2007

Società Italiana di Statistica

Atti del Convegno Intermedio 2007

Proceedings of the 2007 intermediate conference

Risk and Prediction

Rischio e Previsione

UNIVERSITÀ CA' FOSCARI VENEZIA

6-8 giugno 2007

6-8 June, 2007

SESSIONI PLENARIE E SPECIALIZZATE

Plenary and Invited sessions

Si ringrazia per il contributo all'organizzazione del Convegno Intermedio 2007:
Thanks for support are owed to:

ISTAT
Casinò di Venezia
Veneto Banca
DIAMAN srl
G. Giappichelli Editore
InfoCamere
Statsoft
Alternative Investment SGR

Tutti i lavori di questo volume sono stati sottoposti a revisione scientifica da componenti del Comitato Programma
All papers in this volume have been refereed by members of the Program Committee

Prima edizione: giugno 2007

ISBN 88-7178-791-9

© Copyright 2007 by CLEUP sc
"Coop. Libraria Editrice Università di Padova"
Via G. Belzoni, 118/3 – Padova (Tel. 049 650261)
www.cleup.it

Tutti i diritti di traduzione, riproduzione e adattamento,
totale o parziale, con qualsiasi mezzo (comprese
le copie fotostatiche e i microfilm) sono riservati.

SOCIETÀ ITALIANA DI STATISTICA

Sede: Salita de' Crescenzi 26 - 00186 Roma
Tel +39-06-6869845 - Fax +39-06-68806742
sis@caspur.it Web: http://w3.uniroma1.it/sis/

La Società Italiana di Statistica (SIS), fondata nel 1939, è una società scientifica eretta a Ente morale ed inclusa fra gli Enti di particolare rilevanza scientifica. La SIS promuove lo sviluppo delle scienze statistiche e la loro applicazione in campo economico, sociale, sanitario, demografico, tecnologico, produttivo e in molti altri settori di ricerca.

Organi della società

Presidente:	Daniela Cocchi (Università di Bologna)
Segretario Generale:	Cecilia Tomassini (Università del Molise)
Tesoriere:	Maria Felice Arezzo (Università di Roma "La Sapienza")
Consiglieri:	Marcello Chiodi (Università di Palermo), Gianluca Cubadda (Università di Roma Tor Vergata), Agostino Di Ciaccio (Università di Roma Sapienza), Piero Demetrio Falorsi (Istat), Antonio Giusti (Università di Firenze), Enrico Gori (Università di Udine), Giovanna Nicolini (Università di Milano), Nicola Torelli (Università di Trieste)

CONVEGNO INTERMEDIO 2007

COMITATO PROGRAMMA

Presidente: Marcello Chiodi

Membri: Membri: Irene Poli, Giorgio Tassinari, Cecilia Tomassini, Silvano Bordignon, Giorgio Calzolari, Cesare Cislaghi, Alessandro Fassò, Giuseppe Gesano, Pietro Angelo Manfredi, Cristiana Martini, Francesco Mola, Giampaolo Oneto, Cira Perna, Renata Rotondi, Maria Pia Sorvillo.

COMITATO ORGANIZZATORE LOCALE

Presidente: Irene Poli

Membri: Claudio Agostinelli, Luisa Bisaglia, Silvia Bozza, Stefano Campostrini, Margherita Gerolimetto, Francesco Lisi, Christine Mauracher, Claudio Pizzi, Isabella Procidano, Mario Romanizzi.

SIS2007 – SEGRETERIA DEL COMITATO ORGANIZZATORE LOCALE

Sede: Dipartimento di Statistica
Università Ca' Foscari Venezia
San Giobbe, Cannaregio 873,
30121 Venezia, ITALIA
e-mail: sis2007@unive.it
tel: 041 2347418
fax: 041 2347444

Pubblicazioni della Società Italiana di Statistica
SIS Informazioni (notiziario mensile)
Statistical Methods & Applications (quadrimestrale)
Atti delle Riunioni Scientifiche (biennale)
Atti dei Convegni Intermedi (biennale)

ITALIAN STATISTICAL SOCIETY
Head office: Salita de' Crescenzi 26 - 00186 Roma
Tel +39-06-6869845 - Fax +39-06-68806742
E-mail: sis@caspur.it Web: http://w3.uniroma1.it/sis/

The Italian Statistical Society, founded in 1939, is a no profit scientific society with the aim of promoting the development of the Statistical Sciences and their applications in economic, social, medical, demographic, technological and productive fields and in many other working areas.

Executive and Council

Chairman:	Daniela Cocchi (Università di Bologna)
Secretary:	Cecilia Tomassini (Università del Molise)
Treasurer:	Maria Felice Arezzo (Università di Roma "La Sapienza")
Council members:	Marcello Chiodi (Università di Palermo), Gianluca Cubadda (Università di Roma Tor Vergata), Agostino Di Ciaccio (Università di Roma Sapienza), Piero Demetrio Falorsi (Istat), Antonio Giusti (Università di Firenze), Enrico Gori (Università di Udine), Giovanna Nicolini (Università di Milano), Nicola Torelli (Università di Trieste)

2007 INTERMEDIATE CONFERENCE

PROGRAMME COMMITTEE

Chairman: Marcello Chiodi

Members: Membri: Irene Poli, Giorgio Tassinari, Cecilia Tomassini, Silvano Bordignon, Giorgio Calzolari, Cesare Cislaghi, Alessandro Fassò, Giuseppe Gesano, Pietro Angelo Manfredi, Cristiana Martini, Francesco Mola, Giampaolo Oneto, Cira Perna, Renata Rotondi, Maria Pia Sorvillo.

LOCAL ORGANISING COMMITTEE

Chairman: Irene Poli

Members: Claudio Agostinelli, Luisa Bisaglia, Silvia Bozza, Stefano

Campostrini, Margherita Gerolimetto, Francesco Lisi, Christine Mauracher, Claudio Pizzi, Isabella Procidano, Mario Romanizzi.

SIS 2007 LOCAL HEAD OFFICE

Sede: Dipartimento di Statistica
Università Ca' Foscari Venezia
San Giobbe, Cannaregio 873,
30121 Venezia, ITALIA
e-mail: sis2007@unive.it
Tel: + 39-041-2347418 – *Fax:* +39-041-2347444
E-mail: sis2007@unive.it

Publications of the Italian Statistical Society
SIS Informazioni (monthly)
Statistical Methods & Applications (quarterly)
Proceedings of the Scientific Meeting (biyearly)
Proceedings of the Intermediate Conference (biyearly)

Health impact of air pollution at regional administrative level
Impatto sanitario dell'inquinamento atmosferico a livello regionale

Michela Baccini [1]
Departiment of Statistics, University of Florence - Biostatiscs Unit, CSPO, Florence
Pieralberto Bertazzi
Department of Environmental and Occupational Health, IRCCS Maggiore Hospital, Mangiagalli and Regina Elena Foundation and University of Milan
Annibale Biggeri
Departiment of Statistics, University of Florence - Biostatiscs Unit, CSPO, Florence

Riassunto: L'effetto a breve termine dell'inquinamento atmosferico sulla salute è stato ampiamente documentato nella letteratura epidemiologica. La coerenza dei risultati supporta l'interpretazione causale dell'associazione studiata ed è il presupposto per una valutazione d'impatto affidabile. Nel presente articolo è descritto il protocollo di uno studio attualmente in corso che ha come obiettivo la valutazione d'impatto sanitario dell'inquinamento atmosferico in Lombardia. Lo studio si articola in tre fasi: stima di effetto, valutazione dell'esposizione e valutazione di impatto. La prima fase dello studio si basa su una meta-analisi pianificata, mentre un kriging Bayesiano è utilizzato per stimare la superficie di esposizione media sull'intera regione per l'anno 2005. I risultati ottenuti vengono infine combinati per calcolare il numero di decessi e ricoveri ospedalieri attribuibili.

Keywords: Epidemiological time series, meta-analysis, meta-regression, Bayesian kriging, health impact evaluation.

1. Introduction

Quantification of short-term effects of air pollution comes from large meta-analyses conducted in the US and in Europe (Anderson *et al.*, 2004; HEI, 2003). These studies indicate exposure to air pollution at levels presently occurring in urban environments is associated with a short term increase in mortality and with a variety of health conditions, including emergency room visits and hospital admissions for respiratory and cardiovascular diseases.

The replication of epidemiological studies carried out with similar models in different countries and contexts has led to consistent findings, supporting the causal nature of the association and reassuring with regard to the accuracy of effect estimates obtained from epidemiological time series analysis (e.g. Bellini *et al.*, 2007). Causal interpretation of the effect measure and absence of major bias are basis for reliable health impact assessment.

[1] Address of correspondence: Viale Morgagni, 59, 50134 Firenze, Italia - e-mail: baccini@ds.unifi.it

Several studies evaluated impact of air pollution on health (Martuzzi *et al*., 2002, 2006; Medina *et al*., 2004; Kunzli *et al*., 2000; Boldo *et al*., 2006). In Italy, shot term impact of air pollution on mortality has been assessed in 15 of the major Italian cities within the MISA study (Biggeri *et al*., 2004). However any impact evaluation has never been extended out of urban area or in small cities where air pollution level and traffic characteristics could be different from those observed in big cities.
The present paper presents the main characteristics of a study on health impact assessment in Lombardia. The study is actually on going and involves the University of Milan, the Department of Statistics of the University of Florence and the Regional Environmental Protection Agency. It focuses on short-term effects of air pollution on both mortality and hospital admissions. It takes advantage from availability of exposure and mortality/morbidity data at municipality level for addressing the impact evaluation of air pollution on health in the whole region.
Generally speaking health impact assessment consists in three stages:

- risk assessment (i.e. exposure-response function estimation)
- exposure assessment
- disease burden evaluation.

In the present study, inference on the exposure-response functions describing the relationship between air pollution and mortality/morbidity is based on epidemiological time series analyses. First, separate analyses are conducted by city, then Bayesian hyerachical models are specified to combine first stage effect estimates.
Bayesian kriging is performed to predict the continuous surface of exposure levels starting from data collecting by a selected subset of monitoring stations belonging to the regional network.
For assessing impact of air pollution on health, results from the previous points are combined and attributable number of deaths/hospital admissions are obtained. Evaluation of life expectancy reduction associated to attributable mortality and evaluation of costs related to attributable hospital admissions are also planned.
In Section 2 study design is described and daily health and air pollution data are presented. In Section 3 the approach for exposure-response function estimation is described. In Section 4 a model for Bayesian kriging is proposed. In Section 5 methods for health impact evaluation are described. The proposed approach is discussed in section 6.

2. Data

We consider air pollution and mortality/morbidity data from all the municipalities of Lombardia for the period $2000 - 2005$.
Death certificates and hospital admissions data have been obtained from the Local Health Authorities and from regional files, respectively. For each municipality, we focus on daily counts of deaths and hospital admissions of the resident population, occurring inside the municipality area.
Total mortality from all causes excluding external causes (ICD.9: ≤ 800), cardiovascular mortality (ICD.9: 390-459) and respiratory mortality (ICD.9: 460-519) are considered.
A standardized procedure for selecting hospital admissions for cardiac (ICD.9: 390-429) and respiratory (ICD.9: 460-519) acute conditions is used.

Air pollution data have been obtained from the Regional Environmental Protection Agency. The monitoring network established in each city provided air pollutants measurements. Data from monitors with more than 25% of missing measurements during the study period are excluded from the city datasets. Monitoring stations located in sites largely influenced by local traffic are excluded.
The daily mean concentrations of sulfur dioxide (SO_2), nitrogen dioxide (NO_2) and fine particles (PM10) are considered. The daily levels of ozone (O_3) and carbon monoxide (CO) are summarized as maximum 8 hours moving average of the hourly measurements. We avoid O_3 measurements from monitors located near traffic sources, where the scavenger role of nitrogen oxides could have given rise to apparently low levels of ozone.
Daily statistics of pollutants concentration are considered as missing when more than 25% of hourly data were not available. For each city, missing daily data in one monitor were imputed using concentrations measured by the remaining monitors, according to the procedure described in Biggeri *et al.* (2004). Missing data in one day (occurring when data from all monitors were missing) were imputed as average of four days (preceding and following day, the same day of the previous and following weeks).
Meteorological data (temperature and relative humidity) were collected by the same air pollution monitoring networks.

3. Risk assessment

Effect of air pollution on health is evaluated on data from a subset of Lombardia municipalities, including cities with more than 50000 inhabitants, chief towns and municipalities belonging to the administrative district of Lodi, that are treated as a single city. This subset is further reduced excluding municipalities for which air pollution and sanitary data for a minimum of three consecutive years in the period $2000 - 2005$ are not available.
The choice of excluding small municipalities from the risk assessment step relies on considerations about precision of city-specific estimates. In fact sampling variability can be extremely large in presence of small daily counts of sanitary events.
The administrative district of Lodi area is included because of availability of air pollution data coming from monitors placed in country side. This give us opportunity to evaluate air pollution effect in non urban conditions.

3.1 City-specific analysis

At the first stage of the analysis, daily time series of total and cause-specific mortality and morbidity are modeled with respect to each air pollutant, separately for each city.
Separate analyses are performed by age class (less than 65, $65 - 74$ and more than 75 years).
A common model is adopted for all cities. It consists in a Generalized Linear Model for Poisson data, where we control for time-related confounding including in the model cubic regression splines with number of degrees of freedom a priori specified and dependent on age class and outcome (Baccini *et al.*, 2007).
We adjust for confounding of week-day and holidays by dummy variables and for effect of influenza epidemics, specifying for each city an indicator of epidemic days (Biggeri *et al.*, 2004).
The relationship between average daily temperature and mortality, is modeled in a para-

metric way, by introducing in the model a cubic regression spline of air temperature with one degrees of freedom every 8° C. Linear and quadratic terms for relative humidity are included in the model. In order to take into account for lagged effect of meteorological conditions, the mean of current and previous three days temperatures is considered.
For each air pollutant, we use as exposure indicator the average of current day and previous day concentrations. A linear term is used for describing the exposure-response relationship.

3.2 Combined analysis

At the second stage of the analysis, the first stage estimates are combined and sources of heterogeneity among cities are eventually investigated.
Random effects Bayesian meta-analyses of the relationships between air pollutant and outcome variables are performed (Sutton and Abrams, 2001). Let $\hat{\lambda}_c$ and $\hat{\sigma}_c^2$ respectively the estimate of log rate ratio and the estimate of its variance for the c-th city ($c = 1, ..., C$). We postulated that the first stage estimates are independent realizations from Gaussian populations with mean λ_c and known variance $\hat{\sigma}_c^2$

$$\hat{\lambda}_c = \lambda_c + \epsilon_c$$

$$\epsilon_c \overset{indep.}{\sim} N(0, \hat{\sigma}_c^2)$$

and that each city-specific effect λ_c is drawn from a Normal population with mean β and variance τ^2

$$\lambda_c = \lambda + u_c$$

$$u_c \overset{indep.}{\sim} N(0, \tau^2).$$

The two random mechanisms ϵ_c and u_c are assumed to be independent. β represents the average effect adjusted for the inter-city variation τ^2.
The Bayesian formulation needs to specify prior distributions on the hyperparameters β and τ^2. We placed upon these parameters vague proper priors.
Posterior distributions of parameters are obtained with WINBUGS (Spiegelhalter *et al.*, 2000).
The main difference between classical random effects meta-analysis and Bayesian random effects meta-analysis is that the Bayesian approach takes into account for uncertainty on heterogeneity variance estimate, including in the analysis the whole posterior distribution of τ^2, rather than a single estimate.
The posterior distributions of the city-specific parameters λ_c ($c = 1, 2, \ldots, C$) update the first stage estimates taking into account for the information from all enrolled cities. Posterior city-specific distributions are a compromise between first stage city-specific results, that can be unstable for small cities, and overall meta-analytic estimate, usually stable but difficult to be interpreted in presence of heterogeneity among cities.

3.3 Meta-regression

Whatever meta-analysis highlights relevant heterogeneity among cities, the Bayesian random effects model is extended to analyze variability across city in a meta-regression phase (Thompson and Sharp, 1999). Sources of heterogeneity in short term effect of air pollution are investigated specifying regression models, where city-specific effects change

according to city-specific explanatory variables. Several possible effect modifiers can be considered, namely mean level of air pollutant and variables related to geographical and climate characteristics. To avoid *post hoc* data-dredging, explanatory variables are usually introduced into the model one at time.
Denoting with $\hat{\lambda}_c$ the first stage estimate in the c-th city and with $\hat{\sigma}_c^2$ the corresponding estimated variance, we assume

$$\hat{\lambda}_c = \lambda_c + \epsilon_c$$
$$\epsilon_c \overset{indep.}{\sim} N(0, \hat{\sigma}_c^2)$$

and

$$\lambda_c = \beta_0 + \beta_i \times m_{ic} + u_c,$$

where m_{ic} is the observed value of the i-th effect modifier in the c-th city and u_c is a city-specific random effect from a Normal distribution with mean zero and variance τ^2. The random mechanisms which generate ϵ_c and u_c are assumed independent. Non informative priors are used on the model parameters.
In this case, τ^2 expresses the portion of variability among cities which is not explained by the covariate and is usually referred as residual heterogeneity. Inspection of residual heterogeneity distribution is tool for detecting effect modification. If a covariate modifies air pollutant effect, the resulting residual heterogeneity distribution is more concentrated around 0 than the heterogeneity distribution arising from the null model (the meta-analytic model without explanatory variables).
In this study, meta-regression is not only an exploratory and hypothesis generating phase of risk assessment, but it can be used for interpolation purpose, as we better explain in Section 5.

4. Exposure assessment

For exposure assessment, we consider data from the monitoring stations selected according to the criteria described in Section 2. The selected monitors do not provide exposure information for all the Lombardia municipalities, while we are interested in evaluating the health impact of air pollution over the whole region. Then we need a tool for estimating the exposure surface starting from information derived from point data.
Spatial interpolation is a problem of prediction in space. A variety of quantitative interpolation methods have been proposed (Cressie, 1993). Kriging (Matheron, 1963) is one of these methods which is based on the rate at which the covariance between points changes. In this work a Bayesian Gaussian kriging model can be fitted where covariance between points (monitors) is a function of the distance between them (Diggle *et al.*, 1998).

4.1 The Gaussian spatial exponential model

For each pollutant, data consist in yearly averages of mean daily concentrations measured during 2005 by available selected monitors. Our aim is to predict concentration surface over a set of locations representing the centroids of municipalities for which exposure is not directly measured.
We assume that the observed yearly average of mean daily concentrations during 2005 is drawn from a Normal distribution with mean μ_s and known variance ${\sigma_s}^2$:

$$x_s \sim \mathrm{N}(\mu_s, {\sigma_s}^2),$$

where s ($s = 1, 2, \ldots, S$) identifies the monitors. The mean μ_s is the s-th component of the vector μ which is assumed to follow a Multivariate Normal distribution:

$$\mu \sim MVN(\beta, \mathbf{\Sigma}).$$

The elements of the vector $\beta = (\beta_1, \beta_2, \ldots, \beta_S)$ eventually express dependence of air pollutant concentrations over a set of location-specific covariates $(z_{1s}, z_{2s}, \ldots, z_{Ks})$:

$$\beta_s = \gamma_0 + \sum \gamma_k z_{ks}.$$

The variance-covariance matrix $\mathbf{\Sigma}$ expresses spatial dependence among location. The idea is that concentrations measured by closed monitors are similar, then we define a parametric distance function for covariance terms. A common assumption (Cressie, 1993) is for example the exponential decay function:

$$\Sigma_{ik} = \sigma^2 \exp(-\phi\ d_{ij})^\rho,$$

where σ^2 controls the overall variability, d_{ij} is the Euclidean distance between pairs of monitors i and j, ϕ controls the rate of decline of correlation with distance and ρ controls the amount of spatial smoothing.
In kriging we are interested in predicting the mean concentration of air pollutant at a new point location $s^\star$ (say $\mu_{s\star}$) with associate covariates vector $(z_{1s^\star}, z_{2s^\star}, \ldots, z_{Ks^\star})$.
In a Bayesian framework kriging is straightforward since we have just to figure out the predictive distribution of $\mu_{s\star}$. Once prior distributions on unknown parameters are specified, MCMC methods can be used for fitting models and obtaining posterior predictive distribution for $\mu_{s\star}$ (Banerjee *et al.*, 2004). WINBUGS software can be employed at this purpose (Spiegelhalter *et al.*, 2000). See also Biggeri *et al.* (2006) for an epidemiological application.

5. Health impact assessment

Impact of air pollution on mortality and morbidity is first quantified in terms of attributable number of events (deaths/hospital admissions) during 2005. Separate evaluations are done for each air pollutant.
Impact evaluation relies on yearly averages. For each municipality, the following information is available:

- yearly average of the daily number of events by age group during 2005,
- yearly average of daily air pollutant levels during 2005, observed or predicted by Bayesian kriging,
- estimate of air pollutant effect obtained from meta-analysis.

As far as the last point is concerned, it should be stressed that meta-analysis provides both posterior city-specific estimates and overall estimate of effect. If we can assume that the effect of air pollutant is the same over the whole region, health impact assessment can be based on the overall meta-analytic estimate. In this case the same estimate of air pollutant effect is employed for all municipalities. On the contrary, if homogeneity assumption is not plausible, use of posterior city-specific estimates is recommended. In this case a problem also arises concerning the prediction of effect estimates for cities that are not

involved in the risk assessment stage. Prediction can be eventually done on the basis of meta-regression results.
At this stage of the analysis, we assume that the exposure level within municipality is the same for all inhabitants and that the effect of air pollution is linear on a logarithmic scale, according to the model adopted for risk assessment. Theoretically, every concentration of air pollutant has a negative effect on health. However we prefer to provide conservative impact estimates, counting attributable events for exposure levels exceeding a threshold x_0. The threshold definition depends on the specific air pollutant considered and it is the same for all municipalities. This approach is coherent with the idea that it is not possible to reduce air pollution emissions under certain "background" levels. The resulting model is the following:

$$\begin{aligned} y_c = y_{c0} e^{\lambda_c (x_c - x_0)} \quad & \text{if} \quad x_c > x_0 \\ y_c = y_{c0} \quad & \text{if} \quad x_c \geq x_0 \end{aligned}$$

where y_c and x_c are the yearly average of the daily number of deaths/hospital admissions and the yearly average of daily concentrations of air pollutant for the c-th municipality, respectively. y_{c0} is the baseline number of events, i.e. the average daily number of events we would observe for $x_c = x_0$ and λ_c is the coefficient describing the effect of air pollutant in the c-th city.
The number of attributable events is calculated as difference between observed and baseline number of events:

$$AD = y_c - y_{c0} = y_c - y_c / e^{\lambda_c (x_c - x_0)}.$$

Separated attributable deaths/hospital admissions evaluations are obtained by age group. The total number of attributable events is produced by summing over the three age classes. Eventually health impact of air pollutant under simple scenarios of emissions reduction can be evaluated.
Calculation of years of life lost can be performed starting from attributable number of deaths and using age-specific life expectancy provided by life tables. Similarly, starting from attributable number of hospital admissions, total hospitalization costs associated to air pollution can be evaluated.

6. Discussion

Quantifying short term impact of air pollution on health is a relevant task in health policy, because, even if we are in presence of small effects, they act on large populations.
Several studies assessed impact of air pollution in urban context (Martuzzi *at al.*, 2002, 2006; Medina *et al.*, 2004, Biggeri *et al.*, 2004; Kunzli *et al.*, 2000). In the present work, health impact evaluation is extended also to non urban areas and to small cities.
Analysis consists in three steps. First we estimate effect of air pollution using data from the major Lombardia cities, but also from the Lodi area, where several monitoring stations are placed in country site. A meta-analysis of the city-specific estimates is performed and eventually sources of heterogeneity are investigated by meta-regression. In this context meta-regression can be used also for prediction purpose in case relevant heterogeneity among cities is found.

The second stage of the analysis concerns exposure assessment for a recent year (2005). Due to exposure information is not available for all municipalities, we use a Bayesian kriging model to predict the average level of each air pollutant over the whole region, starting from the average concentrations measured by the selected monitors. Variables related to exposure can be eventually included as covariates in the kriging model.
At the third stage of the analysis, effect estimates, exposures and mortality/morbidity information are combined for calculating the number of events attributable of air pollution. The model adopted for health impact assessment is conservative, in the sense that attributable events are calculated only for exposures above a certain threshold.
Health impact assessment is not done day by day, but average daily exposure and average daily number of events are used in combination with effects estimates (Kunzli *et al.*, 2000). Using "averages" instead of daily data should provide similar results if involved distributions are not strongly asymmetric and the degree of correlation between outcome and exposure is not large.
The choice of using exposure at lag 0-1 is motivated by previous published results, that did not highlight delayed effects of air pollution or harvesting phenomena (Schwartz, 2001).
The model adopted assumes linear effect of air pollutants on a logarithmic scale. This linearity assumption relies on previous findings that were carried out on big cities, frequently characterized by high air pollution levels (Bellini *et al.*, 2007). However linearity has never been checked before in studies involving both urban and non urban contexts. Exposure-response function could be locally linear, but different slopes could characterized the relationship, depending on air pollutants level or, for PM10, on chemical composition of particulate. Including the administrative district of Lodi in the risk assessment stage gives us opportunity to address this point.
Higher effect of PM10 on mortality during warm season has been reported in literature (Biggeri *et al.*, 2004; Moolgavkar, 2003). In the present study, season-specific effects of air pollutants can be obtained by introducing an interaction term between exposure and summer indicator in the city-specific model. We expect that using season-specific effects brings to more reliable health impact evaluation.

References

Anderson R., Atkinson R., Peacock J.L.and Marston L. and Konstantinou K. (2004) *Meta-analysis of time series studies and panel studies of particulate matter (PM) and ozone (O3)*, WHO Europe.

Baccini M., Biggeri A., Lagazio C., Lertxundi A. and Saez M. (2007) Parametric and semi-parametric approaches in the analysis of short-term effects of air pollution on health, *Computational Statistics and Data Analysis*, 51, 4324–4336.

Banerjee S., Carlin B. and Gelfand A. (2004) *Hierarchical modeling and analysis of spatial data*, Chapman and Hall, New York.

Bellini P., Baccini M., Biggeri A. and Terracini B. (2007) 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 (in press)*.

Biggeri A., Bellini P. and Terracini B. (2004) Meta-analysis of the italian studies on short term effects of air pollution 1996-2002, *Epidemiologia e Prevenzione*, 28, 1–100.

Biggeri A., Dreassi E., Catelan D., Rinaldi L. and Lagazio C. (2006) Disease mapping

in veterinary epidemiology: a bayesian geostatistical approach, *Statistical Methods in Medical Research*, 15, 337–352.

Cressie N. (1993) *Statistics for spatial data*, John Wiley and Sons, Inc.

Diggle P., Tawn J. and Moyeed R. (1998) Model-based geostatistics (with discussion), *Journal of the Royal Statistical Society C (Applied Statistics)*, 47, 299–350.

HEI (2003) *Revised Analyses of Time Series Studies of Air pollution and Health. Special Report.*, Health Effect Institute: Boston MA.

Kunzli N., Kaiser R., Medina S., Studnika M. and H. C. (2000) Public health impact of outdoor and traffic related air pollution, *Lancet*, 356, 795–801.

Martuzzi M., Galassi C., Ostro B., Forastiere F. and Bertollini R. (2002) *Health impact assessment of air pollution in the eight major Italian cities. Internal Report*, Rome, World Health Organization.

Matheron G. (1963) Principles of geostatistics, *Economic Geology*, 58, 1246–1266.

Medina S., Plasencia A., Ballester F., Mucke H. and Schwartz J. (2004) Apheis: public health impact of pm10 in 19 european cities, *Journal of Epidemiology and Community Health*, 58, 831–836.

Moolgavkar S. (2003) Air pollution and daily mortality in two u.s. counties: season-specific analyses and exposure-response relationships, *Inhalation Toxicology*, 25, 877–907.

Schwartz J. (2001) Is there harvesting in the association of airborne particles with daily deaths and hospital admissions?, *Epidemiology*, 12, 55–61.

Spiegelhalter D., Thomas A., Best N. and Gilks W. (2000) *WinBugs*, Medical Research Council Biostatistics Unit: Cambridge.

Sutton A. and Abrams K. (2001) Bayesian methods in meta-analysis and evidence synthesis, *Statistical Methods in Medical Research*, 10, 277–303.

Thompson S. and Sharp S. (1999) Explaining heterogeneity in meta-analysis: a comparison of methods, *Statistics in Medicine*, 18, 2693–2708.