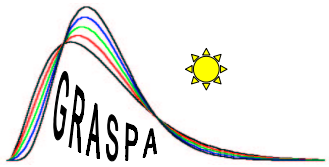

Gruppo di Ricerca per le Applicazioni
della Statistica ai Problemi Ambientali

Working Paper GRASPA n. 12

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Mortality, Temperature and Air Pollution in Palermo, Italy

Lavoro svolto nell'ambito del progetto di interesse nazionale MURST 2000
"Statistica nella valutazione del rischio ambientale"
(*grants* MM13208412_001)

Mortality, Temperature and Air Pollution in Palermo, Italy

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Abstract

The aim of this paper is to show how short-term effects of air pollution can depend on temperature in studying daily deaths in Palermo, Italy. The influence of both temperature and air pollution on mortality has been proved in several studies, but their synergic effect, although suggested by someone, has never been explicitly modelled. The results, concerning mortality for all natural causes and for cardiovascular diseases, suggest a greater effect of some pollutant in hotter days. Also a significant negative influence of sudden changes of temperature is found.

1 Introduction

The relationship between environmental temperature and mortality has been repeatedly studied: a V-like relation has been emphasized in several studies, death rates being lowest on days with 'optimal' average temperatures and becoming progressively higher when weather gets hotter or colder. The threshold value, where mortality reaches its minimum, is usually lower in colder areas than in warmer ones, ranging from 15° to 25° (Mackenbach *et al.*, 1993; Keatinge *et al.*, 2000)

Negative influence of the so-called 'heat-waves' on health has also been proved in different cities, in particular on deaths for respiratory and cardiovascular diseases (Katsouyanni *et al.*, 1988; Kilbourne, 1992; Ramlow and Kuller, 1990; Pan *et al.*, 1995). More recently not only extreme hot temperatures but also non-abnormal increments have been associated with mortality excesses (Saez *et al.*, 1995; Michelozzi *et al.*, 2000).

Low temperatures have also been related to greater deaths counts, but it has been argued that mortality is associated with cold weather because of increased confounding factors including increased incidence of influenza and other respiratory infections and 'season' (Kalkstein, 1993; Kalkstein and Davis, 1989). This latter is a generic not well-defined variable usually understood to be a conglomerate of factors, e.g. diet, psychosocial stress and seasonal variation (Kunst *et al.*, 1993) as mortality time series are always characterized by high values during winter. For instance, in some studies showing de-seasoned relationship between mortality and temperature, the cold-related effect almost disappears (Rossi *et al.*, 1995). Even in studying the interaction between outdoor temperature and sudden infant death syndrome, someone suggests that some cold-related death can be due to *overheating* that is greater when the outdoor temperature is lower (Stanton, 1984).

Short term effects of air pollution, usually assessed by concentration of SO_2, NO_2 O_3 and airborne particles (e.g., TSP, PM_{10}, PM_7) have been investigated in a large body of studies, both on mortality and morbidity (e.g. Zmirou *et al.*, 1998; Hoek *et al.*, 2000; Biggeri *et al.*, 2001; Schwartz, 2000a). Negative effects on the human health seem to exist with modest values,

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lower than those reported in the historical episodes occurred decades ago (Logan, 1953). Unlike temperature, the relationship between mortality and pollutant is not known and it is an issue under investigation, although a linear relationship has been suggested as plausible (Schwartz and Zanobetti, 2000).

Although almost all of the studies have demonstrated the effect of both temperature (at low but especially at high values) and pollutants (especially fine particles) on health, however a possible synergic effect on the mortality has never been investigated in detail. Kalkstein (1993) discusses the possibility of temperature-pollutant interaction and Katsouyanni *et al.* (1993) analyze mortality excesses in Greece during the heat wave in 1987 detecting noticeable differences among Athens, urban cities and rural areas. Also in Sartor *et al.* (1995), elevated outdoor temperatures combined with high concentrations of ozone have been assumed to be the main cause of the observed excess deaths during the heat-wave in August 1994. Finally the works from Zmirou *et al.* (1998) and Hoek *et al.* (2000) show results separately for the cold and warm season, the pollutant-related risks being greater in the latter season than in the former one.

In this paper we explicitly model interaction between air pollution and mortality both for all causes and for cardiovascular diseases by using classical standard Poisson semiparametric regression models.

2 Materials and Methods

Materials

This study analyzes time series from August 1 1996 to December 31 1999 for $T = 1248$ observations. Anonymous individual mortality records, including information on age, sex and ICD.IX code, have been obtained from the regional mortality register of the Sicily Region. A.M.I.A. (the local Agency for environmental management of the city of Palermo) supplied data on daily measurements of air-conditions: meteorological variables include relative humidity (%) and mean temperature (degree Celsius, $^{\circ}C$); air pollution data cover SO_2, NO_2, CO, PM_{10} and O_3.

The analyses reported here consider deaths for all natural causes (code ICD.IX: 1-799, daily mean 13.9) and for cardiovascular diseases (code ICD.IX: 390-459, daily mean=5.6); mortality for respiratory causes was also available but it has not been studied due to the presence of too many sampling zeroes and low counts (the mean was 0.9 and 75% of the days had counts equal to zero or one). Also, ozone and sulfur dioxide were dropped from analysis: SO_2 -pollution is characterized by low concentrations in Palermo because big industrial factories, principal source for SO_2, are absent. O_3 measurements are recorded daily at two stations that are not suitable to measure air pollution because of their location. Detailed descriptive statistics on environmental and epidemiological data used within paper are reported elsewhere (Muggeo, 2000; Biggeri *et al.*, 2001).

Metods

Semiparametric regression models with log link and identity variance function have been used for analysis. Long-term trend has been modelled by means of smoothing splines with degrees of freedom (*df*) selected by BIC (Bayesian Information Criterion). The BIC criterion has been chosen because it seems more appropriate to smooth observations with autocorrelated errors; *Akaike Information Criterion* and its asymptotically equivalent *Cross Validation* select too many *df* and cause negative residual autocorrelation (Stone, 1977; Hart, 1991; Baccini *et al.*, 2001). Temperature and humidity (this variable smoothed term with 3 *df*) has been evaluated as daily mean on 24 hours.

Daily exposure to pollutant at day t was measured by averaging daily means of previous days $t-1, t-2, \ldots$: Schwartz (2000a) discusses how this method allows to approximate the distributed lags models which are more appropriate to describe acute effects decreasing in time. Up three days (mean lag 0-3) have been selected because this term was always the most predictive, i.e. the

one associated with maximum likelihood (or minimum deviance). For instance, for mortality for all causes and PM_{10} the deviance for the models with pollutant assessed at lag 0-1, 0-2 e 0-3 was respectively 1431.7, 1423.2 e 1421.0 with the same df. Note that maximizing the likelihood (or minimizing the deviance) does not imply to maximize the pollutant effect, just to choose the most likely model.

Due to the V-shaped relationship with the response, temperature (TEMP) has been modelled by means of the two following variables: $\texttt{TEMP}_- = \theta - \texttt{TEMP}$ if $\texttt{TEMP} < \theta$ and 0 otherwise and $\texttt{TEMP}_+ = \texttt{TEMP} - \theta$ if $\texttt{TEMP} > \theta$ and 0 otherwise. So whether EXPL includes all the confounding variables (season, influenza epidemics, humidity, holidays, days of week) and POLL means any pollutant, the predictor of the model is:

$$\texttt{EXPL} + \texttt{TEMP}_- + \texttt{TEMP}_+ + \texttt{POLL} + \texttt{POLL}:\texttt{TEMP}_- + \texttt{POLL}:\texttt{TEMP}_+ \tag{1}$$

where : means the interaction (product) of variables.

θ, the 'optimal' value of temperature could be determined by looking at smoothed scatter plot (e.g. Mackenbach *et al.*, 1993), but a likelihood-based approach has been preferred (Halperin, 1963). The log-likelihood for this model may be expressed as $\ell(\boldsymbol{\beta}, \theta)$, with θ a non-linear parameter and $\boldsymbol{\beta}$ the coefficients of the classical explanatory variables in the core model. Given θ the estimate of parameters is $\tilde{\boldsymbol{\beta}}(\theta)$, and the (profile) log-likelihood depending just on θ is $\ell(\tilde{\boldsymbol{\beta}}(\theta), \theta) = \ell(\theta)$. So maximizing $\ell(\theta)$ over the range of temperatures yields $\hat{\theta} = \arg\max \ell(\theta)$. Assuming $\theta = \hat{\theta}$ the log-likelihood of the full model depends just on the linear parameters $\boldsymbol{\beta}$ and so classical GAMs may be fitted. Only to estimate $\tilde{\boldsymbol{\beta}}(\theta)$ and then θ, the core model (1) without $\texttt{POLL} + \texttt{POLL} : \texttt{TEMP}_- + \texttt{POLL}:\texttt{TEMP}_+$ has been used, and the nonparametric smoothing splines have been replaced with (parametric) basis splines to get treatable model-matrix required to compute $\ell(\theta)$.

To test the effect of sudden change of temperature, the variable CHANGE has been added in the model (1); at day t this variable is measured as the range of 24 hourly measurements for TEMP in the previous day $t-1$. Finally, residuals from the fitted model have been used to test the residual (partial) autocorrelation and some lack of fit in the model. Including interaction terms between temperature and pollutant according to the (1), implies to model the (log) relative risk of any pollutant (hereafter RR) as linear function of temperature, i.e.

$$\log \mathrm{RR}_{\texttt{POLL}}(\texttt{TEMP}) = \beta + \gamma \times \texttt{TEMP}_- + \delta \times \texttt{TEMP}_+ \tag{2}$$

instead of assuming it constant during the year, i.e. $\log \mathrm{RR} = \beta$. γ and δ are the parameters modelling the interaction of the pollutant with low ($\texttt{TEMP} < \theta$) and high ($\texttt{TEMP} > \theta$) temperatures respectively. β in the formula (2) measures the effect at the 'minimum mortality temperature', i.e. when $\texttt{TEMP} = \theta$. Of course the variance also depends on temperature:

$$\begin{aligned} v(\log \widehat{\mathrm{RR}}_{\texttt{POLL}}(\texttt{TEMP})) \quad = \quad & v(\hat{\beta}) + v(\hat{\gamma}) \times \texttt{TEMP}_-^2 + 2 \times cov(\hat{\beta}, \hat{\gamma}) \times \texttt{TEMP}_- \\ & + v(\hat{\delta}) \times \texttt{TEMP}_+^2 + 2 \times cov(\hat{\beta}, \hat{\delta}) \times \texttt{TEMP}_+ \end{aligned} \tag{3}$$

An interesting question in studying temperature-pollutant effects on health, is whether only extreme values, i.e. heat-waves or unusual picks of air pollution, are associated with increases of mortality: this can be achieved by measuring the influence of each day on the estimates. The $\Delta\beta$ statistics measures the impact of each observation t on the parameter estimates and so it can be used to assess the influence of 'unusual days' on the parameters of interest, i.e. γ and in particular δ in the (2). The influence of the t^{th} observation on the generic estimate $\hat{\beta}_j$ is the difference between $\hat{\beta}_j$ and the estimate in the data-set without the t^{th} observation, $\hat{\beta}_{j(t)}$,

$$\hat{\beta}_j - \hat{\beta}_{j(t)} \approx \Delta_t \hat{\beta}_j = \frac{\widehat{\boldsymbol{V}(\boldsymbol{\beta})}_j \, x_{tj}(y_t - \hat{y}_t)}{(1 - h_{tt})} \tag{4}$$

where $\boldsymbol{V}(\boldsymbol{\beta})_j$ is the j^{th} row of the covariance matrix of estimates and h_{tt} is the t^{th} element on the main diagonal of the hat-matrix. By dividing $\Delta_t \beta_j$ by the standard error $se(\hat{\beta}_j)$, the resulting

standardized delta beta measures the impact on the Wald value ($w_j = \hat{\beta}_j / se(\hat{\beta}_j)$) and so this value may be assumed as a 'lack-of-significance' statistic.

The larger this diagnostic measure, the greater the influence of day t on $\hat{\beta}_j$. The $\Delta\beta$ statistic has been used to assess the sensitivity of the estimates for the parameters in (2) with respect to abnormal days.

3 Results

The break-point for the V-shaped relationship between mortality and temperature has been estimated separately for the two different responses variables (plots not shown); it is higher for total mortality ($\hat{\theta}_{tot} = 23.5°C$) and lower for deaths for cardiovascular diseases ($\hat{\theta}_{card} = 18.6°C$). For total mortality this threshold value is higher than the one reported in Netherlands (Kalkstein and Davis, 1989) and in England and lower with respect to Athens (Keatinge *et al.*, 2000); however the estimation method is quite different because we applied a likelihood based approach instead of simple inspection of scatter-plots. Visual inspection of plots (not shown) proved that profile log-likelihood $\ell(\theta)$ was not strictly concave but there was just one global maximum.

Parametric linear modelling for the temperature does not change substantially neither the deviance nor the pollutants effect estimates: for instance in the total mortality model the estimated percentage increases of RR for CO ($\times$10mg/m^3), NO_2 ($\times 10\mu$g/m^3) and PM_{10} ($\times 10\mu$g/m^3) are 3.09, 1.98 and 3.34 versus the same estimates in the model with smoothed temperature equal to 3.15, 2.21 and 3.52 respectively.

Interactions between temperature and different pollutants (CO, NO_2 and PM_{10}), have been included in the model according to (2). One model for each pollutant has been estimated to avoid collinearity problems in the linear predictor.

Table 1 shows the parameter estimates just for the main effect of each pollutant and its interactive effects with temperature, i.e. $(\hat{\beta}, \hat{\gamma}, \hat{\delta})$ together with their Wald statistics (absolute value). Usually if $w > 1.96$ the parameter is considered significant at 95%.

Table 1: Beta coefficients ($|w|$, Wald statistics value) for the temperature-pollutant interaction on mortality for natural causes (code 1-799) and cardiovascular diseases (code 390-459). Estimates from the full interaction or according to the parsimonious model (by dropping non-significant terms) are shown.

	Pollutants					
Parameters	CO(mg/m^3)		NO_2($\times 10\mu$g/m^3)		PM_{10}($\times 10\mu$g/m^3)	
	full	reduced	full	reduced	full	reduced
All Causes (1-799)						
POLL	.0374(2.6)	.0304(4.5)	.0127(1.0)	.0146(2.1)	.0329(3.2)	.0244(4.0)
POLL : TEMP$_-$	-.0010(0.6)	–	.0003(0.2)	–	-.0013(1.0)	–
POLL : TEMP$_+$	.0055(0.6)	–	.0065(1.8)	.0062(2.0)	.0119(3.3)	.0133(4.1)
Card.Dis.(390-459)						
POLL	.0421(2.0)	.0507(4.8)	.0024(0.1)	.0246(2.0)	.0179(1.1)	.0328(3.1)
POLL : TEMP$_-$	.0013(0.3)	–	.0049(1.3)	–	.0038(1.2)	–
POLL : TEMP$_+$	.0043(0.7)	–	.0078(2.3)	.0053(2.1)	.0081(2.7)	.0062(2.5)

For each pollutant and response variable two models have been estimated: the full one where all interaction terms (two parameters γ and δ according to formula (2)) are included, and the reduced one where the non significant coefficients have been dropped.

The results are very clear for CO and PM_{10}: no interactive effect exists between temperature and CO, neither on total mortality nor on mortality for cardiovascular diseases; the risk is therefore constant during the year. For PM_{10} there is evidence of synergic effect during the hot days with mean temperature greater then $23.5°C$ in both models for mortality (all causes and cardiovascular diseases). This is proved by a significant δ coefficient both in the full interaction model ($w_\delta = 3.3$)

and in the reduced one ($w_\delta = 4.1$). The results are similar on the cardiovascular causes related mortality although the coefficients are smaller.

The findings concerning NO_2 are somehow doubtful. As for total mortality, the Wald value of the δ coefficient is near its limit of significance, in both models (full and reduced), but on cardiovascular disease deaths, interaction with temperature seems confirmed.

Table 2: Estimated percentage changes in RR[95% CI] from $10\mu g/m^3$ PM_{10} and NO_2 exposure for different temperatures: mortality for all natural causes and for cardiovascular diseases according to the 'full-interaction' models.

	All Causes (1-799)		*Card.Dis.(390-459)*	
Temperature	$NO_2(\times 10\mu g/m^3)$	$PM_{10}(\times 10\mu g/m^3)$	$NO_2(\times 10\mu g/m^3)$	$PM_{10}(\times 10\mu g/m^3)$
$12(^\circ C)$	1.57[0.06, 3.12]	1.82[0.41, 3.25]	3.53[1.13, 6.00]	4.38[2.12, 6.69]
$17(^\circ C)$	1.48[0.29, 2.62]	2.48[1.46, 3.51]	1.03[-1.7, 3.87]	2.48[0.19, 4.71]
$18(^\circ C)$	1.42[0.20, 2.65]	2.61[1.56, 3.68]	0.54[-2.7, 3.85]	2.04[-0.5, 4.69]
$25(^\circ C)$	2.27[0.00, 4.59]	5.20[3.21, 7.23]	5.36[0.22, 10.7]	7.20[2.79, 11.8]
$30(^\circ C)$	5.63[1.02, 10.4]	11.6[7.01, 16.4]	9.53[1.92, 17.7]	11.6[4.85, 18.8]

In modelling interaction terms, the relevant relative risks and their variances depend on temperature (see formulas (2) and (3)): Table 2 presents the estimated percentage change in RR, i.e. $\Delta\widehat{RR} = (e^\beta - 1) \times 100$ with respect to the four seasonal mean temperatures and an arbitrary value of $30^\circ C$ and Figure 1 shows graphically these results.

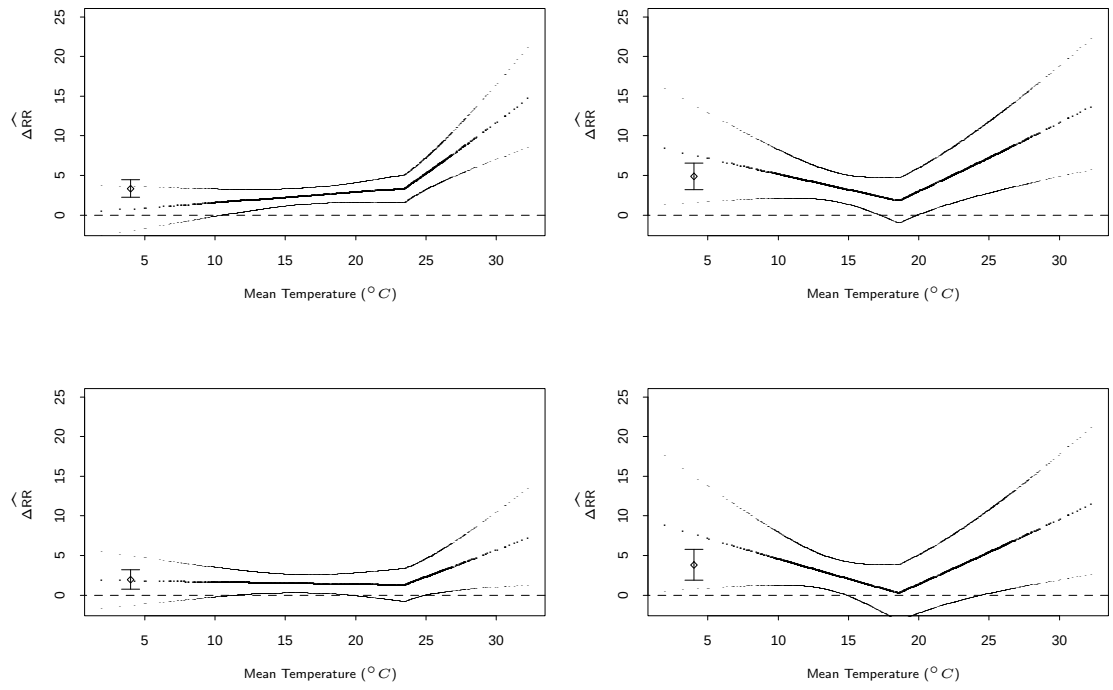

Figure 1: Estimated percentage changes (95%CI bands) in RR from $10\mu g/m^3$ exposure of PM_{10} (top) and NO_2 (bottom) as function of temperature ('full-interaction' models): mortality for all natural causes (left side) and for cardiovascular diseases (right side). On each plot the bar shows the estimated RR from 'only-main-effect' models.

As estimates from Table 1 suggest, the increases in RR are much more evident during hot days than during cold ones; instead, only in mortality from cardiovascular causes there is some evidence of cold related pollutant effects (see right side in Figure 1).

Independently of the V-shaped relation between temperature and mortality also confirmed and its interaction with the pollutants, an effect of sudden changes of temperature has been found significant in all the models. This variable has been fitted in the model as logarithmic transformation of the difference between maximum and minimum of the daily temperature (i.e., the range) in previous day: the relevant estimated change in the relative risk is approximatively equal to 1%. Standard deviation of the 24 measurements of previous day was also tested as an alternative to the range, but although it was also significant, the latter provided a better fit.

Sensitivity Analysis

The first problem is to check the linearity of the interaction terms between each pollutant and the two variables $\texttt{TEMP}_-$ and $\texttt{TEMP}_+$. Although Figure 2 shows the smoothing estimate only for the interaction temperature-PM_{10} in all-causes mortality, also in models for mortality from cardiovascular diseases and NO_2, no systematic departure from linearity has been revealed. This allows us to put major reliance in the model (2).

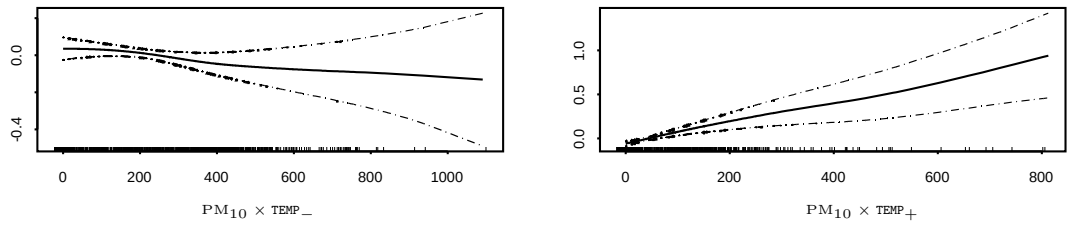

Figure 2: Smoothing estimated relationships between the mortality and interactions temperature-PM_{10}: cold temperatures (left) and hot temperatures (right).

In order to evaluate the impact of extreme values of the temperature and pollutant on the estimates of the interaction coefficients, the delta-beta statistics have been calculated for the $\hat{\delta}$ parameters for PM_{10} and NO_2 respectively on both the response variables. In the Figure 3 this diagnostic measurements for the interaction PM_{10}-$\texttt{TEMP}_+$ in all-causes mortality model has been jointly plotted versus the temperature and PM_{10}: the aim is to assess how high values in temperature and pollutant may influence the estimate.

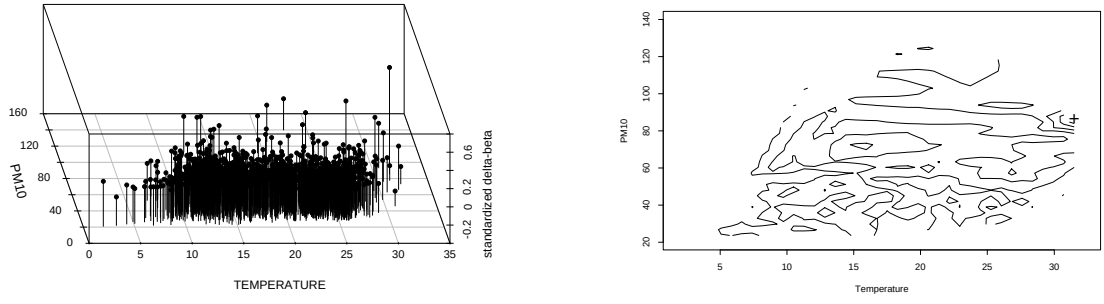

Figure 3: Standardized delta-beta for the δ coefficient modelling the interaction of the PM_{10} with hot days in the full-interaction model: 3D plot (left side) and contour plot (right side) with the highest delta-beta signed by "+"

It is evident no particular pattern may be observed among the delta-beta (in particular, see

the level-curves in the contour plot), as there is just one observation with big influential value on the estimate $\hat{\delta}$, all others being with negligible values. This observation (with standardized delta-beta 0.77) corresponds to a day with rather high values both in temperature ($31.5°C$) and in PM_{10} ($85.4\mu g/m^3$). However also removing this day, the interaction term remains significant: in particular the Wald value decreases to 2.53. Approximatively the same pattern has been found in the various delta-beta statistics for the models of interest: even if the day with high values of temperature and pollutant has a big effect in the estimates the interaction parameter, however this observation does not modify the findings. As also appears in Table 1, only for NO_2 in the all-causes mortality model the interaction is some doubtful: by dropping the influential day, $\hat{\delta}$ becomes non-significant.

Finally sensitivity of the model was also tested with respect to degrees of freedom for seasonality. By modelling the long-term trend with large *df* (40, as selected by the AIC), no substantial difference has been appreciated in the analysis of the interaction.

4 Discussion

Short term effects of both air pollution and ambient temperature have been established by several studies in different areas, being the risk in days with high values of both air pollution and temperature equal to sum of the two independent effects. In this paper we have emphasized that their possible synergic effect is likely with respect to NO_2 and PM_{10} in particular: this implies that the risk during hot days with high levels of air pollution is greater than the sum of two separated risks. Figure 4 summarizes the difference between additive and synergic effect of temperature and PM_{10} on total mortality; non parametric estimate is also showed checking similarity with interaction model instead of the main-effects one.

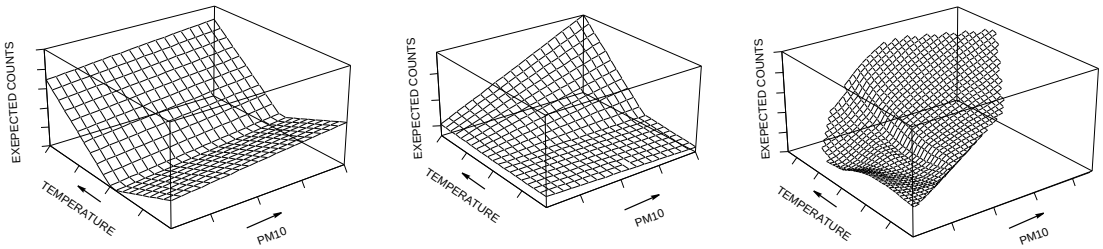

Figure 4: Total mortality as function of the temperature and pollutant. Left side: expected values from additive effect (just main effect model); Middle side: expected values from synergic effect (interaction terms according to formula (2)); Right side: bivariate smoothing estimate.

Moderate air temperature is very comfortable for man (Erikson *et al.*, 1956), and exposure to higher or lower temperatures can cause stress on the circulatory and other body system as has been supported by the results in thermophysiologic experiments. However, although some author confirmed cold-related mortality, someone reported that season reduces the cold effect (Bowie and Prothero, 1981; Marshall *et al.*, 1988). But the hot effect is well understood instead: hot reduces thermoregulatory capacity to maintain normal body temperature determining a greater probability of hyperthermia (Pan *et al.*, 1995).

Our findings highlight that possible synergic effects between temperature and air pollution concern just the hot days; cold-related effect of air pollution has never marked in our results. Mechanisms by which humans adapt to excessive temperatures include increase in respiratory rates (Isselbacher *et al.*, 1980) and so this can increase the exposure to air pollution; also mortality increases on hot days might result in part from increased photochemical smog (Shumway *et al.*, 1988; Kunst *et al.*, 1993). These effects could increase the influence of air pollution just during the hot days and not the cold ones.

Comparing results from all-causes and cardiovascular-diseases mortality, the interaction with hot was evident just for PM_{10}, while the NO_2 effect being dependent on just one influential observation. The PM_{10}-hot temperature effect is more accentuate in total mortality instead of cardiovascular disease one; this would mean that heat-related mortality is largely attributable to the direct effects of exposure of the human body to hot instead of cardiovascular stress. In fact findings from Kunst *et al.* (1993) suggest heat-induced cardiovascular stress is very modest.

Still unlike all-causes mortality, on cardiovascular-diseases deaths there is also some evidence of cold-pollutant interaction (see Figure 1, right side), although the relevant parameters are statistically not significant. Results by thermophysiologic experiments hint that exposure to cold results in increases in blood pressure, blood viscosity and heart rate (Keatinge *et al.*, 1986; Clark and Edholm, 1985). Then, the high values of these factors suggest that cold-induced cardiovascular stress is quite prevalent during the winter (Stout and Crawford, 1991; Marshall *et al.*, 1988): this would agree with the findings of this study where the pollutant-cold interaction was associated to increases of risk just for cardiovascular disease deaths. However speculation on this aspect needs much more evidence.

Other weather conditions have not been found interacting with mortality-temperature-air pollution: in particular humidity, that should reduce evaporation of sweat and impairs body coding (Clark and Edholm, 1985).

As shown in other studies (Saez *et al.*, 1995; Michelozzi *et al.*, 2000) and stressed here by means of delta-beta statistics, not only heat-waves but also non-abnormal increments of temperature are associated with death risk excess. Days with mean temperature greater than $23.5°C$ (the optimal temperature value) are quite frequent in the year (almost 25% in Palermo) and in particular during summer (more than 75%). Assuming a smaller temperature tolerability for cardiovascular diseases deaths, as noticed in this study, the findings would be worse.

Harvesting effect, even if present, has been shown to be 'non-absorbing' both in the temperature effects (Kalkstein, 1993), and in the pollutant ones (Zeger *et al.*, 1999; Schwartz, 2000b, 2001); so it should be negligible also with respect to their interaction, although further investigations are needed.

Other results detected in this study, and of course needed of substantial extra evidence, include the different threshold values for all causes and cardiovascular diseases deaths and effects of the sudden changes of temperature; also it is perhaps worth noting that the hot-related effects do not concern CO at all. In particular, provided the existence of hot-related effect, the possible influence of sudden changes becomes quite crucial, because the greenhouse effect is expected to lead (and probably it is already leading) to increases both in mean values of temperature and in its variability.

It worth noting that an alternative approach to assess the joint effect of temperature and pollutant (and also every meteorological condition) on mortality was performed by Kalkstein (1991) which used principal component analysis to classify days into categories. This synoptic effect is motivated by the fact that weather conditions are never independent and so analyzing independent variables (like temperature, air pollution, humidity and so on) it is not very realistic. However if interest is in estimating the direct effects on health of some specific risk factor, such as temperature and air pollution, using single variables could be more proper. By the way, whichever the approach, the interaction temperature-air pollution seems an useful and also indispensable topic to be investigated, because the intensity of such factors is increasing in the city. What might be the joint effect of increasing temperature and even stationary levels of air pollution in large city where the car-related pollution is quite oppressive?

However speculation about these possible new findings might be meaningful only when the same results would appear in other studies. To date, threshold value has never been estimated by statistical procedure and even no difference between disease-group death has never been investigated. Any more no systematic model-based approach has been carried out to study interactions among health, weather and air pollution.

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