
Air pollution exposure and hospital admission: time-series versus case-control approach

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1. Introduction

Urban air quality and its impact on health remains a major concern for the international scientific community; numerous testimonies then followed as to the short and long-term effects of atmospheric pollution on the incidence of oncologic, respiratory and cardiovascular events, as well as are an increase in the overall mortality rate (1-6).

Emergency hospital admission rates for respiratory was taken as good indicator of the acute effects of urban-air pollution (7, 8). The American National Morbidity, Mortality and Air Pollution Study (NMMAPS) (9) and the European Air Pollution and Health Project (APHEA) (10, 11), along with the Meta-analysis of the Italian studies on short-term effects of air pollution (MISA) (12, 13) and the Environmental Modular Advanced Compact System project (EMECAS)(14) are some of the most valuable investigations of primary importance to have been carried out in the last few years on hospitalisation for cardiovascular and respiratory events due to air pollution (15).

Literature contains mainly reports of observations based on different design, as time-series (16-24) or, al-

though less frequently, case control studies (25-28). However, unfortunately, data obtained by different approaches are difficult to compare because based on different study populations, making investigation into the advantages and disadvantages of these approaches of difficult execution. Other research fields have attempted to analyse associations using different approaches applied to the same data-base (29), but rarely has this been attempted in the analysis of the association between air pollution and public health (30, 31).

The research reported here aims at making a contribution to this field by proposing an in-depth examination of the comparability of the estimates obtained by differing approaches.

2. Objectives

The main objective of this study is to analyse the association between urban pollution and hospital admissions for respiratory and cardiovascular causes among residents in the city of Torino, northern Italy, in the years 2000-2003, using both time-series and case control approaches, with the scope of evaluating the advantages and disadvantages of the two designs.

3. Methods

3.1 Database

Hospital admission information was obtained from the regional files of the hospital discharge register (HDR), managed by the “Servizio Sovrazonale di Epidemiologia dell’ASL 5” (Piedmont Region). The study was based on 43,997 patients residents in the city of Torino, hospitalised in the years 2000-2003 for dysfunctions in the respiratory (ICD 460-519) or in the cardiovascular apparatus (ICD 390-459). Only emergency admissions were taken into consideration in this study, so as to evidence any acute effects determined by exposure to polluting agents.

Total suspended particulates (TSP) measured in $\mu\text{g}/\text{m}^3$, are the most commonly used predictors of urban pollution (17, 20, 27, 28). The average of TSP levels and meteorological data for three days before hospitalisation were considered (7, 12, 27, 28). As there is a strong correlation between pollution levels with season and relative humidity (measured in average daily percentages), average daily temperature (expressed in Centigrade) and the month of admission to hospitals (classified as summer/winter (20)), have been taken as the main predictors for the seasonal control. Other confounding factors include a qualitative variable of 7 levels that represent the days of the week when the adverse health event took place.

3.2 Study Designs and Statistical Analyses

To estimate the risk of hospitalisation for respiratory causes associated to TSP exposure, this study took the following approaches into consideration:

1. time-series analysis (32): a design based on time-series analyses was chosen in an effort to determine the extent that the measured urban pollution level influenced the number of persons admitted to hospital units with acute episodes of respiratory events. The statistical analyses were based on Poisson regression models (assuming that the hospital admissions at time t are distributed as a Poisson distribution). Results are expressed in terms of an increase in the risk percentage (IR%ts), associated with its relative 95% confidence interval (95%CI_{ts}) to a $10\mu\text{g}/\text{m}^3$ increase in TSP, adjusted by the considered confounding factors. Spline modelling was applied for the analysis of temperature and relative humidity (*a parametric curve which approximates the dispersion of data*), where the degrees of freedom are chosen so as to optimise the function of the

Generalized Cross Validation, an adaptation function of the model, whilst, at the same time minimizing the self-correlation of the residuals. Moreover, the approach included modelling as potential confounding factors: (i) seasonal and long term factors, by means of a variable taking values 1 to the number of the days in the study; (ii) the day of the week, using six dummy variables.

2. Case-control (33): on the basis of the primary diagnosis codified according to the International Classification of Diseases (ICD IX), patients hospitalised for respiratory (ICD 460-519, $N_{\text{Resp.}} = 14754$) or cardiovascular (ICD 390-459, $N_{\text{Card.}} = 29243$) causes separately were defined as *Cases*. Patients hospitalised in the same period with a diagnosis other than that of the cardio-circulatory and/or respiratory apparatus, or correlated with than were paired to the cases according to age and gender ($N_{\text{control.}} = 108,472$).

A conditional logistic regression model was fitted to estimate the OR and relative 95% Confidence Interval adjusted for the confounding factors considered. The results were expressed in terms of a percentage increase of the risk (IR%cc), determined by a $10\mu\text{g}/\text{m}^3$ increase in the TPS levels and its relative 95% confidence interval (95%CI).

In both designs the analysis were performed separately for respiratory causes, [acute diseases (ICD 460-469) and asthma (493)], and cardiovascular causes [circulatory (ICD 390-429) and cerebrovascular (ICD 430-438)].

4. Results

There was a total number of 14,754 and 29,243 patients admitted with a diagnosis of respiratory (ICD 460-519) and cardiovascular (ICD 390-459) disorders respectively. Subjects affected by respiratory problems were, on average, aged 35 (standard deviation 34), whilst subjects hospitalised for cardiovascular conditions averaged 71 years of age (standard deviation 13).

Table 1 reports the first /middle and third quartile of TSP, Humidity and Temperature, separately for the autumn-winter and spring-summer seasons.

Whatever the approach adopted, the analyses showed an increase in the hospitalisation risk associated to an increase in pollution, with, as expected, differences in the precision of the estimate. Moreover if the 95%CI show a general comparability of the results, the risks

Table 1. TSP, Humidity and Temperature levels in the city of Turin in the years 2000-2003.

	Autumn/Winter	Spring/Summer
	Quartiles	
	first - middle - third	first - middle - third
TSP	84.67 - 113.42 - 145.78	53.92 - 66.19 - 79.70
Humidity	65.34 - 76.71 - 84.38	55.51 - 62.86 - 71.62
Temperature	3.58 - 7.08 - 10.3	16.65 - 20.03 - 23.61

estimated using the case-control design show an higher variability

The analyses carried out on the overall number of respiratory tract diseases using the time series approach show a 0.5% increase of hospital admission risk due to a TSP increase of 10 µg/m3 [IR%st=0.50% (IC95%st: 0.06 ; 0.92%)]; the case control approach provided a higher estimate, although the confidence interval shows the comparability of the estimates obtained with the previous approach [IR%cc=0.91% (IC95%cc: 0.50 ; 1.32%)] (Fig. 1).

Considering the cardiovascular hospital disorders, the analysis based on time series approach show a 0.74% increase of hospital admission risk due a TSP increase of 10 µg/m3 [IR%st=0.74% (IC95%st: 0.43 ;

1.05%)]; using the case-control approach, a lower increase of hospital admission risk was estimated [IR%cc=0.30% (IC95%cc: 0.001 ; 0.70)] (Fig. 2).

When the specific pathology groups were examined it was noted that the difference between the two approach are more evident; (Figs. 1 and 2).

5. Discussion

The principal objective of this study was to compare the risk estimated using two different approaches in the analysis of the association of air pollution exposure and hospital admission for respiratory causes. The results obtained using both time series and case-control approaches, were generally comparable with the risk shown in literature (13).

The time series design, thanks to the adoption of appropriate smoothing methods, allows for a better control of atmospheric factors such as the temperature and relative humidity, which have a strong seasonal component and may introduce distortions in the estimates obtained by the unidirectional approach. Although there has been criticism as to the application of the time series approach (36) as it has been evidenced that the

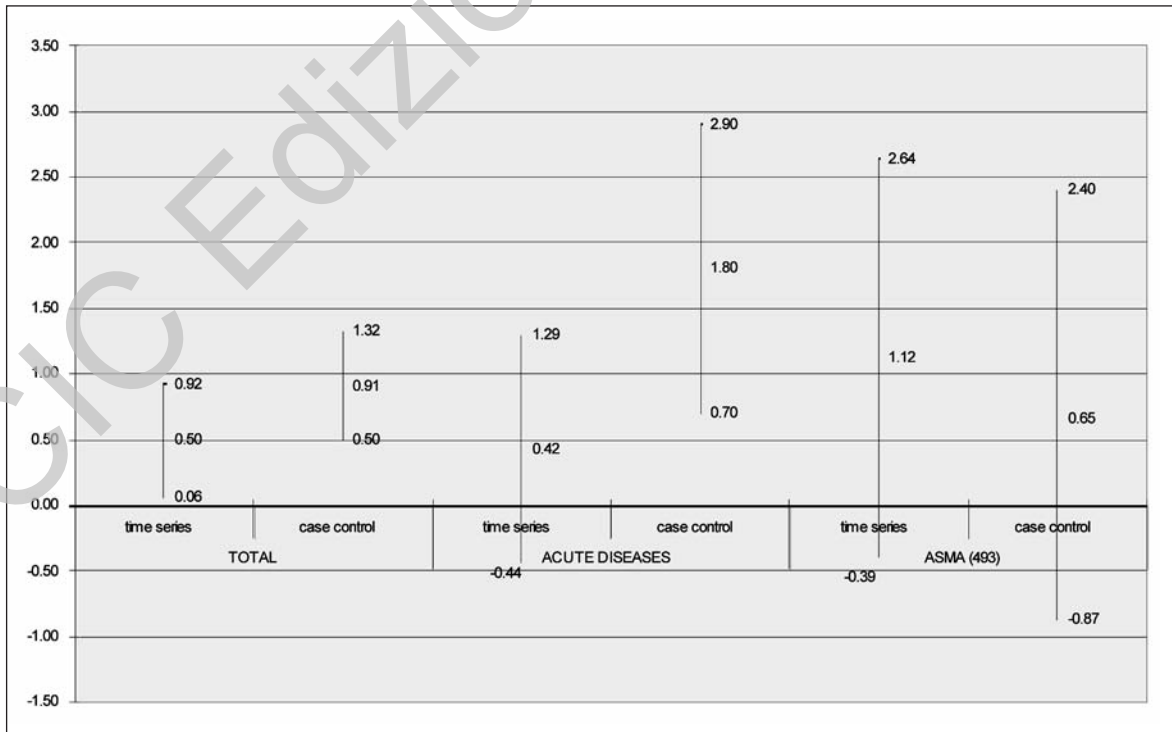


Figure 1. Percent increase of respiratory hospital admission risk due a TSP increase of 10 µg/m3

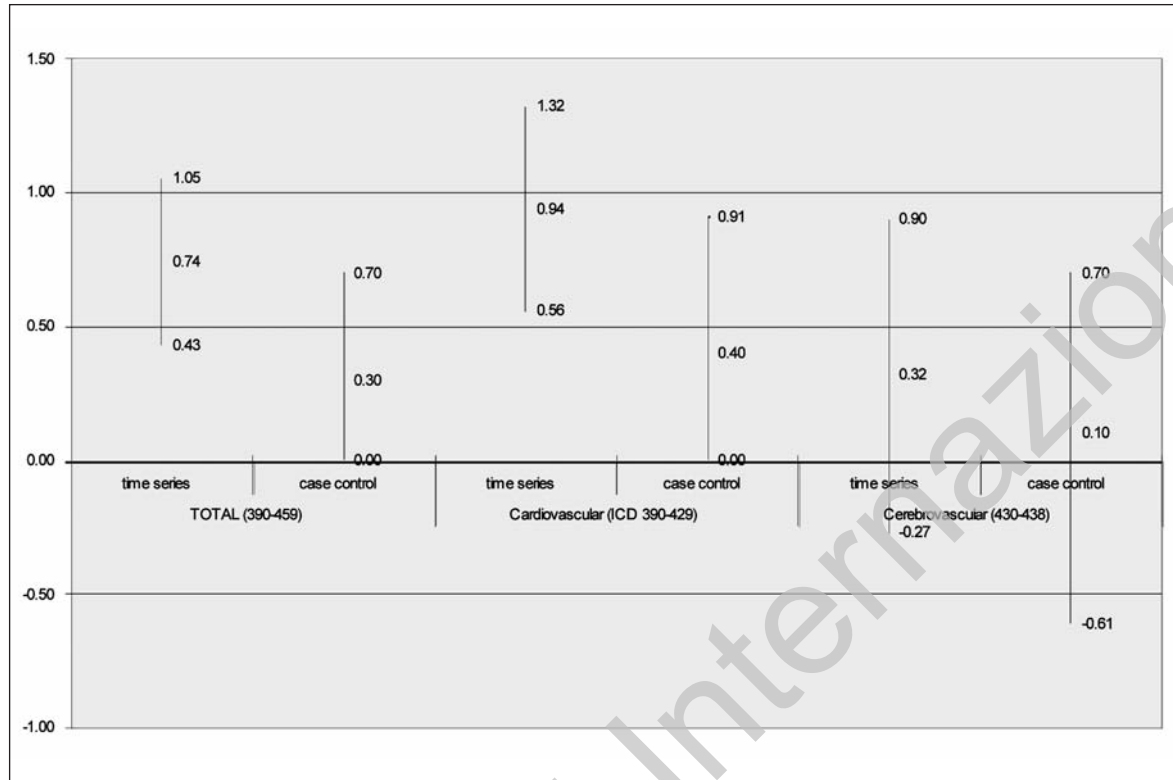


Figure 2. Percent increase of cardiovascular hospital admission risk due a TSP increase of 10 $\mu\text{g}/\text{m}^3$.

results of such an approach are overly model dependant, and, in particular, that the association between exposure and pollutant and the consequent adverse effect/s on health, it has been shown to be sensitive to the choice of the degrees of freedom allowed to the smoothing function.

The case-control approach takes into the model the time occurrence of the events even for the series of controls. It has a natural base-line, not influenced by exposure, so that the occurrence among cases and controls can be compared. It needs no adjustments for complex cyclical trends or for introducing smoothing parameters. One key difference between time series and case-control design is to account for seasonality and time trend. Another important difference is that the case-control estimates a combination of acute and chronic effects because the outcomes accumulate over long time periods and could be triggered by either cumulative or short-term peak exposures. As a direct consequence, chronic effects may not be separable from the acute effects of exposure. Nonetheless, the case-control approach has the attractive feature that it allows for the assessment of effect modification, i.e. for identifying subject characteristics, such as age, sex, health status,

which make individual susceptible to the effect of air pollution. In our study, some fundamental differences among the two approaches did come to light. This was particularly evident when the risk estimated using a time-series design was compared to those obtained using a case-control approach, where there was a notably higher variability of the estimated risks. Such an element is crucial in the assessment of the seasonal confounding factors. Indeed, it is in the very difference in the capacity to control an important factor in this type of study such as the seasonal influence, that the cause of this result may be search for.

In conclusion, with all due limits, our results seem to offer comparable risks, in particular for the total respiratory and cardiovascular diseases, even if the results from case-control designs give constantly higher and more unstable results. However, the lack of statistical significance evidenced by the confidence intervals, may well stimulate further investigations into the age-old debate as to the risks urban pollution poses on health. Further research will be carried out in order to evaluate the association between urban pollution and acute respiratory and cardiovascular symptoms considering also other designs proposed in the literature.

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