Original Contribution

Short-Term Association Between Ambient Air Pollution and Risk of Hospitalization for Acute Myocardial Infarction: Results of the Cardiovascular Risk and Air Pollution in Tuscany (RISCAT) Study

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Air pollutant levels have been widely associated with increased hospitalizations and mortality from cardiovascular disease. In this study, the authors focused on pollutant levels and triggering of acute myocardial infarction (AMI). Data on AMI hospitalizations, air quality, and meteorologic conditions were collected in 6 urban areas of Tuscany (central Italy) during 2002–2005. Levels of particulate matter with an aerodynamic diameter ≤10 μm (PM$_{10}$) (range of 4-year mean values, 28.15–40.68 μg/m$^3$), nitrogen dioxide (range, 28.52–39.72 μg/m$^3$), and carbon monoxide (range, 0.86–1.28 mg/m$^3$) were considered, and increases of 10 μg/m$^3$ (0.1 mg/m$^3$ for carbon monoxide) were analyzed. A time-stratified case-crossover approach was applied. Area-specific conditional regression models were fitted, adjusting for time-dependent variables. Stratified analyses and analyses in bipollutant models were performed. Pooled estimates were derived from random-effects meta-analyses. Among 11,450 AMI hospitalizations, the meta-analytical odds ratio at lag2 (2-day lag) was 1.013 (95% confidence interval (CI): 1.000, 1.026) for PM$_{10}$, 1.022 (95% CI: 1.004, 1.041) for nitrogen dioxide, and 1.007 (95% CI: 1.002, 1.013) for carbon monoxide. More susceptible subgroups were elderly persons (age ≥75 years), females, and older patients with hypertension and chronic obstructive pulmonary disease. This study adds to evidence for a short-term association between air pollutants and AMI onset, also evident at low pollutant levels, suggesting a need to focus on more vulnerable subjects.

Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; PM$_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM$_{10}$, particulate matter with an aerodynamic diameter ≤10 μm.
myocardial infarction (AMI) (9–11). In particular, results of the HEAPSS Study (Health Effects of Air Pollution among Susceptible Subpopulations), performed in 5 European cities, supported the hypothesis that exposure to traffic-related air pollution increases the risk of AMI (10). In a case-control study performed in Worcester, Massachusetts, Tonne et al. (12) analyzed traffic near homes and distance from major roadways as proxies for exposure to traffic-related air pollution, suggesting that long-term exposure to elevated levels of traffic may increase the occurrence of AMI. In a recent review, Bhaskaran et al. (13) concluded that there is some evidence that short-term fluctuations in air pollution affect the risk of myocardial infarction, but they also underlined a need for further studies to clarify the nature of these associations and identify populations at major risk.

In the present study, we evaluated the relations between air pollutants and hospital admissions for AMI in some urban areas of Tuscany, using a case-crossover approach. Area-specific analyses and meta-analyses were performed, taking into account different lag structures in the relation between air pollution exposure and health events, the influence of meteorologic parameters, individual susceptibility factors, and the associations in bipollutant models.

**MATERIALS AND METHODS**

**Air quality and meteorologic data**

For the study period (January 2002–December 2005), we obtained daily air pollution data from the Regional Agency for Environmental Protection of Tuscany monitoring system. Particulate matter with an aerodynamic diameter ≤10 μm (PM$_{10}$), nitrogen dioxide, and carbon monoxide were considered.

In a first step, we selected 29 monitoring sites, classified as “urban background” sites (based on European Union and Italian air quality legislation), to represent the exposure of the general population in urban areas. In a second step, daily averages of hourly concentrations of PM$_{10}$ and nitrogen dioxide and the daily 8-hour maximum moving average for carbon monoxide were calculated for each site. We conducted a correlation analysis between sites in order to define areas with plausible homogeneous air quality levels. Six areas, delimited by administrative boundaries, were identified (approximately 1,500,000 inhabitants; 42.5% of the total population of Tuscany) (Figure 1). Some areas included only 1 municipality (Arezzo, area 1; Pistoia, area 5; Prato, area 6) and other areas had more municipalities.
(metropolitan area of Florence, area 2; Pisa and Livorno coastal area, area 3; Lucca area, area 4). Monitoring sites with daily series data which covered almost 75% of the whole study period were included. Finally, for each pollutant, we calculated a daily area value by averaging the daily means of the selected monitoring sites. In the rare situation where data were missing for case days and/or all control days, these days were excluded from the analyses. During the study period, the methods and instruments of environmental monitoring were homogeneous and consistent with quality assurance criteria.

The Regional Agency for Environmental Protection of Tuscany also provided meteorologic data on air temperature (in degrees Celsius), relative humidity (%), and apparent temperature.

Health data

Data on hospitalized cases of AMI (International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), code 410 as the primary discharge diagnosis) were obtained from the Acute Myocardial Infarction Registry of Tuscany (14). The Acute Myocardial Infarction Registry of Tuscany is a population-based registry that has been operating in Tuscany since the late 1990s. In Tuscany, subjects in hospital discharge and mortality databases are identified by a personal identification number, based on the fiscal code, which allows investigators to anonymously perform electronic record linkage among multiple information sources. (In Italy, ethics committee approval and informed consent from patients are not required for observational studies based on anonymous data.)

In the present analysis, only hospitalized AMI events were considered. A validation study of a random sample of hospitalized AMI patients enrolled in 2003 (380 cases) showed that AMI diagnoses in the Tuscan AMI registry largely comply with the AMI definition used in the 2003 American Heart Association Scientific Statement (15). According to the 2003 American Heart Association criteria, 94.6% of the events in the validation sample fulfilled criteria for definite (86.0%), probable (1.3%), or possible AMI (7.3%) (14).

Between 2002 and 2005, 13,554 hospitalized AMI events were recorded in the 6 study areas. Several exclusions were made to increase the specificity of the study. To limit the study to first events, we excluded 1,870 patients who had been hospitalized for AMI during the 3 years preceding the index hospitalization. In addition, 234 patients admitted to hospitals outside the index area were excluded. Thus, a total of 11,450 patients were included in the analysis. For each subject, the following information was available: age, gender, municipality of residence, and up to 5 secondary diagnoses. According to the secondary discharge diagnoses of the index hospitalization and to diagnoses of hospital admissions occurring in the previous 3 years, patients were classified as affected by diabetes (ICD-9-CM code 250), hypertension (ICD-9-CM code 401–405), or chronic obstructive pulmonary disease (COPD) (ICD-9-CM code 490–496). On the basis of the previous hospitalizations only, patients were considered to be affected by heart conduction disorders or cardiac arrhythmia (ICD-9-CM codes 426–427, excluding codes 427.1, 427.2, and 427.5), by heart failure (ICD-9-CM code 428), or by a previous hospitalization for cardiac disease (ICD-9-CM codes 390–429).

Statistical analyses

An area-specific case-crossover approach was applied to evaluate the short-term association between daily air pollutant levels and the risk of hospitalization for AMI. The case-crossover design was developed from the case-control design to study the associations of transient exposures with acute events. With this design, the investigator samples only cases and compares each subject’s exposure during a time period just before a case event (the hazard period) with the subject’s exposure at other times (the control periods) (16). Because there is perfect matching on all measured and unmeasured individual characteristics that do not vary or that vary slowly over time (i.e., age, gender, body mass index), this design intrinsically adjusts for those characteristics.

According to the methods of Levy et al. (17), controls were selected on the same day of the week as cases, within the same month of the same year. Area-specific conditional logistic regression models were fitted to calculate odds ratios and their 95% confidence intervals for an increase of 10 μg/m² in pollutant levels (0.1 mg/m³ for carbon monoxide). The models included adjustment for a set of time-dependent variables, such as influenza epidemics, population decreases during vacation periods, holidays, and apparent temperature.

Many studies have documented the J-shaped relation between high summer temperatures and total mortality (18, 19) and hospital admissions (20). On the contrary, a few studies have depicted the relation between cold temperatures and mortality as linear with a negative slope, with prolonged effects (21). In our study, we combined these 2 components. The left side of the curve was approximated by a linear term of the apparent temperature averaged from the previous 6 days (lag1–6) (up to 9°C) to catch the latent effect of cold temperatures. The effects of high temperatures are generally more immediate, with an exponential relation. For these reasons, we used a lago–1 term for apparent temperature, and we introduced into the model a piecewise linear spline for the apparent temperature, with 2 knots chosen by means of a univariate regression spline model. This statistical procedure, performed with STATA software (Stata Corporation, College Station, Texas), selects the regression spline model that best predicts the outcome variable from 1 continuous predictor, suggesting the best knot positions.

To evaluate immediate and delayed effects, we analyzed the associations between pollutant exposure and AMI occurrence while taking into account different lag patterns, using single-day lags from lag0 (current day concentration) to lag5 (5 days before the event day). We also used cumulative lags: the average between the same day and the previous 2 days (lag0–2), the average between the same day and the previous 5 days (lag0–5), and the average between the previous 3 days and the previous 5 days (lag0–5). After selection of the lag with the maximum association, we assessed the presence of effect modification in patients with or without a specific condition by introducing interaction
terms into the models and evaluating the results using a likelihood ratio test ($\chi^2$). Furthermore, we performed analyses stratified by gender, age (<75 years or ≥75 years), season of hospitalization (cold: October–March; warm: April–September), and the presence of comorbid conditions. In each area, we also applied bipollutant models in which all possible pairs of pollutants were simultaneously included in the model. Finally, we combined area-specific results using meta-analysis (22). We tested for heterogeneity using the $Q$ statistic, and $P$ values were calculated on the basis of the $\chi^2$ distribution. Conservatively, we chose a random-effects approach regardless of whether or not there was significant heterogeneity among areas.

Analyses were carried out using the STATA statistical package, version 10.0.

RESULTS

Study population and AMI patients

Overall, 11,450 patients hospitalized for AMI were included in the study (Table 1). Patients were more likely to be male (61.0%). Nearly half of the patients (50.9%) were aged 75 years or older. The mean age for the whole series was 72.8 years (standard deviation, 13.0). Females were significantly older than males (mean ages were 78.0 years and 69.4 years, respectively; $t$ test: $P < 0.001$). Events occurred more frequently during the cold season (54.8%). Regarding comorbidity, 36.8% of patients were classified as affected by hypertension, 19.5% by diabetes, 9.2% by COPD, 8.3% by heart failure, and 7.1% by cardiac arrhythmia or conduction disorders. A previous hospital admission for cardiac disease was observed in 27.6% of patients.

Air pollution levels

Data on air pollutant levels and meteorologic variables are shown in Table 1. Area 5 had a high percentage of days with missing values for the pollutants under study, because the monitoring sites had been activated at the end of 2003. Mean air pollutant levels were heterogeneous, mainly for PM$_{10}$ (range, 28.15–40.68 $\mu$g/m$^3$) and nitrogen dioxide (range, 28.52–39.72 $\mu$g/m$^3$). In all areas, annual mean PM$_{10}$ values were higher than the World Health Organization value for protection of human health (20 $\mu$g/m$^3$) (23), and in area 4, they were even higher than limits imposed...
by European Union directive and national legislation (40 μg/m³). Nitrogen dioxide and carbon monoxide values in all areas were above the European Union and World Health Organization limits. Spearman correlation coefficients (rs) showed that, in all areas, PM10 was positively correlated with nitrogen dioxide (range of rs, 0.44–0.71); it was also correlated with carbon monoxide, but with lower coefficients (range of rs, 0.22–0.60). Nitrogen dioxide was strongly associated with carbon monoxide, with very high coefficients in 4 areas (rs/C², 0.671). All pollutants were negatively associated with temperature in all areas.

**Association of AMI hospital admissions and air pollution levels**

Table 2 shows the associations between an increase in each pollutant and hospital admission for AMI from lag0 to lag5, derived from meta-analyses. The 3 pollutants showed similar trends, with increased associations up to lag2 and lower estimates from lag2 to lag5. For nitrogen dioxide and carbon monoxide, the positive association remained up to lag3, but the risk estimates at this lag were imprecise. For these reasons, lag2 was chosen as the lag with the maximum association for all 3 pollutants, and it was used to perform stratified analyses. This choice was also justified by the lower heterogeneity among areas reported at lag2 with respect to the other lag patterns; however, all P values from heterogeneity testing were statistically nonsignificant, suggesting that the null hypothesis of homogeneity between areas could not be rejected. Thus, at lag2, pooled estimates showed odds ratios of 1.013 (95% confidence interval (CI): 1.002, 1.013) for PM10, 1.007 (95% CI: 1.002, 1.013) for nitrogen dioxide, and 1.007 (95% CI: 1.002, 1.013) for carbon monoxide.

Associations between pollutants and AMI hospitalization are shown by area in Table 3. Area 2 had the largest sample size and hence the most precise estimates. Except for the negative associations with carbon monoxide in area 5 and some less precise estimates due to a limited sample size in area 1, we noticed homogeneous risk estimates among the areas, highlighting overall positive associations between pollutants and AMI events.

Because a considerable portion of the missing data were in area 5, this area was excluded from the main models (pooled estimates at lag2). Results of this sensitivity analysis were very similar to those for the whole data set (data not reported).

Table 4 shows results from the analyses stratified by gender, age, season of hospitalization, and comorbidity. All P values for the interaction terms were statistically

### Table 2. Association Between Air Pollutant Levels and Hospitalization for Acute Myocardial Infarction in Single Lag Models for a 10-μg/m³ Increase in Pollutant Level (0.1 mg/m³ for Carbon Monoxide), Tuscany, Italy, 2002–2005a

<table>
<thead>
<tr>
<th>Lag, days</th>
<th>PM10</th>
<th>Nitrogen Dioxide</th>
<th>Carbon Monoxide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
</tr>
<tr>
<td>0</td>
<td>1.004</td>
<td>0.991, 1.017</td>
<td>1.011</td>
</tr>
<tr>
<td>1</td>
<td>1.011</td>
<td>0.997, 1.024</td>
<td>1.020</td>
</tr>
<tr>
<td>2</td>
<td>1.013</td>
<td>1.000, 1.026</td>
<td>1.022</td>
</tr>
<tr>
<td>3</td>
<td>1.009</td>
<td>0.990, 1.028</td>
<td>1.028</td>
</tr>
<tr>
<td>4</td>
<td>1.007</td>
<td>0.994, 1.019</td>
<td>1.026</td>
</tr>
<tr>
<td>5</td>
<td>1.001</td>
<td>0.989, 1.013</td>
<td>1.009</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; OR, odds ratio; PM10, particulate matter ≤10 μm in diameter.

### Table 3. Estimated Local and Combined Odds Ratios for Acute Myocardial Infarction Hospitalization Associated With a 10-μg/m³ Increase in Air Pollutant Levels (0.1 mg/m³ for Carbon Monoxide) at Lag2 (2-Day Lag), Tuscany, Italy, 2002–2005

<table>
<thead>
<tr>
<th>Study Area</th>
<th>PM10</th>
<th>Nitrogen Dioxide</th>
<th>Carbon Monoxide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
</tr>
<tr>
<td>1</td>
<td>0.984</td>
<td>0.898, 1.078</td>
<td>1.064</td>
</tr>
<tr>
<td>2</td>
<td>1.006</td>
<td>0.987, 1.026</td>
<td>1.019</td>
</tr>
<tr>
<td>3</td>
<td>0.999</td>
<td>0.957, 1.042</td>
<td>1.026</td>
</tr>
<tr>
<td>4</td>
<td>1.032</td>
<td>1.004, 1.061</td>
<td>1.027</td>
</tr>
<tr>
<td>5</td>
<td>1.005</td>
<td>0.962, 1.050</td>
<td>1.027</td>
</tr>
<tr>
<td>6</td>
<td>1.020</td>
<td>0.985, 1.056</td>
<td>1.011</td>
</tr>
<tr>
<td>All areas combined</td>
<td>1.013</td>
<td>1.000, 1.026</td>
<td>1.022</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; OR, odds ratio; PM10, particulate matter ≤10 μm in diameter.

nonsignificant (data not reported). Nevertheless, in the stratified analyses, gender, age, and season showed some associations with the response to levels of pollutants. For PM$_{10}$ and nitrogen dioxide, estimates were larger in females and in elderly people. For carbon monoxide, no associations were found after stratification by gender and age. For all 3 pollutants, the risks of AMI events were higher during the cold season. None of the comorbid conditions examined showed any suggestions of effect modification in analyses of the whole series. Nevertheless, it is noteworthy that the presence of hypertension (odds ratio $\approx 1.034$, 95% CI: 0.995, 1.074) and COPD (odds ratio $\approx 1.058$, 95% CI: 1.011, 1.108) was associated with the response to PM$_{10}$ levels among patients aged 75 years or older.

Results of bipollutant analyses performed at lag 2 in the whole series showed that the excess risk for PM$_{10}$ and carbon monoxide disappeared (Table 5). Otherwise, for nitrogen dioxide and carbon monoxide, a borderline-significant association still remained when the pollutant was analyzed with PM$_{10}$.

**DISCUSSION**

The pooled results for the 6 urban areas of Tuscany indicated a short-term adverse association between air pollution and AMI hospitalizations. Analyses of different lag patterns suggested a delayed (lag 2) association with pollutants.

Similar short-term associations have been previously observed for hospitalization for a first AMI episode (10, 24, 25), for ischemic heart disease (26), for emergency room admission for AMI or angina (27), and for cardiac hospital readmission of AMI survivors (9).

Our data showed that the excess risk of AMI hospitalization was also present at low levels of pollutants, such as carbon monoxide and nitrogen dioxide (i.e., annual mean

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### Table 4. Association Between Air Pollutant Levels and Hospitalization for Acute Myocardial Infarction at Lag 2 (2-Day Lag) for a 10-ug/m$^3$ Increase in Pollutant Level (0.1 mg/m$^3$ for Carbon Monoxide), Tuscany, Italy, 2002–2005$^a$

<table>
<thead>
<tr>
<th>Variable</th>
<th>PM$_{10}$</th>
<th>Nitrogen Dioxide</th>
<th>Carbon Monoxide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.003</td>
<td>0.977, 1.030</td>
<td>1.013</td>
</tr>
<tr>
<td>Female</td>
<td>1.025</td>
<td>1.003, 1.047</td>
<td>1.048</td>
</tr>
<tr>
<td>Age group, years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;75</td>
<td>1.005</td>
<td>0.976, 1.035</td>
<td>1.019</td>
</tr>
<tr>
<td>$\geq$75</td>
<td>1.017</td>
<td>0.999, 1.036</td>
<td>1.028</td>
</tr>
<tr>
<td>Season</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warm (April–September)</td>
<td>0.997</td>
<td>0.962, 1.033</td>
<td>1.009</td>
</tr>
<tr>
<td>Cold (October–March)</td>
<td>1.016</td>
<td>0.999, 1.032</td>
<td>1.025</td>
</tr>
<tr>
<td>Comorbid conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.013</td>
<td>0.983, 1.043</td>
<td>0.990</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.025</td>
<td>0.980, 1.073</td>
<td>1.028</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>1.035</td>
<td>0.966, 1.109</td>
<td>1.010</td>
</tr>
<tr>
<td>Cardiac arrhythmia</td>
<td>0.993</td>
<td>0.943, 1.046</td>
<td>0.982</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1.003</td>
<td>0.918, 1.096</td>
<td>1.000</td>
</tr>
<tr>
<td>Hospitalization for cardiac disease</td>
<td>0.999</td>
<td>0.996, 1.034</td>
<td>0.981</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; OR, odds ratio; PM$_{10}$, particulate matter $\leq$10 $\mu$m in diameter.

$^a$ Pooled results from stratified analyses.
nitrogen dioxide levels were lower than the World Health Organization guideline value). These results are consistent with those of the study by Bell et al. (28), which also showed associations between short-term exposure to ambient carbon monoxide and cardiovascular hospitalizations at levels lower than the current regulatory standard. The data agree with the suggestion that some airborne pollutants do not seem to have a threshold level at low concentrations (29).

As is well known, air pollution is a complex mixture of particulate and gaseous compounds that originate from the same sources and are strictly correlated. Particulate air pollution itself is a complex mix of particles varying in size and chemical composition (1), all factors influencing the toxicity of particulate matter. In particular, “fine particulate matter” (i.e., particulate matter with an aerodynamic diameter \( \leq 2.5 \mu m \) \( (PM_{2.5}) \)) is associated with a substantially higher risk of myocardial infarction than “coarse fraction” particulate matter \( (PM_{2.5-10}) \) (24). Furthermore, traffic emissions are only one of numerous sources of airborne particulates, especially considering \( PM_{10} \). Therefore, carbon monoxide and nitrogen dioxide are considered better markers of traffic-related air pollution (1).

Our data agree with those of previous studies showing a mostly consistent association between carbon monoxide and nitrogen dioxide and cardiac admissions (27) and a reduction in the association with \( PM_{10} \) when carbon monoxide and nitrogen dioxide are controlled for (30).

Our results suggest that there are subgroups in the population (the elderly, females, patients with cardiopulmonary comorbidity) that are more susceptible to airborne pollutants. Elderly people showed a slightly larger association with increasing concentrations of \( PM_{10} \) and nitrogen dioxide. The vulnerability of elderly people is well documented. Barnett et al. (31) studied daily myocardial infarction hospital admissions, reporting higher associations with \( PM_{2.5} \), carbon monoxide, and nitrogen dioxide among subjects aged 65 years or older. Lanki et al. (10) reported a larger association between carbon monoxide or particle number concentration and the risk of first, nonfatal AMI among subjects aged 75 years or older.

Females showed greater risks for \( PM_{10} \) and nitrogen dioxide. Few investigators have conducted separate analyses by gender, and conflicting results have been reported. D’Ippoliti et al. (25) found higher risks in women than in men. On the other hand, in the study by Koken et al. (32), males tended to have higher numbers of hospital admissions for AMI and other cardiovascular diseases. Zanobetti et al. (33) found weak evidence of a larger association for males in emergency hospital admissions for myocardial infarction. In our series, females were approximately 9 years older than men, and the difference in age might help to explain the different association with pollutants.

In our data, the relation between comorbidity and susceptibility to pollution was more complex. In fact, no association was observed in the whole series. On the other hand, some associations with hypertension and COPD were observed in older patients. Few studies have investigated the potential susceptibility associated with comorbidity. The study by D’Ippoliti et al. (25) showed some indications of a greater association for patients with a secondary diagnosis of heart conduction disorders. Previous admissions for COPD appeared to increase the risk of AMI hospitalization in the study by Zanobetti et al. (33), and some research has focused on the major cardiovascular health risks in patients with diabetes. The study by von Klot et al. (9) on cardiac readmissions in myocardial infarction survivors suggested a specific vulnerability to traffic-related pollutants among patients affected by some cardiovascular conditions.

In the analyses stratified by season, significant association estimates were obtained in the cold season, whereas no association was observed in the warm season. This result is coherent with the higher levels of pollutants observed during winter in the studied areas. Our finding seems to contrast with the findings of other studies, although results are not conclusive. Zanobetti et al. (27) found stronger associations between carbon monoxide, nitrogen dioxide, and \( PM_{2.5} \) and myocardial infarction hospital admissions during the warm season; however, this could be explained by differences in the distribution of pollutant levels in different seasons between Europe and the United States. The same results were obtained by D’Ippoliti et al. (25). In the study by Linn et al. (34), a significant excess risk for particulate matter was reported only in winter.

Some limitations of this study should be considered. Firstly, measurements of fine and ultrafine particulate matter and particle composition (organic carbon, metals, sulfate) were not available, and we limited the analyses to \( PM_{10} \). Indoor pollution sources were ignored, and pollution measured by outdoor monitoring sites may not be a good measure of overall personal exposure, especially for gaseous pollutants, as suggested by a recent study comparing personal exposure with ambient exposure (35). In addition, we selected monitoring sites in order to represent the background exposure of the general population, assuming homogeneous exposure throughout the area. Diagnostic misclassification could have affected the categorization of the individual comorbid conditions; the use of hospital discharge data to identify people affected by some chronic conditions, such as hypertension, diabetes, and COPD, could have a low sensitivity. Finally, the use of hospital admission data did not allow us to explore the association of other important risk factors for myocardial infarction with individual susceptibility, such as smoking habits, diet, and other lifestyle factors.

In conclusion, our study adds further evidence for an association between short-term increases in ambient air pollutant levels and AMI onset. The associations were evident at pollutant levels even lower than those of the current regulatory standards. Results suggest that some population subgroups are more susceptible.

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