

PULMONARY DISEASES

Air pollution and respiratory status in asthmatic children: Hints for a locally based preventive strategy. AIRE study

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Abstract. Respiratory health effects of short-term exposure to ambient air pollution have been examined in 120 'asthma-like' school-aged children in some areas of Emilia-Romagna (urban-industrial and rural area). They kept a daily diary, through 12 weeks, for respiratory symptoms, PEF measurements, drug consumption and daily activity. The average daily concentrations of air pollutants in the same period (TSP, NO₂, CO, PM_{2.5}) were higher in the industrial than the rural area. Asthma was diagnosed in 77% of cases, 85% of subjects took medical treatments for respiratory disease in the last year and 90% used medicine for respiratory diseases. Significantly lower variations in PEF, between morning and evening, were observed in the rural area, considering only the asthmatic or cough subsets of children. Symptom prevalence was higher in the urban-indus-

trial area than the rural area; the most frequent symptoms were cough, phlegm and stuffed nose. The two area populations are homogeneous in individual features, family susceptibility, passive smoking exposure and atopy. The differences observed in the frequency of daily reported symptoms could be attributed to external situations like the different reported exposures to pollutants. Although most analyses revealed non-significant associations, panel analysis showed a significant statistical risk for the cough and phlegm group by an increase of 10 µg of TSP (RR 1.0017, 95% CI: 1.0002–1.0033) in the entire group. In the *urban-industrial* panel we observed a significant association between cough and phlegm together and PM_{2.5} (RR 1.0044, 95% CI: 1.0011–1.0077). The results of this investigation should be used in orienting local political decisions.

Key words: Air pollution, Asthma, Children, Panel study, Short-term respiratory symptoms

Introduction

Growing urbanization has led to an increase in exposure to air pollutants, associated with respiratory diseases. The evaluation of short-term health effects from air pollution represents one of the most interesting priorities in prevention-oriented research [1].

It is of interest to study the adverse health effects of air pollution in children since their respiratory system is growing and is more sensitive to air pollution. Attention is focused, in particular, on children with chronic respiratory symptoms, most vulnerable to air pollution effects [2].

Asthma is the most common and increasing chronic respiratory disorder in the US population: children account for the largest proportion of this increase [3].

Although a strong genetic component is undoubtedly responsible for the development of asthma and atopic disorders, environmental risk factors acting early in life are also important. Paediatric asthma is

one of major public health concerns in Europe and represents an enormous burden on family and society. It is a drain on healthcare resources (direct costs: medication use, emergency and hospitalization care) and may also deprive children of educational achievement and social interaction (indirect costs: days lost from school, care-giver costs, environmental adaptation costs) [4].

Different studies have shown an association between air pollution and respiratory effects in asthmatic children [5, 6], such as reduced lung function, increases in asthma attacks, use of bronchodilators, respiratory symptoms and hospital admissions [7].

Repeated peak expiratory flow (PEF) measurements are widely used in epidemiological study to assess the severity of asthma and as an indicator of bronchial hyper-reactivity. They are also used to measure changes of pulmonary function in relation to environmental exposure. Children with asthma have a greater variation in PEF than children with no respiratory symptoms [8].

The PEACE European study ('Pollution Effects on Asthmatic Children in Europe') has shown weaker associations between PEF and symptom incidence in asthmatic children [9, 10]. The present study called Asma Infantile Ricerca in Emilia-Romagna (AIRE) was carried out in some areas of the Emilia-Romagna region to investigate associations between this kind of respiratory diseases and air pollution.

These areas are characterized by different kinds of urbanization and industrialization. The main hypothesis is that the daily variation of respiratory health conditions in children with chronic respiratory symptoms is associated with daily variation of air pollutants. The goal of the study is to verify the strength of association of interest between areas characterized by different kinds of urbanization and industrialization.

The results of this investigation could be used in orienting local political decisions.

Methods

Study population

A population-based survey was conducted in the period February–May 1999 (12 weeks) in the two areas of the Emilia-Romagna region previously described: an urban-industrial area (ceramic district) and a rural area, characterized by low vehicle traffic, low population density and low industrialization. The survey was conducted to investigate the frequency of respiratory diseases in 6–11 year-old children attending primary school.

A panel study was then carried out; according to PEACE and SIDRIA questionnaires [8, 11, 12], children were selected if a positive answer was given to at least one of the following questions in the questionnaire filled in by parents:

1. Has your child suffered in the past 12 months from a wheezy chest, apart from colds?
2. Has your child suffered in the past 12 months from attacks of shortness of breath with wheezing?
3. Has your child had dry cough at night in the past 12 months, apart from coughing with a cold or chest infection?
4. Has a doctor said your child was suffering from asthma?

Final panel size was 120 children: 118 (1.6% drop out) were included in the final analysis. They were characterized by skin prick tests, basal spirometry measure and a detailed questionnaire on individual features, familiarity, medicine consumption, domestic environment (house features, pets presence) and family habits (passive smoking exposure, child habits). Atopy was defined as at least one positive reaction to the skin prick test. Children kept a daily diary, for a period of 12 weeks, from February to April 1999, for respiratory symptoms, PEF measurements

(three measurements in the morning and in the evening), drug consumption and daily activity.

Exposure assessment

In the same time period (12 weeks), pollution and meteorological data were collected. Daily mean concentrations of TSP, NO₂ and CO were obtained from fixed monitoring stations. An *ad hoc* monitoring of PM_{2.5} concentrations was also implemented: three gravimetric sequential samplers of PM_{2.5} were located in the same fixed monitoring stations (two in the urban-industrial area, one in the rural area). It is not possible to draw conclusions on the yearly mean value of exposure to PM_{2.5} in the different areas, nor to evaluate the seasonal variability of concentrations, because of the short time of the study (a continuous monitoring from March to May, 1999).

We excluded daily average measurements with more than 25% of missing hourly data (NO₂, TSP, PM_{2.5}) or if more than 25% of 8 h moving average calculated with at least 75% of valid data (CO) was lacking.

Information on air pollutants, as well as meteorological data (daily average temperature and relative humidity) was provided by the Regional agency for health prevention and environmental protection (ARPA) in Emilia-Romagna Region.

Pollens may be important confounders for asthma-like symptoms; we tested a dichotomous variable for both areas to take into account the overcoming of a preset threshold of graminaceae concentration in the air: data were provided by ARPA.

Health effect measurements

At the beginning of the panel study, parents and children were instructed to complete daily diaries concerning respiratory symptoms and medication use. Daily diaries of respiratory symptoms provide a powerful method for assessing the impact of short-term changes in human health due to environment [13].

During the study period, participants performed PEF measurements twice a day with portable mini peak flow meters, once in the morning before breakfast and once in the evening before going to bed. Subjects were instructed to perform the PEF measurements before any airway medication was taken. Each measurement consisted of three tests and participants were asked to note all three readings in the diary. The highest of the three PEF readings was used for the analysis. We also considered a PEF variability-linked measurement, called Δ PEF and obtained, for each day and each subject, as

$$\frac{|\text{PEF}_m - \text{PEF}_e|}{0.5(\text{PEF}_m + \text{PEF}_e)} \times 100,$$

where PEF_m was the maximum morning measurement and PEF_e the maximum evening one [8, 14]. This index is a measure of short-term daily variability weighted on individual base line.

The diary was also used to record occurrences of acute respiratory symptoms and the use of medication. Symptoms included were: cough, phlegm, runny or stuffed nose, waking up with breathing problems, shortness of breath, wheeze, attacks of shortness of breath with wheeze, eye irritation and sore throat [7, 15]. Fever and headache are considered as confounders and were controlled for influenza epidemics. We analyzed cough, phlegm, runny or stuffed nose alone, cough and phlegm together [8, 16]. Symptomatic children were judged to be those with at least one daily reported symptom.

To assess the use of medication, subjects were required to write down name and quantity of the medication used. Medicines were coded into three groups according to mode of use (aerosol, spray and pills) and in six categories according to pharmacological active principle (antibiotics, antihistamines, antiphlogistics, inhalants, drops, cortisones). Inhaled cortisone is included in aerosols, as drug group, and in inhalants, as drug category.

Statistical methods

Data were firstly investigated by descriptive statistics, means, standard deviations, and interquartile ranges to summarize daily pollution and meteorology data, including time plots to examine possible confounding trends in the data, and exposure correlation matrices to determine the degree of intercorrelation that could suggest confounding or co-linearity effects in regression analysis. Prevalence and incidence of respiratory symptoms were calculated for each day of study.

The analysis was conducted for the two areas (urban-industrial and rural) separately and both together, by using the day as the unit of analysis. Associations of both symptoms (total symptoms and separate groups) and daily mean ΔPEF with air pollutants were analyzed with regression models.

First an ecological analysis on the number of symptoms was conducted, then a panel analysis to take into account the repeated measures and the heterogeneity of individuals in the study.

In the ecological analysis, the outcome variable is the number of daily symptoms. A preliminary time series analysis of the drug assumption was done to check for the autocorrelation of these series: using the ARIMA model. The core model was fitted including variables controlling for potential time trend, deviation of the current daily temperature from the average of three preceding days, quadratic temperature to consider potential non-linear trend in the meteorology variables, humidity as linear term, the subject's symptom status on the previous day to account for

autocorrelation [13], and the ARIMA fitted series for medicine consumption.

The outcome variables were the number of total symptoms, and the number of symptoms in different groups considered for the lag 0, 1, 2, 3 and average of three preceding days (lag 0–3). Before including each single pollutant in the basic model, it was verified that there was no autocorrelation in the model's residuals.

Panel analysis

To take into account the heterogeneity of children, the associations between variation in PEF, presence or absence of symptoms and air pollution were analyzed by means of regression analysis based on generalized linear model (both fixed and random effects, LME) for longitudinal data (mixed model) [17–20].

The urban-industrial and rural panel were combined to increase the power of the study; we also analyzed them separately, to assess differences between panels.

Two models were setup, one for the variation in PEF analysis and one for the symptom analysis [11, 16, 21–24].

In the first model (ΔPEF) we adjusted for gender, medicinal use (four typologies were considered: antihistamines, inhalants and two kinds of ENT drops) and symptomatic status (defined as having asthmatic symptoms or not); we included temperature, humidity and one pollutant at a time as fixed effects. Correlation of residuals was checked. This kind of analysis was also conducted for the two groups atopic and non-atopic.

In the second model (presence or absence of symptoms) we adjusted for gender, medicinal use (as the previous analysis) and symptomatic status of the previous day to correct for the autocorrelation of the symptom series; we included temperature, humidity and one pollutant at a time as fixed effects. The analyses were conducted, for cough and phlegm together and for cough, phlegm and runny or stuffed nose alone [8].

In these models residuals were found to be normally distributed and non-autocorrelated.

Results

Questionnaires

Children included in the panel totalled 118: 67 lived in the urban-industrial area and 51 in the rural area, as reported in Table 1.

Among the children included in the panel, the range of reported respiratory disease incidence during life runs from 20% (pneumonia) to 75% (bronchitis); 32% reported heavy respiratory disease in the first 2 years. The same diseases during the last 12 months were obviously less frequent (5% pneumonia, 50% bronchitis).

Table 1. Panel composition: residence, sex and age of children included in the panel

Residence	No of subjects	% subjects	Mean age	% male
Casalgrande (urban-industrial)	6	5	7.2	33
Castelnuovo Monti (rural)	31	26	7.7	48
Pavullo (rural)	20	17	7.9	55
Sassuolo (urban-industrial)	61	52	7.8	69
Total	118	100	7.8	59

Night-time cough in the last 12 months had a frequency of 73%, subjects with attacks of shortness of breath with wheeze (63% during life, 42% in the last 12 months) had reported a mean of 3.2 attacks in the last year (SD: 2.05, IC: 1.15–5.25). Asthma was diagnosed in 77% of cases with a mean age at the date of diagnosis of 3.5 years; in the last year the mean number of attacks was 2.7 between asthmatic children. 85% of subjects took medical treatments for respiratory disease in the last year and 90% used medicine for these diseases.

Panel children reported allergy to one or more considered allergens in 70% of cases: the allergic situation was relevant, especially for the high amount of children with sneeze attacks or nose irritation (rhinitis). Skin prick tests were for these allergens: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Parietaria officinalis*, *Alternaria alternata (tenuis)*, *Phleum pratense* (timothy grass), *Betula*, dog and cat fur. The results of the prick tests are reported in Table 2.

As shown, 67% of subjects are positive to at least one allergen, and these are considered as atopic subjects. The two areas considered in the panel study showed no differences in the prick test results, as reported in Table 2.

Detailed questionnaires revealed that 40% of children lived next to a crossroads, 33% lived near a road with bus flow and 39% lived near a road with lorry flow. The exposure to indoor passive smoking was evaluated in terms of presence of persons who smoke every day (46%). Children had similar demographic, household, allergy and habit characteristics in the areas included.

The PEF variability was significantly lower in asymptomatic than symptomatic children, taking into account the two different areas; results are shown in Table 3 (Mann–Whitney non-parametric test, $p < 0.001$).

Furthermore, significantly lower variations in PEF were observed in the rural area, taking into account

Table 2. Number and prevalence of subjects resulting positive to prick-test in the two considered areas

Positivity to allergens	Urban-industrial		Rural		Two areas	
	No	%	No	%	No	%
No allergen	72	61	82	69.4	36	30.4
Only one allergen	8	6.8	6	5.1	14	11.9
Two allergens	8	6.8	6	5.1	14	11.9
Three allergens	10	8.5	2	1.7	12	10.2
Four allergens	9	7.6	10	8.5	19	16.1
Five or more allergens	11	9.3	12	10.2	23	19.5
At least one allergen (total)	46	39	36	30.6	82	69.6

‘At least one allergen’ + ‘No allergen’ = 100% (118 children).

* Category ‘At least one allergen’ is the sum of the other categories excluded ‘No allergen’.

Table 3. Δ PEF descriptive statistics in the two areas for symptomatic and asymptomatic children

Statistics	Δ PEF urban-industrial			Δ PEF rural		
	Symptomatic	Asymptomatic	Total	Symptomatic	Asymptomatic	Total
Min	1.4781	4.3926	5.0668	2.8077	3.9089	4.6238
Mean	8.9997	7.7371	8.2718	9.1432	6.7228	7.3814
Median	9.1940	7.7270	8.3285	8.3999	6.3367	7.2513
Max	15.3605	12.6659	11.6336	26.4264	12.3946	12.5264
SD	2.5814	1.7669	1.2502	4.2815	1.6462	1.5845

Table 4. Total number of days when children presented symptoms and when children did not present symptoms

Symptoms	Child-day occurrence		Child-day presence %
	Presence occurrence ^a	Absence occurrence ^b	
Cough	1627	7022	18.81
Phlegm	986	7663	11.40
Stuffed nose	1656	6993	19.15
Woken up at night	110	8539	1.27
Shortness of breath	356	8293	4.12
Breath with wheeze	217	8432	2.51
Attacks	54	8595	0.62
Ocular irritation	577	8072	6.67
Sore throat	292	8357	3.38
Headache	305	8344	3.53
Fever	134	8515	1.55

^a Presence: when 1 child presents the symptom in 1 day. Presence occurrence: sum of the presence for all children in all days.

^b Absence: no presence. Absence occurrence: sum of the absence for all children in all days.

Total number of child-days = number of children in the whole panel * total number of study days.

only the asthmatic or cough subsets of children ($p = 0.037$ and $p = 0.024$ respectively).

The prevalence of symptoms per child-day is reported in Table 4; the symptoms with the highest frequencies were cough, phlegm and stuffed nose.

Symptom prevalence is higher in the urban-industrial area than the rural area, and this is true for all symptoms during almost the entire study period.

The drugs most used per child-days were inhalants (15.3%), followed by antihistamines (12.3%), anti-phlogistics (3.2%), drops (4.6%), antibiotics (1.6%) and cortisones (1.1%).

Air pollution levels

The mean temperature in the period was lower in the rural area (9.07 °C) than in the industrial area (11.28 °C). The average daily concentrations of air pollutants were higher in the industrial area than in the rural area: daily mean NO₂ concentrations were 69.52 µg in the urban area and 34.81 µg in the rural area, TSP were 111.41 and 45.34 µg, PM_{2.5} were 53.07 and 29.11 µg, CO were 1.54 and 1.22 mg respectively. In the industrial area, temperature was negatively correlated with NO₂ and CO, and was positively correlated with TSP and PM_{2.5}. The correlations were high between TSP and PM_{2.5} (0.613). In the rural area, temperature was negatively correlated with TSP and PM_{2.5} and was positively correlated with NO₂ and CO.

The correlations in daily air pollution concentrations between the areas were 0.658 for PM_{2.5}, 0.457 for NO₂ and lower for the other pollutants.

Regressions

Aggregated analysis

Graphs of the Partial AutoCorrelation Function (PACF) showed no autocorrelation in the residuals of

the selected models, after the introduction of the single pollutant. As already mentioned, models were performed for both rural and urban-industrial areas.

All symptoms: no statistically significant association between the presence of at least one symptom and pollution was observed.

Subset of symptoms: within this study population, some subsets were sampled according to reported symptoms: cough, phlegm, runny or stuffed nose symptoms, asthma-like symptoms, and sore throat and ocular irritation. No statistically significant associations between health and pollution were found.

Panel analysis

APEF

In the panel analysis we studied first the entire panel, then the two areas separately and finally the two groups of atopic and non-atopic children. Initially we analyzed the daily PEF variation for each subject in study.

The results for the entire panel are shown in Figure 1.

There was no significant statistical association between pollutants and PEF variations, although higher relative risks were found for particles in the urban-industrial area compared to the rural one and among non-atopic children compared with atopic ones.

Symptoms

For the symptom analysis with mixed effects model we considered the individual symptoms, cough, phlegm and runny or stuffed nose, and all these together, and at least one other symptom as dichotomous variables and cough and phlegm together. We analyzed the two areas together and separately. In the two areas together we observed significant statistical risk for the cough and phlegm group by an increase

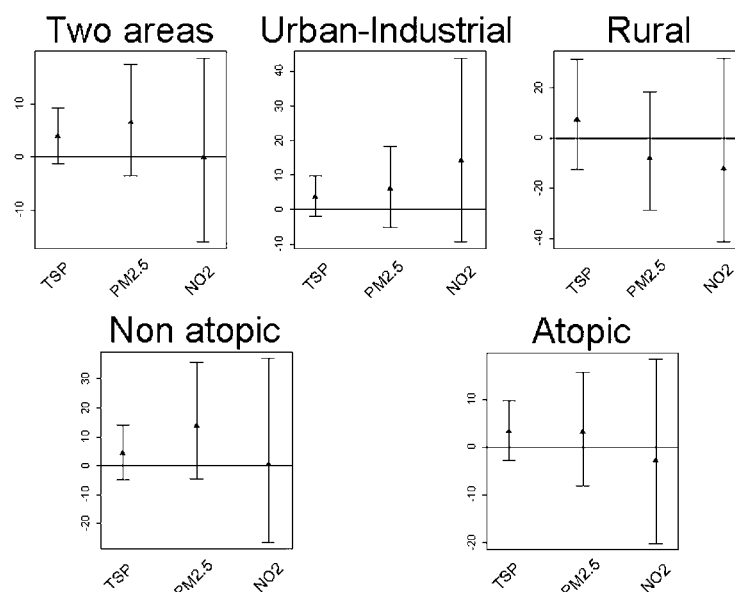


Figure 1. Percent log relative risk increments in PEF variation related to 10 µg increase of pollutants in different settings. Legend: y axis: RR * 100 (increments per 10 µg increase of pollutants) (IC 95%).

of 10 µg of TSP (RR: 1.0017, IC: 1.0002–1.0033), as shown in Figure 2.

In the *urban-industrial* panel we observed significant associations between cough and phlegm together (mainly due to recurrent respiratory infections) and PM_{2.5} (RR: 1.0044 IC: 1.0011–1.0077) by 10 µg increase, as we could see in Figure 3. In the *rural* panel, there were no significant associations between any kind of symptoms and any kind of pollutant, as shown in Figure 4.

No significant variations in the previous results were found when pollens were included in the models.

Discussion

Asthma and allergic disorders are some of the leading causes of chronic illness in childhood. An increasing trend has been observed in many industrialized countries. Paediatric asthma is a major public health concern in Europe and represents an enormous burden on family and society [4].

In this study school-aged children were considered because they were already beyond the first three years of life (when asthma is not well-defined) and were exploring new environments and were exposed to new

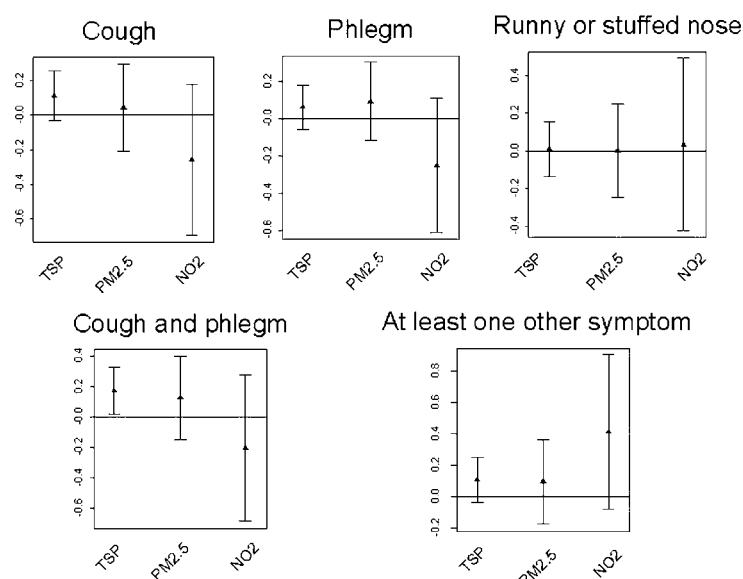


Figure 2. Percent log relative risk increments in symptoms related to 10 µg increase of pollutants (two areas). Legend: y axis: log RR * 100 (increments per 10 µg increase of pollutants) (IC 95%).

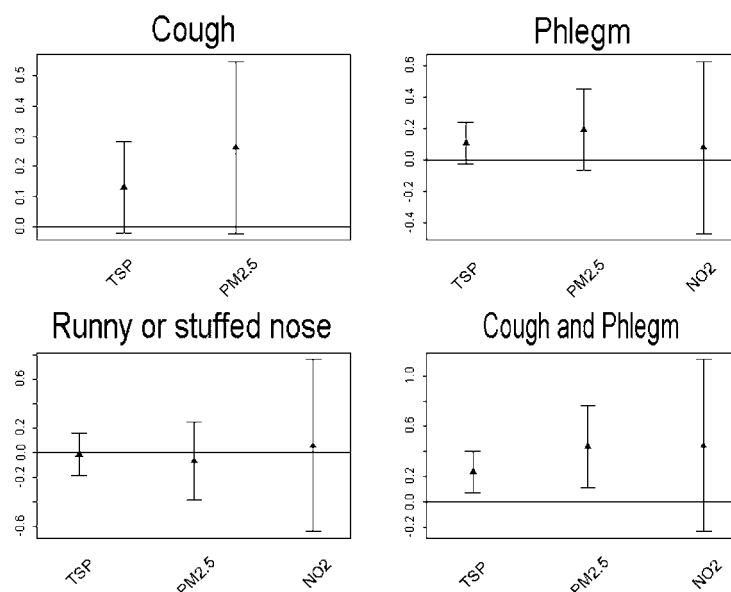


Figure 3. Percent log relative risk increments in symptoms related to 10 µg increase of pollutants (Urban-Industrial area). Legend: y axis: log RR * 100 (increments per 10 µg increase of pollutants) (IC 95%).

sources of contamination in school buildings and playgrounds [25].

International data of ISAAC study showed a wide variation among countries in asthma prevalence; in Italy, the prevalence of asthma was 9% [26, 27].

Following the definition given in the SAPALDIA study [14], PEF analysis is a measure of respiratory performance variation. A larger variability has been found for the rural area between symptomatic and asymptomatic (mean: 9.14, SD: 4.28; mean: 6.72, SD: 1.64 respectively) than in the urban-industrial area (mean: 8.9, SD: 2.58; mean: 7.7, SD: 1.77 respectively), suggesting that in the rural area the difference

between a good respiratory health status and a bad one is greater than in the urban-industrial one.

A long-term exposure to air pollution for urban-industrial inhabitants could be adduced as effect confounder, therefore the effects reported for the rural area would be the best approximation of the real peak effect measure.

No associations between air pollutants and increase in PEF variations in both areas, together or separately, were found.

In the present study PEF was measured at home twice a day: this can cause problems with compliance due to the measurement's dependence on panel sub-

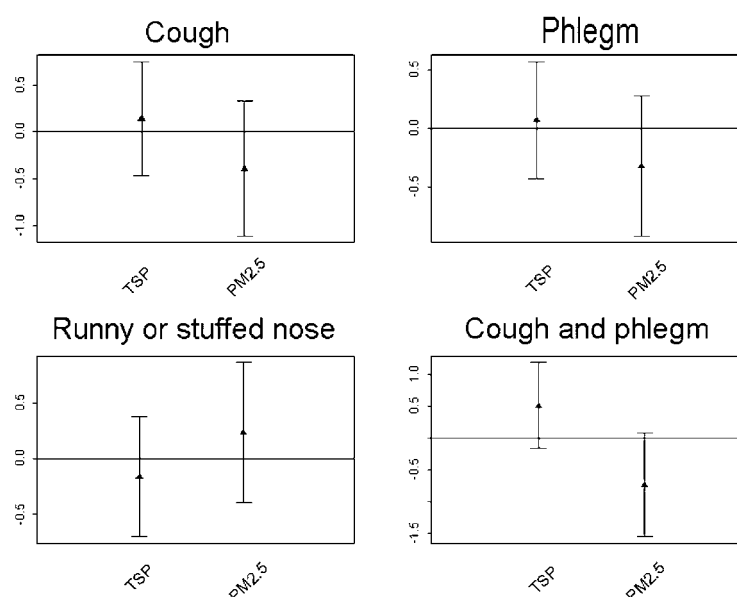


Figure 4. Percent log relative risk increments in symptoms related to 10 µg increase of pollutants (rural area). Legend: y axis: log RR * 100 (increments per 10 µg increase of pollutants) (IC 95%).

jects. Moreover, performing only two measurements in the day span could lead to underestimation of the real level of diurnal variation in PEF [8].

The significant associations between PEF and pollutants reported in literature were observed, generally, in particular subsets of subjects (i.e. those with doctor-diagnosed asthma, those with symptoms of asthma but no doctor's diagnosis of asthma and those with nocturnal cough but no other symptoms of asthma).

In view of the previous considerations, in the present study the investigation of the associations between PEF measures and pollutants will be carried out and studied in detail.

In a panel study in Utah, a negative association between concentrations of PM_{10} and PEF was found; a positive association of PM_{10} concentrations with bronchodilator use and prevalence of acute respiratory symptoms was also recorded [28].

Hoek and Brunekreef have found no association between prevalence of acute respiratory symptoms and the concentration of PM_{10} , but mean prevalence of the combination of upper and lower respiratory symptoms was higher in the classes of days with higher PM_{10} concentrations [23].

Timonen and Pekkanen [7] have found no consistent associations between air pollution and respiratory symptoms, except for SO_2 concentrations and upper respiratory symptoms.

In both the Harvard Six Cities study and the Uniontown-State College diaries, fine particles (1–2.5 μm) were much more strongly associated with asthma-related responses than coarse particle mass (2.5–10 μm). Hence for acute asthma-related responses as well as daily mortality, fine particles are considered a stronger predictor of response than are coarse particles [29].

In the present panel of asthmatic children, we observed a significant statistical association between the increase of symptoms of cough and phlegm (mainly due to recurrent respiratory infections?) and the increase in exposure to particles.

However, the association was evident only in the urban-industrial area, where both measures of particles (TSP and $PM_{2.5}$) show a significant association. Panel children selected in the two areas are homogeneous according to individual features, familiarity, passive smoking exposure, atopy (in terms of frequencies and kind), medicine consumption, house features, pets presence, child habits.

Thus the differences observed in the frequency of daily reported symptoms could be attributed to external situations like the different reported exposures to pollutants. This supports the need for a strict health status surveillance.

It is not possible to compare properly distinct situations even in different monitoring periods and in relation to various methods, used in previous studies, because of the smaller availability of data for $PM_{2.5}$

in Italy and their diminished reliability owing to the limited experience in this kind of measurement.

The study results supply the baseline information about $PM_{2.5}$ pollution in some areas of the Emilia-Romagna region.

Therefore it seems correct and necessary to address fine and ultra fine particulate (PM_{10} , $PM_{2.5}$ and smaller) as more relevant indicators for health surveillance and prevention.

As a future step it might be interesting to study the adverse health effects of PM_1 and $PM_{0.1}$ in heavy air polluted areas [30].

Pollens as confounders might be another interesting issue if we could know the dispersion of pollens in the two areas separately [22]. Unfortunately, only overall area distributions are available.

A limitation to the power of the study comes from having included one pollutant at a time to exclude errors due to the multi-collinearity of compounds that makes it difficult to recognize the univocal effects of a single pollutant [31].

A common limitation of these kind of studies is the individual exposure approximation with the monitoring stations concentrations. The $PM_{2.5}$ distribution improves this necessary approximation because of the higher uniformity of the spatial distribution of the fine particles.

Conclusions

In Europe, very few studies have dealt with the $PM_{2.5}$ air pollution respiratory effects: one of the first results of this investigation is to respond to the need to move towards monitoring of fine and ultrafine particles (PM_{10} , $PM_{2.5}$ and lower fractions), also at local level.

This statement is also supported by the following points:

- $PM_{2.5}$ (and lower fractions) air concentration monitoring is more representative of wide areas than TSP and PM_{10} ones [32–34].
- outdoor fine and ultrafine particles are mainly produced by traffic pollution (which is a direct and important (if not the major) concern even in industrial areas [35].

Another point that emerges from this study is the clear relationship between air pollution and respiratory effects whenever properly investigated taking into account the individual environmental co-variables (endogenous factors, pollen, etc). As a matter of fact, recurrent respiratory infections are more strongly associated with particle air pollution than asthma attacks.

In particular these, and some other relationships observed, even though not clearly statistically significant, suggested a real impact of urban-industrial air quality on children's respiratory status.

Taken at local level, all these findings imply the need to focus preventive action on traffic reduction-

moderation, also in industrial areas since they act as a traffic-attracting pole.

Moreover, as these effects have been assessed among children, some concluding comments should be made.

Respiratory health in children would benefit in the long term from a substantial reduction in air pollution exposure from traffic [36] and other indoor and outdoor sources.

Even though asthma and child respiratory disease currently represent an important health and economic burden in developed societies, they must be regarded as potentially more serious future problems in terms of both absolute and relative figures (i.e. cardiovascular diseases, diabetes, hypertension, are faced in developed countries in a more and more effective way) [37].

More generally, the achievement of lower environmental stress would enable a better quality of life.

References

- MacNee W, Donaldson K. Exacerbations of COPD. Environmental mechanism. *Chest* 2000; 117: 390S–397S.
- Boezen HM, van der Zee SC, Postma DS, et al. Effects of ambient air pollution on upper and lower respiratory symptoms and peak expiratory flow in children. *Lancet* 1999; 353: 874–878.
- Teague WG, Bayer CW. Outdoor air pollution. Asthma and other concerns. *Child Environ Health* 2001; 48: 1167–1183.
- von Mutius E. The burden of childhood asthma. *Arch Dis Child* 2000; 82: ii2S2–ii2S5.
- Dockery and Pope (1994).
- Pope et al. (1995).
- Timonen KL, Pekkanen J. Air pollution and respiratory health among children with asthmatic or cough symptoms. *Am J Respir Crit Care Med* 1997; 156: 546–552.
- Timonen KL, Nielsen J, Schwartz J, et al. Chronic respiratory symptoms, skin test results and lung function as predictors of peak flow variability. *Am J Respir Crit Care Med* 1997; 156: 776–782.
- Brunekreef B. PEACE study. *Eur Respir Rev* 1998; 8(52).
- Viegi G. Air pollution epidemiology and the European Respiratory Society (ERS): The PEACE project. *Eur Respir Rev* 1998; 8: 1–3 (Editorial).
- Romieu I, Meneses F, Ruiz S, et al. Effects of air pollution on the respiratory health of asthmatic children living in Mexico City. *Am J Respir Crit Care Med* 1996; 154: 300–307.
- Issued by funding: Commission of the European Communities in the framework of the 'ENVIRONMENT' RTD Programme. Coordinator: Brunekreef B. Effects of short-term changes in urban air pollution on the respiratory health of children with chronic respiratory symptoms. Technical Report: Study procedure for collaborative study. Wageningen, the Netherlands, August 1993.
- Schwartz J, Wypij D, Dockery D, et al. Daily diaries of respiratory symptoms and air pollution: Methodological issues and results. *Environ Health Persp* 1991; 90: 181–187.
- Künzli N, Zemp Stutz E, Perruchoud AP, et al. Peak flow variability in the SAPALDIA study and its validity in screening for Asthma-related conditions. *Am J Respir Crit Care Med* 1999; 160: 427–434.
- Saskia C, van der Zee, Hoek G, Boezen HM, et al. Acute effects of urban air pollution on respiratory health of children with and without chronic respiratory symptoms. *Occup Environ Med* 1999; 56: 802–813.
- Nuntavarn Vichit-vadakan, Ostro B, Chestnut LG, et al. Air pollution and respiratory symptoms: Results from three panel studies in Bangkok, Thailand. *Environ Health Persp* 2001; 109: 381S3–387S3.
- Delfino RJ, Coate BD, Zeiger RS, Seltzer JM, Street DH, Koutrakis P. Daily asthma severity in relation to personal ozone exposure and outdoor fungal spores. *Am J Respir Crit Care Med* 1996; 154: 633–641.
- Burton P, Gurrin L, Sly P. Extending the simple linear regression model to account for correlated responses: An introduction to generalized estimating equations and multi-level mixed modelling. *Stat Med* 1998; 17: 1261–1291.
- Goldestein H. Multilevel mixed linear model analysis using iterative generalized least squares. *Biometrika* 1986; 73: 43–56.
- Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika* 1986; 73: 13–22.
- Neas LM, Dockery DW, Koutrakis P, Tollerud DJ, Speizer FE. The association of ambient air pollution with twice peak expiratory flow rate measurements in children. *Am J Epidemiol* 1995; 141: 111–122.
- Neas LM, Dockery DW, Burge H, Koutrakis P, Speizer FE. Fungus spores, air pollutants, and other determinants of peak expiratory flow rate in children. *Am J Epidemiol* 1996; 143: 797–807.
- Hoek G, Brunekreef B. Acute effects of a winter air pollution episode on pulmonary function and respiratory symptoms of children. *Arch Environ Health* 1993; 48: 328–335.
- Schwartz J, Kirsi L, Timonen, Pekkanen J. Respiratory effects of environmental tobacco smoke in a panel study of asthmatic and symptomatic children. *Am J Respir Crit Care Med* 2000; 161: 802–806.
- von Ehrenstein OS. Asthma, allergies and respiratory health. In: Tamburlini G, von Ehrenstein OS, Bertollini R (eds), *Children's health and environment: A review of evidence*. Joint WHO Regional Office for Europe/EEA. *Environ Issue Report* 2002; 29(Part II): 44–65.
- Worldwide Variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. *Lancet* 1998; 351: 1225–1232.
- Frequency of Childhood asthma in various Italian regions. Results from ISAAC. Collaborating group of ISRDCE (Italian Studies of Respiration Disorders in Childhood and the Environment). *Epidemiol Prev* 1997 21: 235–242.

28. Pope CA III, Dockery DW, Spengler JD, Raizenne ME. Respiratory health and PM10 pollution: A daily time series analysis. *Am Rev Respir Dis* 1991; 144: 668–674.
29. Schwartz J, Neas LM. Fine particles are more strongly associated than coarse particles with acute respiratory health effects in schoolchildren. *Epidemiology* 2000; 11: 6–10.
30. Peters A, Wichmann HE, Tuch T, Heinrich J, Heyder J. Respiratory effects are associated with the number of ultra fine particles. *Am J Respir Crit Care Med* 1997; 155: 1376–1383.
31. MISA Collaborative Group. Meta-analysis of the Italian studies on short-term effects of air pollution. *Epidemiol Prev* 2001; (Suppl 2).
32. Oglesby L, Künzli N, Roosli M, et al. Validity of ambient levels of fine particles as surrogate for personal exposure to outdoor air pollution – Results of the European EXPOLIS-EAS Study (Swiss center Basel). *J Air Waste Manage Assoc* 2000; 50: 1251–1261.
33. Roosli M, Braun-Fahrlander C, Künzli N, Oglesby L. Spatial variability of different fractions of particulate matter within an urban environment and between urban and rural sites. *J Air Waste Manage Assoc* 2000; 50: 1115–1124.
34. Hoek G, Meliefste K, Cyrus J, et al. Spatial Variability of fine particle concentrations in three European areas. *Atmos Environ* 2002; 36: 4077–4088.
35. Holgate ST, Samet JM, Koren HS, Maynard RL. *Air pollution and health*. London: Academic Press, 1999.
36. Kunzli et al. (2000).
37. McMichael A. *Human frontiers, environments and disease past patterns, uncertain futures*. Cambridge: University Press, 2001.
38. Viegi G, Paoletti P, Carrozzi L, et al. Prevalence rates of respiratory symptoms in Italian general population samples, exposed to different levels of air pollution. *Environ Health Persp* 1991; 94: 95–99.
39. Viegi G, Paoletti P, Prediletto R, et al. Prevalence of respiratory symptoms in an unpolluted area of Northern Italy. *Eur Resp J* 1988; 1: 311–318.

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