THE ROLE OF AIR POLLUTION AS A POTENTIAL CONFOUNDER OF THE ASSOCIATION BETWEEN TEMPERATURE AND MORTALITY IN CYPRUS

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Abstract

Purpose: This study is the first to examine the effect of extreme weather on mortality in Cyprus. It aims to investigate the individual effect of meteorological indicators on mortality, as well as the role of air pollution as a potential confounder of heat related health effects.

Methods: The analysis concentrated on the warm periods (April to September) of the years 2007-2009. A Generalized Linear Model (GLM) with quasi-Poisson regression included a temperature function and was adjusted for relative humidity and seasonality. The temperature function was developed under a newly-developed framework of Distributed Lag Non-Linear Models, to capture non-linearities and lag effects simultaneously. The GLM was extended to examine the confounding effect of air pollution.

Results: High temperatures had a significant effect on mortality, independent of humidity and seasonality. Mortality risk increased steeply above a temperature threshold at 33.7ºC. A direct heat effect was shown, with high risk on the current and next two days of a severe heat event. PM_{10} was not found to be significant: the strength of the temperature-mortality relation remained after the inclusion of air pollution in the model.

Conclusions: The study indicated that high temperatures result in increased mortality rates in Cyprus, independent of humidity and seasonality, whereas air pollution does not have a confounding effect on the mortality-temperature relation.

Keywords

Extreme weather, heat effect, temperature, particulate matter, Cyprus.

1. Introduction

The interest in the impact of extreme weather on human health has been growing. Climatic change, characterized by larger temperature fluctuations, results in increased occurrence of heat waves and the thermal stress caused by such phenomena is expected to lead to higher levels of heat-related mortality worldwide [1-2]. Related literature has shown that heat waves are associated with increased mortality, not only for heat-related conditions such as heat stroke. Despite the variation observed amongst different diseases, there is a consistent evidence of association between high temperatures and all-cause mortality, as well as with mortality due to cardiovascular, cerebrovascular and respiratory causes [3-9].

Several studies have additionally shown that air pollutants can be confounders of the association between temperature and mortality, and have quantified the confounding effect, which has been shown to differ between locations [10-12]. On the other hand, some of the studies that have examined the role of air pollutants have shown that they have no effect on the mortality-temperature relation [13-14]. Due to the conflicting results, additional studies to examine confounding of air pollution on the relation between temperature and mortality are warranted.

The combined effects of meteorology and air pollution on public health have never been explored in detail for Cyprus. The current study is the first to examine the effect of extreme weather on mortality in Cyprus. More specifically, the present study investigates the role of air pollution as a potential confounder of the association between meteorological indicators and mortality and, especially, of the heat related health effects.

1.1. The study area

The island of Cyprus is situated in the Eastern part of the Mediterranean Sea, 33°E and 35°N of the Equator, with an area of 9,251 km^2. It has a typical Mediterranean climate characterized by hot dry summers from June to September and rainy changeable winters from November to March, separated by short autumn and spring seasons of rapid change in October, April and May. The average temperature in the warmer months (July and August) is around 36 degrees Celsius (°C). The predominantly clear skies and high sunshine amounts give large seasonal and daily differences between temperatures of the sea and the interior of the island, which also cause considerable local effects, especially near the coast [15].

Specifically, during summertime, the island is mainly under the influence of a shallow trough of low pressure extending from the great continental depression centered over Southwest Asia. This results in high temperatures with almost cloudless skies. Rainfall is almost negligible during this time of the year. However, isolated thunderstorms may sometimes occur, contributing to less than 5% of the total annual rainfall [15]. It has been well documented that the depressions affecting the area of Cyprus are associated with different types of weather. Climatological studies have shown that showery weather is associated mainly with depressions coming from the west, i.e. the main body of the Mediterranean Sea, whereas cold and mainly dry weather is predominant with depressions coming from the north [16-18]. Weather connected with dust events is largely associated with depressions affecting the area from the east and south, commonly referred to as “Saharan Events”, which are associated with extreme concentrations of dust in the atmosphere, resulting in low visibility and poor air quality, and are responsible for increased levels of particulate matter (PM) in the atmosphere [19-20].

Therefore, in the Mediterranean environment of Cyprus, the extremely high levels of temperature during summertime together with the so-called "Saharan Events" are expected to be associated with increased mortality.

1.2. Theoretical background

The effect of increased temperatures on mortality has been consistently shown to be non-linear, following a U-, V-, J-, or inverse J-shaped curve, where minimum mortality is found within a certain temperature or temperature range, at moderate temperatures, and an increase in mortality below and above the threshold, with higher mortality at temperature extremes. The aforementioned shapes of the relation between mortality and weather indicators have been identified in many different areas around the world, including Europe, the United States and China [4, 6, 10; 21-24].

In addition, many studies have shown evidence of the so-called "delayed effect". They have indicated that temperature can affect not only deaths occurring on the same day, but on several subsequent days, where the converse is also true: deaths on each day depend on the effect of the same day's temperature as well as the lag effects of the previous days' temperatures [21, 25- 26].

The relationship between temperature and mortality may be confounded by measured or unmeasured confounders. Confounding factors are present when a covariate is associated with both the outcome and exposure of interest, but is not a result of the exposure. A basic issue in modelling is to control properly for all the potential confounders [27]. Such confounders have been shown to be certain meteorological indicators, like relative humidity, as well as seasonality and long-term trends [6, 21, 22, 24].

Particulate matter (PM_{10}) has been associated with daily mortality in many studies [28-30] and several studies have, thus, used PM_{10} as a possible confounder in the mortality-temperature relation [3, 12, 31-33].

2. Methods

2.1. Data collection

Daily mortality data were provided by the Ministry of Health of the Republic of Cyprus, for each of the five districts in Cyprus (Nicosia, Limassol, Larnaca, Paphos, Ammochostos) for the period between the years 2004 and 2009. They involve deaths of people that lived permanently in the free areas of Cyprus. The data include all-cause mortality excluding external causes, as classified in the European shortlist of causes of death (Eurostat Shortlist-65 causes of death).

Daily meteorological data were collected by the Cyprus Meteorological Service in the five main urban centers of the island, for the time period between 2004-2010. The meteorological parameters that were used for the purpose of this study include daily values of surface maximum temperature (in °C) and mean values of relative humidity at 8:00 LST and 13:00 LST (in %).

The air pollutant that has been chosen to be included in our model is the concentration of particulate matter, with an aerodynamic diameter of less than 10 μm (PM_{10}). Daily data for particulate matter were obtained from the Department of Labour Inspection of the Ministry of Labour and Social Insurance. More specifically, the daily averages of suspended particulate matter (PM_{10} in (μg/m^3) were taken from the records of five stations (Agia Marina Xyliatou, Nicosia, Larnaca, Limassol and Paphos), using gravimetric monitoring techniques, for the years 2007-2010. The average of the five stations was used as a measure for daily PM_{10} of Cyprus. Where missing data existed in any of the five stations, the average was calculated as the average of the data of the remaining stations.

The final period for our analysis, for which daily temperature, mortality and air pollution data were available, was the years 2007-2009. The analysis concentrated on the warm periods (April to September) of each year, to examine heat effects. Cyprus was considered as a total area, using the combined data from all the stations, but separate analyses were also performed for Nicosia (urban area) and Limassol (coastal area).

2.2. Statistical modeling

A Generalized Linear Model (GLM) was implemented, with quasi-Poisson regression to allow for overdispersion. Models under the general GLM modeling framework have been widely applied in epidemiological studies of the impact of meteorology or air pollution on human health [3, 6, 24, 29].

A temperature function was first entered in GLM. The function was developed based on the recent methodology of Distributed Lag Non-Linear Models (DLNM), which had the advantage of capturing simultaneously any non-linearities and lag effects of the temperature-mortality relation [15, 18, 34]. More specifically, a V-shaped temperature function, with a hot threshold and constraints along the strata of lags 0-1, 2-5 and 6-10, fit the data. The GLM was also adjusted for relative humidity, long- and short-term seasonality.

Finally the GLM was extended to examine the confounding effect of air pollution on this relation. Air pollutants, such as PM_{10}, have been shown to have a monotonic, linear exposure-response relationship and their linear effect has been examined in previous studies [5, 31-32, 35]. Therefore, a linear term for air pollution was added in the model. In addition, the average of the current and the previous day (lags 0 and 1), was calculated and included in the model, similar to previous studies [3, 5, 31-32]. Sensitivity analysis was performed with the inclusion of interaction terms in the model, to examine the potential synergy between temperature and air pollution.

3. Results

The total area of Cyprus was examined first. The V-shaped temperature-mortality relation had a high temperature threshold at 33.7°C, above which mortality risk increased steeply. The results showed that high temperatures had a significant effect on mortality in Cyprus (p-value<0.001 and p-value=0.018 respectively for the first two components of the lag-stratified temperature function), independent of humidity and seasonality. The air pollution term for PM_{10} was not found to be significant (p-value=0.5526) in the GLM model, and the significance of the effect of temperature on mortality remained after the inclusion of air pollution in the model. Additional results that included interaction terms for the quantification of the potential synergy between temperature and air pollution similarly showed that these were not statistically significant.

Table 1 shows the relative risk increment per degree of heat sustained over each lag interval and per day (effect of lags in the same strata interval is equal), both for the unadjusted model and for the model adjusted for air pollution, for the years 2007-2009.

Table 1: Summary results for Relative Risk (RR) increment- Cyprus, 2007-2009

(Threshold temperature: 33.7°C).

Lags	Adjusted Model[1] RR (per day) (95% CI)	Adjusted Model[1] RR (per lag interval)	Unadjusted Model[2] RR (per day) (95% CI)	Unadjusted Model[2] RR (per lag interval)
0-1	3.948% (2.083 to 5.848%)	7.897%	3.872% (2.026 to 5.752%)	7.745%
2-5	1.256% (0.221 to 2.302%)	5.025%	1.229% (0.200 to 2.269%)	4.917%
6-10	0.628% (-0.207 to 1.471%)	3.142%	0.623% (0.212 to 1.465%)	3.115%
Total 0-10	**17.199% (10.842, 23.921%)**		**16.872 % (10.621, 23.476%)**	

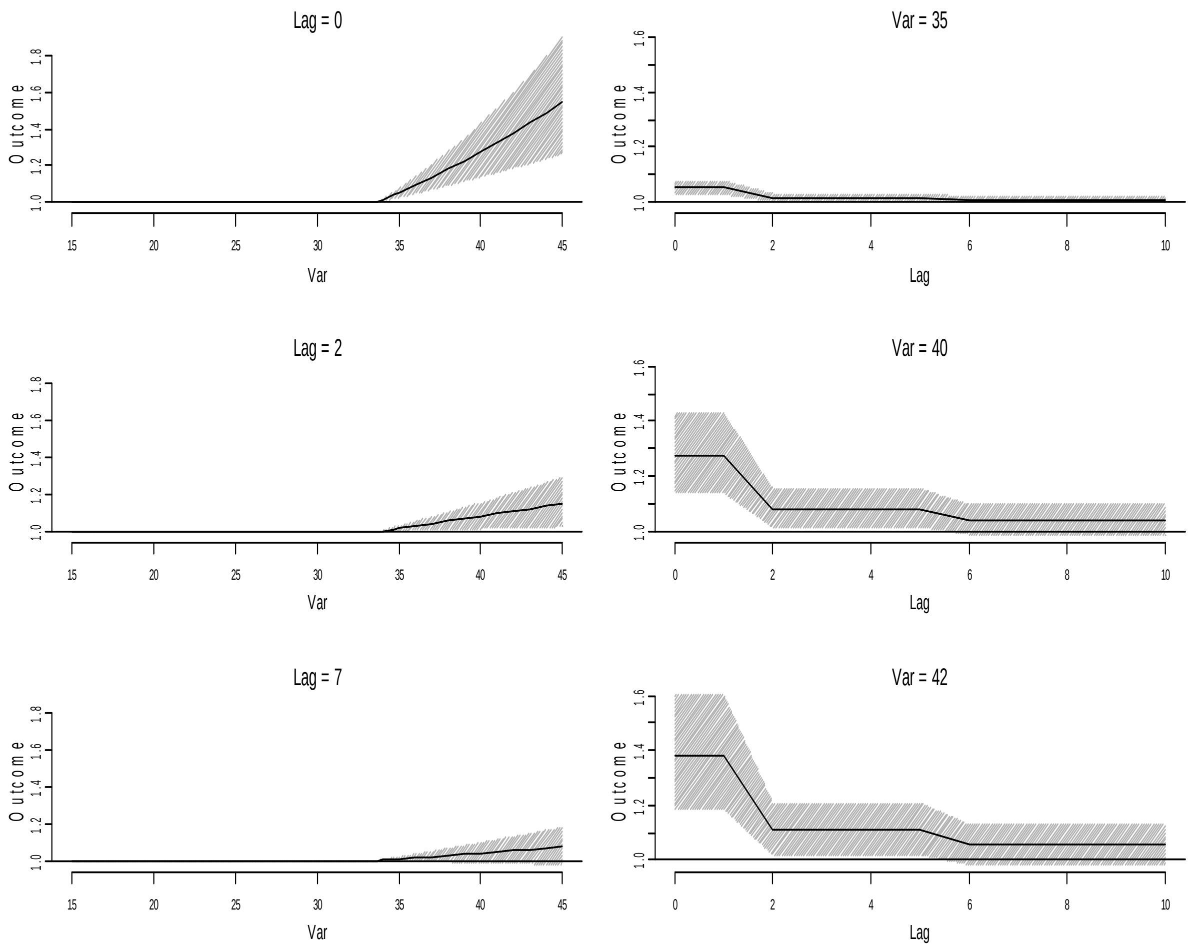
[1] With air pollution; [2]without air pollution

The table additionally shows the estimated overall effect of maximum temperature on all-cause mortality for a 1⁰C increase in temperature above the threshold (i.e. from 33.7⁰C to 34.7⁰C), along all 10 lags. The overall effect is computed by summing the log relative risks of each lag.

Looking at Table 1, we see that the effect of heat is much more pronounced for lags 0-1. For example, the effect in lags 0-1 for the adjusted model that includes air pollution is 7.9%, which shows that a 1⁰C increase in maximum temperature above the threshold of 33.7⁰C was associated with an estimated 7.9% increase in all-cause mortality in Cyprus, around 2.5 times higher than the effect of the next days (lags 6-10). Similarly, the effect for each of lags 0 or 1 was around 4%, more than 4 times higher than the effect of the next few days (e.g., each of lags 6-10). The effect is slightly higher than the corresponding effect of the unadjusted model for the same period. Comparing the adjusted and unadjusted model effects, we can see that air pollution was not a confounder in the models.

Figure 1 shows the risk of mortality for different lags (0, 2 and 7) and different temperatures (35⁰C, 40⁰C, 42⁰C), when we adjust for air pollution (PM_{10}).

Figure 1: Relative risk for different lags (0. 2 and 7) and temperatures (35⁰C, 40⁰C and 42⁰C), when we adjust for air pollution- Cyprus, 2007-2009 (Threshold temperature: 33.7⁰C).



First, the non-linear V-shaped relation between temperature and mortality is depicted in the three graphs for lags 0, 2 and 7 (graphs on the left). These three graphs show the increase in effect for higher temperatures, which is much more pronounced for lag 0, the same day (upper left graph). The three graphs for temperatures 35⁰C, 40⁰C and 42⁰C (graphs on the right) show that the effect of heat is much more pronounced for higher temperatures (e.g. 42⁰C), where the risk is much higher in the first couple of days compared to longer lags, and this is more obvious for higher temperatures, with a more sharp drop from lag 1 to lag 2. Overall, Figure 1 shows that high temperatures (i.e. temperatures above the threshold of 33.7^{0}C) have a much stronger effect at lag 0, compared to lags 2 or 7, and this effect is much stronger at higher temperatures; for example it is 40% higher at 42^{0}C, compared to 35^{0}C. At 35^{0}C the risk is negligible more than two days after the event (lags higher than 2). The mortality effect at 35^{0}C has a smoother shape, compared to the sudden drop for a temperature above 40^{0}C, at 42^{0}C, for longer lags.

In addition to the total area of Cyprus, Nicosia (urban area) and Limassol (coastal area) were also examined separately, for comparative purposes. Similar results were obtained in terms of the role of air pollution as a potential confounder on the association between temperature and mortality: the term for PM_{10} was not found to be significant (p-value=0.511 for Nicosia and p-value=0.417 for Limassol), whereas the significance of the effect of temperature on mortality remained after the inclusion of air pollution in the model, without any significant changes in relative risk between the adjusted and unadjusted models. The effect of heat on mortality was found to be lower for Nicosia, compared to Limassol or the total area of Cyprus. For example, the relative risk for lags 0 and 1 was 0.682% (95% confidence interval (CI): -0.949% to 2.340%) for Nicosia, while for Limassol it was 21.369% for the same lags (95% CI: 5.680% to 39.385%). The overall effect for lags 0-10 was found to be 5.469% (95% CI: 0.7177%, 10.4445%) for Nicosia, compared to 58.4757 % (95% CI: -18.6851%, 208.8554%) for Limassol. An interesting finding was that the relative risk for the coastal area of Limassol for lags 6-10 was negative (-9%; 95% confidence interval from -18.5% to 1.6%), indicating a reduction of heat related deaths in lags 6-10.

4. Discussion

This study has shown an immediate or direct health effect of heat in Cyprus, with higher risk within the current and next day of a severe heat event, compared to the effect in longer lags, as we move further from the event. For example, the effect during the same or next day was around 4%, indicating that a 1^{o}C increase in maximum temperature above the hot threshold of 33.7^{o}C was associated with an estimated 4% increase in all-cause mortality during the same and next day, more than 4 times higher than the effect of each of the next few days. The delayed effect of heat could be seen vice versa: a death due to high temperatures is not only due to the thermal stress of the same day, but also of the previous couple of days. The results of a pronounced direct effect of heat (lags 0-1, compared with longer lags) on all-cause mortality agree with previous studies that have shown that the heat effect is immediate [4, 21, 24, 35].

In addition to the immediate effect of heat, the results showed that the effect on public health is much more pronounced for higher temperatures, with a sharp drop from lag 1 to lag 2. For example, it is 40% higher at 42^{0}C, compared to 35^{0}C. At the temperature of 35^{0}C the risk is negligible more than 2 days away from the event (lags greater than 2). The effect for temperatures of 35^{0}C and 37^{0}C is smoother, compared to the sudden drop for temperatures above 40^{0}C, as we move further away from the event (e.g. at lag 7 or one week after the event).

Air pollution (PM_{10}) has not been found to significantly confound the effect of high temperature on mortality in Cyprus for the period 2007-2009. When comparing the adjusted and unadjusted effects (with and without air pollution in the model), it was found that PM_{10} did not affect the exposure-response coefficients: the effect in the adjusted model was slightly higher compared to the unadjusted model in the same period, but the difference was statistically non-significant. Additional results that included interaction terms for the quantification of the potential synergy between temperature and air pollution similarly showed that these were not statistically significant. Similar studies that have examined the role of air pollution as a possible confounder have shown conflicting results. The findings of the present study thus provide additional evidence in literature of another geographical area where air pollution does not appear to have a significant effect on the mortality-temperature relation [13-14, 36].

Apart from the examination of the whole island of Cyprus as a total area, separate analyses were performed for Nicosia (urban area) and Limassol (coastal area), for comparative purposes. In general, air pollution (PM_{10}) was not found to be a confounder of the temperature-mortality relationship in any of the geographical areas under examination. The risk of mortality appeared to be lower in Nicosia compared to Limassol. This finding could suggest an adaptation to high temperatures in urban areas as opposed to coastal areas, and could be an interesting topic for future investigation. It should also be mentioned here that the mean levels of air pollution were higher in Limassol compared to Nicosia, with a daily mean of 45.9 $\mu g/m^3$ and 42.9 $\mu g/m^3$ respectively, with similar standard deviations (17.5 μg/m3 and 17.8 $\mu g/m^3$, respectively). Interestingly enough, an indication of the so called "harvesting effect" or "mortality displacement" appeared for Limassol, with the relative risk for lags 6-10 being negative, showing a deficit of deaths in lags 6-10. Mortality displacement is evidence that deaths have been accelerated by a short amount of time [37-38]. This reduction in mortality for Limassol, one week or so after the event, suggests that the heat wave affected especially those whose health was already so compromised that would have died in the short term anyway and whose events were only accelerated by a brief period of time by the effect of exposure.

5. Conclusions

The current study was the first to examine and quantify the effect of high temperatures on all-cause mortality and investigate the role of air pollution as a potential confounder of this association, in the Mediterranean island of Cyprus.

In summary, the results have shown that high temperatures during the warm months of the year in Cyprus can result in increased mortality rates, independent of relative humidity, secular trends or seasonality, whereas air pollution (PM_{10}) does not appear to have a significant confounding effect on the mortality-temperature relation. The significance of the effect of temperature on mortality remained after the inclusion of air pollution in the model, whereas examination for the quantification of the potential synergy between temperature and air pollution showed that it was not significant.

Future work in this area could consider a longer time period, which was not possible at this stage due to data availability. In addition, it would be worth examining the effect on the mortality-temperature relation of other air pollutants, such as ozone. An in-depth investigation of differences between urban and coastal areas could also provide more insight to the topic.

The results of the current study can be used for the development of early Heat-Health warning systems for the population in Cyprus and for implementing preventive measures, targeting climatic variables.

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