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Modelling temperature effects on mortality: multiple segmented relationships with common break-points

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Abstract

A model for estimation of temperature effects on mortality is presented in this paper. The model is able to capture jointly the typical features of every temperature-death relationship, i.e. nonlinearity and delayed effect of cold and heat over few days. Through a segmented approximation along with a spline-based distributed lag parameterization, estimates and relevant standard errors of the cold- and heat-related risks and of the heat-tolerance are provided. The model is applied to two data-sets of mortality time series in Italy.

Keywords: temperature effects, breakpoints, segmented regression, distributed lag, equality constraints.

1 Introduction

Statistical models aimed to investigate temperature effects on heath are acquiring considerable importance largely due to greenhouse effect and consequent global warming (Bloomfield, 1992). Specifically, quantifying death excesses related to temperature is crucial to assess how the mortality pattern could change owing to variations in climate (e.g. Langford and Bentham, 1995; McGeehin and Mirabelli, 2001; Beniston, 2002). In studying temperature effects on mortality one is confronted with two noticeable features which have to be taken into account in the data modelling process: i)nonlinearity of the death-temperature relationship and ii)delayed effect of temperatures (both cold and heat). Catching adequately such features is important to obtain reliable results and meaningful parameter estimates.

Nonlinearity between outdoor temperature and mortality has been acknowledged since a long time by several authors (e.g. Gover, 1938; Kunst *et al.*, 1993;

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Keatinge *et al.*, 2000) with a U-, J- or V-shape relationship which has been emphasized in many studies: mortality increases as temperature gets colder or hotter and reaches its minimum at some optimal value. Lately, Pattenden *et al.* (2005) argue about chance of assuming a range (rather than a single value) of optimal temperatures, leading to a 'bath-type' shaped curve having two breakpoints, for the cold and the heat distinctly. In this case, only extreme temperatures act on health, whereas in the wide middle range no risk occurs. Nonlinearity is usually modelled by nonparametric splines (Curriero *et al.*, 2002) or quadratic terms (Braga *et al.*, 2001, 2002; Schwartz *et al.*, 2004) or by means of a piecewise linear parameterization (Kunst *et al.*, 1993; Nafstad *et al.*, 2001; Gouveia *et al.*, 2003; Muggeo, 2004; El-Zein *et al.*, 2004). Besides predicted number of death excesses at fixed temperature values, the last approach is able to provide directly also estimates of the cold- and heat-related risks (for $1°C$ increases, say) and of the threshold temperature value where mortality reaches its minimum. This 'optimal' value, which represents the breakpoint of the segmented curve, is sometimes referred as MMT (Minimum Mortality Temperature) and it is usually assumed as a measurement of the heat tolerance (Curriero *et al.*, 2002). Many authors have recognized the heat tolerance to be an important and meaningful parameter to be used to summarize the temperature-mortality curve, but in spite of this no thorough (careful-detailed) statistical model appears to be available; the most studies have determined the MMT by visual inspection of the, possibly smoothed, scatter-plots of death versus temperature.

Delay is a relatively recent issue, but assessment of lagged effects is worthwhile to estimate the so-called distributed lag (DL) curve. The DL curve is useful to compute the prolonged effect and to quantify the so-called 'harvesting': that is, how much of the temperature-induced mortality excesses are followed by deficits (Braga *et al.*, 2001; Pattenden *et al.*, 2005). The final question is whether the temperature acts only on susceptible individuals whose life is shortened by a few days or weeks. To account for delayed effects, different time lags for temperature and/or their combinations have been considered by several authors; for instance means of the temperature at different lag intervals (mean lag 0-1, mean lag 2-5,...) is a common practice in epidemiological studies (Kunst *et al.*, 1993; Gouveia *et al.*, 2003; Pattenden *et al.*, 2005). However, as discussed nextly, including temperature as mean of lags implies strong constraints on the DL curve.

To obtain simultaneous estimates and standard errors of the three parameters describing the mortality-temperature curve, the 'simple' (i.e. based on a unique lag-temperature variable) segmented approximation, although useful, might suffer from some drawbacks since estimation depends on the strength of the V-shaped relationship. The more clear-cut the curve, the better the estimate (Muggeo, 2003). In turn, the strength of the relationship depends on the both left and right slopes, namely on the both cold and heat risks. One could select the lag with 'the best' curve, but this is a nontrivial task as it is common knowledge that the cold effect persists for days, while hot has a more immediate effect (e.g. Keatinge *et al.*, 2000; Braga *et al.*, 2001); thus the left slope is remarkable at long lags while the right slope is steeper at short lags. Seeking a compromise between shorter and longer lags, e.g. by means of some lag-averaged variable, is unlikely to lead notable improvement.

Therefore, due to the weight of topic, it is of practical and theoretical importance to develop a unified framework aimed to estimate temperature effects on mortality. In this paper we propose a parameterization which allows to obtain joint estimates of DL curves for both cold and heat risks, while providing 'efficient' estimate of the MMT. Efficient in that its estimate is independent of any particular lag-specific relationship, and at the same time it condenses information from each relationship at different lag.

The proposed modelling framework is detailed throughout section 2, while section 3 is devoted to illustration through the analysis of a few daily time series of mortality and temperature. The section 4 concludes the paper with some remarks and brief discussion

2 Methods

In a previous work, Muggeo (2003) illustrates a simple algorithm to fit segmented relationships in regression models, with linear predictor $\alpha Z + \beta(Z - \psi)_+$, where Z is the variable having a segmented relationship with the response (on the link scale), α is the left slope and β is the difference-in-slopes parameter when Z exceeds the breakpoint ψ. Starting from an initial estimate of the breakpoint, the method carries on by fitting iteratively a specific 'working' linear model and gaining at each step an improved estimate of the breakpoint via the current estimates of the model parameters.

To begin with, note that the iterative working linear model being fitted may alternatively be expressed by

$$\alpha Z + \beta U + \delta\{\tilde{\beta} V\} \tag{2.1}$$

where $\tilde{\beta}$ and $\tilde{\psi}$ are estimates known from the previous iteration, and $U = (Z - \tilde{\psi})_+$ and $V = -I(Z > \tilde{\psi})$ are simple variables depending on $\tilde{\psi}$. To emphasize this dependence a more correct could be $\tilde{U}$ and $\tilde{V}$, but we have simplified notation and suppressed the 'tilde' in the formulas. Note that expression (2.1) is substantially equal to the original one described in Muggeo (2003), the only difference being that the variable $\{\tilde{\beta} V\}$ (rather than V) has to be included; this implies that the updated estimate of the breakpoint is now given by $\hat{\psi} = \tilde{\psi} + \hat{\delta}$ and the standard error corresponding to $\hat{\delta}$ is the (approximate) standard error of the (current) estimate $\hat{\psi}$.

This fairly simple re-formulation of the 'working' iterative model underlies the whole modelling framework described in this paper.

Let Z the temperature variable, usually daily mean; a starting model for the analysis of mortality-temperature could be a two-breakpoints segmented model expressed via the left and right slopes directly (and not the difference-in-slopes parameter):

$$\beta_1(Z - \psi_1)_- + \beta_2(Z - \psi_2)_+ \tag{2.2}$$

where β_1 is the log-risk for cold temperatures (i.e. the left slope, when $Z < \psi_1$) and β_2 is the heat-related log risk when temperature exceeds the second threshold (the right slope, $Z > \psi_2$). In the optimal range $[\psi_1, \psi_2]$ mortality is constant at its minimum value and the risk (i.e. the slope) is zero.

Simple algebra show that the constructed variables relevant to cold and heat for model (2.2) are given by $U_1 = (Z - \tilde{\psi}_1)_-$ and $V_1 = -I(Z < \tilde{\psi}_1)$, and $U_2 = (Z - \tilde{\psi}_2)_+$ and $V_2 = -I(Z > \tilde{\psi}_2)$, and hence the 'working' model to be estimated iteratively to fit model (2.2) is

$$\beta_1 U_1 + \beta_2 U_2 + \delta_1\{\tilde{\beta}_1 V_1\} + \delta_2\{\tilde{\beta}_2 V_2\} \tag{2.3}$$

and $\hat{\psi}_j = \tilde{\psi}_j + \hat{\delta}_j$ for the cold ($j = 1$) and heat ($j = 2$) threshold. Model (2.2), or equivalently its working version (2.3), assumes the effect of Z to be specific to the same-day (i.e. lag 0) exposure. To allow the cold and heat effects to be spread over a few days, lagged variables have to be included to take into account the distributed effects. Hence a natural extension of the (2.3) is

$$\sum_{l_1=0}^{L_1-1} \beta_{1l_1} U_{1l_1} + \sum_{l_1=0}^{L_1-1} \delta_{1l_1}\{\tilde{\beta}_{1l_1} V_{1l_1}\} + \sum_{l_2=0}^{L_2-1} \beta_{2l_2} U_{2l_2} + \sum_{l_2=0}^{L_2-1} \delta_{2l_2}\{\tilde{\beta}_{2l_2} V_{2l_2}\}$$

which models the effect from current day (lag 0) up to lag $L_1 - 1$ and $L_2 - 1$, respectively for cold and heat. Here it is plain the rational of using DL: environmental exposure may produce risk not only on the same day of exposure but also on the succeeding days after (through L days, say). Then mortality count at day t depends on the same-day exposure (lag 0, $Z_{t-0} = Z_0$) plus contributions from exposures of preceding days: one-day before ($Z_{t-1} = Z_1$), two-days before ($Z_{t-2} = Z_2$) and so on through $L - 1$ days before ($Z_{t-L+1} = Z_{L-1}$).

In the model above the U_{jl_j} and V_{jl_j} variables are defined as in the unlagged case (2.3), the only difference being that they are computed using lagged temperature (Z_{l_j}) and lag-specific breakpoint ($\tilde{\psi}_{l_j}$); actually such model assumes a segmented relationship at every lag, each with its own parameters, cold and heat risks and thresholds as well. However, while different risks are plausible (leading to the well-known DL curve), lag-specific heat tolerances become difficult to interpret. Furthermore as discussed nextly, breakpoint estimation depends heavily on the magnitude of the relevant parameter describing the segmented curve. Hence in fitting an unconstrained segmented curve at each lag, one could be in trouble in estimating cold-thresholds for short lags as well as heat-thresholds for longer lags. All this causes unstable estimating procedure (final results depending strongly on starting values of the thresholds) as well as unstable and then meaningless breakpoint estimates. To overcome such drawbacks the proposal is to constrain the MMTs to be the same among the several lagged relationships, namely $\psi_{1l_1} = \psi_1 \, (l_1 = 0, 1, \ldots, L_1 - 1)$ and $\psi_{2l_2} = \psi_2 \; (l_2 = 0, 1, \ldots, L_2 - 1)$. Such equalities imply that the search of the common breakpoints has to be independent of any specific lag, then the equality $\delta_{jl_j} = \delta_j$ also have to hold. Under the foregoing constraints the working linear predictor becomes

$$\sum_{l_1=0}^{L_1-1}\beta_{1l_1}U_{1l_1}+\delta_1\left\{\sum_{l_1=0}^{L_1-1}\tilde{\beta}_{1l_1}V_{1l_1}\right\}+\sum_{l_2=0}^{L_2-1}\beta_{2l_2}U_{2l_2}+\delta_2\left\{\sum_{l_2=0}^{L_2-1}\tilde{\beta}_{2l_2}V_{2l_2}\right\} \quad (2.4)$$

Now, as in the single-lag case (2.3), the unique breakpoint estimates are given by $\hat{\psi}_j = \tilde{\psi}_j + \hat{\delta}_j$ and SE$(\hat{\psi}_j) \approx$ SE$(\hat{\delta}_j)$ for $j = 1, 2$. Because of constraints on the breakpoints, the terms being included are $L_1 + 1$ (rather than $2L_1$) for the cold and $L_2 + 1$ (rather than $2L_2$) for the heat and the two variables $\left\{\sum_l \tilde{\beta}_l V_l\right\}$-type are the ones controlling for the breakpoint estimation. Note this exemplification is allowed just by using the re-parameterization in the (2.1).

Each segmented relationship (from 0 to $L_j - 1$) contributes to estimation of ψ_j making things easier: stabler the algorithm, and more importantly, narrower the final standard errors of the MMTs; namely, making irrelevant any issue on 'the more predictive lag'. It is worth emphasizing also that even coefficients having opposite sign, possibly due to the mortality displacement (for instance negative coefficients for the heat effect) describe a change in slope and accordingly they take part in the MMT estimation as well. This is a nontrivial advantage as the more the information on slope-change is, the more accurate the estimate of the MMTs is. Figure 1 displays such constrained segmented parameterization.

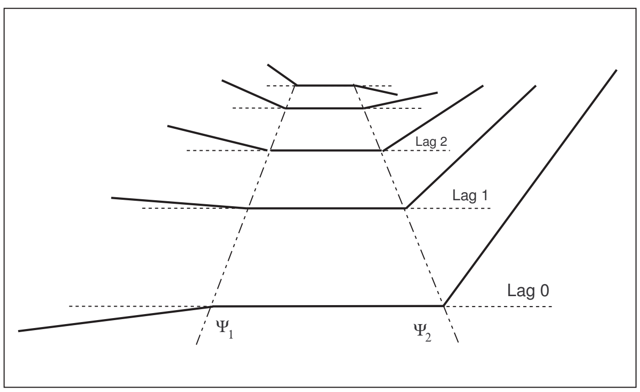

Figure 1: The proposed constrained segmented parameterization for the temperature-mortality relationship: equality constraints for the threshold values in the different lag-specific relationship are imposed while the lag-varying slopes are separately modelled by B-splines. A V-shaped model is obtained as $\psi_1 = \psi_2$.

So far, two breakpoints estimation has been discussed. However whether the popular V-shaped relation has to be fitted, further simplifications occur. In particular since $\psi_1 = \psi_2$ the model is

$$\beta_1(Z-\psi)_- + \beta_2(Z-\psi)_+ \quad (2.5)$$

and because this has to imply $\delta_1 = \delta_2$, the iterative 'working' linear predictor simplifies to

$$\sum_{l_1=0}^{L_1-1} \beta_{1l_1} U_{1l_1} + \sum_{l_2=0}^{L_2-1} \beta_{2l_2} U_{2l_2} + \delta \left\{ \sum_{l_1=0}^{L_1-1} \tilde{\beta}_{1l_1} V_{1l_1} + \sum_{l_2=0}^{L_2-1} \tilde{\beta}_{2l_2} V_{2l_2} \right\} \tag{2.6}$$

which has $L_1 + L_2 + 1$ parameters to be estimated, with the single breakpoint being given by $\hat{\psi} = \tilde{\psi} + \hat{\delta}$.

Models (2.4) and (2.6) constrain the breakpoint(s) to be same among the different lags, but the slopes describing the distributed lag curves (of cold and heat) are actually unconstrained. Although in general model fitting could lead to some results, collinearity among the lagged variables 'U_{jl_j}' can cause large standard errors of the β-parameters and hence poor estimates of the shape of the DL curves; so some parametric function is assumed to get more accurate and reliable estimates of the lag-pattern. This is useful to obtain a smooth curve which is more plausible from a biological standpoint and allows to gain narrower standard errors by reducing the degree of collinearity and the number of parameters to be estimated. Such an approach has been first proposed by Almon (1965) in a econometric context, its introduction in the analysis of epidemiological time series seems to originate from Wyzga (1978) and further applications include works by Braga *et al.* (2001, 2002) and Schwartz *et al.* (2004). However these works assume that the β-parameters follow polynomial functions which sometimes may heavily depend on outliers. A better alternative is represented by splines which allow local, rather than global, fitting (de Boor, 2001); here we use B-splines to smooth the shape of DL curves. Let $[B_1, \ldots, B_{i_j}, \ldots, B_{P_j}]$ the generic spline basis on the $l_j = \{0, 1, \ldots, L_j - 1\}$ variable with P_j degrees of freedom (i.e. columns) depending on proper knot vector and degree, usually cubic. Given two B-spline basis, the shape of the DL curve for cold and heat separately, can be expressed by a linear combination of single columns:

$$\beta_{1l_1} = \sum_{i_1=1}^{P_1} b_{1i_1} B_{i_1}(l_1) \qquad \beta_{2l_2} = \sum_{i_2=1}^{P_2} b_{2i_2} \breve{B}_{i_2}(l_2)$$

where B and $\breve{B}$ stand for the spline bases for cold and heat with P_1 and P_2 degrees of freedom respectively. Now it easily seen that the lagged effects $\sum \beta U$ in the (2.4) or in the (2.6) are modelled as a function of the P_j constructed variables (rather than the L_j original ones); for instance for the cold it is

$$\sum_{l_1=0}^{L_1-1} \beta_{1l_1} U_{1l_1} = \sum_{l_1=0}^{L_1-1} \left\{ \sum_{i_1=1}^{P_1} b_{1i_1} B_{i_1}(l_1) \right\} U_{1l_1} = \sum_{i_1=1}^{P_1} b_{1i_1} \left\{ \sum_{l_1=0}^{L_1-1} B_{i_1}(l_1) U_{1l_1} \right\}$$

By putting such expressions into (2.4) or (2.6) it is clear that estimation is carried out in terms of the $P_1 + P_2$ transformed variables whose b coefficients and their covariance matrix are used to get the original point estimates and relevant covariance matrices of the β parameters. For instance, using matrix notation for the cold it is

$$\hat{\boldsymbol{\beta}}_1 = \boldsymbol{B}\hat{\boldsymbol{b}}_1 \qquad \widehat{\text{cov}}(\hat{\boldsymbol{\beta}}_1) = \boldsymbol{B}\widehat{\text{cov}}(\hat{\boldsymbol{b}}_1)\boldsymbol{B}'$$

where $\boldsymbol{B}$ is the $L_1 \times P_1$ B-spline matrix and the components of $\hat{\boldsymbol{\beta}}_1$ are the lag-specific estimated effects having standard errors extracted from the main diagonal of the matrix $\widehat{\text{cov}}(\hat{\boldsymbol{\beta}}_1)$. Thus the total net effect is given by the sum of the estimated single effects, namely $\sum_{l_1} \hat{\beta}_{1l_1} = \mathbf{1}'\hat{\boldsymbol{\beta}}_\mathbf{1}$ with standard error $\text{SE}(\sum_{l_1} \hat{\beta}_{1l_1}) = (\mathbf{1}'\text{cov}(\hat{\boldsymbol{\beta}}_1)\mathbf{1})^{1/2}$ being $\mathbf{1}'$ a row-vector of ones with appropriate length. Analogous formulas hold for the heat effects estimate.

A plot of the 'lag-specific estimates versus lag indices' represents an estimate of the DL curve from which useful information may be drawn: the shape of the curve itself may be used to evaluate what is the pattern of the risks with respect to time (days), whether the environmental exposure has an immediate or delayed effect and whether harvesting occurs. With this respect, the total effect provides a measure of the net amount of deaths induced by temperature.

3 Application

The method illustrated in the previous section is applied to daily time series of all-natural (ICD.IX 1-799) deaths and average air temperature (expressed in degrees Celsius, $^\circ C$) recorded in two Italian cities: Milano 1980-89 (average daily death and temperature 30.7 and $14.6^\circ C$ respectively) and Bologna 1998-2002 (average daily death and temperature 11.5 and $14.3^\circ C$ respectively). Plots of raw data (counts vs. time and counts vs. temperature) reveal the classical pattern of mortality with noticeable picks during the winter months and some excesses of mortality during summertime especially at higher temperature values.

Here the aim is to estimate the effect of temperature on mortality. In particular, topics of interest concern the determination of the heat tolerance (MMT) and of the DL curve associated with heat and cold and the final assessment whether the apparent effect of temperatures is compensated by a deficit.

Figure 2 displays smoothed point estimate of the temperature-mortality curve (adjusted for seasonality) at different lags for the two considered cities. The plot emphasizes how the slopes of cold (heat) are steeper at longer (shorter) lags, making difficult to select the most predictive relationship. The constrained segmented DL overcomes this issue and allows to take into account information from each lag making estimate of MMT more accurate. Note that also the information on the negative right slope shares in estimating the MMT.

We pursue the analysis by using Poisson log-linear regression, modelling the log-expected count of death at day t as a function of seasonality and temperature. Temperature has been included via a constrained segmented DL with a single threshold up to $L_1 = L_2 = 15$ lags for cold and heat. Both the DL curves are based on cubic B-spline with one knot at 7.5 (five constraints overall, i.e. $P_1 = P_2 = 5$). For each considered city, estimates from two different models are displayed in Table 1: in M_1 long-term trend and seasonality have been fitted by categorical variables month plus year, while a nonparametric smoother based on regression splines with 7 degrees of freedom per year has been used in M_2. For each fitting log-likelihoods from the present model and from an alternative approach is also displayed: to model nonlinear

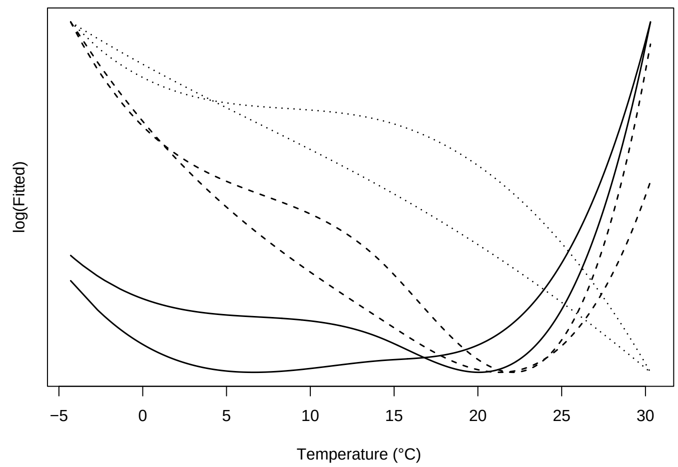

Figure 2: Smoothed estimated mortality-temperature curve at different specific lags for Milano and Bologna dataset: lag 0 (continuous line), lag 7 (dashed line) and lag 15 (dotted line). The scales of the fitted curves at different lag are not comparable from each other.

multi-lag relationship, Braga *et al.* (2001, 2002); Schwartz *et al.* (2004) assume both linear and quadratic terms at each lag and constrain the relevant coefficients to fit fourth-degree polynomials. However to get comparable results, B-splines rather than polynomials have been used, therefore observed differences should be attributed to the different parameterization (segmented versus quadratic).

Table 1: Point estimates and 95% Wald-based confidence intervals (in parentheses) of the temperature parameters from some fitted models: cumulative cold- and heat- related risks and MMT.

		Temperature parameters estimate			– log-likelihood‡	
City	model†	Cold(×10)	Heat	MMT	A	B
Milano	M_1	-0.163	0.146	25.9	11602.4	11701.2
		(-0.193, -0.129)	(0.115, 0.178)	(25.5, 26.3)		
	M_2	-0.045	0.134	26.2	11531.6	11605.2
		(-0.094, 0.004)	(0.095, 0.173)	(25.8, 26.6)		
Bologna	M_1	-0.079	0.095	24.6	4800.5	4812.0
		(-0.155, -0.002)	(0.041, 0.149)	(23.4, 25.8)		
	M_2	0.059	0.094	25.8	4779.1	4789.3
		(-0.048, 0.166)	(0.017, 0.171)	(24.7, 26.9)		

† M_1: seasonality modelled by categorical variables 'year+month'

† M_2: seasonality modelled by natural spline with 7 df per year

‡ Poisson log-likelihood according to the proposed approach (segmented, A) and an alternative (quadratic, B). See text

Figure 3 displays the DL curves for cold and heat for models M_1: positive (negative) values in the curve of cold (heat) suggests harvesting which does not seem occurring in a relevant way. By summing up such lag-specific estimates, the total (net) effect estimates, as reported in Table 1, are obtained.

Results suggest that the proposed piecewise-linear model performs better then the quadratic formulation: the log-likelihoods are always lower, although such differences are sometimes small. However what is worth stressing, is that the constrained segmented DL model while accounting jointly for linearity and distributed effects, provides meaningful estimates of the temperature-mortality curve: cold and hot risks (lag-specific and total) and MMT. In particular, the estimates of the unique breakpoint measuring the heat tolerance appear to be quite accurate, with fairly narrow confidence intervals. That arises from the equality constraint set among the several lagged relationships: indeed, as just discussed previously, each difference-in-slope contributes to estimation of the MMT parameter independently of its sign.

Substantially, results agree with many epidemiological papers with heat effects occurring more promptly, within five days approximatively, and the cold ones being more persistent, from three days through two weeks (Zanobetti *et al.*, 2003; Pattenden *et al.*, 2005).

It is also worth to highlight how the long-term smoother impacts the es-

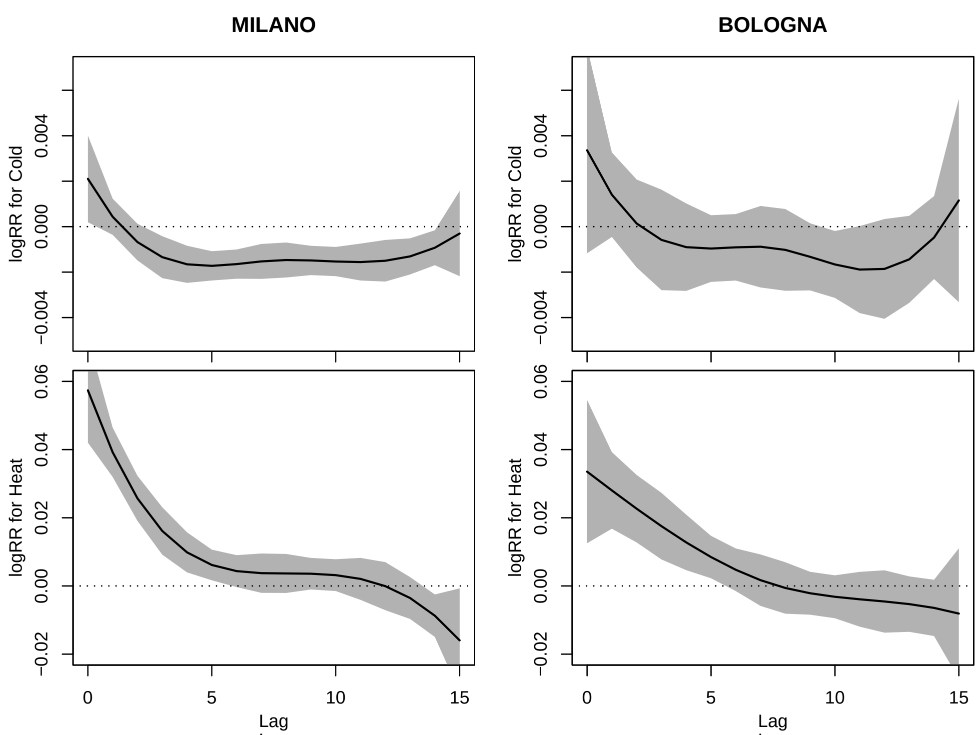

Figure 3: Point estimates and 95% confidence intervals of the Distributed Lag curves for the cold and heat effect in Milano and Bologna. Each curve is based on a five-order B-spline (cubic spline with one knot at 7.5)

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timate of the temperature effects. While heat and MMT estimates are substantially unchanged, severe controlling for seasonality (i.e. undersmoothing) tends to capture death excesses in winter and, as a consequence, the cold effect falls and disappears: the relevant confidence intervals in the M_2 models include the zero. Hence in practice care is needed in selecting the appropriate smoothness for seasonality since results for cold might be seriously misleading.

Two-threshold models have been tried for both the datasets, but problems of convergence occurred, suggesting that one breakpoint were sufficient. Issues on estimation of two-breakpoints models and on model selection, will be tackled in the Conclusions section.

4 Conclusions

In this paper we have presented an unified model-based approach to quantify the temperature effects on mortality accounting for the major features that characterize the data. By means of a multi-lag segmented approximation with equality constraints on the breakpoints and spline-based smoothers for the DL curves, nonlinearity and delayed effects are simultaneously taken into account leading to parameter estimates with important physical meaning. A piecewise linear parametrization is quite attractive: for instance, Curriero *et al.* (2003) in re-visiting their previous analyses use a piecewise formulation rather than a nonparametric approach (Curriero *et al.*, 2002); smoothing of the DL via B-spline is useful also to rule out the noise from the lag-specific estimates while guaranteeing enough flexibility. The estimating procedure lies just on iterative fitting of proper linear model, therefore its implementation is also favored in practice; an R function is available on request from the author.

Hence there is a number of advantage in using the proposed approach. Either lag-specific and total risks for $1°C$ increase are obtained for both the cold and heat and in addition an unique breakpoint (MMT) estimate is also provided, which can be interpreted as a measurement of the heat-tolerance. In this connection, the equality constraints appear to be a quite 'lucky' (good) choice, since those enable to estimate the breakpoints with sufficient accuracy. Likewise the computational aspect is also involved: constraints assure some stability of the estimating procedure and initial values to start the algorithm become substantially unimportant.

For the V-shape model, testing procedure on the existence of the breakpoint also look better: the Davies test (Davies, 1987) is understood to gain some power due to increased information on the difference-in-slope parameter. Moreover in the two analyzed data-sets, interpretability is also matched with better fit (with respect to one provided by an alternative approach), although this may be not always true.

Estimates depend on the choices of lags (L_1, L_2) and on the B-spline used to model the distributed effects. While different B-splines are not expected to twist the results provided that enough of flexibility is guaranteed, lag selection will do so. Selecting longer lags (upon to 30, say) can be useful to exploit possible longer effects, although many parameters can lead to increase the uncertainty of the net effect estimate. Likelihood-based criteria can be employed to select the lags (L_1, L_2) and of the order of the B-spline (P_1, P_2).

The paper does not discuss methods to discriminate among one- or two-breakpoint models (namely between the (2.6) and (2.4)). The null hypothesis to be tested is $H_0 : \psi_1 = \psi_2$, which is a non-standard hypothesis for several reasons; some simulations have shown the likelihood ratio statistic having a nonstandard distribution and the relevant statistic test being greatly biased. However a few rules of thumb can be used: one could look at the confidence intervals of the thresholds, and select the one-breakpoint model when the CIs are overlapped; alternatively the choice can be driven via any likelihood-based criterium (e.g. the AIC or the BIC) and finally bootstrap procedures may be applied, although these are not favored in practice since epidemiological studies often involve many years with quite a lot of observations. However a limited experience on some real and simulated datasets suggest that computational problems often indicate that the fitting model is unlikely.

Finally it should be noted that while the paper is specifically devoted to temperature-mortality relationship, the proposed method and algorithm could be applied to broader contexts where a segmented relationship is met in the levels of some stratification variable and a common breakpoint has to be estimated (Kim *et al.*, 2004).

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