the other hand, TSP is correlated with PM10, which is assumed in the literature to be homogeneously distributed over urban areas [56]. High concentration of PM10 was associated with a significant reduction in lung function and an increase in new cases of asthma over time (Canadian Council of the Minister of the Environment) [57]. In study performed, seasons and days of the week for hospital admission remain important confounding factors.

V. Conclusions

Epidemiological studies of health and air pollution in this European region are still scarce. Our investigations provide evidence for an adverse effect of airborne particles and a protective effect of air humidity on respiratory health and give an overview of the situation in a city of this region.

From the results of our study we conclude that in the exposed city area, air pollution with particles decreases between the Study- Part 1 and Study- Part 2 periods and exceeds the PM10 annual European threshold and the TSP annual American standard along the total study period. Climate parameters are modified during the study periods, possibly by global warming. On the other hand, climate parameters modify the adverse respiratory health effects of particles. In the exposed city area, there is a weak adverse effect of TSP on COPD incidence increase and on chronic bronchitis incidence and hospitalization (disease exacerbation) at a specific age, 15-64 years. Humidity interferes with effects of TSP on respiratory health**,** and manifests a protective effect on chronic bronchitis and asthma (especially in individuals over 45 years of age). Seasonality, air temperature, days of the week, infections, age groups, difference in distribution by age groups of population from different areas, population density and urban-rural differences are verified as important confounders.

New studies should address the effect-modification by meteorological factors, on the basis of multicentre studies in this European region. Improved exposure assessment demands more sophisticated measurements of airborne particulates including PM10, PM2.5, as well as UFP (ultra-fine particles) and/or particle number concentrations. Spatial representation should be improved by taking different stations into consideration. A reduction of air pollution in the investigated area can only be successful when all countries in this European region will improve their air quality.

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