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Keywords: UBRE; hospital admissions; Milano; non-linear temperature effect.

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1 Introduction

Ambient temperature is recognized to be an important factor in determining health status of human beings. Evidence shows that an ideal temperature can be identified and that when ambient temperature is different than ideal temperature, mortality and morbidity among exposed population increase (Donaldson et al. (2003)). Moreover, the persistence of high temperature –a heat wave– may have a stronger effect than the same temperature experienced in non consecutive days. The cumulative effect, in other words, may be stronger than the sum of the effects. The effect of temperature on hospital admissions can be analyzed using generalized additive models (GAM, (Hastie and Tibshirani (1990))) in which the daily number of admissions is the response variable and a measure of daily temperature is included among the covariates. GAM are widely used in investigating epidemiological time series, for instance, they are the typical choice in modeling the effect of pollutant concentration on health (see *Epidemiology*, vol. 16, issue 4 on Ozone and mortality). There are various reasons to choose GAM in this context: we can model a non gaussian response; we can estimate a non linear effect of some of the covariates without a prior assumption on its form; we will be able –thanks to the additive structure of the model– to distinguish the effect of each covariate. We can assess whether or not a cumulative effect is in place by adding, to the basic temperature-admissions model, one or more further temperature-related covari-

ates measuring the heat wave (sections 3 and 4). In this context the selection of the model plays an important role, being the main evidence of relevance of heat waves in explaining the number of hospital admissions. Things are further complicated by the fact that a lot of competing models, quite similar to each other, are considered. To select among alternative models we employ Un-Biased Risk Estimator (UBRE), which is a very convenient choice from a practical point of view, but we also deepen the results of model selection employing a resampling technique (section 5).

2 Data

In order to understand the relationship between meteorological variables and frequency of hospital admissions, we collect data on the number of health episodes in a given population and its level of exposure to temperature. This ideally implies knowledge of actual personal exposure, in practice we restrict our analysis to Milano urban population and we consider meteorological data measured at a weather station located in the town center; these are assumed to be representative of the exposure of all urban population (Richardson and Best (2003)).

Weather conditions are seldom the direct and unique reason for admission to the hospital, usually adverse meteorological patterns favor acute health episodes in people weakened by existing pathologies or belonging to population groups which are more fragile, like the elderly and the youngest. We consider hospital admissions due to all non-incident causes (all codes ICD-IX except 800-999) of people aged more than 75 years, occurred in all hospitals located in Milano during summer periods (June-July-August) of years 1995 to 2003. In order to consider relevant admissions to the hospital, only those events corresponding to admissions not required by the general practitioner, not related to a surgical event and not scheduled to last less than one day are selected. We exclude events for which the reason for admission is not specified. Daily hospital admissions data are obtained from the Regional Health Informative System.

Meteorological data for the period 1995-2003 are obtained from the Regional Agency for Environmental Protection (ARPA Lombardia). Hourly data are collected on temperature, rain, wind velocity and direction and, from year 2000, humidity.

In the end, due to the presence of missing data in meteorological time series we could use observations for 812 days. The average number of admissions per day is 38.91 (s.d. 9.78), the range is 13 to 108; data are depicted in figure 1.

3 Definition of heat wave

If we accept that heat waves pose a risk on health, as is maintained in various sources (a partial list of these is in table 1), it is also natural to expect the excess mortality and morbidity due to a heat wave to depend on its characteristics: the duration and the temperature level which is reached. Table 1 outlines a number of definitions of heat wave, it is worth to look through them in order to determine the main distinctive elements before discussing how to measure it for our purposes.

Proposed definitions differ both qualitatively and quantitatively. Qualitative differences concern the variables involved or the pattern which defines the heat wave. Distinctive ele-

Source	Definition of Heat Wave
(a) Merriam Webster dictionary (online)	A period of unusually hot weather
(b) EM-DAT: The OFDA/CRED International Disaster Database - www.em-dat.net - Universit Catholique de Louvain - Brussels - Belgium	Long lasting period with extremely high surface temperature.
(c) Environment Canada (2001)	A period of more than three consecutive days of $T^{(\max)}$ at or above 32°C. The same definition is used in Nashold et al. (1996), Lene and Grymes (1997), Donoghue et al. (2003).
(d) Michelozzi et al. (2004)	A h.w. is experienced if Maximum Apparent Temperature greater than 90th percentile and an increase of 2°C compared with the previous day has occurred.
(e) National Weather Service (U.S.)	(1) A period of abnormally and uncomfortably hot and unusually humid weather. Typically a heat wave lasts two or more days. (2) Heat Advisory: Issued within 12 hours of the onset of the following conditions: heat index of at least 40.56°C but less than 46.11°C for less than 3 hours per day, or nighttime lows above 26.67°C for 2 consecutive days.
(f) Netherlands Royal Meteorological Institute (as in Huynen et al. (2001))	At least 5 days with $T^{(\max)} > 25^\circ\text{C}$ of which at least 3 with $T^{(\max)} > 30^\circ\text{C}$
(g) Meehl and Tebaldi (2004)	(1) Several consecutive nights with no relief (high nighttime temperature) (2) Let T_1, T_2 be, respectively, the percentiles 97.5 and 81 of the distribution of temperature. A h.w. is then a period of consecutive days for which: $T^{(\max)} > T_1$ for at least three days; mean of daily max greater than T_1 ; $T^{(\max)} > T_2$ for the whole period.
(h) Kalkstein and Sheridan (1999)	No definition of heat wave, but the authors discuss threshold temperature above which mortality increase, these are 29°C for Montreal; 33°C for Toronto.

Table 1: Some alternative definitions of what a heat wave is.

ments are: the inclusion of other than temperature meteorological variables like humidity (*d*) (letters refer to table 1); the minimum duration (which is not set only in case (*d*)); which temperature is considered, many authors do not refer only to maximum temperature, suggesting that the lack of relief due to high nighttime temperature (*g.1, e.1*) or, more generally, high mean temperature (*f, g.2*) may be relevant as well.

As far as quantitative differences are concerned, we must recall that, as the analysis of Donaldson et al. (2003), among others, showed, the relationship between temperature and health is strongly dependent on the local climate (in more intuitive terms it depends on the meteorological condition which the population is used to). Then, it is intuitively clear that the temperature threshold above which a heat wave is said to occur should depend on the climate of the area and also on the period we refer to. This is apparent in the definitions of table 1 when percentiles of the distribution of temperature are used (*d, g*), those definitions which use fixed values (*c, e, f, h*) should be considered valid only for the area they refer to.

We define a heat wave as a minimum of n consecutive days ($n = 2, 3$) during which the daily maximum temperature is above a threshold. Since a reasonable threshold should be relative to (local) usual weather, we define the threshold as a quantile of the probability distribution of daily maximum temperature. Different thresholds arise depending on the particular quantile which is chosen and on whether a stationary or non stationary model for temperature is used.

Let $T_t^{(\max)}$ represent the observations of maximum temperature on day t and let y_t be the calendar year to which day t belongs.

The simplest choice of a threshold is a constant value for the whole observation period:

this corresponds to a stationary model, $T_t^{(\max)} \sim F(\cdot) \forall i$, the threshold is then the q -quantile of F , $s_i = \hat{F}^{-1}(q) \forall i$, where \hat{F} is the empirical distribution function. In practice, we use fixed thresholds at $30^\circ C$, $31^\circ C$, $32^\circ C$, $33^\circ C$.

We also consider thresholds based on non stationary models for temperature: we assume first that mean of temperature varies as a smooth function f of time

$$T_t^{(\max)} = g(t) + \varepsilon_t \quad \varepsilon_t \sim IID(\mathcal{N}(0, \sigma^2)), \quad (1)$$

alternatively, we assume that the temperature distribution is the same for all days in each calendar year,

$$T_t^{(\max)} \sim F_{y_t}(\cdot). \quad (2)$$

The threshold, according to model (1), is $s_t = \hat{g}(t) + \hat{\sigma}\Phi^{-1}(q)$ where estimates are obtained fitting a GAM with a spline function with 3 equivalent degrees of freedom for g . According to model (2) we define $s_t = \hat{F}_{y_t}^{-1}(q)$. Examples of threshold computed according to the three methods are in figure 1, where the relationship between occurrence of heat waves and spikes in the number of admissions is also pointed out.

It is worth noting that the above definitions lead to significantly different thresholds in Milano because the relevant time series of maximum daily temperature is non stationary.

We should recall that we are trying to assess the characteristics that a heat wave should have to qualify as a source of additional risk for the health of the elderly. The types of thresholds considered can be discussed on this respect and with respect to adaptation, which is a well known concept in scientific discussion related to changes in climate conditions (IPCC (2001)). Adaptation, in the context of the relationship between health and temperature, means that if the base temperature increases, exposed population get used to it (either due to physiological changes or –more likely in such a short period– due to a greater risk awareness and consequent changes in the behavior) so that adverse effects take place at higher levels than before. A constant threshold over the years corresponds to the idea that the population does not adapt: loosely speaking, what is harmful in year 1995 is harmful to the same extent in year 2003. A continuously varying threshold means a continuous adaptation, a threshold which varies year by year correspond to assuming that people adapt from year to year.

On this respect all three definitions can be criticized, the less reasonable is the one assuming continuous adaptation, while the others, albeit imperfect, may be advocated: a constant threshold, in particular, is reasonable if we assume that few years is too short a period to significantly adapt to new conditions. We may draw a conclusion on whether adaptation takes place or not during the period under consideration by comparing the fit of the models employing different threshold definitions.

4 Models

For each of the heat wave definitions in section 3 we consider a set of alternative models, each employing a different measure of intensity of the heat wave.

Besides heat wave variables, all models may include as covariates maximum daily temperature and calendar effects: day of the week to allow for event scheduling, year and day of the year (*yday*) to control for time trend and seasonality. Day of the week (*wday*) and

year (*year*) have been included into the models through sets of dummy variables while the covariate day of the year (*yday*), transformed on a $[0, 1]$ scale (0 being the 1st of June, 1 being the 31st of August), is included into the models through a spline, thus allowing for a non-linear effect. Other meteorological variables are not significant and hence are dropped. This may appear surprising, especially for humidity which is expected to worsen the effect of heat. When humidity is included in a model along with temperature, however, its role is not clear, for example in Ballester et al. (1997) humidity is not significant, in Tobías and Saez (2004) and Pauli and Rizzi (2005) it has a protective effect.

Finally, we include in the model a variable which is null unless the day belongs to a heat wave or immediately follows it; this variable is chosen among: duration of the heat wave (D_t); maximum temperature observed during the heat wave (M_t); position of the day within the heat wave (P_t); cumulative temperature within the heat wave (C_t); same as P_t but the first day after a heat wave has value equal to the last day of the heat wave ($P_t^{(L)}$); same as C_t but the first day after a heat wave has value equal to the last day of the heat wave ($C_t^{(L)}$). Variable D is included in the linear predictor as factor, while variables C , $C^{(L)}$, P , $P^{(L)}$ are included as smooth functions.

Being then X_t the number of events occurred in day t , we assume $X_t \sim \text{Poisson}(\lambda_t)$ where

$$\log(\lambda_t) = \alpha + \sum_{j=1}^6 \beta_j \text{wday}_t^{(j)} + \sum_{i=1996}^{2003} \gamma_i \text{year}_t^{(i)} + g(\text{yday}_t) + \text{temp}, \quad (3)$$

where $\text{wday}_t^{(j)}$ and $\text{year}_t^{(i)}$ are dummy variables for days of the week and calendar years, respectively ($\text{wday}_t^{(1)}$ is 1 if day t is a Monday and 0 otherwise, with obvious extension for $j = 2, \dots, 6$; $\text{year}_t^{(i)}$ is 1 if day t is in year i and 0 otherwise); yday_t is the time within year scaled to be in $[0, 1]$.

For the temperature model (*temp*) part we consider the alternative specifications listed in table 2. Choice of model and of the degree of smoothness for the non linear components is decided by UBRE (Wahba (1990)) which is a modification of more usual criteria such as GCV or AIC to be preferred in GAM when scale parameter is known (Hastie and Tibshirani (1990), Wood (2000)). UBRE score is given by $\frac{D}{n} + 2\frac{p}{n}$, where D is the deviance (twice the difference between the log-likelihood for the saturated model and the log-likelihood for the present model), and p is the total degrees of freedom (including the estimated d.o.f. of the smooth functions). UBRE is a very convenient choice from a computational point of view, is readily available in most statistical software and is the preferred choice in most applied works. On the other hand, criteria such as UBRE are judged to be unstable as a tool for model selection, meaning that little difference among datasets may lead to different models selected (Hastie et al. (2001)).

5 Results

As already pointed out, the selection of the model plays in this work an important role, being the main evidence of relevance of heat waves in explaining the number of hospital admissions. Things are not made easier by the fact that a lot of competing models, quite similar to each other, are considered.

Alternative “temperature models” in (3)	
<i>no temp. model</i>	(α)
$f(T_t^{(\min)})$	(β)
$f(T_t^{(\text{mean})})$	(γ)
(a) $f(T_t^{(\max)})$	(δ)
(b) $f(T_t^{(\max)}) + \text{as.factor}(D_t)$	
(c) $f(T_t^{(\max)}) + s(M_t)$	
(d) $f(T_t^{(\max)}) + s(P_t)$	
(e) $f(T_t^{(\max)}) + s(C_t)$	
(f) $f(T_t^{(\max)}(1 - S_t)) + \text{as.factor}(D_t)$	
(g) $f(T_t^{(\max)}(1 - S_t)) + s(M_t S_t)$	
(h) $f(T_t^{(\max)}(1 - S_t)) + s(P_t)$	
(i) $f(T_t^{(\max)}) + s(P_t^{(L)})$	
$f(T_t^{(\text{mean})}) + s(C_t^{(L)})$	(κ)
(j) $f(T_t^{(\max)}) + s(C_t^{(L)})$	(ζ)

Table 2: Legend of alternative temperature components of models. S_t is a variable which is equal to 1 if day t belong to a heat wave and 0 otherwise; $T_t^{(\max)}$ is maximum daily temperature on day t . Legend in leftmost column is used in section 4 and can be referred to different choices of heat wave definition, that in rightmost column is used in 5 and is always referred to h.w. defined as at least two days above $32^\circ C$. For the sake of brevity we write *as.factor* instead of explicitly representing dummy variables when used and s for smooth functions.

Model comparison based on UBRE is summarized in table 3. The UBRE score for model not including heat waves ((a) in table 2) is 0.218, higher than most of the scores for models in table 3. The improvement of model prediction ability, measured by UBRE score, induced by the inclusion of a measure of high temperature persistence suggests the relevance of the heat wave effect. Best model according to UBRE is based on heat waves defined as at least two days with maximum temperature above $31^\circ C$ (figure 1, bottom row) and $C_t^{(L)}$ as heat wave intensity measure.

In order to improve on UBRE, alternative criteria have been proposed, sometimes with interesting results. We, however, adopt a different approach: we want to stick with UBRE as the basic criterion, because of the computational and practical advantages, but we want to keep into account its variability in drawing conclusions.

In order to allow for the variability of the UBRE score in choosing among I models we resample (with replacement) the time series B times and for each sample we reckon UBRE scores according to the models under consideration, obtaining, for each model $i = 1, \dots, I$ a sample $UBRE_i^{*b}$, $b = 1, \dots, B$. Then, we compare models based on resampling

model	Constant threshold				Smooth threshold				Yearly threshold			
	30	31	32	33	0.8	0.85	0.9	0.95	0.8	0.85	0.9	0.95
Minimum duration: 2 day												
(b)	0.209	0.206	0.218	0.224	0.210	0.233	0.216	0.218	0.219	0.202	0.190	0.220
(c)	0.203	0.213	0.220	0.220	0.211	0.214	0.164		0.214	0.165	0.173	0.188
(d)	0.139	0.128	0.148	0.158	0.175	0.178			0.149	0.165	0.163	
(e)	0.133	0.127	0.150	0.164	0.163	0.172	0.200	0.179	0.139	0.167	0.156	0.206
(f)	0.298	0.280	0.257	0.263	0.256	0.270	0.249	0.233	0.271	0.266	0.242	0.262
(g)	0.289	0.284	0.266	0.262	0.236	0.241	0.166		0.250	0.168	0.178	0.179
(h)	0.176	0.141	0.155	0.160	0.229	0.224			0.197	0.257	0.258	
(i)	0.140	0.125	0.126	0.136	0.166	0.169			0.157	0.150	0.163	
(j)	0.131	0.123	0.128	0.143	0.145	0.163	0.191	0.174	0.148	0.154	0.157	0.162
Minimum duration: 3 day												
(b)	0.209	0.206	0.218	0.224	0.210	0.233	0.216	0.218	0.219	0.202	0.190	0.220
(c)	0.206	0.212	0.220		0.209	0.190			0.214	0.164	0.168	
(d)	0.139	0.128	0.148	0.159	0.174	0.178			0.149	0.165	0.164	
(e)	0.133	0.127	0.149	0.163	0.157	0.170	0.201	0.212	0.139	0.167	0.156	0.213
(f)	0.298	0.280	0.257	0.263	0.256	0.269	0.250	0.250	0.271	0.266	0.242	0.261
(g)	0.292	0.281	0.244		0.233	0.236			0.249	0.167	0.174	
(h)	0.178	0.141	0.155	0.160	0.229	0.227			0.200	0.255	0.251	
(i)	0.140	0.125	0.127	0.143	0.165	0.170			0.157	0.150	0.164	
(j)	0.131	0.123	0.129	0.147	0.139	0.162	0.190	0.168	0.148	0.154	0.158	0.164

Table 3: UBRE scores for alternative models differing for the variables included in the linear predictor (see table 2) and the definition of heat wave. The UBRE score for model not including heat wave effect is 0.218.

distributions of UBRE scores of different models in order to compare them.

This analysis is performed for the models marked with Greek letters in table 2: we limit ourselves to six models, a reference null model including only calendar variables, three models including daily temperature as a covariate through, respectively, daily minimum, daily mean and daily maximum and two models including heat wave effect, where a heat wave is defined as a minimum of two days with temperature above $31^{\circ}C$.

Resampled UBRE scores are pairwise dependent, the comparison of the (marginal) resampling distributions of the $UBRE_i$ may then be misleading, so we compare models i and j by looking at the probability distribution of $\Delta_{ij}^{*b} = UBRE_i^{*b} - UBRE_j^{*b}$. Prior to presenting the results it is worth noting that many of the alternative models are quite similar to each other, so we expect the model confidence set to include many different models. It would be surprising, for instance, to find a strong difference between models (d) and (i) or between (e) and (j) which differ only for the value of one covariate in a few data points. The comparison (figure 2) allows to conclude that models (κ) and (ζ) improve on all other models to substantially the same extent; models (β), (γ) and (δ) improve on reference model and are substantially equivalent to each other. Hence, evidence shows that allowing for heat wave effect improves on predictive performance while choice of temperature measure does not lead to substantial changes.

Another approach we consider to complement model selection decision is the bumping procedure suggested in Tibshirani and Knight (1995). The authors consider the problem of determining the best among a set of models indexed by a parameter θ which has to be estimated by minimizing a criterion $R(\mathbf{z}; \theta)$, so that $\hat{\theta} = \operatorname{argmin}_{\theta} R(\mathbf{z}; \theta)$. In our case the

criterion R is minus the penalized log likelihood (Wood (2000))

$$R(\mathbf{z}; \theta) = -l(\mathbf{z}; \theta) + \frac{1}{2} \sum_j \nu_j J(\phi_j).$$

The parameter θ has components $(\alpha, \beta, \gamma, \phi_1, \dots, \phi_d)$ where α , β and γ are introduced in equation (3) and ϕ_j is the vector of coefficients of the i -th smooth component (that is, is the vector of coefficients multiplying the basis function of the spline). We recall that all models involve a smooth component modeling seasonality ($g(\text{yday}_t)$ in equation (3)) and one or two smooth components related to temperature, (f and s in table 2). The log-likelihood is then $l(\mathbf{z}; \theta) = \sum_{t=1}^n (z_t \ln \lambda_t - \lambda_t)$ with λ_t as in equation (3) and \mathbf{z} the vector of daily observations. For each smooth function in the model a penalization factor $\nu_j J(\phi_j)$ is applied which is smaller the smoother is the spline determined by ϕ_j , ν_j is the smoothing coefficient determining the smoothness of the final estimate and is chosen according to UBRE criterion. Tibshirani and Knight (1995) suggest drawing bootstrap samples \mathbf{z}^{*b} and consequently obtain a bootstrap sample for the estimate of θ : $\theta^{*b} = \operatorname{argmin}_{\theta} R(\mathbf{z}^{*b}; \theta)$ (including choice of smoothing coefficients ν_i .) This sample is then used to obtain the bumping estimate of θ , $\hat{\theta}^B = \operatorname{argmin}_{\theta} R(\mathbf{z}; \theta^{*b})$, but can also be used to obtain confidence sets for models. If $\theta^{*1}, \dots, \theta^{*B}$ is the sequence of bootstrap estimates ordered according to the value of the criterion R ($R(\mathbf{z}; \theta^{*i}) \leq R(\mathbf{z}; \theta^{*j})$ if $i < j$) an approximate confidence set of level α is given by $\{\theta^{*1}, \dots, \theta^{*[\alpha B]}\}$, being $[\alpha B]$ the integer part of αB .

Pairwise comparison of resampled penalized likelihood suggests the same conclusion drawn based on resampled UBRE scores: models (κ) and (ζ) lead to the highest scores; models (β), (γ) and (δ) are a second best; (α) is ruled out.

The most interesting result is that the model not including any heat wave effect is always ruled out. The conclusion that heat wave effect has to be included into the model is then confirmed.

Non linear contributions to the linear predictor of final model are depicted in figure 3 which confirms the increasing risk posed by the temperature but also the worsening effect of persistence of high temperature. Heat wave effect is depicted in figure 3(c), risk increases as cumulative temperature during the heat wave gets higher, when a certain level is reached, however, the additional risk decrease, this may be due to a harvesting effect. If we compare the curve for maximum daily temperature estimated within the model with heat wave explicitly allowed for (figure 3(a)) and the one reported in figure 3(b) and relative to no-heat-wave model, we see that the latter is much more steep in its final part. Finally, the comparison of normal probability plots of deviance residuals (figure 3(d) and (e)) reveals that the inclusion of the heat wave effects improves model fit, especially in the right tail of the distribution.

6 Discussion

We examine data on hospital admissions in Milano in order to understand the relationship between temperature and number of hospital admissions. In particular, we want to assess the additional effect of heat waves, if any, with respect to the effect of daily temperature alone.

For this purpose we compare a basic model, in which mean daily number of admissions is explained by daily maximum temperature and calendar variables only, and alternative models including an additional heat wave effect. A number of different alternative criteria based on the pattern of daily maximum temperature in consecutive days are used to define heat wave measures to be compared. Criteria are based on different plausible assumptions on the sensitivity of the population to surrounding climate.

The choice of the heat wave measure to be used and, thus, the uncertainty on model selection is investigated using a resampling scheme in which we replicate the model selection process to check the stability of its conclusions.

Results of model selection are strongly in favor of the inclusion of heat wave effect in the model. The stress due to high temperature cumulate from day to day and the risk of hospitalization increases the more hot days are experienced consecutively.

In order to appreciate the increase in estimated risk we compare (figure 4) the relative risk due to temperature computed for summer 2003 according to the base model and the model allowing for heat wave effect selected by UBRE. The relative risk is computed on a day by day basis and is the ratio of expected number of episodes for day t according to model including temperature and expected number of events according to the model not including temperature (taken as baseline risk). In the Poisson model this reduces to the exponential of the temperature part of the model.

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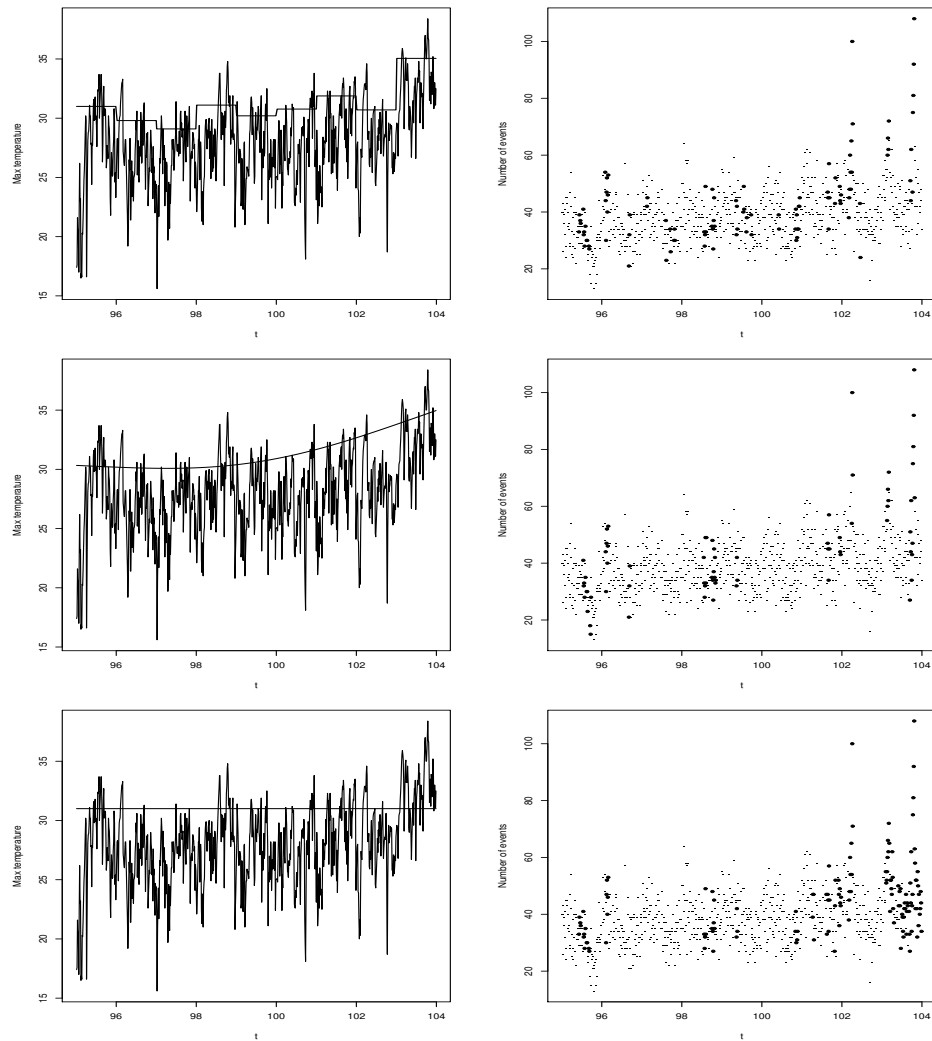


Figure 1: Observed heat waves defined as (from top to bottom): at least two consecutive days with $T^{(\max)}$ higher than the 85-th percentile of the year distribution; at least three consecutive days with maximum temperature higher than the 85-th percentile of $T^{(\max)}$ distribution computed according to a smooth trend model; at least two consecutive days with $T^{(\max)} > 31^\circ C$.

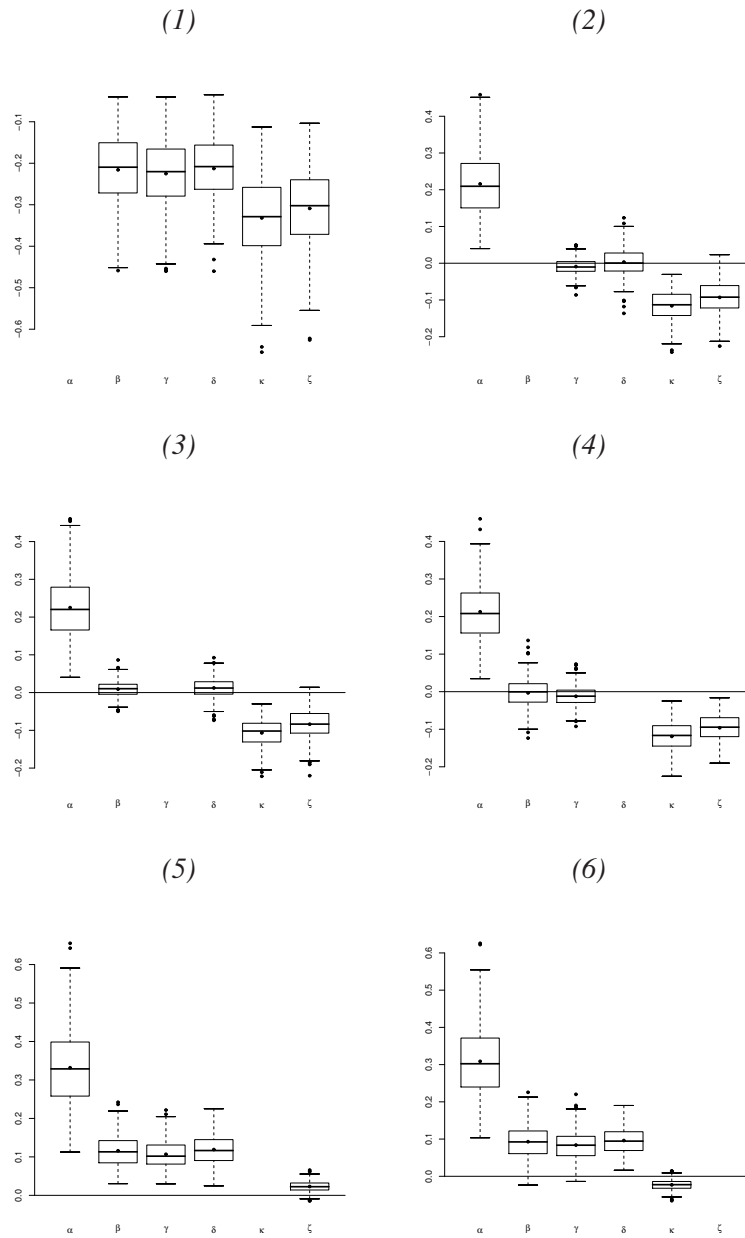


Figure 2: Boxplots of resampling distributions of $\Delta_{ij}^{*b} = \text{UBRE}_i^{*b} - \text{UBRE}_j^{*b}$, panel (j) depicts boxplots for Δ_{ij}^{*b} for each $i \neq j$.

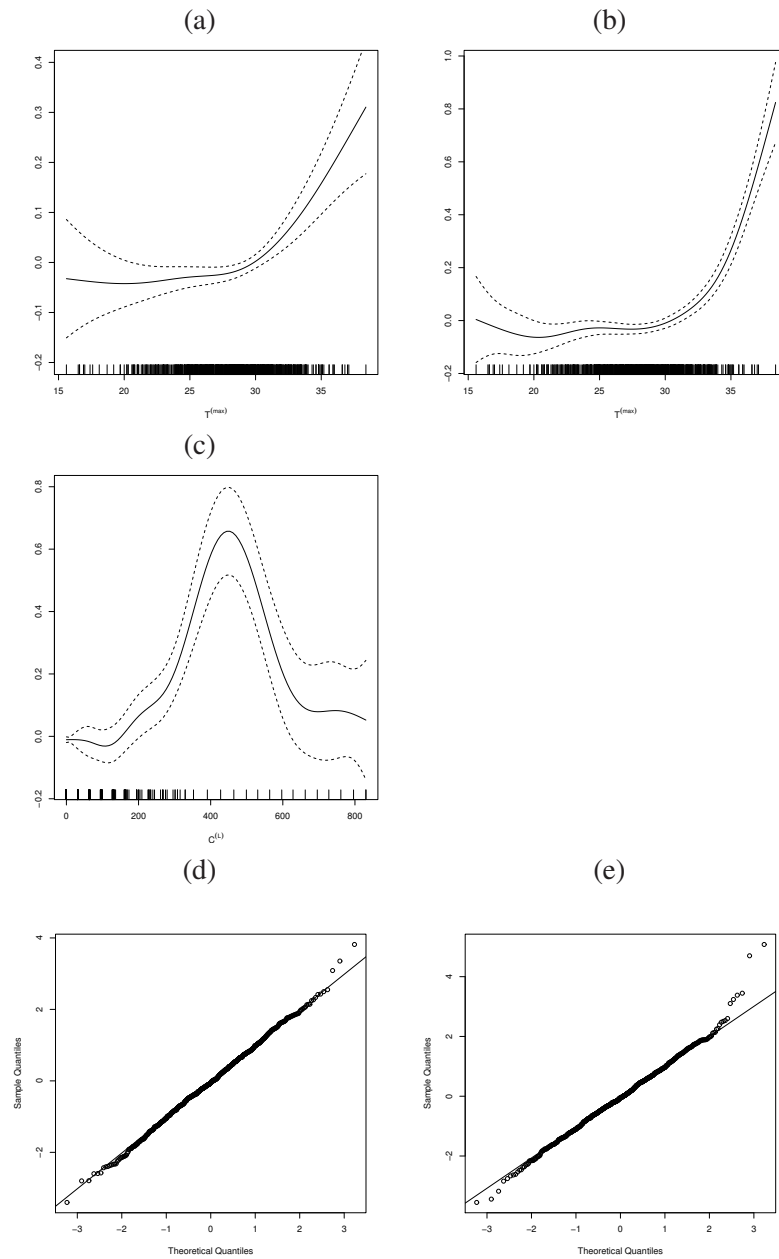


Figure 3: Comparison of model including $T^{(\max)}$ and $C^{(L)}$ (on the left) and model including $T^{(\max)}$ only (on the right). Top row is $f(T^{(\max)})$; middle row is $s(C^{(L)})$; bottom row is normal probability plot of deviance residuals.

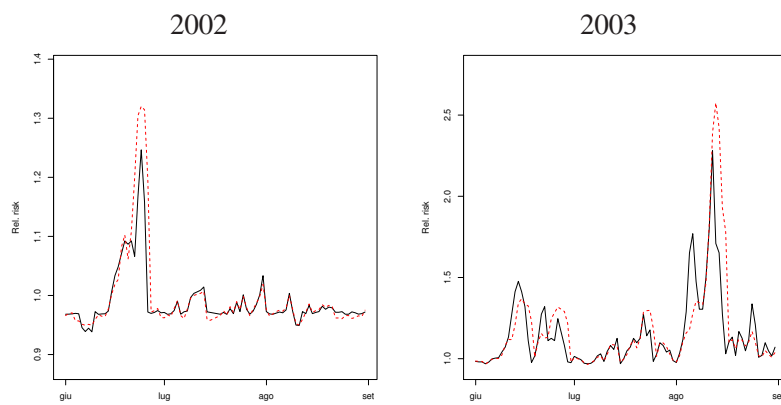


Figure 4: Comparison of relative risks estimated from model with $T^{(\max)}$ only (solid black line) and best model according to UBRE (dashed red line).

Acknowledgements

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