Long-Term Exposure to Urban Air Pollution and Mortality in a Cohort of More than a Million Adults in Rome

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BACKGROUND: Few European studies have investigated the effects of long-term exposure to both fine particulate matter (≤ 2.5 µm; PM2.5) and nitrogen dioxide (NO2) on mortality.

OBJECTIVES: We studied the association of exposure to NO2, PM2.5, and traffic indicators on cause-specific mortality to evaluate the form of the concentration–response relationship.

METHODS: We analyzed a population-based cohort enrolled at the 2001 Italian census with 9 years of follow-up. We selected all 1,265,058 subjects ≥ 30 years of age who had been living in Rome for at least 5 years at baseline. Residential exposures included annual NO2 (from a land use regression model) and annual PM2.5 (from a Eulerian dispersion model), as well as distance to roads with > 10,000 vehicles/day and traffic intensity. We used Cox regression models to estimate associations with cause-specific mortality adjusted for individual (sex, age, place of birth, residential history, marital status, education, occupation) and area (socioeconomic status, clustering) characteristics.

RESULTS: Long-term exposures to both NO2 and PM2.5 were associated with an increase in non-accidental mortality [hazard ratio (HR) = 1.03 (95% CI: 1.02, 1.04) per 10-µg/m3 NO2; HR = 1.04 (95% CI: 1.03, 1.05) per 10-µg/m3 PM2.5]. The strongest association was found for ischemic heart diseases (IHD) [HR = 1.10 (95% CI: 1.06, 1.13) per 10-µg/m3 PM2.5], followed by cardiovascular diseases and lung cancer. The only association showing some deviation from linearity was that between NO2 and IHD. In a bi-pollutant model, the estimated effect of NO2 on mortality was independent of PM2.5.

CONCLUSIONS: This large study strongly supports an effect of long-term exposure to NO2 and PM2.5 on mortality, especially from cardiovascular causes. The results are relevant for the next European policy decisions regarding air quality.

We conducted a follow-up to determine vital status using the Rome Municipal Register during the period October 2001–December 2010. We retrieved information on deceased individuals and considered subjects as lost to follow-up when they moved out of the city. The underlying cause of death [coded according to the International Classification of Diseases, 9th Revision (ICD-9; WHO 1977)] for deceased subjects was retrieved from the Lazio regional health information system.

The RoLS is part of the National Statistical Program for the years 2011–2013 and was approved by the Italian Data Protection Authority.

**Air pollution exposure assessment.** We used a land use regression (LUR) model to estimate annual NO$_2$ concentrations for each residence. The LUR model has been described previously (Cesaroni et al. 2012a). Briefly, in 2007 we measured NO$_2$ concentrations using Ogawa passive samplers (Ogawa & Co. USA Inc., Pompano Beach, FL, USA) at 78 sites during three 1-week periods in February, May, and October. We assigned to each sampling location a single NO$_2$ level, the mean of the three measurements. We used several land-use, GIS, and traffic variables to predict log NO$_2$ levels in multivariable linear regression. The best-fitting regression model had a determination coefficient ($R^2$) of 0.704. The model was validated using leave-one-out cross validation; the $R^2$, adjusted $R^2$, and root mean square error of the regression analysis between measured and estimated concentrations was 0.61, 0.61, and 5.38, respectively.

Residential exposure to PM$_{2.5}$ was estimated using a 1 km–grid dispersion model (the flexible air quality regional model (FARM), a three-dimensional Eulerian model of the transport and multiphase chemistry of pollutants in the atmosphere (Gariazzo et al. 2007, 2011)]. [For further details on the dispersion model, its validation, and the comparison of the results from the NO$_2$ and PM$_{2.5}$ models with actual measurements are provided in Supplemental Material, pp. 2–3 (http://dx.doi.org/10.1289/ehp.1205862).]

We applied the estimated annual means from the 2007 NO$_2$ LUR model and from the 2005 PM$_{2.5}$ dispersion model to all addresses from October 1996 through December 2010. For each individual subject and each year of the follow-up, we calculated the average exposure since October 1996, weighted for the time of residence in each location.

We used two GIS indicators at the sub-neighborhood level (the sum of the number of vehicles per day multiplied by the length of the roads in meters within the buffer) categorized in quintiles of the distribution. The size of the buffer was slightly larger than that used by Beele et al. (2008). For the GIS variables, we used the address of the individual subjects at the baseline.


**Covariates.** We considered age, sex, and several variables at the baseline as potential confounders: marital status (married, single, separated/divorced, or widowed), place of birth (Rome or other), level of education (university, high school, secondary, or primary), and occupation [top qualified non-manual employed (i.e., managers, university and high school professors, researchers); other non-manual employed; manual labor employed; other employed (i.e., armed forces and retail sales); housewife; unemployed; retired; other].

Some studies have shown that neighborhood socioeconomic level is associated with smoking, after accounting for individual education and occupation (Diez Roux et al. 2003). Therefore, we adjusted estimates for a five-level small-area (census block) socioeconomic position index that is based on 2001 census data in Rome (5,500 census blocks, average population of 500 subjects per block) and was derived based on a factor analysis including education, occupation, house ownership, family composition, crowding, and immigrant status (Cesaroni et al. 2010). In addition, because data on lifestyles were unavailable, we adjusted a subset of models for preexisting comorbidities related to smoking habits or diet [diabetes (ICD-9 code 250), chronic obstructive pulmonary disease (COPD; ICD-9: 490–492, and 496), and hypertensive heart disease (ICD-9: 401–404)] that were identified based on the principal and up to five secondary diagnoses indicated on hospital discharges from October 1996 to October 2001 (Gan et al. 2011).

In a sensitivity analysis, we performed a frailty model to investigate the role of both neighborhood and district (Rome is divided into 94 neighborhoods and into 19 districts).

We explored the shape of relationships between exposures and outcomes by replacing the linear term in the base model with natural splines with 2, 3, or 4 degrees of freedom (df) (Eisen et al. 2004), which capture potential nonlinearity in the data without overfitting. We used the Bayesian information criterion (BIC) and the likelihood ratio test to compare the relative goodness of fit of the models.

We used STATA10 (StataCorp, College Station, TX, USA) for all statistical analyses with the exception of the frailty models and spline plots, for which we used R (R Foundation, Vienna, Austria). Because R was not able to deal with a large number of records for the amount of computer memory available, for the spline and frailty analyses we studied a 20% random sample of the study population and used fixed time-weighted exposures between October 1996 and October 2001. We applied the appropriate weights to natural spline models to plot effects for the entire population.
Results

A total of 1,265,058 residents were included in the study. The average exposure levels of the population (mean (SD, range, 25th percentile, 50th percentile, 75th percentile)) at baseline were 43.6 µg/m³ (8.4, 13.0–75.2, 38.5, 44.5, 49.2) for NO₂, and 23.0 µg/m³ (4.4, 7.2–32.1, 20.3, 23.9, 26.0) for PM₂.₅. The average distance to an HTR was 232 m (224, 2–946, 80, 165, 308), and the average traffic intensity within a 150 m buffer zone was 4.1 × 10⁶ vehicles/m (5.3 × 10⁶, 0–88.9 × 10⁶, 0.6 × 10⁶, 5.4 × 10⁶, 5.5 × 10⁶). We found a high correlation between NO₂ and PM₂.₅ exposures (0.79). Figure 1 maps the concentrations of the two pollutants in Rome. The highest levels of air pollution are in the city center and in the eastern part of Rome. The resolution of the exposure model for NO₂ is clearly higher than for PM₂.₅.

From October 2001 to December 2010 (average length of follow-up: 8.3 years), 9.5% of the study population emigrated, and 12% died. There were 144,441 non accidental deaths (95.8% of all deaths), and the crude mortality rate (CMR) was 13.8 per 10,000 person-years. Cardiovascular causes were responsible for 40% of all deaths (CMR = 5.8) [including IHD (15% of deaths, CMR = 2.2) and cerebrovascular diseases (9% of deaths, CMR = 1.3)]; respiratory diseases and lung cancer accounted for 6% (CMR = 0.8) and 8% of all deaths (CMR = 1.2), respectively. The majority of the cohort (75.3%) did not change address from October 1996 to the end of follow-up, whereas a change in address within the city was registered for the other 311,728 residents.

Residents with higher levels of NO₂ exposure were older, better educated, and more likely to live alone, closer to HTRs, and more exposed to traffic compared with residents who had lower levels of exposure [see Supplemental Material, Table S1 (http://dx.doi.org/10.1289/ehp.1205862)].

Air pollution and mortality. Although there was little or no evidence of an association between any of the indices of exposure and non accidental, cardiovascular disease, or IHD mortality based on the crude model (model 1, adjusted for sex only), there was strong evidence of an association between all exposure indicators and these outcomes when we adjusted for personal characteristics and area-based socioeconomic position (model 2) (Table 1). The variables most responsible for the differences between the two models were education, occupation, and area-based socioeconomic position index (data not shown). The magnitude of the estimated effects on non accidental mortality was similar for NO₂ and PM₂.₅, with a gradual increase in mortality across the quintiles of NO₂ and PM₂.₅, as well as categories of traffic intensity and distance to HTRs. Although the p_trend was < 0.05 in the association between proximity to HTRs and mortality, only those living < 50 m from an HTR had a statistically significant higher mortality risk compared with those living ≥ 250 m from an HTR. Associations with the different exposure indexes followed similar patterns for cardiovascular disease and IHD mortality, and the estimated effects were stronger for IHD mortality than all other causes.

Table 2 shows the results of cerebrovascular, respiratory, and lung-cancer mortality. There was evidence of an association between PM₂.₅ exposure and cerebrovascular mortality, with an 8% higher risk per 10-µg/m³ PM₂.₅ (model 2; 95% CI: 1.04, 1.13), but associations with NO₂ and proxy measures of traffic exposure were weaker and not statistically significant. There was some evidence of an effect of NO₂ and traffic intensity on respiratory disease mortality. There was strong evidence of an association between lung-cancer mortality and both NO₂ and PM₂.₅, but not with proxy measures of traffic exposure. Estimated associations with NO₂ and PM₂.₅ were similar or slightly stronger for all outcomes when we also adjusted for preexisting comorbidity [see Supplemental Material, Table S2 (http://dx.doi.org/10.1289/ehp.1205862)].

Associations with 10-µg/m³ increases in NO₂ and PM₂.₅ (performed on a 20%
### Table 1. Adjusted HRs (95% CI) of nonaccidental, cardiovascular, and IHD mortality according to different air pollution exposure indices, Rome 2001–2010.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Cases</th>
<th>HR* (95% CI)</th>
<th>HR* (95% CI)</th>
<th>Cases</th>
<th>HR* (95% CI)</th>
<th>HR* (95% CI)</th>
<th>Cases</th>
<th>HR* (95% CI)</th>
<th>HR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonaccidental causes (n = 144,441)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Quintiles of NO₂a</td>
<td>21,496</td>
<td>1.00</td>
<td>1.00</td>
<td>8,400</td>
<td>1.00</td>
<td>1.00</td>
<td>3,181</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Q2</td>
<td>23,521</td>
<td>1.00 (0.98, 1.02)</td>
<td>1.04 (1.02, 1.06)</td>
<td>9,443</td>
<td>1.00 (0.97, 1.03)</td>
<td>1.04 (1.01, 1.08)</td>
<td>3,651</td>
<td>1.04 (0.99, 1.09)</td>
<td>1.09 (1.04, 1.15)</td>
</tr>
<tr>
<td>Q3</td>
<td>30,272</td>
<td>1.00 (0.99, 1.01)</td>
<td>1.05 (1.03, 1.07)</td>
<td>12,647</td>
<td>0.98 (0.98, 0.99)</td>
<td>1.06 (1.03, 1.09)</td>
<td>5,183</td>
<td>1.02 (0.98, 1.07)</td>
<td>1.10 (1.05, 1.15)</td>
</tr>
<tr>
<td>Q4</td>
<td>32,820</td>
<td>1.00 (0.98, 1.01)</td>
<td>1.06 (1.04, 1.07)</td>
<td>14,093</td>
<td>0.99 (0.96, 1.01)</td>
<td>1.06 (1.03, 1.09)</td>
<td>5,869</td>
<td>1.06 (1.01, 1.10)</td>
<td>1.13 (1.08, 1.19)</td>
</tr>
<tr>
<td>Q5</td>
<td>36,332</td>
<td>1.01 (0.99, 1.03)</td>
<td>1.07 (1.05, 1.09)</td>
<td>15,738</td>
<td>1.00 (0.98, 1.03)</td>
<td>1.07 (1.04, 1.10)</td>
<td>5,869</td>
<td>1.06 (1.01, 1.10)</td>
<td>1.13 (1.08, 1.19)</td>
</tr>
<tr>
<td>IQR NO₂ (10.7 μg/m³)</td>
<td>1.01 (1.00, 1.01)</td>
<td>1.02 (1.01, 1.03)</td>
<td>1.00 (0.99, 1.01)</td>
<td>1.03 (1.02, 1.04)</td>
<td>1.02 (1.01, 1.04)</td>
<td>1.05 (1.03, 1.07)</td>
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</tr>
</tbody>
</table>

### Table 2. Adjusted HRs (95% CI) of mortality according to different air pollution exposure indices, Rome 2001–2010.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Cerebrovascular disease (n = 13,576)</th>
<th>Respiratory disease (n = 8,825)</th>
<th>Lung cancer (n = 12,208)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>HR* (95% CI)</td>
<td>HR* (95% CI)</td>
<td>HR* (95% CI)</td>
</tr>
<tr>
<td>Quintiles of NO₂a</td>
<td>1,935</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Q2</td>
<td>2,141</td>
<td>0.97 (0.91, 1.03)</td>
<td>1.02 (0.96, 1.09)</td>
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<tr>
<td>Q3</td>
<td>2,330</td>
<td>0.94 (0.89, 1.00)</td>
<td>1.01 (0.96, 1.08)</td>
</tr>
<tr>
<td>Q4</td>
<td>3,151</td>
<td>0.94 (0.88, 0.99)</td>
<td>1.01 (0.96, 1.06)</td>
</tr>
<tr>
<td>Q5</td>
<td>3,519</td>
<td>0.95 (0.90, 1.00)</td>
<td>1.02 (0.97, 1.09)</td>
</tr>
<tr>
<td>IQR NO₂ (5.8 μg/m³)</td>
<td>0.97</td>
<td>0.040</td>
<td>0.459</td>
</tr>
</tbody>
</table>

### Notes
- Quintiles of NO₂: Q1 = 36.5; Q2, 36.5–42.7; Q3, 42.7–46.2; Q4, 46.2–50.4; Q5, > 50.4 μg/m³. Quintiles of PM₁₀: Q1, ≤ 19.4; Q2, 19.4–22.5; Q3, 22.5–24.8; Q4, 24.8–28.6; Q5, > 28.6 μg/m³. Quintiles of traffic intensity (>10): Q1, < 0.05; Q2, 0.25–1.83; Q3, 1.83–3.23; Q4, 3.23–6.66; Q5, > 6.66.
random using the standard Cox model (model 2), the frailty model with districts, and frailty model with neighborhoods [see Supplemental Material, Table S3 (dx.doi.org/10.1289/ehp.1205862)]. The effect estimates in the 20% sample were similar to those obtained for the entire data set, with the only exception of the PM$_{2.5}$–lung cancer association, which was clearly underestimated.

Figure 2 shows estimated concentration–response curves (natural splines, 2 df) for non-accidental mortality, cardiovascular, IHD, and lung-cancer mortality for NO$_2$ (Figure 2A) and PM$_{2.5}$ (Figure 2B) based on a 20% random sample of the study population. In general, the results showed no evidence of deviation from linearity (based on BIC), with the only exception being the association between NO$_2$ exposure and IHD mortality (likelihood ratio test comparing the linear and the spline model with 2 df gave a $p$-value = 0.028, although with very similar BIC). Results were similar for natural splines with 3 or 4 df (data not shown).

Despite the high correlation between the two pollutants, the estimated effect of a 10-$\mu$g/m$^3$ increase in NO$_2$ on nonaccidental mortality was still statistically significant when adjusted for PM$_{2.5}$ in a bi-pollutant model [model 2; HR = 1.02 (95% CI: 1.01, 1.03)]. In contrast, the estimated effect of PM$_{2.5}$ decreased when adjusted for NO$_2$ [HR = 1.01 (95% CI: 0.99, 1.02) for a 10-$\mu$g/m$^3$ increase in PM$_{2.5}$ compared with HR = 1.04 (95% CI: 1.03, 1.05) based on the single pollutant model]. Adjusting for proximity to an HTR or traffic intensity in separate models of NO$_2$ and PM$_{2.5}$ did not change estimates for either pollutant (data not shown).

Figure 3 presents the adjusted HRs, 95% CIs, and $p$-values for interaction (likelihood ratio test) for nonaccidental, cardiovascular, IHD, and lung-cancer mortality per 10-$\mu$g/m$^3$ NO$_2$ and PM$_{2.5}$, by sex, level of education (high = university; middle = high school, low = secondary and primary school), age group, area-based socioeconomic position, and residential stability (movers: those who changed residence during the study). There was some suggestion of effect modification by age (with < 60-year-olds at higher risk than ≥ 75-year-olds), by residential stability (with non-movers at higher risk than movers), and by sex (with men at higher risk than women) for nonaccidental and cardiovascular mortality (for PM$_{2.5}$ only).

**Discussion**

We found statistically significant positive associations between long-term exposure to NO$_2$ and PM$_{2.5}$ and nonaccidental, cardiovascular, IHD, and lung-cancer mortality in the adult population of Rome. In addition, exposure to PM$_{2.5}$ was associated with cerebrovascular mortality, whereas NO$_2$ exposure was associated with respiratory mortality. Proximity to HTRs and high traffic intensity were associated with nonaccidental, cardiovascular, and IHD mortality. Despite the high correlation of the pollutants, NO$_2$ was significantly associated with mortality when adjusted for PM$_{2.5}$, although the estimated effect of PM$_{2.5}$ was no longer significant. There was no evidence of deviation from linearity of the effects of either NO$_2$ or PM$_{2.5}$ on nonaccidental, cardiovascular, and lung-cancer mortality. The estimated effects on nonaccidental mortality tended to be stronger in males, younger subjects (< 60 years of age), and non-movers.

Average exposure of the cohort was slightly higher than in other study populations from Europe or North America, but near the values being discussed as potential European standards (40 µg/m$^3$ for NO$_2$ and 20 µg/m$^3$ for PM$_{2.5}$). The mean concentrations of NO$_2$ and

![Figure 2](image-url). Estimated concentration–response curves (solid lines) and 95% CIs (dashed lines) for nonaccidental causes, cardiovascular disease, IHD, and lung cancer for NO$_2$ (A) and PM$_{2.5}$ (B). Cox models adjusted for sex, marital status, place of birth, education, occupation, and area-based socioeconomic position on a 20% sample of the cohort.
Figure 3. Adjusted HRs (95% CIs) and p-values for interaction for cause-specific mortality per 10-µg/m³ elevation in NO₂ (A) and PM₂.₅ concentrations (B), by population characteristics and cause of death.
PM$_{2.5}$ (in Rome: 44 µg/m$^3$ and 23 µg/m$^3$, respectively) ranged from 32.1 and 4.1 µg/m$^3$ in Canada (Gan et al. 2011) to 39 µg/m$^3$ NO$_2$ in Germany (Gehring et al. 2006), and to 28.3 µg/m$^3$ PM$_{2.5}$, respectively, in the Netherlands (Beelen et al. 2008).

The associations we found for the selected causes of mortality were comparable with, but slightly lower than, those reported in other European and North American settings (Crouse et al. 2012). The 4% (95% CI: 3, 5%) higher risk of nonaccidental mortality per 10-µg/m$^3$ PM$_{2.5}$ in Rome was comparable to the 6% higher risk (95% CI: 3, 9%) reported based on a meta-analysis of five studies (Abbey et al. 1999; Beelen et al. 2008; Gehring et al. 2006; Laden et al. 2006; Pope et al. 2002), whereas the 3% (95% CI: 2, 3%) estimated increase in risk per 10-µg/m$^3$ NO$_2$ was lower than the meta-analytic estimate of 6% (95% CI: 4, 8%) based on four European studies (Beelen et al. 2008; Filleul et al. 2005; Gehring et al. 2006; Nabratu et al. 2004) [data reported in Cesaroni et al. (2012b)].

As expected, associations with IHD and cardiovascular mortality were stronger than with other causes of death (Crouse et al. 2012; Jerrett et al. 2009; Lepule et al. 2012). Linear association between the pollutant exposures and cause-specific mortality were reported in some previous studies (Crouse et al. 2012; Gan et al. 2011). The shapes of the NO$_2$ curves were similar to estimates reported for a study population in Olso, Norway (Naess et al. 2007).

Although stronger estimated effects for non-movers may simply reflect improved exposure estimation, evidence of higher risks in men compared with women deserves additional attention. Evidence of sex differences in susceptibility to air pollution is controversial. In the United States, an association between exposure to PM$_{10}$ (particles with a diameter ≤ 10 µm) and mortality was reported for women in the Nurses’ Health Study (Puett et al. 2008) but not for men in the Health Professionals Follow-Up Study (Puett et al. 2011). However, Gan et al. (2011) reported strong evidence of an effect of black carbon on coronary heart disease mortality (after adjusting for NO$_2$ and PM$_{2.5}$) in men but not women. We estimated the strongest effects in the youngest age group of our population (< 60 years), consistent with a previous study (Naess et al. 2007).

Our study has several strengths. It is the largest European cohort study of the effects of both NO$_2$ and PM$_{2.5}$ and provides the statistical power to detect the effects of different indices of exposure on mortality. Residential history and several individual characteristics were available, and we had estimates of both NO$_2$ and PM$_{2.5}$ at the residences of all subjects.

This study has some limitations. The RoLS is a cohort built on administrative data and information on individual risk factors such as smoking habits, diet, alcohol consumption, and obesity were not available. As previously done in the literature, we adjusted the models for preexisting diabetes, COPD, and hypertensive heart disease—conditions which share the lifestyle risk factors cited (Gan et al. 2011). We adjusted also for small-area socioeconomic position, which could be a predictor of smoking habits independent of personal characteristics (Diex Roux et al. 2003). The adjustment for preexisting conditions might have led to an underestimation of the effect, because the comorbidities might act as intermediate variables (Gan et al. 2011).

To further investigate the role of smoking, we selected 7,845 adult subjects from the study population for whom information on smoking habits was available from another investigation (the Italian Studies on Respiratory Disorders in Childhood and Environment (SIDRIA) study; Cesaroni et al. 2008). Once we adjusted for all covariates used in model 2 in a logistic regression model predicting ever smoking, there was no evidence of an association between exposure to NO$_2$ or PM$_{2.5}$ and ever smoking (all odds ratios close to 1.0), indicating that smoking is unrelated to the exposures and thus an unlikely confounder. Moreover, when we added smoking status in a survival analysis (model 2) restricted only to SIDRIA participants, the association between the air pollution exposures and nonaccidental mortality did not change (data not shown).

To analyze frailty and concentration–response curves we had to use a 20% random sample of the population, but these alternate models provided only slightly different estimates of the effects for nonaccidental, cardiovascular, and IHD mortality. Therefore, we expect that frailty analyses of the entire population would be comparable. On the other hand, PM$_{2.5}$ effect estimates for lung cancer based on the 20% sample were quite different (close to unity) from estimates based on the entire population, and therefore the relative spline plot should be interpreted cautiously.

To estimate NO$_2$ and PM$_{2.5}$ exposure we used both an LUR model based on measurements carried out on 2007 and a dispersion model based on simulation for the year 2005, respectively. Both models were independently validated [see Supplemental Material, pp. 2–3 (http://dx.doi.org/10.1289/ehp.1205862)]. PM$_{2.5}$ and NO$_2$ were highly correlated, but PM$_{2.5}$ estimates had a lower resolution than estimates for NO$_2$. We are fairly confident that the spatial gradient of pollutants within the city remained stable over time. Rome is a city that changes very slowly, as two NO$_2$ LUR models developed using measures taken 12 years apart showed very similar results both in terms of estimates of exposure of the population (the correlation was 0.96) and in their associations with natural mortality (Cesaroni et al. 2012a). We took into account the changes of address (and exposure) during the follow-up in the main time-dependent analyses. Conversely, we used time-weighted exposure for the 5 years before enrollment, without taking account of changes of address, for frailty models and spline curves. We have evaluated that the bias introduced in this way is negligible because the results on the entire population based on 1996–2001 average exposure were similar to those obtained with time-dependent exposure (data not shown).

Conclusions

Long-term exposure to NO$_2$ and PM$_{2.5}$ was associated with increased mortality in this large population-based cohort. We found the strongest associations with IHD, followed by cardiovascular and lung-cancer mortality. The estimated effect of NO$_2$ persisted after adjusting for PM$_{2.5}$, and the shapes of the concentration response for both pollutants showed no evidence of deviation from linearity for all causes except cancer. European policy decision regarding environment and public health should be made with consideration of the specific scientific research results on the health effects of air pollution, such as those provided here.

References


