



Practice of Epidemiology

Health Impact Assessment of Fine Particle Pollution at the Regional Level

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Since the year 2000, evaluation of the impact of air pollution on people's health has drawn the attention of the general public and has led decision-makers to develop specific health policies. In most of the health impact assessment literature, investigators have reported on long- and short-term effects of air pollution. Here the authors present results of a health impact assessment of short-term effects of particulate matter $\leq 10 \mu\text{m}$ in diameter (PM_{10}) in the Lombardy region of Italy (2003–2006). The impact was evaluated in terms of numbers of attributable deaths under several counterfactual scenarios of air pollution reduction based on World Health Organization guidelines and European Union limits. The authors found that annual average PM_{10} levels exceeding the World Health Organization threshold of $20 \mu\text{g}/\text{m}^3$ and the European Union limit of $40 \mu\text{g}/\text{m}^3$ were responsible for 302 and 109 attributable deaths per year, corresponding to attributable community rates of 13 and 5 deaths per 100,000 inhabitants per year, respectively. A 20% reduction in existing PM_{10} levels could reduce by more than 30% the burden of short-term deaths linked to ambient air pollution. Therefore, policies for air pollution reduction appear to be necessary in order to protect and improve individual and community health.

air pollution; attributable risk; Bayesian analysis; particulate matter; public health; shrunken estimator

Abbreviations: CrI, credibility interval; EU, European Union; MISA, Meta-Analysis of the Italian Studies on Short-Term Effects of Air Pollution; PM_{10} , particulate matter $\leq 10 \mu\text{m}$ in diameter; RS, reduction scenario; WHO, World Health Organization.

Since the year 2000, evaluation of the impact of air pollution on people's health has drawn the attention of the general public and has led decision-makers to develop specific health policies (1). In most of the health impact assessment literature, investigators have reported on the long- and short-term effects of air pollution. Several contributions focused on impact assessment carried out in European cities and elsewhere (2–8). In Italy, results of multicity impact assessments were published by the World Health Organization (WHO) (9) and as part of the MISA (Meta-Analysis of the Italian Studies on Short-Term Effects of Air Pollution) project (10).

On the basis of public health considerations, the WHO Air Quality Guidelines (11) suggest a target of $20 \mu\text{g}/\text{m}^3$ for annual average concentrations of particulate matter $\leq 10 \mu\text{m}$ in diameter (PM_{10}). The European Commission's 2008 directive on air quality, which defines the legal obligations of European Union (EU) member states, is less stringent and sets a yearly average limit of $40 \mu\text{g}/\text{m}^3$ (12).

Large meta-analyses conducted in the United States and Europe have indicated that exposure to air pollution at levels currently present in urban environments is associated with a short-term increase in mortality and with a variety of health conditions (13, 14). The replication of epidemiologic studies carried out with similar models in different countries and contexts has led to consistent findings, supporting a causal interpretation of the effect measure and the absence of major bias, which are the basis for reliable health impact assessment (15).

Here we present results of a health impact assessment of short-term effects of PM_{10} in the Lombardy region of Italy (Figure 1). Lombardy, a 23,865-km² area in northwestern Italy, has 9.8 million inhabitants (a population density of 412 inhabitants/km²), 12 provinces, and 1,546 municipalities. It is the most populated region of Italy and ranks first in gross internal product (20% of the total Italian gross product) and gross product pro capita (€33,648). Milan is the capital city.

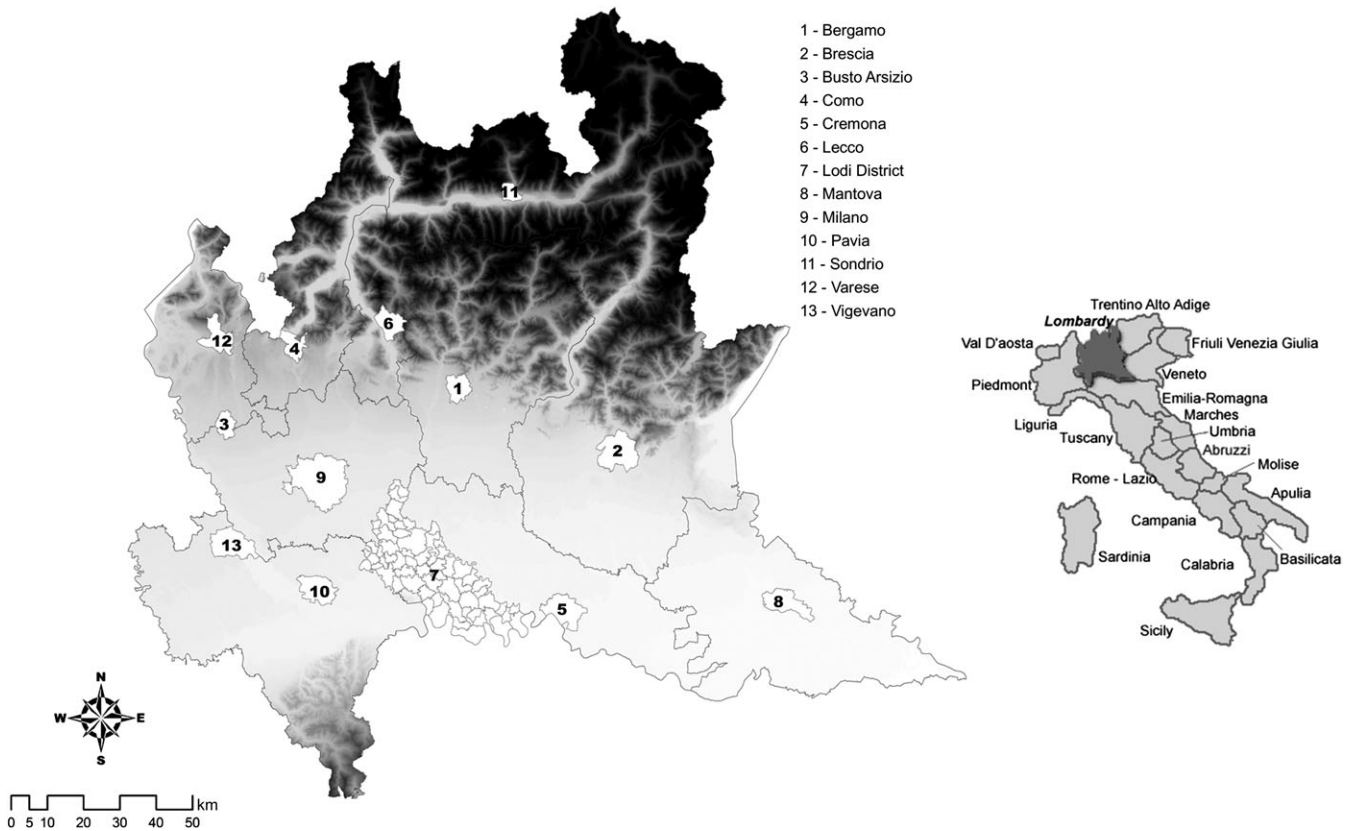


Figure 1. The Lombardy region of Italy. The 13 study areas considered in the meta-analysis are highlighted in white.

The region can be geographically and economically divided into 3 zones: the mountain range of the Alps; the sloping foothills; and the immediate facing plains, where one finds the highly industrialized provinces of Varese, Como, Lecco, Bergamo, and Brescia. The service sector is concentrated in the Milan area, and the large Po River plains have a rich agricultural sector (16). The population is concentrated in the Milan conurbation and the Alpine foothills of the above-mentioned provinces (6.5 million inhabitants, a density of 1,200 inhabitants/km²). Since the 1980s, while remaining the most important industrial area of the country, Lombardy has shown marked growth in the service sector.

The area's climate depends on altitude and the presence of inland waters. The temperature shows high annual variations (in Milan, the average temperature is 1.5°C in January and 24°C in July), and thick fog is frequent between October and February. The basin of the Po River, where most of the major cities are located, is bordered on 3 sides by mountains, and Atlantic weather disturbances are frequently unable to cross the Alpine barrier, consequently providing no air mass exchange. Wind speed measured in the Po River basin is among the lowest in Europe. This causes frequent phenomena of thermal inversion, with smog and pollution being trapped close to the ground. This unfavorable context and these climate characteristics create a high level of air pollution. Lombardy has exceeded the EU PM₁₀ limit since 1996, when the limit

was first issued. Road transport can be considered the main source of air pollution in the urban areas considered in this study. For example, in the district of Milan, road transport is estimated to be responsible for 63% of total PM₁₀ emissions (17).

In the present study, we assessed the health impact of PM₁₀ in Lombardy during the period 2003–2006. We evaluated the impact of PM₁₀ in terms of number of attributable deaths, assuming several counterfactual scenarios of air pollution reduction. We focused on short-term evaluation because it allows for immediate appraisal of deaths prevented by reduction policies, while for long-term effects the impact is highly speculative in nature because of latency time and the role of cumulative exposure.

We propose an original approach to assess the health impact of air pollution at the regional level that is characterized by the use of local data for estimation of the concentration-response function and by the specification of several counterfactual scenarios defined in terms of both annual average PM₁₀ concentrations and daily concentrations. In particular, we applied 2 different methods for calculation of attributable deaths. The first, which we named the “macro” approach, is appropriate for evaluating impacts under scenarios defined in terms of annual mean air pollutant concentration, and the second, named the “micro” approach, is used when the counterfactual scenarios are defined in terms of daily levels of PM₁₀.

MATERIALS AND METHODS

Data

We considered air pollution and mortality data for the period covering 2003–2006 for 13 areas in Lombardy: 11 cities with more than 50,000 inhabitants, 1 smaller town (Sondrio) that is the capital of an Alpine administrative province, and all of the municipalities belonging to the administrative agricultural district of Lodi, collapsed into a single epidemiologic time series. We did not consider the smaller municipalities in estimating air pollutant effects because precision is poor in the presence of small daily death counts.

The air quality monitoring network of the Lombardy Regional Environmental Protection Agency provided the daily time series of PM₁₀ measurements, temperature, and relative humidity values. All of the monitoring stations were located at sites not greatly influenced by local traffic and therefore provided measurements of the background levels of PM₁₀. For each municipality, missing daily values at one monitor were imputed using concentrations measured by the remaining monitors, and a daily time series of PM₁₀ levels was obtained by averaging data over the available monitors (10).

Death certificates were obtained from the regional mortality register. We considered mortality from all causes, excluding external causes (*International Classification of Diseases*, Ninth Revision, codes below 800). For each area, we focused on daily numbers of deaths occurring in the resident population inside the area and in municipalities within a 10-km radius from the border.

Effect estimates

Health impact was evaluated for each area in terms of the number of attributable deaths, combining the concentration-response functions derived from a Bayesian meta-analysis of the 13 study areas and the observed daily time series of PM₁₀ concentrations and mortality over the study period.

Inference on the concentration-response function was made up of 2 steps: an area-specific analysis and a Bayesian combined analysis. At the first stage, we estimated the short-term effect of PM₁₀ separately for each area. For specificity reasons, in estimating the air pollutant effect we considered only deaths of the resident population occurring inside the area. By excluding deaths occurring outside the area, we obtained less precise estimates, but we avoided possible bias due to classifying as exposed those persons who did not experience the PM₁₀ levels observed in their residence area.

We specified a Poisson regression model for the daily number of deaths (10, 18). Analysis was age-adjusted (<65, 65–74 years, and ≥75 years). We controlled for time-related confounding, effects of temperature and humidity, and influenza epidemics. The average of current-day and previous-day concentrations (lag 0–1) was used as the indicator of PM₁₀ exposure. We modeled the air pollution effect using a linear term. Analyses were performed with R 2.11.0 software (19).

At the second stage of the analysis, a Bayesian random-effects meta-analysis of the first-stage area-specific estimates was performed (20). Random-effects meta-analysis

allows one to obtain estimates of the second-stage area-specific effects (β_i), or shrunken estimates. Under the classical approach, shrunken estimates ($\hat{\beta}_i$) combine the area-specific estimates obtained in the first step of the analysis ($\hat{\lambda}_i$) and the overall estimate from meta-analysis ($\hat{\beta}$). Each location-specific estimate is pulled towards the overall effect estimate, proportionally to its variance $\hat{\sigma}_i^2$:

$$\hat{\beta}_i = \frac{\hat{\sigma}_i^2}{\hat{\sigma}_i^2 + \tau^2} \hat{\beta} + \left(1 - \frac{\hat{\sigma}_i^2}{\hat{\sigma}_i^2 + \tau^2}\right) \hat{\lambda}_i.$$

These estimates are more stable than the area-specific estimates because they borrow strength from all locations while reflecting heterogeneity among areas. The overall amount of shrinkage depends on the heterogeneity parameter τ^2 . Under the Bayesian approach, the posterior distribution of the area-specific parameters β_i can be obtained by updating the first-stage area-specific estimates using information from all analyzed areas (21–23).

Posterior distributions of the model parameters were obtained with WinBugs (24).

Health impact assessment

The impact of air pollution on mortality was quantified in terms of the number of attributable deaths. The model assumes that the exposure level within each area is homogeneous. For each area, we considered the deaths of residents occurring inside the area or in municipalities within a 10-km radius from the border of the area. We excluded events occurring elsewhere. The main rationale for this choice is that a person experiencing the air pollution level of his or her residence area on a certain day could be admitted to the hospital of a neighboring municipality and then die within few days due to the effects of this exposure.

We used 2 different approaches, which we called the “macro” and “micro” approaches, for health impact assessment. The macro approach relies on the yearly average of the number of deaths and the yearly average of PM₁₀ levels (1). Under the micro approach, impact calculation was made day by day using the series of daily death counts and daily PM₁₀ levels.

If the distribution of the PM₁₀ daily concentrations is not strongly asymmetric and the degree of correlation between outcome and exposure is not large, the macro approach approximates the results we would obtain by applying the day-by-day, micro approach. Despite this correspondence, the opportunity to use one approach or the other depends on the chosen counterfactual scenario. While using macro modeling is the simplest way to quantify the impact under counterfactual scenarios defined in terms of yearly average, the micro approach also allows evaluation of the impact under counterfactual scenarios defined in terms of daily concentration.

The effect of air pollution is assumed to be linear without any threshold on a logarithmic scale. We counted the events attributable to exposure levels exceeding a given threshold T_0 . Let y_i be the yearly average of the number of deaths (under the macro approach) or the daily number of deaths (under the micro approach) for the i th area. Let x_i be the yearly

average of the PM₁₀ concentrations (under the macro approach) or the daily concentration of PM₁₀ (under the micro approach) for the *i*th area. Given a certain value of the coefficient which describes the effect of air pollution in the *i*th area (for simplicity, we indicated this value with $\hat{\beta}_i$), we assumed that above the threshold T_0 ,

$$y_i = y_{i0} \exp(\hat{\beta}_i(x_i - T_0)), \quad x_i > T_0,$$

where y_{i0} is the baseline number of deaths, that is, the expected number of events (yearly average or daily count, depending on the approach) we would observe for $x_i = T_0$.

The number of events attributable to PM₁₀ levels exceeding the threshold (i.e., attributable deaths (AD)) was then calculated as the difference between the observed number of events and the baseline number of events:

$$AD_i = y_i - y_{i0} = y_i \left(1 - \frac{1}{\exp(\hat{\beta}_i(x_i - T_0))} \right) = y_i AF_i,$$

with AF_i representing the attributable fraction of deaths. When making a calculation under the micro approach, the total number of attributable deaths over a time span was obtained by summing the number of attributable deaths from each day.

We evaluated the impact using different values of $\hat{\beta}_i$ sampled from the posterior distribution of the area-specific effect, obtaining a whole posterior distribution of the number of attributable deaths for each area.

The percentage of deaths attributable to the exposure and the attributable community rate per 100,000 inhabitants per year were also calculated for each area (25, 26). These measures allowed relative evaluation of the PM₁₀ impact and comparison among areas.

Counterfactuals

The health impact assessment was conducted by specifying different reduction scenarios (RS). We used the following scenarios under the macro approach:

RS0: $T_0 = 20 \mu\text{g}/\text{m}^3$, that is, the WHO Air Quality Guideline threshold (11) for PM₁₀ annual average;

RS1: $T_0 = 40 \mu\text{g}/\text{m}^3$, that is, the EU limit for PM₁₀ annual average (12);

RS2: T_0 equal to a reduction of 20% in the observed concentration of PM₁₀, provided it is greater than $20 \mu\text{g}/\text{m}^3$; and

RS3: T_0 equal to a reduction of 20% in the observed concentration of PM₁₀, provided it is greater than $40 \mu\text{g}/\text{m}^3$.

We chose the RS2 and RS3 counterfactual scenarios according to the EU regulation, which asks for a progressive reduction of 20% in the observed concentrations until the limit is reached for all of the contexts in which the limit cannot currently be reached (12).

When applying the micro approach, we considered a further scenario:

RS4: PM₁₀ concentrations not exceeding $50 \mu\text{g}/\text{m}^3$ more than 35 days per year, that is, the EU limit for daily averages (12).

We estimated the number of attributable deaths under the RS4 scenario by averaging 100 different pseudodata obtained by constraining to the threshold a different random set of days exceeding the $50 \mu\text{g}/\text{m}^3$ level, so that the number of days with a PM₁₀ concentration above the limit was set equal to 35 per year.

RESULTS

The 13 study areas represent approximately 35% of the Lombardy population (Table 1). The municipality of Milan has 1,299,633 inhabitants, which is 14% of the regional population. The average PM₁₀ level across the 13 areas was $45.4 \mu\text{g}/\text{m}^3$, with the highest values being observed in Cremona, Milan, and Lodi. In Figure 1, the areas considered in the meta-analysis are highlighted in white. These areas are the most densely populated in the region and hence the most polluted.

Effect estimates

Posterior distributions of the effect measures were summarized as posterior mean values and credibility intervals. Lower and upper bounds of a $(1 - \alpha)\%$ credibility interval are defined as the $(\alpha/2)$ th and $(1 - \alpha/2)$ th percentiles of the posterior distribution, respectively. For example, the 25th and 75th percentiles define the 50% credibility interval for the parameter of interest. Effect estimates were expressed in terms of the percentage of variation in mortality associated with an increase of $10 \mu\text{g}/\text{m}^3$ in PM₁₀ concentrations at lag 0–1.

In Table 2 we show, for each of the examined areas, the posterior mean of the percent variation with its 50% and 90% credibility intervals (27, 28). The pooled meta-analytic estimate of percent variation in natural mortality was 0.30 (90% credibility interval (CrI): $-0.21, 0.70$; 50% CrI: $0.14, 0.50$). We obtained the posterior distribution of the heterogeneity statistic I^2 (the percentage of total variability due to heterogeneity between areas) (29). There was little evidence of heterogeneity across zones ($I^2 = 4.23$, 90% CrI: $0.10, 28.17$). Still, the posterior effect estimate was higher for the Milan area (0.63, 90% CrI: $0.28, 1.02$; 50% CrI: $0.48, 0.78$) than for the other areas, with the posterior distribution for this city being shifted upward from the overall marginal posterior effect distribution (Figure 2).

Health impact estimates

The health impact of PM₁₀ is presented by area in Table 3. Over the course of the study period, 11 areas exceeded the EU limit of $40 \mu\text{g}/\text{m}^3$ (RS1), and all 13 exceeded the WHO threshold of $20 \mu\text{g}/\text{m}^3$ (RS0). The number of attributable deaths under the counterfactual scenario RS0 was approximately 3–4 times the number of attributable deaths under the counterfactual scenario RS1. The total number of attributable deaths per year in the 13 study areas was 302 assuming the $20 \mu\text{g}/\text{m}^3$ limit, while it was 109 assuming the $40 \mu\text{g}/\text{m}^3$ limit. In both cases, most of the attributable deaths (76% and 82% of the total, respectively) were observed in Milan, which contained approximately 50% of the entire study population.

Assuming a reduction of 20% in the observed concentrations in all areas (RS2), the total number of prevented deaths

Table 1. Characteristics of the 13 Areas Included in a Health Impact Assessment of Short-Term Effects of Particulate Matter $\leq 10 \mu\text{m}$ in Diameter, Lombardy, Italy, 2003–2006

Study Area	Population in 2007	Annual Average No. of Deaths From Natural Causes ^a		PM ₁₀ Concentration, $\mu\text{g}/\text{m}^3$			Average Temperature ($^{\circ}\text{C}$)
		Within a 10-km Radius From the Area Border	Inside the Area	Mean	5th Percentile	95th Percentile	
Bergamo	115,781	1,166	1,064	46.1	13.2	105.4	14.0
Brescia	189,742	1,223	1,155	49.4	14.5	108.7	12.9
Busto Arsizio	80,633	676	614	44.7	10.4	103.0	12.9
Como	83,175	786	698	43.6	15.5	93.5	12.5
Cremona	71,998	768	723	53.5	20.3	115.2	13.1
Lecco	47,325	468	422	38.4	11.0	86.8	14.0
Lodi district	219,670	1,945	1,945	52.6	16.1	114.6	13.1
Mantova	47,649	546	508	50.6	17.2	102.4	11.4
Milan	1,299,633	11,416	10,218	52.5	16.2	120.8	14.5
Pavia	70,207	744	684	44.4	12.3	95.4	16.7
Sondrio	22,214	195	190	42.8	11.0	93.6	12.5
Varese	82,037	816	742	29.6	11.2	56.2	13.2
Vigevano	60,738	572	508	42.2	5.9	100.5	14.7

Abbreviation: PM₁₀, particulate matter $\leq 10 \mu\text{m}$ in diameter.

^a *International Classification of Diseases*, Ninth Revision, codes below 800.

was 101. The scenario RS3 involved only the 11 areas in which the $40 \mu\text{g}/\text{m}^3$ limit was not currently being met. Assuming a 20% reduction in these areas (or a smaller reduction when

Table 2. Area-Specific Effects of Particulate Matter $\leq 10 \mu\text{m}$ in Diameter (PM₁₀) on Natural Mortality and the Overall PM₁₀ Effect, Lombardy, Italy, 2003–2006^a

Area	Posterior Mean of % Variation	50% CrI ^b	90% CrI ^c
Bergamo	0.33	0.13, 0.57	-0.34, 0.88
Brescia	0.13	-0.13, 0.46	-0.77, 0.71
Busto Arsizio	0.27	0.05, 0.54	-0.51, 0.85
Como	0.30	0.09, 0.56	-0.48, 0.88
Cremona	0.25	0.04, 0.53	-0.61, 0.83
Lecco	0.18	-0.05, 0.51	-0.79, 0.79
Lodi district	0.32	0.12, 0.54	-0.30, 0.80
Mantova	0.34	0.13, 0.58	-0.42, 0.93
Milan	0.63	0.48, 0.78	0.28, 1.02
Pavia	0.29	0.08, 0.56	-0.53, 0.90
Sondrio	0.28	0.06, 0.56	-0.61, 0.91
Varese	0.40	0.17, 0.63	-0.36, 1.09
Vigevano	0.24	0.01, 0.52	-0.59, 0.81
Overall	0.30	0.14, 0.50	-0.21, 0.70

Abbreviations: CrI, credibility interval; PM₁₀, particulate matter $\leq 10 \mu\text{m}$ in diameter.

^a Effects are expressed in terms of the percent variation in natural mortality associated with an increase of $10 \mu\text{g}/\text{m}^3$ in PM₁₀ concentration at lag 0–1.

^b 25th–75th percentiles.

^c 5th–95th percentiles.

this was sufficient to reach the $40 \mu\text{g}/\text{m}^3$ limit), the total number of prevented deaths per year was 93.

Table 4 shows the percentage of attributable deaths and the attributable community rate under the RS0 and RS1 scenarios. Areas with the largest risk attributable to PM₁₀ were Milan, Cremona, Lodi, and Mantova. Deaths attributable to exceeding the WHO limit of $20 \mu\text{g}/\text{m}^3$ amounted to 1.4% of all natural deaths among the studied areas. The percentage of deaths attributable to exceeding the EU limit of $40 \mu\text{g}/\text{m}^3$ was 0.5. In terms of attributable community rate, 13 and 5 deaths per 100,000 inhabitants per year were attributable to yearly average PM₁₀ levels exceeding $20 \mu\text{g}/\text{m}^3$ and $40 \mu\text{g}/\text{m}^3$, respectively.

Satisfying the condition of the PM₁₀ daily limit of $50 \mu\text{g}/\text{m}^3$ not being exceeded more than 35 days per year (RS4) would have resulted in an annual average slightly above $40 \mu\text{g}/\text{m}^3$ for the Milan area but notably would have avoided some PM₁₀-related deaths even in areas with lower yearly average PM₁₀ concentrations (Table 5).

DISCUSSION

We related PM₁₀ levels to immediate health effects on the populations of the most urbanized cities in the Lombardy region and the agricultural province of Lodi. It is reasonable to expect that the health impact of air pollution in all of Lombardy is mainly produced in these areas.

We evaluated the number of deaths we would have observed in the years 2003–2006 had the air pollution levels been different. Note that because no threshold has been proven for the toxic effects of air pollutants, the counterfactuals are arbitrary. A natural background level (i.e., from nonanthropogenic sources) of $7.5 \mu\text{g}/\text{m}^3$ was used in previous impact calculation (1). However, it is questionable whether any such

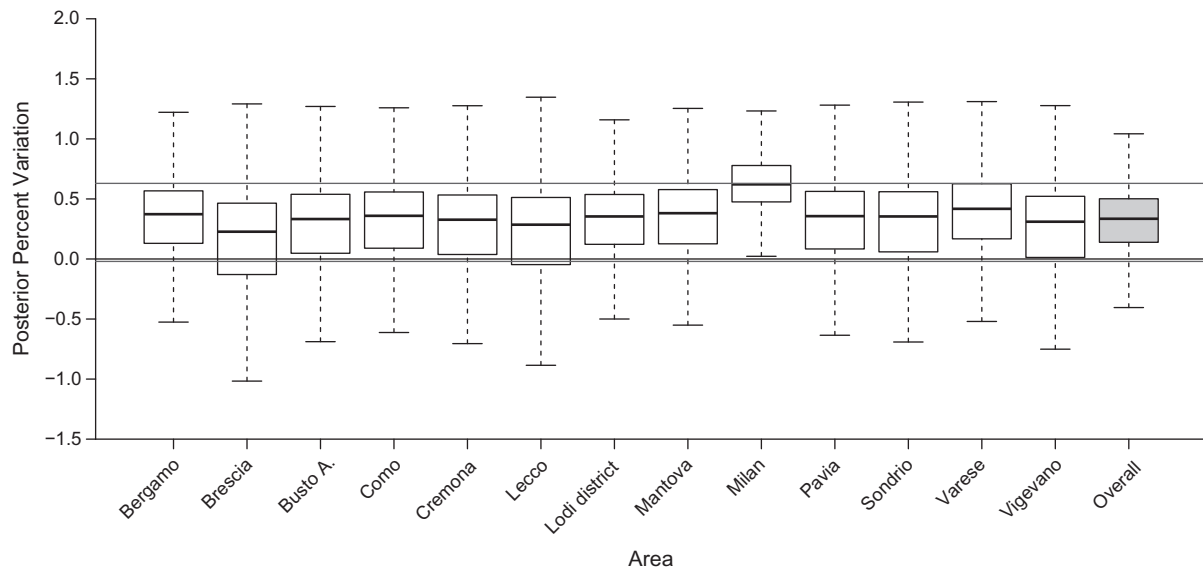


Figure 2. Multiple box-and-whiskers plots of the posterior distributions of the area-specific effects of particulate matter $\leq 10 \mu\text{m}$ in diameter (PM₁₀) and of the overall PM₁₀ effect (in gray), Lombardy, Italy, 2003–2006. The gray lines indicate a symmetric interval of 2 standard deviations around the posterior mean of the overall effect. Effects are expressed in terms of percent variation in natural mortality associated with an increase of $10 \mu\text{g}/\text{m}^3$ in PM₁₀ concentrations at lag 0–1.

Table 3. Annual Average Concentration of Particulate Matter $\leq 10 \mu\text{m}$ in Diameter (PM₁₀) and Expected Number of Deaths Attributable to PM₁₀ Evaluated With the “Macro Approach” Under Different Counterfactual Reduction Scenarios, by Area, Lombardy, Italy, 2003–2006

Area	Average PM ₁₀ Concentration ^a , $\mu\text{g}/\text{m}^3$	Scenario									
		RS0 ^b		RS1 ^c		RS2 ^d			RS3 ^e		
		AD	50% CrI	AD	50% CrI	PM ₁₀ Threshold ^f , $\mu\text{g}/\text{m}^3$	AD	50% CrI	PM ₁₀ Threshold ^g , $\mu\text{g}/\text{m}^3$	AD	50% CrI
Bergamo	46.1	10.2	4.0, 17.1	2.4	0.9, 4.0	36.9	3.6	1.4, 6.1	40	2.4	0.9, 4.0
Brescia	49.4	4.7	-4.7, 16.8	1.5	-1.5, 5.4	39.5	1.6	-1.6, 5.7	40	1.5	-1.5, 5.4
Busto Arsizio	44.7	4.6	0.8, 9.1	0.9	0.2, 1.7	35.8	1.7	0.3, 3.3	40	0.9	0.2, 1.7
Como	43.6	5.7	1.7, 10.5	0.9	0.3, 1.6	34.9	2.1	0.6, 3.9	40	0.9	0.3, 1.6
Cremona	53.5	6.4	1.0, 13.5	2.6	0.4, 5.5	42.8	2.0	0.3, 4.3	42.8	2.0	0.3, 4.3
Lecco	38.4	1.6	-0.4, 4.4	0	0, 0	30.7	0.7	-0.2, 1.9	40	0	0, 0
Lodi district	52.6	19.9	7.7, 33.5	7.7	3.0, 13.0	42.1	6.4	2.5, 10.9	42.1	6.4	2.5, 10.9
Mantova	50.6	5.6	2.1, 9.6	1.9	0.7, 3.3	40.5	1.9	0.7, 3.2	40.5	1.9	0.7, 3.2
Milan	52.5	231.3	174.7, 284.3	89.5	67.5, 110.2	42.0	75.3	56.7, 92.6	42	75.3	56.7, 92.6
Pavia	44.4	5.2	1.5, 9.9	0.9	0.3, 1.8	35.5	1.9	0.5, 3.6	40	0.9	0.3, 1.8
Sondrio	42.8	1.2	0.2, 2.3	0.1	0.0, 0.3	34.2	0.4	0.1, 0.9	40	0.1	0, 0.3
Varese	29.6	3.0	1.3, 4.8	0	0, 0	23.7	1.9	0.8, 3.0	40	0	0, 0
Vigevano	42.2	3.0	0.2, 6.7	0.3	0.0, 0.7	33.8	1.2	0.1, 2.6	40	0.3	0, 0.7

Abbreviations: AD, attributable deaths; CrI, credibility interval; PM₁₀, particulate matter $\leq 10 \mu\text{m}$ in diameter; RS, reduction scenario.

^a Annual average PM₁₀ concentration observed over the study period (2003–2006).

^b Assumes that the $20 \mu\text{g}/\text{m}^3$ World Health Organization limit for annual average PM₁₀ concentration is not exceeded.

^c Assumes that the $40 \mu\text{g}/\text{m}^3$ European Union limit for annual average PM₁₀ concentration is not exceeded.

^d Assumes a 20% reduction in the annual average concentration of PM₁₀, provided it is greater than $20 \mu\text{g}/\text{m}^3$.

^e Assumes a 20% reduction in the annual average concentration of PM₁₀, provided it is greater than $40 \mu\text{g}/\text{m}^3$.

^f Threshold for the annual average concentration of PM₁₀ under scenario RS2.

^g Threshold for the annual average concentration of PM₁₀ under scenario RS3.

Table 4. Annual Average Concentration of Particulate Matter ≤ 10 μm in Diameter (PM_{10}), Expected Number of Deaths Attributable to PM_{10} , Percentage of Attributable Deaths, and Attributable Community Rate per 100,000 Inhabitants Under the RS0 and RS1 Counterfactual Reduction Scenarios, Lombardy, Italy, 2003–2006

Area	Average PM_{10} Concentration, ^a $\mu\text{g}/\text{m}^3$	Scenario					
		RS0 ^b			RS1 ^c		
		AD	%AD	ACR	AD	%AD	ACR
Bergamo	46.1	10.2	0.87	8.8	2.4	0.21	2.1
Brescia	49.4	4.7	0.38	2.5	1.5	0.12	0.8
Busto Arsizio	44.7	4.6	0.68	5.7	0.9	0.13	1.1
Como	43.6	5.7	0.73	6.8	0.9	0.11	1.1
Cremona	53.5	6.4	0.83	8.9	2.6	0.34	3.6
Lecco	38.4	1.6	0.34	3.4	0	0.00	0.0
Lodi district	52.6	19.9	1.02	9.1	7.7	0.40	3.5
Mantova	50.6	5.6	1.03	11.7	1.9	0.35	4.0
Milan	52.5	231.3	2.03	17.8	89.5	0.78	6.9
Pavia	44.4	5.2	0.70	7.4	0.9	0.12	1.3
Sondrio	42.8	1.2	0.62	5.4	0.1	0.05	0.4
Varese	29.6	3.0	0.37	3.7	0	0.00	0.0
Vigevano	42.2	3.0	0.52	4.9	0.3	0.05	0.5
Total		302.4	1.42	12.6	108.7	0.51	4.6

Abbreviations: ACR, attributable community rate; AD, attributable deaths; PM_{10} , particulate matter ≤ 10 μm in diameter; RS, reduction scenario.

^a Annual average PM_{10} concentration observed over the study period (2003–2006).

^b Assumes that the 20 $\mu\text{g}/\text{m}^3$ World Health Organization limit for annual average PM_{10} concentration is not exceeded.

^c Assumes that the 40 $\mu\text{g}/\text{m}^3$ European Union limit for annual average PM_{10} concentration is not exceeded.

level could reasonably be reached through any reduction strategy in urbanized areas. We used the WHO value of 20 $\mu\text{g}/\text{m}^3$ as a background threshold value for the annual average PM_{10} concentration. This represents a target level to be reached in the future but is not reachable in the next few years (11). The EU limit of 40 $\mu\text{g}/\text{m}^3$ was chosen as a second counterfactual. This is greatly above the PM_{10} concentrations considered dangerous. By setting this limit, the EU delineated a point above which arguments on health protection should prevail over arguments based on economic considerations. We also evaluated 2 other counterfactual scenarios. We calculated the number of prevented deaths due to decreasing pollution concentrations of 20% of the actual measured values, provided that the annual average was above 20 $\mu\text{g}/\text{m}^3$ or 40 $\mu\text{g}/\text{m}^3$. Since a 20% reduction of emissions is a realistic target, as is also stated in the European legislation, these scenarios allowed us to appraise how far we are from the 2 targets.

In the design of epidemiologic time-series studies, only the present population is usually considered, because any immediate effect of air pollution on persons not present is questionable. We followed this approach in order to avoid exposure misspecification bias in the estimated concentration-response relation, while in health impact assessment we applied the effect estimates to a larger set of events: deaths among the resident population occurring inside the area or in municipalities within a 10-km radius from the border of the area. In

fact, considering only the deaths occurring inside the municipality of interest could cause considerable underestimation of impact, linked to the catchment area of the nearest hospitals and to the fact that in Lombardy 40%–50% of deaths occur in hospitals (30). In the analysis, we used the lag 0–1 concentration for comparability with the current literature and consistency with the evidence that PM_{10} has an immediate effect on mortality in comparable populations (31, 32). However, note that this choice can give rise to a certain degree of underestimation of the air pollutant impact if the PM_{10} effect 2 days or a few more days after the concentration peak is not negligible (18, 32).

We calculated the number of deaths attributable to PM_{10} exposure, regardless of the life expectancy of those who died. Although we cannot exclude the possibility that PM_{10} exposure can partly precipitate death in very frail people by a period of several days to a few weeks, there is evidence that the observed effects are not due primarily to this short-term mortality displacement (10, 33). Therefore, we expect that the observed impact would not be negligible, even in terms of loss of life expectancy.

The model adopted assumes a linear effect of air pollutants on a logarithmic scale, relying on previous findings from studies carried out in large cities, which are frequently characterized by high air pollution levels (15). In the study by Cohen et al. (2), the burden of disease attributable to air

Table 5. Annual Average Concentration of Particulate Matter ≤ 10 μm in Diameter (PM₁₀) and Expected Number of Deaths Attributable to PM₁₀ Evaluated With the "Micro" Approach Under the Counterfactual Scenario RS4^a, Lombardy, Italy, 2003–2006

Area	Average PM ₁₀ ^b Concentration, $\mu\text{g}/\text{m}^3$	Average PM ₁₀ Concentration Expected Under RS4, $\mu\text{g}/\text{m}^3$	No. of Attributable Deaths	50% Credibility Interval
Bergamo	46.1	38.9	3.0	1.2, 5.0
Brescia	49.4	40.9	1.4	−1.4, 5.0
Busto Arsizio	44.7	37.9	1.3	0.2, 2.6
Como	43.6	38.6	1.3	0.4, 2.4
Cremona	53.5	43.2	2.1	0.3, 4.5
Lecco	38.4	35.3	0.3	−0.1, 0.7
Lodi district	52.6	42.8	6.5	2.5, 11.0
Mantova	50.6	42.6	1.5	0.6, 2.6
Milan	52.5	40.2	96.6	73.1, 118.4
Pavia	44.4	38.2	1.4	0.4, 2.7
Sondrio	42.8	37.6	0.3	0.1, 0.6
Varese	29.6	29.0	0.2	0.1, 0.4
Vigevano	42.2	36.3	0.8	0.0, 1.8

Abbreviations: PM₁₀, particulate matter ≤ 10 μm in diameter; RS, reduction scenario.

^a Assumes that the daily limit of 50 $\mu\text{g}/\text{m}^3$ for PM₁₀ is not exceeded more than 35 days per year (the European Union limit for daily averages).

^b Annual average PM₁₀ concentration observed over the study period (2003–2006).

pollution was evaluated defining an upper bound for the annual average concentration. For cities with annual average PM₁₀ concentrations exceeding 100 $\mu\text{g}/\text{m}^3$, a maximum concentration equal to 100 $\mu\text{g}/\text{m}^3$ was used for health impact assessment, because a linear exposure model could produce unrealistically large estimates of attributable mortality in the most extremely polluted regions. The annual average concentrations of PM₁₀ observed in Lombardy are not so high as to justify the use of an upper bound.

Because of a lack of statistical power, we did not assess the impact of PM₁₀ by age class. In fact, in most of the included cities, the age-specific estimates of the air pollutant

effect relied on a very small number of daily events, particularly in the younger age classes. Using the age-adjusted effect estimates, we probably underestimated the impact of PM₁₀, because we did not account for the likely larger vulnerability and higher baseline risk of elderly persons. For the same reason, we did not assess the impact by specific cause of death, even if this could have, in principle, improved the specificity of our evaluation.

Large national/continental meta-analyses on short-term effects of air pollutants usually show a substantial heterogeneity of the effect. This implies that the portability of the effect estimates is questionable and that when performing impact

Table 6. Daily Average Number of Deaths, Concentration of Particulate Matter ≤ 10 μm in Diameter (PM₁₀), Posterior Mean of the City-Specific PM₁₀ Effect, and Expected Number of Attributable Deaths Under Different PM₁₀ Reduction Scenarios for the City of Milan as Compared With the MISA Study, Lombardy, Italy^a

	Daily Average No. of Deaths	PM ₁₀ Concentration, $\mu\text{g}/\text{m}^3$		City-Specific Distribution of % Variation		No. of Attributable Deaths Under Different Scenarios	
		Mean	95th Percentile	Posterior Mean	90% Credibility Interval	RS0 ^b	RS1 ^c
MISA (1996–2002)	29.1	56.3	135.1	0.36	0.09, 0.63	137	62
Lombardy health impact assessment (2003–2006)	31.3	52.5	120.8	0.63	0.28, 1.02	231	89

Abbreviations: MISA, Meta-Analysis of the Italian Studies on Short-Term Effects of Air Pollution; PM₁₀, particulate matter ≤ 10 μm in diameter; RS, reduction scenario.

^a Effects are expressed in terms of percent variation in natural mortality associated with an increase of 10 $\mu\text{g}/\text{m}^3$ in PM₁₀ concentrations at lag 0–1.

^b Assumes that the 20 $\mu\text{g}/\text{m}^3$ World Health Organization limit for annual average PM₁₀ concentration is not exceeded.

^c Assumes that the 40 $\mu\text{g}/\text{m}^3$ European Union limit for annual average PM₁₀ concentration is not exceeded.

analysis we should use specific estimates for the population considered (25). This is the reason why we derived the effect estimates to be used for attributable death calculation from the same population. However, even within Lombardy, we found some evidence of heterogeneity, and we found a larger effect for the city of Milan than for the other areas. For this reason, we used posterior area-specific distributions, which appropriately reflect differences among locations.

The effect estimates appeared to be increasing for the metropolitan area of Milan from the period 1996–2002 to the more recent time span of 2003–2006 (Table 6). The percent variation in total natural mortality associated with an increase of $10 \mu\text{g}/\text{m}^3$ in daily PM_{10} concentrations was 0.36 in the first period (MISA study (10)) and 0.63 in the second period. The range of PM_{10} concentrations did not change greatly enough to support the hypothesis that the observed difference was due to a nonlinear concentration-response curve (the mean and 95th percentile of daily PM_{10} levels were 56.3 and 135.1, respectively, in 1996–2002 vs. 52.5 and 120.8, respectively, in 2003–2006). The observed discrepancy could simply be due to sampling variability, but it was shown elsewhere that PM_{10} effect estimates have increased over time even in other Italian cities (31); hence, we cannot exclude more complex explanations. The increasing trend in the effect could have been induced by the improvement in PM_{10} measurement in the most recent years, which probably reduced exposure misclassification (instruments for measuring particulate concentrations in the Lombardy air quality monitoring network were upgraded after 2002, with a gain in precision and accuracy). A more interesting hypothesis is that the observed change in the estimated effect was caused by variation in PM_{10} composition over time (for example, an increasing proportion of particulate matter $\leq 2.5 \mu\text{m}$ in diameter in total suspended particles) or by effect modification involving meteorologic conditions. Finally, the observed discrepancy could be due to an increase in the vulnerable fraction of exposed persons related to sociodemographic phenomena such as aging, changes in the economic status of the population, or immigration. Regarding aging, the aging index for the Lombardy region, calculated as the number of persons aged 65 years or over per hundred persons under age 14, increased from 123.5 in 1995 to 143.1 in 2008 (34).

Concerning the impact, the number of attributable deaths we found for Milan was larger than the number of attributable deaths calculated with the same approach for the 1996–2002 period, despite the fact that the PM_{10} levels decreased over time (Table 6): The reduction in average PM_{10} concentration seems to have been compensated for by the larger effect estimate in the more recent period. This result, coupled with the likelihood that an aging population will increase vulnerability to air pollution, makes further development of policies for pollution reduction both crucial and urgent.

The goal of the WHO threshold of $20 \mu\text{g}/\text{m}^3$ is still out of reach, but we showed that even less stringent policies could bring about a relevant reduction in the number of attributable deaths. The health impact in the 13 study areas was 1.4% of the total number of natural deaths when considering the annual PM_{10} concentration limit of $20 \mu\text{g}/\text{m}^3$ and 0.5% when considering the limit of $40 \mu\text{g}/\text{m}^3$ (which was met by only 2 cities). Given the mortality rate and the air pollutant level observed

during the study period, approaching the $20 \mu\text{g}/\text{m}^3$ limit through a reduction of current annual PM_{10} concentrations by 20% in all municipalities with an annual average above $20 \mu\text{g}/\text{m}^3$ would have prevented about 33% of the mortality burden (31% if the 20% reduction policy had been restricted to only those municipalities with an annual average above $40 \mu\text{g}/\text{m}^3$).

The mortality burden attributable to exceeding the EU yearly limit of $40 \mu\text{g}/\text{m}^3$ for the annual average contributed to 93% of the mortality burden under the RS4 scenario (in which the daily limit of $50 \mu\text{g}/\text{m}^3$ for PM_{10} was not exceeded more than 35 days per year). In this specific situation, these 2 counterfactual scenarios provided quite similar results, but this could not be true under different distributions of daily PM_{10} levels.

In conclusion, we estimated that in the major cities of Lombardy, annual average PM_{10} levels exceeding the WHO limit of $20 \mu\text{g}/\text{m}^3$ and the EU limit of $40 \mu\text{g}/\text{m}^3$ were responsible for 13 and 5 deaths per 100,000 inhabitants per year, respectively. At the same time, we estimated that a 20% reduction in the existing PM_{10} levels could reduce by more than 30% the burden of short-term deaths linked to ambient air pollution exposure. Empirical studies showing an increase in life expectancy in parallel with the decrease in ambient fine-particulate air pollution add credibility to these estimates and underline their relevance to public health goals (35). Therefore, policies for the reduction of air pollution appear to be necessary, and their implementation will be rewarding in terms of the protection and improvement of individual and community health.

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REFERENCES

1. Künzli N, Kaiser R, Medina S, et al. Public-health impact of outdoor and traffic-related air pollution: a European assessment. *Lancet*. 2000;356(9232):795–801.

2. Cohen AJ, Anderson HR, Ostro B, et al. Mortality impacts of urban air pollution. In: Ezzati M, Lopez AD, Rodgers A, et al, eds. *Comparative Quantification of Health Risks: Global and Regional Burden of Disease Due to Selected Major Risk Factors*. Vol 2. Geneva, Switzerland: World Health Organization; 2004.
3. Medina S, Plasencia A, Ballester F, et al. Apheis: public health impact of PM₁₀ in 19 European cities. *J Epidemiol Community Health*. 2004;58(10):831–836.
4. Ballester F, Medina S, Boldo E, et al. Reducing ambient levels of fine particulates could substantially improve health: a mortality impact assessment for 26 European cities. *J Epidemiol Community Health*. 2008;62(2):98–105.
5. Boldo E, Medina S, LeTertre A, et al. Apheis: health impact assessment of long-term exposure to PM_{2.5} in 23 European cities. *Eur J Epidemiol*. 2006;21(6):449–458.
6. Boldo E, Linares C, Lumbreras J, et al. Health impact assessment of a reduction in ambient PM_{2.5} levels in Spain. *Environ Int*. 2011;37(2):342–348.
7. Li Y, Gibson JM, Jat P, et al. Burden of disease attributed to anthropogenic air pollution in the United Arab Emirates: estimates based on observed air quality data. *Sci Total Environ*. 2010;408(23):5784–5793.
8. Orru H, Teinmaa E, Lai T, et al. Health impact assessment of particulate pollution in Tallinn using fine spatial resolution and modeling techniques. *Environ Health*. 2009;8:7. (doi:10.1186/1476-069X-8-7).
9. Martuzzi M, Mitis F, Iavarone I, et al. *Health Impact of PM₁₀ and Ozone in 13 Italian Cities*. Copenhagen, Denmark: Regional Office for Europe, World Health Organization; 2004.
10. Biggeri A, Bellini P, Terracini B. Meta-Analysis of the Italian Studies on Short-Term Effects of Air Pollution—MISA 1996–2002 [in Italian]. *Epidemiol Prev*. 2004;28(suppl 4-5): 4–100.
11. World Health Organization. *Air Quality Guidelines: Global Update 2005. Particulate Matter, Ozone, Nitrogen Dioxide and Sulfur Dioxide*. Geneva, Switzerland: World Health Organization; 2005. (http://www.euro.who.int/_data/assets/pdf_file/0005/78638/E90038.pdf). (Accessed June 1, 2011).
12. Directive 2008/50/EC of the European Parliament and of the Council of 21 May 2008 on ambient air quality and cleaner air for Europe. *Offic J Eur Union*. 2008;51(6):L152/1–L152/44. (<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:152:0001:0044:en:pdf>). (Accessed June 1, 2011).
13. Anderson HR, Atkinson RW, Peacock JL, et al. *Meta-Analysis of Time Series Studies and Panel Studies of Particulate Matter (PM) and Ozone (O₃)*. Report of a WHO Task Group. Copenhagen, Denmark: World Health Organization Regional Office for Europe; 2004.
14. Health Effects Institute. *Revised Analyses of Time Series Studies of Air Pollution and Health. Special Report*. Boston, MA: Health Effects Institute; 2003.
15. Bellini P, Baccini M, Biggeri A, et al. The Meta-Analysis of the Italian Studies on Short-Term Effects of Air Pollution (MISA): old and new issues on the interpretation of the statistical evidences. *Environmetrics*. 2007;18(3):219–229.
16. Dallari F, Curi S. *Competitive Pattern of the Lombardy Logistic System* [in Italian]. (LIUC Papers in Ethics, Law and Economics no. 223, Technology Series 15). Castellanza, Italy: Libera Università Carlo Cattaneo; 2008.
17. ARPA Lombardia—Regione Lombardia. *INEMAR, Inventario Emissioni in Atmosfera. Emissioni in Lombardia nel 2008—Revisione Pubblica*. Milan, Italy: Lombardy Regional Agency for the Environment; 2008–2009. (<http://www.ambiente.regione.lombardia.it/inemar/webdata/main.seam>). (Accessed June 1, 2011).
18. Samoli E, Peng R, Ramsay T, et al. Acute effects of ambient particulate matter on mortality in Europe and North America: results from the APHENA study. *Environ Health Perspect*. 2008; 116(11):1480–1486.
19. R Development Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2008. (<http://www.R-project.org>). (Accessed June 1, 2011).
20. Sutton AJ, Abrams KR. Bayesian methods in meta-analysis and evidence synthesis. *Stat Methods Med Res*. 2001;10(4): 277–303.
21. Post E, Hoaglin D, Deck L, et al. An empirical Bayes approach to estimating the relation of mortality to exposure to particulate matter. *Risk Anal*. 2001;21(5):837–842.
22. Le Tertre A, Schwartz J, Touloumi G. Empirical Bayes and adjusted estimates approach to estimating the relation of mortality to exposure of PM(10). *Risk Anal*. 2005;25(3):711–718.
23. Ades AE, Lu G, Higgins JP. The interpretation of random-effects meta-analysis in decision models. *Med Decis Making*. 2005;25(6):646–654.
24. Lunn DJ, Thomas A, Best N, et al. WinBUGS—A Bayesian modelling framework: concepts, structure, and extensibility. *Stat Comput*. 2000;10(4):325–337.
25. Steenland K, Armstrong B. An overview of methods for calculating the burden of disease due to specific risk factors. *Epidemiology*. 2006;17(5):512–519.
26. Wacholder S. The impact of a prevention effort on the community. *Epidemiology*. 2005;16(1):1–3.
27. Louis TA, Zeger SL. Effective communication of standard errors and confidence intervals. *Biostatistics*. 2009;10(1):1–2.
28. Sterne JA, Davey Smith G. Sifting the evidence—what’s wrong with significance tests? *BMJ*. 2001;322(7280):226–231.
29. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557–560.
30. Cadum E, Berti G, Biggeri A, et al. The results of EpiAir and the national and international literature [in Italian]. *Epidemiol Prev*. 2009;33(6 suppl 1):113–119; 123–143.
31. Biggeri A, Baccini M. Short-term effects of air pollution in Italy: risk heterogeneity from 1996 to 2005 [in Italian]. Gruppo Col-laborativo EpiAir. *Epidemiol Prev*. 2009;33(6 suppl 1):95–102.
32. Stafoggia M, Faustini A, Rognoni M, et al. Air pollution and mortality in ten Italian cities. Results of the EpiAir Project [in Italian]. *Epidemiol Prev*. 2009;33(6 suppl 1):65–76.
33. Zanobetti A, Schwartz J, Samoli E, et al. The temporal pattern of mortality responses to air pollution: a multicity assessment of mortality displacement. *Epidemiology*. 2002;13(1):87–93.
34. Istituto Regionale di Ricerca della Lombardia. *Società, Governo e Sviluppo del Sistema Lombardo*. Milan, Italy: Istituto Regionale di Ricerca della Lombardia; 2010. (<http://www.irer.it/lombardia2010/societa-governo-e-sviluppo-del-sistema-lombardo>). (Accessed June 1, 2011).
35. Pope CA III, Ezzati M, Dockery DW. Fine-particulate air pollution and life expectancy in the United States. *N Engl J Med*. 2009;360(4):376–386.