WP 2: Health impacts of extreme weather/heat waves, 1990-2004

The health impacts of heat and heat-waves

Lead Author(s): Paola Michelozzi
Contributing authors: Daniela D'Ippoliti, Ursula Kirchmayer, Manuela De Sario, Claudia Marino, Francesca de'Donato, Carlo A. Perucci

Table of contents

1 Introduction

The interest in evaluating the health impact of heat and heat waves has become a hot topic world wide, in particular in Europe climate change models show that over the next century heat waves will become more intense, more frequent and longer lasting, especially in the Mediterranean region, but also in northern areas currently not very susceptible to heat waves (Meehl and Tebaldi 2004). These changes will contribute to the burden of disease and premature deaths, particularly in the populations with the fewest resources to adapt (IPCC 2007).

Two main types of epidemiological methods have been applied to assess the heat-related mortality in human populations: time series studies and the analysis of specific heat wave episodes ("episode analysis") (Basu & Samet 2002).

Time series studies analyse day-to-day variations both in temperature and mortality counts within a specific geographic location and represent the best choice when the aim is to describe the shape of the dose-response relationship and to quantify the impact through an evaluation of possible threshold values of the curve and the slope of the linear segment.

On the other hand, episode analyses have been employed to provide a better insight of the impact of individual heat wave events and on the specific characteristics of the population at risk. The number of excess deaths attributable to the heat wave is evaluated by a comparison of deaths observed during the episode and the expected mortality baseline (i.e. a period before the heat wave or the same period in previous years) (Basu & Samet 2002).

In general, evidence provided from time series studies and episode analyses have limited statistical power as they refer to a specific place, time and population and the lack of methodological standards makes comparisons of results across geographical areas problematic (Whitman et al. 1997). To overcome these limitations, efforts have recently been made to establish an international collaboration between experts in public health, meteorology, epidemiology and biostatistics to provide estimates of the impact of heat and heat waves on health through the EU-funded projects "Assessment and Prevention of Acute Health Effects of Weather Conditions in Europe" (PHEWE) and "Improving Public Health Responses to extreme weather/heat-waves" (EuroHEAT). In the present chapter, the main findings from these two multi-centre studies are discussed, with special focus on their different analytical approaches.

2 Impact of high temperatures on mortality in Europe

Since the early 90s, time series studies performed in areas with different climates, both in the United States and Europe, have consistently provided evidence of increased mortality in association with hot weather, also showing a geographical variability of heat-related mortality (Kunst et al. 1993, Saez et al. 1995, Ballester et al. 1997, Alberdi et al. 1998, Michelozzi et al. 2000, Braga et al. 2002, Curriero et al. 2002, Dìaz et al. 2002a, Diaz et al. 2002b, Hajat et al. 2002, O'Neill et al. 2003). In particular, high temperatures seem to have a stronger impact in temperate regions, where these extreme events occur rarely (Keatinge et al. 2000, Braga et al. 2001, Curriero et al. 2002).

The observed heterogeneity can be explained by the demographic and socio-economic characteristics of a specific population that define their susceptibility to heat, as well as the preventive measures and actions put in place (WHO 2003).

Comparisons between single studies should be made with caution due to differences in the age structure of populations and the methodologies employed, especially the definition of baseline mortality rates. The PHEWE project has recently provided estimates of the impact of heat on mortality and hospital admissions, for the warm and cold season, using a standardized time series approach for 15 European cities representing a broad range of geographical, climatic, cultural and socio-economic conditions (Athens, Barcelona, Budapest, Dublin, Helsinki, Ljubljana, London, Milan, Paris, Prague, Rome, Stockholm, Turin, Valencia, and Zurich) (Michelozzi et al. 2007). A European database of meteorological variables, air pollution levels and health indicators was developed under the same standardized protocol. The primary aim of this study was to describe the city-specific association between high temperatures and mortality using maximum apparent temperature as the exposure variable. In order to reduce heterogeneity among cities, the results were pooled into two groups, the Mediterranean cities (Athens, Rome, Barcelona, Valencia, Turin, Milan and Ljubljana) and the Northern-continental cities (Prague, Budapest, Zurich, Paris, Helsinki, Stockholm London and Dublin) (Baccini et al. 2008).

Mortality outcomes for all natural causes (ICD-9: 1-799), cardiovascular (ICD-9: 390-459) and respiratory diseases (ICD-9: 460-519) were considered. To estimate the impact of heat wave on mortality GEE models (Liang and Zeger 1986) were used. The effect of heat was expressed in terms of percent variation in mortality associated to 1°C increase in apparent temperature above a city-specific threshold identified by the segmented regression technique (Muggeo 2003).

Results showed a significant association between high temperatures and mortality with a typical a J-shaped relationship in most cities with differences both in the strength of the relationship (slope) and in the threshold values above which mortality quickly increased. The pooled and city-specific estimates of the threshold value and of the effect of high temperatures are reported in Table 1. Further details are reported in the original article (Baccini et al. 2008)

PHEWE results (Baccini et al. 2008) have shown that during the warm season an increase of 1°C in apparent temperature above the threshold (29.4°C and 23.3°C in Mediterranean and Northern-Continental cities, respectively) was associated to a greater increase in daily mortality in Mediterranean cities (+3.12%) than in Northern-Continental cities (+1.84%) (Baccini et al. 2008). At the city level, the greatest increase in daily mortality were observed in Athens (+5.54% for 1°C over 32.7°C), Rome (+5.25% for 1°C over 30.3°C) and Milan (+4.29% for 1°C over 31.8°C). Furthermore, the impact of high temperatures was greatest in the elderly, particularly for respiratory and cardiovascular causes of death. A significant effect on cardiovascular mortality was found only in the Mediterranean cities, while for respiratory causes an effect was observed in both Mediterranean and Northern Continental cities.

PHEWE results shown that the effect of high temperature was immediate, with a lag of 0-3 days, confirming findings from previous studies (Braga et al. 2001, Curriero et al. 2002). Furthermore, there is consistent evidence among cities that the excess in mortality declines in the subsequent days up to negative values (‘harvesting’ effect), then returns to the baseline mortality level, as observed in other studies (Alberdi et al. 1998, Braga et al. 2001, Huynen et al. 2001, Braga et al. 2002, Diaz et al. 2002b, Hajat et al. 2002); the ‘harvesting’ effect was stronger in Mediterranean cities than in the north-continental cities. However, it is relevant to point out that in both groups of cities the mortality displacement only partially compensates the increase in mortality associated to heat.

Heat appears to have a stronger impact on respiratory and cardiovascular mortality than on total mortality, and the association were stronger for the 75+ age group, confirming that this subgroup is particularly susceptible to the effect of heat. Another important finding is that the impact of high temperatures changes within the summer season; the first episodes are the most dangerous as populations are not yet acclimatised. This aspect should be considered when planning preventive actions, since the first heat waves may cause the largest depletion of the pool of susceptible individuals.

3 Impact of heat waves on mortality in Europe

Time series studies provide mean estimates of heat-related mortality on the entire study period, thus suggesting that the effect of individual episodes is underestimated (Hajat et al. 2006).

In episode analysis of specific heat waves, mortality count or rates during these events are generally compared with rates several days before or during the same period in the previous year to estimate the excess mortality during specific periods of extreme heat.

Several epidemiological studies, mainly from the United States and Europe, have shown marked short-term increases in the number of deaths heat waves (Huynen *et al*. 2001, Naughton *et al*. 2002, Michelozzi *et al*. 2004, Kovats & Ebi 2006). Such studies have been carried out in countries with different climatic conditions and have demonstrated that hot weather predominantly affects people with a limited adaptive response living in urban areas; these susceptible subgroups include the elderly, infants, people with chronic diseases and socially deprived groups (Basu & Samet 2002, O'Neill *et al*. 2003, Schwartz 2005).

Episode analysis also show that populations are most vulnerable to early summer heat waves, when they are not become acclimatized to hot weather, especially in countries where heat waves occur infrequently (Diaz et al. 2002b, Hajat et al. 2002, Kyselý 2004). The duration of the heat wave episode also appears to be important, with the largest impact on mortality during the more prolonged heat wave episodes (Diaz et al. 2002b, Hajat et al. 2002, Kyselý 2004). Two well documented heat waves are the 1995 Chicago heat wave (Whitman et al. 1997) and the 2003 European heat wave (Brücker 2005, Kosatsky 2005). The heat wave that hit Chicago during July 1995 was associated with a 31% increase in mortality with at least 700 excess deaths observed, most of which were classified as heat-related and occurred mainly among males and non-Hispanics aged 65 years or older (Whitman et al. 1997).

During August 2003, most European countries were affected by an intense heat wave that caused more than 50.000 deaths, especially among the very old (Brücker 2005, Kosatsky 2005, Robine 2003). The highest anomalies were reached between the 1st and 13th August (IPCC 2007). During this period, the greatest excess in mortality were observed in France (+34.7%), Portugal (+25.9%), Spain (+16.7%), Luxembourg (+16.6%), Italy (+11.9%), Germany (+9.6%) and Switzerland (+9.2%). Other countries like Slovenia, Croatia, England and Wales, Belgium and the Netherlands were affected to a lesser extent (about 4%) (Sardon 2007).

Thanks to the collaboration already established with the PHEWE project, the project "Improving Public Health Responses to extreme weather/heat waves" (EuroHEAT), coordinated by the World Health Organization in Rome and funded by the European Commission started in 2004. The EuroHEAT study had the objective of estimating the effect of heat-waves on mortality in a subgroup of cities already included in the PHEWE project and others (Athens, Barcelona, Budapest, London, Milan, Munich, Paris, Rome and Valencia), using an integrated and standardized approach to allow comparisons of results among the selected cities.

Mortality data for all natural causes (ICD-9: 1-799), cardiovascular (ICD-9: 390-459), cerebrovascular (ICD-9: 430-438) and respiratory causes (ICD-9: 460-519) were analysed to study the association with high temperatures during specific heat waves episodes between 1990-2004. The project focused on the elderly (age ≥65 years) because of their greater vulnerability due to pre-existing chronic diseases and an impaired thermoregulatory system (Kenney & Munce 2003).

A standardized definition of heat wave was is not available, and throughout the literature different definitions and methodological approaches have been used to estimate the health impact associated to heat waves exposure (Smoyer et al. 1998, Hajat et al. 2002, Weisskopf et al. 2002, Kysely et al. 2004, Michelozzi et al. 2004, Paldy et al. 2005). According to a meteorological definition, a heat-wave is a prolonged period of extreme high temperatures (Robinson 2001). In the EuroHeat study heat wave episodes were defined as days with maximum apparent temperature and minimum temperature above the 90th percentile of the monthly distribution in each city (minimum two consecutive days above the threshold). Minimum temperatures were specifically included to account for high night time temperatures. Heat waves were also characterized in terms of duration and intensity. Duration was classified in two levels: short duration <4 days and long duration ≥4 days; also intensity was classified in two levels: low intensity for temperature values lower than 95th percentile and high intensity for temperature values higher than 95° percentile of its monthly distribution.

The impact of heat was estimated as percent variation in mortality during heat waves days compared to days without heat-wave using GEE models (Liang and Zeger 1986). To assess the impact of heat during summer 2003, when a major heat-wave hit several European countries, the analysis was performed comparing estimates for 2003 with those of all other available years for each city.

Results revealed that high values of both, maximum apparent temperature and minimum temperature were associated with an increase in mortality. The impact, in terms of the increase in daily mortality during heat waves days, was heterogeneous among cities ranging between +7.6% in Munich to +33.6% in Milan (Table 2). Investigating the characteristics of heat episodes, the long duration (more than 4 days) had the greatest impact on health, with an excess in mortality +1.5 times greater in Milan, Rome and Budapest +3 times greater in Barcelona.

EuroHEAT was the first project to evaluate the effect of 2003 heat wave using a standardised methodology which would ensure a valid comparison of results among cities. During summer 2003 an important increase in temperatures was observed in all cities considered, except for Athens. At the same time, the number of heat waves associated deaths in 2003 was much higher when compared to episodes during other years of the study period.

4 Discussion and conclusions

Considering the projected long-term changes in climate presented in the latest IPCC Assessment Report, an increase in the frequency and intensity of heat waves is expected in Europe, especially in central, southern and eastern areas (IPCC 2007). Therefore, heat-related mortality may become a relevant threat even in those cities, and areas, usually not exposed to extreme temperatures during summer. In developed countries, as a consequence of the continuous growth of the elderly population, the fraction of vulnerable subgroups living in urban areas is expected to increase substantially, thus enhancing the impact of heat on health (IPCC 2007). The recent PESETA study estimated that in Europe by 2070 more than 70.000 annual deaths can be attributed to heat waves if no preventive action is taken (Confalonieri et al. 2007).

Results from the PHEWE project using a time series approach, have shown that during the warm season a 1°C increase in maximum apparent temperature above the threshold was associated to a greater increase in daily mortality in Mediterranean cities (+3.12%) than in Northern-Continental cities (+1.84%) (Baccini et al. 2008). At a city level, the greatest increases in daily mortality were observed in some Mediterranean cities (Athens, Rome and Milan . These coefficients represent daily population averaged effects of high temperatures over the entire study period, and the effect of anomalous extreme values of exposure such as heat waves contributed to the overall estimate but was weakened within the time series.

The EuroHEAT project represents the first attempt to evaluate the impact of heat waves on mortality in the elderly population in Europe using a standard heat wave definition. The estimated impact of heat waves was analysed through an episode analysis approach and expressed as the average increase in mortality during “heat wave days” with respect to the mortality level during the other days in the time series. The EuroHEAT results have revealed that the effect of heat wave is largely heterogeneous among cities, with the highest effects observed in the two Italian cities and the lowest in Valencia and Munich.

Such heterogeneity may be explained by the levels of exposure to the heat extreme and by the different susceptibility of the resident population. Moreover, in large metropolitan areas, the effect of high temperatures may be exacerbated by the "urban heat island effect" that depends on local climatic factors as well as on building types and land cover characteristics posing an additional risk to the resident population during heat waves (Jones et al. 1982, Rooney et al. 1998, Smoyer 1998, de'Donato et al. 2008). However, exposure levels alone may not account for all the observed heterogeneity. For example, in Valencia, only a small impact of heat waves was observed despite the high temperatures recorded during summer (daily mean of Tappmax=35.6°C). Possible alternative explanations of the observed heterogeneity are the proportion of aged population, the health status and the socio-demographic characteristics of populations, the population density, that may increase the sensitivity to such extreme events, and the adaptation measures and actions in place (WHO 2003).

During the summer of 2003, a large part of Europe, extended from northern Spain to Czech Republic and from Germany to Italy, was affected by an intense heat wave that was responsible for more than 50.000 excess deaths, especially among the very old (Brücker 2005, Kosatsky 2005, UNEP 2004). Average monthly temperatures were far above the long-term mean in June and August, and the extreme weather conditions were exceptionally persistent (over 20 days) (UNEP 2004, Fink et al. 2004). EuroHEAT findings confirm that summer 2003 was characterized by extreme meteorological conditions in most cities, with the highest anomalies in Barcelona, Paris and Milan in both mean (+5.5°C, +3.5°C and +6.8°C respectively) and maximum apparent temperature (over the 90^{th} percentile) (+3.7°C, +4.1°C, +6.0°C respectively). In most cities minimum temperature were also above mean values, in particular in Barcelona, Milan, Paris and Rome and this seems to exacerbate the health impact as local populations are not relieved from the high daytime temperatures. The impact of the 2003 heat wave had an exceptional impact in Paris, typically characterized by a temperate climate where extreme high temperatures occur rarely (Ledrans et al. 2006, Bouchama 2004). In Paris, as well as in Valencia, Rome, Barcelona and Milan, it is worth noting that an impact on mortality

was also observed on "isolated" hot days (not classified as heat waves), due to the fact that the summer 2003 as a whole was anomalous. It has been estimated that the probability of extreme rare events like that of 2003, will increase with global warming also in areas within Europe currently not susceptible like France, Germany and the Balkans (Stott et al. 2004, Meehl & Tebaldi 2004).
Results from the EuroHEAT project show a limited or no impact of the 2003 heat wave in Budapest and Munich, where meteorological anomalies occurred, but probably were not as severe as in the other European continental cities. In Athens, summer 2003 was comparable to other summers in the study period both in meteorological terms (number heat wave days) and in terms of the impact on mortality, due to the fact that the intense hot, dry spell that dominated Central Europe from June to mid-August did not reach the Greek Peninsula (UNEP 2004).

Although heat wave-related mortality is a recurring phenomenon on a yearly basis in many locations, the number of excess deaths is strongly correlated with the type of heat wave and its meteorological characteristics. A general finding of the EuroHEAT project, is that heat-waves of long duration and high intensity have the greatest impact on health. Previous studies showed that the effects of heat waves are more evident at the beginning of the summer season, when vulnerable people have not had enough time to acclimatize to the high temperatures (Smoyer 1998, Diaz J et al. 2002b, Hajat et al. 2002, Kysely et al. 2004, Paldy et al. 2005). Our results showed that this is not a general rule but is strongly dependant on the location, and presumably early heat waves are more dangerous in populations where these extreme events occur infrequently. Another possible explanation is that the pool of susceptible individuals can be depleted by the initial heat wave episodes leaving those individuals more able to cope with extreme temperatures later in summer. As a consequence, reductions in mortality may be observed shortly after a severe heat episode, a phenomenon known as "harvesting effect". Public health interventions need to address these aspects in order to prevent a possible additional burden of disease during the summer season considering that the population at risk may vary in the course of the summer.

Table 1. Pooled and city-specific estimates of the effect of high temperatures on daily mortality during the warm season (from Baccini et al., Epidemiology 2008).

	Threshold (°C) (95% CrI/CI)[a]		% Change (95% CrI/CI)[a]	
Region				
North-continental	23.3	(22.5 to 24.0)	1.84	(0.06 to 3.64)
Mediterranean	29.4[b]	(25.7 to 32.4)	3.12	(0.60 to 5.72)
City				
Athens	32.7	(32.1 to 33.3)	5.54	(4.30 to 6.80)
Barcelona	22.4[c]	(20.7 to 24.2)	1.56	(1.04 to 2.08)
Budapest	22.8	(21.9 to 23.7)	1.74	(1.47 to 2.02)
Dublin	23.9	(20.7 to 27.1)	−0.02	(−5.38 to 5.65)
Helsinki	23.6	(21.7 to 25.5)	3.72	(1.68 to 5.81)
Ljubljana	21.5	(15.0 to 28.0)	1.34	(0.32 to 2.37)
London	23.9	(22.6 to 25.1)	1.54	(1.01 to 2.08)
Milan	31.8	(30.8 to 32.8)	4.29	(3.35 to 5.24)
Paris	24.1	(23.4 to 24.8)	2.44	(2.08 to 2.80)
Praha	22.0	(20.4 to 23.6)	1.91	(1.39 to 2.44)
Rome	30.3	(29.8 to 30.8)	5.25	(4.57 to 5.93)
Stockholm	21.7	(18.2 to 25.3)	1.17	(0.41 to 1.94)
Turin	27.0	(25.2 to 28.9)	3.32	(2.53 to 4.13)
Valencia	28.2	(23.7 to 32.7)	0.56	(−0.35 to 1.47)
Zurich	21.8	(16.5 to 27.0)	1.37	(0.49 to 2.25)

[a]95% credibility interval for regional meta-analytic estimates and 95% confidence interval for city-specific estimates.
[b]Excluding Barcelona.
[c]Mean apparent temperature.

Table 2: Estimated effect of heat-waves on total mortality at age 65+ (% increase and 90% CI), 1990-2004

City	% increase	90% CI	
Athens	21.6	18.5	24.8
Barcelona	15.6	11.0	20.4
Budapest	21.1	17.3	24.9
London	10.4	8.6	12.2
Milan	33.6	28.5	39.0
Munich	7.6	3.8	11.5
Paris	11.4	10.0	12.9
Rome	26.8	23.4	30.4
Valencia	8.5	1.2	16.3

References

1. Alberdi J, Diaz J, Montero J, Miron I. Daily mortality in Madrid community 1986-1992: Relationship with meteorological variables. Eur J Epidemiol 1998; (14)571-578.
2. Baccini M, Biggeri A, Accetta G, Kosatsky T, Katsouyanni K, Analitis A, Anderson HR, Bisanti L, Danova J, D'Ippoliti D, Forsberg B, Medina S, Paldy A, Rabczenko D, Schindler C, Michelozzi P. Effects of apparent temperature on summer mortality in 15 European cities: results of the PHEWE project. Epidemiology 2008; 19 (5) 711-9
3. Ballester F, Corella D, Perez-Hoyos S, Saez M et al. Mortality as a Function of Temperature. A Study in Valencia, Spain, 1991-1993. Int J Epidemiol 1997; 26:(3)551-561.
4. Bouchama A. The 2003 European heat wave. Intensive Care Med 2004;30:1–3.
5. Braga A, Zanobetti A, Schwartz J. The Time Course of Weather Related Deaths. Epidemiology 2001; 12:(6) 662-667.
6. Basu R, Samet J. Relation between elevated ambient temperature and mortality: A review of the epidemiologic evidence. *Epidemiol Rev* 2002;24:190-202.
7. Braga A.L.F., Zanobetti A, Schwartz J. The Effect of Weather on Respiratory and Cardiovascular Deaths in 12 U.S. Cities. Environ Health Perspect 2002; 110:(9)859-863.
8. Brücker G. Vulnerable populations: lessons learnt from the summer 2003 heat waves in Europe. Eurosurveillance 2005; 10:(7-9)
9. Confalonieri, U., B. Menne, R. Akhtar, K.L. Ebi, M. Hauengue, R.S. Kovats, B. Revich and A. Woodward, 2007: Human health. Climate Change 2007: Impacts, Adaptation and Vulnerability. Contribution of Working Group II to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change, M.L. Parry, O.F. Canziani, J.P. Palutikof, P.J. van der Linden and C.E. Hanson, Eds., Cambridge University Press, Cambridge, UK, 391-431.
10. Curriero F, Heiner K, Samet JM, Zeger SL, Strug L, Patz JA. Temperature and mortality in 11 cities of the Eastern United States. *Am J Epidemiol* 2002;155:80-87.

11. de'Donato, F. K.; Stafoggia, M.; Rognoni, M.; Poncino, S.; Caranci, N.; Bisanti, L.; Demaria, M.; Forastiere, F.; Michelozzi, P.; Pelosini, R., and Perucci, C. A. Airport and city-centre temperatures in the evaluation of the association between heat and mortality. Int J Biometeorol. 2008 Mar; 52(4):301-10.
12. Diaz J, Garcia R., Velazquez de Castro F., Hernandez E., Lopez C., Otero A. Effects of extremely hot days on people older than 65 years in Seville (Spain) from 1986 to 1997. Int J Biometeorol 2002a; 46:145-149.
13. Diaz J, Jordán A, Garcia R, López C, Alberdi JC, Hernández E, et al. Heat waves in Madrid 1986-1997: effects on the health of the elderly. Int Arch Occup Environ Health 2002b; 75:163-170.
14. Fink AH, Brucher T, Kruger A, Leckebusch GC, Pinto JG, Ulbrich U. The 2003 European summer heatwaves and drought – synoptic diagnosis and impacts. Weather 2004;59:209-216.
15. Hajat S, Kovats R, Atkinson R, Haines A. Impact of hot temperatures on death in London: a time series approach. J Epidemiol Comm Health 2002; 56:367-372.
16. Hajat S, Armstrong B, Baccini M, Biggeri A, Bisanti L, Russo A, Paldy A, Menne B, Kosatsky T. Impact of high temperatures on mortality. Is there and added heat wave effect? *Epidemiology* 2006;17:632-638.
17. Huynen M, Martens P, Schram D et al. The Impact of Heat Waves and Cold Spells on Mortality Rates in the Dutch Population. Environ Health Perspect 2001; 109:463-470.
18. IPCC. Climate change 2007: The physical science basis. Contribution of working group I to the fourth assessment report of the intergovernmental panel on climate change. [Solomon S, Qin D, Manning M, Chen Z, Marquis M, Averyt KB, Tignor M, Miller HL]. United Kingdom and New York, NY, USA. Cambridge University Press: 996 pp.
19. IPCC. Alcamo, J., J.M. Moreno, B. Nováky, M. Bindi, R. Corobov, R.J.N. Devoy, C. Giannakopoulos, E. Martin, J.E. Olesen, A. Shvidenko, 2007: Europe. Climate Change 2007: Impacts, Adaptation and Vulnerability. Contribution of Working Group II to the Fourth Assessment Report of the Intergovernmental Panel on Climate

Change, M.L. Parry, O.F. Canziani, J.P. Palutikof, P.J. van der Linden and C.E. Hanson, Eds., Cambridge University Press, Cambridge, UK, 541-580.

20. Jones TS, Liang AP, Kilbourne EM, Griffin MR, Patriarca PA, Wassilak SG,Mullan RJ, Herrick RF, Donnell HD, Choik K, Thacker SB. Morbidity and mortality associated with the July 1980 heat wave in St Louis and Kansas City, Mo. JAMA 1982;247:3327-3331
21. Keatinge WR, Donaldson GC, Cordioli E, Martinelli M, Kunst AE, Mackenbach JP, et al. Heat related mortality in warm and cold regions of Europe: observational study. BMJ 2000; 321:670-673.
22. Kenney WL, Munce TA. Invited review: Aging and human temperature regulation. *J Appl Physiol* 2003;95:2598-2603.
23. Kosatsky T. The 2003 European heat waves. Eurosurveillance 2005; 10:(7-9).
24. Kovats RS, Ebi KL. Heatwaves and public health in Europe. Eur J Public Health 2006;16(6):592-9.
25. Kunst A, Looman C, Mackenbach J. Outdoor Air Temperature and Mortality in the Netherlands: A Time-Series Analysis. Am J Epidemiol 1993; 137:(3)331-341.
26. Kyselý J. Mortality and displaced mortality during heat waves in the Czech Republic. Int J Biometeorol 2004; 49:91-97.
27. Ledrans M. Impact sanitaire de la vague de chaleur de l'été 2003: synthèse des études disponibles en août 2005. BEH 2006;19-20:130-7.
28. Liang K-Y, Zeger S L. (1986). Longitudinal data analysis using generalized linear models. Biometrika, 73, 13-22.
29. Meehl GA, Tebaldi C. More Intense, More Frequent, and Longer Lasting Heat Waves in the 21st Century. Science 2004;305:994. DOI: 10.1126/science.1098704.
30. Michelozzi P, Fano V, Forastiere F, Barca A, Kalkstein LS, Perucci CA. Weather conditions and elderly mortality in Rome during summer. World Meteorological Organization Bulletin 2000; 49:(4) 348-55.
31. Michelozzi P, de' Donato F, Accetta G, Forastiere F, D'Ovidio M, Perucci CA Impact of Heat Waves on Mortality - Rome, Italy, June-August 2003. MMWR 2004; 53:369-371.

32. Michelozzi P, Kirchmayer U, Katsouyanni K, Biggeri A, McGregor G, Menne B, Kassomenos P, Anderson HR, Baccini M, Accetta G, Analytis A, Kosatsky T. Assessment and prevention of acute health effects of weather conditions in Europe, the PHEWE project: background, objectives, design. *Environ Health* 2007;6:12.
33. Muggeo V. Estimating regression models with unknown break-points. *Stat Med* 2003;22:3055-71.
34. Naughton M.P, Henderson A, Mirabelli MC, Kaiser R, Wilhelm JL, Kieszak SM, et al. Heat-Related Mortality During a 1999 Heat Wave in Chicago. Am J Prev Med 2002; 22:(4)221-227.
35. O'Neill MS, Zanobetti A, Schwartz J. Modifiers of the Temperature and Mortality Association in Seven US Cities. *Am J Epidemiol* 2003;157:1074-1082.
36. Paldy A, Bobvos J, Vamos A, Kovats RS, Hajat S. The effect of temperature and heat waves on daily mortlity in Budapest, Hungary, 1970-2000. In: Eds. Kirch W, Menne B. Bertollini R. Extreme weather events and Public Health Responses. Berlin Springer 2005.
37. Robine JM, Cheung SL, Le Roy S, Van Oyen H, Griffiths C, Michel JP, Hermann FR. Death toll exceeded 70,000 in Europe during the summer of 2003. C R Biol 2008; 331 (2): 171-8.
38. Robinson PJ. On the definition of a Heat Wave. Journal of Applied Meteorology 2001; 40:762-775.
39. Rooney C, McMichael AJ, Kovats RS, Coleman M.P. Excess mortality in England and Wales, and in Greater London, during the 1995 heatwave. J Epidemiol Community Health 1998; 52:482-486.
40. Saez M, Sunyer J, Castellsagué J, Murillo C, Antó JM. Relationship between Weather Temperature and Mortality: A Time Series Analysis Approach in Barcelona. International Journal of Epidemiology 1995; 24:(3)576-582.
41. Sardon JP. The 2003 heat wave. Euro Surveill 2007;12(3)
42. Schwartz J. Who is Sensitive to Extremes of Temperature? A Case-Only Analysis. Epidemiology 2005;16:(1)67-72.

43. Smoyer KE. A comparative analysis of heat waves and associated mortality in St. Louis, Missouri - 1980 and 1995. Int J Biometeorol 1998; 42:44-50.

44. Stott PA, Stone DA, Allen MR. Human contribution to the European heatwave of 2003. Nature 2004;432:610-614.

45. UNEP (United Nations Environment Programme) - GRID Europe. Impacts of summer 2003 heat wave in Europe. Environment Alert Bulletin, March 2004. http://www.grid.unep.ch/product/publication/download/ew_heat_wave.en.pdf

46. Weisskopf M, Anderson H, Foldy S et al. Heat Wave Morbidity and Mortality, Milwaukee, Wis, 1999 vs 1995: An Improved Response? Am J Public Health 2002; 92:(5)830-833.

47. Whitman S, Good G, Donoghue DR, Benbow N, Shou W, Mou S. Mortality in Chicago attributed to the July 1995 Heat Wave. Am J Public Health 1997; 87:(9)1515-1518.

48. WHO. Methods of assessing human health vulnerability and public health adaptation to climate change. By Kovats S, Ebi KL & Menne B. Health and Global Environmental Change Series, No.1 2003, 111 pages.