

Assessment and prevention of acute health effects of weather conditions in Europe. The PHEWE project: background, objectives, design

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Abstract

Background

The project “Assessment and prevention of acute health effects of weather conditions in Europe” (PHEWE) aimed at assessing the association between weather conditions and acute health effects, during both warm and cold seasons in 16 European cities with widely differing climatic conditions and to provide information for public health policies.

Methods

The PHEWE project was a three-year pan-European collaboration between epidemiologists, meteorologists and experts in public health.

Meteorological, air pollution and mortality data from 16 cities and hospital admission data from 12 cities were available from 1990 to 2000. The short-term effect on mortality/morbidity was evaluated through city-specific and pooled time series analysis. The interaction between weather and air pollutants was evaluated and health impact assessments were performed to quantify the effect on the different populations. A heat/health watch warning system to predict oppressive weather conditions and alert the population was developed in a subgroup of cities and information on existing prevention policies and of adaptive actions was gathered.

Results

Main results were presented in a symposium at the conference of the International Society of Environmental Epidemiology in Paris on September 6th 2006 and will be published as scientific articles. The present article introduces the project, including the description of the database and the framework of the applied methodology.

Conclusions

The PHEWE project offers the opportunity to investigate the relationship between temperature and mortality in 16 European cities, representing a wide range of climatic, socio-demographic and cultural characteristics; the use of a standardized methodology allows for direct comparison between cities.

Background

Interest in the impact of weather on human health is increasing, especially in the light of potential climate changes. The rapid increase of greenhouse gases in the atmosphere is expected to increase both mean temperature and temperature variability around the world.[1][2] Climatologists project that, in temperate climates, a 2-3°C increase in average summer temperatures doubles the frequency of periods characterized by extremely high temperatures.[3] Such changes would be characterized by the increased frequency and intensity of heat waves, and could lead to an increase in heat related illness episodes and deaths.

The association between high and low temperatures and mortality has been investigated in several studies. Most investigations have focused on the effect of temperature on health during extreme events (heat waves, cold spells) through descriptive (episode analysis) and analytical (time series) approaches. A review of the epidemiological studies on the effect of high temperatures on mortality conducted after 1970 identified sensitive groups among the elderly, persons with pre-existing cardiovascular and respiratory diseases and/or those of low socioeconomic status.[4] The heat effect appears within few days of exposure and some harvesting is observed.[4][5] The heterogeneity of the impact of heat on health reflects geographical, climatic and cultural variability, as well as different capacities to adapt to extreme heat and cold and needs to be addressed more in depth in a large scale study.[4][5][6][7]

Recently, studies on the effect of high temperatures on morbidity provided evidence of an increase in emergency hospital admissions for specific causes in young children and persons over 75 years of age, though with a smaller effect for admissions than for mortality.[8] Schwartz et al. reported an effect of heat on cause-specific admissions within a few days after exposure and a short-term displacement of the events (harvesting effect).[9]

In the 1990s, the APHEA (Air Pollution and Health: an European Approach) project investigated the short-term effects of air pollution on health throughout Europe.[10] In the time series analysis

performed for this project, temperature was considered an important confounder of the association between air pollution and mortality.[11]

The project “Assessment and Prevention of Acute Health Effects and Weather Conditions in Europe” (PHEWE) was initiated in 2002, with the general aim to assess the association between weather and acute health effects (daily mortality and hospital admissions) in Europe and to provide information for public health policy on preventive and adaptive actions. The specific objectives of the program were:

- to create a European database of meteorological variables and health indicators;
- to perform time series analysis using a standardized methodology to evaluate the short term health effects of weather conditions on daily mortality and daily hospital admissions, both during warm and cold seasons;
- to investigate the role of air pollution as a potential effect-modifier using a standardized methodology;
- to define a synoptic weather classification system in different European areas, and to evaluate synoptic categories associated with increased mortality and morbidity;
- to experiment the use of Heat/health watch warning systems (HHWWS) to predict in advance high risk weather conditions;
- to produce a health impact assessments of weather conditions on mortality;
- to define public health actions aimed at the prevention of adverse health effects of weather in Europe.

Methods

The database

The project collected data from 16 European cities, representing a large spectrum of climatic conditions: Athens, Barcelona, Budapest, Krakow, Dublin, Helsinki, Ljubljana, London, Milan, Paris, Prague, Rome, Stockholm, Turin, Valencia, and Zurich, including about 30 million European

citizens (Table 1). The number of city residents ranges between 6,8 M (London) to 260.000 (Ljubljana), with the percentage of the elderly population (over 75 years) between 5% (Helsinki) and 10% (Barcelona). The gender and age-adjusted mortality rate is highest in Budapest (1093.6) and lowest in Milan (439.4).

Health data

Mortality data were provided from 16 cities, and hospital admission data from 12 cities for all available years in the period 1990-2000 (Table 1), all referring to the city residents, and to events that occurred in the city, except for Dublin, where hospital admissions referred also to non residents. Taking into account the results of previous studies, [12][13][14] and the biological plausibility of the health effects, [7] [15][16][17] the following causes of death and hospital admission were selected for all ages combined and specific age groups (0-14 yrs, 15-64 yrs, 65-74 yrs, 75+ yrs): all causes (excluding external causes), ICD-9: 1-799; cardiovascular diseases, ICD-9: 390-459; cerebrovascular diseases, ICD-9: 430-438; respiratory diseases, ICD-9: 460-519.

Data from cold and warm seasons were analyzed separately, defining summer as the months from April to September and winter as the months between October and March.

Table 2 gives an overview of the mean daily number of deaths by cause and season. Data on cerebrovascular mortality were not available in three cities (Athens, Paris, Zurich). For all other causes the mean daily counts were lower in the summer season.

Emergency hospital admission records for the same causes (plus influenza, ICD-9: 487) were selected, following the APHEA-2 project protocol.[10] Only main causes of admission were considered. In table 3 mean daily admission counts are summarized by cause and season. Two cities could not provide all requested causes (Paris, Zurich). Generally, admission counts were higher in the cold season, especially for respiratory diseases.

Meteorological variables

For each city, data were retrieved from a weather station located in the city centre as well as from the nearest airport weather station for the study period. The following meteorological variables,

recorded every three hours, were collected: air temperature, dew point temperature, wind speed, wind direction, sea level pressure, total cloud cover, solar radiation, precipitation, visibility. Quality control included a descriptive overview of the variables in all cities, detecting possible errors and extreme values, testing for homogeneity and correcting erroneous values where possible.

Table 4 gives an overview of the daily mean values observed in the participating cities. Mean summer temperatures ranged between 12.0 °C in Helsinki and 23.5 °C in Athens, in Valencia the lowest inner-city temperature range was reported. Relative humidity levels were highest in Dublin (81%) and lowest in Athens (57%). In winter, the lowest temperature was observed in Helsinki (-0.9°C), and the highest in Valencia (13.7°C), which is also the city with lowest relative humidity (69%) and the smallest temperature range.

Previous studies have used a variety of exposure measures, including maximum, minimum or average temperature, apparent temperature, humidity and dew point temperature but to date there is no standard indicator of heat or cold stress.[18][19] [5] [20][21] In the present study, maximum apparent temperature (Tappmax) was chosen as the exposure variable, which is an index of thermal discomfort based on air temperature and dew point temperature.[22] Tappmax is defined as the highest value of the 3-hourly apparent temperature values, using the following formula:

$$AT = -2.653 + 0.994 \text{ Temp} + 0.0153 (\text{Dew})^2$$

where AT is apparent temperature, Temp is the air temperature in °C and Dew is the dew point temperature in °C.[23][24]

For Barcelona, where 3 hour meteorological data were not available, the daily average apparent temperature was used.

Air pollution data

The data collected within the APHEA-2 project were updated and integrated according to that project's procedures.[10] The following pollutant measurements were recorded at each monitoring station (maximum 6): SO₂ (mean 24-hours), TSP or Black Smoke (mean 24-hours), PM10- if

available-(mean 24-hours), NO₂ (maximum 1 hour, mean 24-hours), O₃ (maximum 1 hour, maximum 8-hours moving average) CO (maximum 8-hour moving average).

The selection of the monitors was based on local criteria, mainly on the completeness of measurements and representation of population exposure. A standardized procedure was used to fill-in days with missing data.[10]

Other variables

Through a complementary questionnaire information on other confounders and potential effect modifiers was gathered from each city, such as holidays and unusual events during the study period (strike in the health services or transportation, flood, earthquake), percentage of households with air conditioning facilities and annual restrictions on home heating use. Questions on the city population, and on details concerning data quality were also included, which were useful in order to characterize the different city populations (Table 1) and necessary to complete the Health Impact Assessment.

City-specific analysis

For the city-specific analyses a Generalized Equation Estimation (GEE) approach was proposed as an extension of Generalized Linear Models to analyze longitudinal data, when the observations on different subjects (clusters) can be assumed independent and the observations on the same subject correlated.[25]

For each city, there was an outcome variable (number of deaths or hospital admissions) and several covariates (confounders, apparent temperature, other meteorological variables), observed on different days. A marginal Poisson distribution of the dependent variable and correlation between observations during one summer (winter) were assumed, while observations from different summer (winter) periods were considered independent.

An exploratory analysis indicated the appropriate dependence structure within a season to be used in the GEE. Dynamic regression models were combined with a genetic algorithm for the semi-

automatic selection of the best model over a large model space, covering different specifications of the correlation structure within a cluster.[26]

A first order autocorrelation structure within a season resulted to be appropriate both for mortality and hospital admissions.

The common model applied to single city analysis took into account potential confounding effects of holidays, day of the week, seasonality and long-term time trend, barometric pressure, wind speed and air pollution levels, all modeled in parametric terms.

An indicator of influenza epidemics was included in the model for cold season analyses (except for respiratory causes).[27] Models for hospital admission analysis in the warm season included the moving average of total admission counts (ICD 9: <800) to offset population reduction during summer holidays.

Exposure modeling

Based on the results of previous studies, the maximum apparent temperature of current and previous 3 days (lag 0-3) for the warm season and lag 0-15 for the cold season was chosen as the indicator of exposure; the delayed effect of the exposure was further investigated by distributed lag models in a sensitivity analysis.

The shape of the exposure-response curve between apparent temperature and log mortality/hospital admission rate was investigated, with a flexible approach, introducing a cubic regression spline for apparent temperature into the model.

For mortality, during the warm season a “turning point” or “threshold” was identified. The effect of high temperatures on summer mortality was also investigated focusing on the slope above the city-specific threshold of the exposure-response curve. City-specific thresholds were obtained a priori by a maximum likelihood approach, treating the apparent temperature corresponding to the minimum of exposure-response curve as an unknown parameter.[28]

For hospital admissions the effect of high temperatures in summer was investigated using a dummy variable for maximum apparent temperatures above the 90th percentile.

The delayed effect of exposure on health outcomes was investigated using constrained and unconstrained distributed-lag models that simultaneously included variables for the same day and up to 5, 10, 15, 20, 25, 30 and (for hospital admissions) 40 days.

The impact of high temperatures on mortality was investigated with health risk assessment analyses.

Pooled analysis

In the second stage, the city-specific effect estimates were combined to obtain pooled estimates.

Overall exposure-response curves were obtained through a fixed effect meta-analytical approach using the pooled data set and through a second stage meta-analytical approach,[29] while the city-specific effect estimates and the city-specific curves for distributed-lag and time-varying effects were pooled by a hierarchical Bayesian modeling approach.

To reduce heterogeneity, pooled results were obtained grouping the cities, according to a priori defined meteorological and geographical criteria, distinguishing between Mediterranean cities and Continental/North Atlantic cities.

Second stage models including potential effect modifiers as covariates were applied in order to explore heterogeneity. Such effect modifiers included variables on climate and health of the population, variables on air pollution levels and the correlation between air pollution concentrations and the meteorological variables.

Confounding and synergistic effect of meteorological and air pollution variables

Based on the models defined in the city-specific and pooled analysis, further exploration of the confounding effects of air pollutants was carried out. Possible effect modification of the temperature-mortality effect by air pollutant levels was investigated using meta-regression models.

Heat/health watch warning system (HHWWS)

In five cities (Rome, Barcelona, London, Paris, Budapest), experimental heat/health watch warning systems were developed based on the results of the time series analysis. An air-mass-based climatologic index was developed, using a synoptic climatologic approach. Feeding the forecast

data for upcoming days (up to 72 hours) into the model, can predict the arrival of an oppressive air mass.

Public health policies

An overview of existing prevention programs in the participating cities was obtained by the implementation of a questionnaire. Moreover, physiological and behavioral adaptation measures, experiences with heat health warning systems, urban planning, housing standards, and socio-economic determinants of vulnerability were summarized in a comprehensive literature review. The quantification of the effect of heat/air masses exposures in the different populations was addressed through health impact assessment (years-of-life-lost approach).

Results and Discussion

While previous studies focused on single cities, the present project investigated the health impact of weather on a large scale through a variety of climate conditions and of socio-economic and demographic characteristics, applying the same methodology, thus allowing for comparison between the city specific results.

Previous studies showed that the temperature level corresponding to the minimum mortality level varies from city to city and across different latitudes according to the local climate and probably reflecting adaptation by the local population to the temperature range in both the hot and cold season.[12] [20] [30][31][32][33][34] The analysis of the heterogeneity of the effect in European areas was accounted for in the present project, describing city-specific “change points” of the dose-response relationship and the specific shape of the dose-response curves. In the pooled analysis, heterogeneity was reduced grouping the cities according to a priori geographical and meteorological characteristics.

Few studies have examined the effect of heat on outcomes other than mortality. In Chicago, during the July 1995 heat wave an 11% increase in hospital admissions was observed, with 35% of the increase among patients over 65 years.[35] More recently, studies performed in London and 12 US

cities reported an increase of admissions for specific causes in the elderly and evidence of a harvesting effect.[8][9] To date, the present study is the largest one to investigate weather and hospital admissions in Europe.

In the present study, the role of meteorological variables other than temperature was investigated, assuming that they may contribute to the negative health effects.[22][24] Therefore, an exposure indicator including dew point temperature was chosen for the time series analysis,[36][37] and the excess mortality/morbidity associated with specific air masses was explored using a climatologic classification based on synoptic indexes.[38][39][40]

This project focused on time series rather than on heat wave episodes, using an approach, that has been successfully used in the analyses of the effects of air pollution. Such methods have the advantage that the population under study serves as its own control, and covariates that vary between subjects, but not over time, are not potential confounders.[39][40]

Evidence that the increase in mortality is followed by a deficit that (partly) compensates the negative effect (harvesting) is contradictory.[41] In the present study the heterogeneity of mortality/morbidity displacement patterns between cities was systematically investigated.

There is much disagreement in literature concerning human acclimatization to changing weather.[22] [36] [42][43] While the issue was examined by comparing the threshold temperature in different geographic locations, the possibility of a short-term acclimatization was also evaluated by comparing the dose-response function in the first period of the summer with the effects modeled in the later part of the season. This allowed also for comparison of the impact of the first heat wave in one summer with the following ones.

Given the small number of events (mortality and admissions), a unique definition of winter and summer season was chosen in order to reach a reasonable statistical power, and sensitivity analysis was performed, focusing on the three central summer months (June-August).

The relationship between increase in air pollution levels and acute health effects has been well described in the USA and in Europe.[40] [11] The levels of some of the pollutants associated with

increase in mortality and hospital admissions are higher during the summer period in many European areas. A synergistic effect of warm temperature and air pollution on mortality has been suggested from time series analysis conducted in Athens, whereas no effect modification detected in a study in Philadelphia, USA.[44][45] The present study investigated the independent effect of meteorological variables of that of ambient air pollution, and explored whether there is synergy between the two factors.

The development and evaluation of HHWS in a subset of European cities represents an innovation in the field of climate and health research in Europe. After the 2003 heat wave, the need for early warning systems based on a standardized protocol and using the same evaluation criteria has become a major topic of public health policies.

These results of the health impact assessment will contribute to policy development, public health decision-making, and will be an important input for cost-benefit analysis and risk communication. Guidelines for preventive strategies and health care actions taken to lessen morbidity and mortality effects can then be based on evidences arising from this project, namely the literature review, the investigation of the state-of-the-art in the participating cities (feasibility), and the identification of susceptible populations.

Conclusions

The PHEWE project offers the opportunity to investigate the relationship between temperature and mortality in 16 European cities, representing a wide range of climatic, socio-demographic and cultural characteristics; the use of a standardized methodology allows for direct comparison between cities. The analysis of the effect of weather on hospital admissions in 12 cities is an innovation in Europe. The evidence arising from the project's results, namely the literature review, the investigation of the state-of-the-art in the participating cities (feasibility), and the identification of susceptible populations (target groups), offer an important contribution for guidelines for preventive strategies and health care actions taken to lessen morbidity and mortality effects. The

results of this project contribute to policy development, public health decision-making, and will be an important input for cost-benefit analysis and risk communication.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

PM coordinated the project and participated in all methodological discussions. UK coordinated the data collection, dealt with administrative and financial issues, organized the meetings and contributed to the writing of the present paper. KK was the leader of the Epidemiology and Statistics working group, shared the methodological decisions with PM and AB, supervised the analysis on winter mortality and was responsible for the investigation of air pollutants as potential confounders or effect modifiers. AB shared the development of the methodology with PM and KK and supervised summer mortality analysis. GMG was responsible for the development of HHWWS in five cities and was the leader of the Meteorology working group. BM was responsible for all public health related issues and the organisation of the final work shop. PK carried out the analysis of meteorological indicators for all cities. HRA was the leader of the Public Health working group. MB and AA participated in the methodological discussion and carried out mortality analysis for summer and winter, respectively. GA contributed to the methodological discussion and carried out hospital admission analysis. TK performed health impact assessment of heat on mortality in collaboration with AB and MB and developed and implemented the city specific questionnaire for the assessment of prevention programmes in place. All authors read and approved the final manuscript.

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References

1. McMichael AJ: **Global Environmental Change and Human Population Health: A Conceptual and Scientific Challenge for Epidemiology.** *Int J Epidemiol* 1993, **22(1)**:1-8.
2. Meehl GA, Zwiers F, Evans J, Knutson T, Mearns L, Whetton P: **Trends in extreme weather and climate events: issues related to modelling extreme in projections of future climate change.** *Bull Amer Meteor Soc* 2000, **81**:427-36.
3. WHO/WMO/UNEP: *Climate and health: The potential impacts climate change.* Geneva, Switzerland; 1996.
4. Basu R, Samet J: **Relation between elevated ambient temperature and mortality: a review of the epidemiologic evidence.** *Epidemiol Rev* 2002, **24**:190-202.
5. Curriero FC, Heiner KS, 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.
6. Keatinge W, Donaldson G: **Mortality Related to Cold and Air Pollution in London after Allowance for Effects of Associated Weather Patterns.** *Environ Res* 2001: Section A[86], 209-216.
7. Eurowinter Group: **Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe.** *Lancet* 1997,**349**:1341-1346.

8. Kovats RS, Hajat S, Wilkinson P: **Contrasting patterns of mortality and hospital admissions during hot weather and heat waves in Greater London, UK.** *Occup Environ Med* 2004, **61(11):893-8.**
9. Schwartz J, Samet JM, Patz JA **Hospital admissions for heart disease: the effects of temperature and humidity.** *Epidemiology* 2004, **15(6):755-61.**
10. Katsouyanni K, Schwartz J, Spix C, Touloumi G, Zmirou D, Zanobetti A, Wojtyniak B, Vonk JM, Tobias A, Ponka A, Medina S, Bacharova L, Anderson HR: **Short term effects of air pollution on health: a European approach using epidemiologic time series data: the APHEA protocol.** *J Epidemiol Community Health* 1996, **50 Suppl 1:S12-8**
11. Katsouyanni K, Touloumi G, Spix C, Schwartz J, Balducci F, Medina S, Rossi G, Wojtyniak B, Sunyer J, Bacharova L, Schouten JP, Ponka A, Anderson HR: **Short term effect of ambient sulphur dioxide and particulate matter on mortality in 12 cities: results from time series data from the APHEA project. Air Pollution and Health: a European Approach.** *BMJ* 1997, **314(7095):1658-63.**
12. Ballester F, Corella D, Perez-Hoyos S, Saez M, Hervas A: **Mortality as a function of temperature. A Study in Valencia, Spain, 1991-1993.** *Int J Epidemiol* 1997, **26:551-561.**
13. Kunst AE, Looman C, Mackenbach J: **Outdoor air temperature and mortality in the Netherlands: a time-series analysis.** *Am J Epidemiol* 1993, **137:331-341.**
14. Rooney C, McMichael AJ, Kovats RS, Coleman MP: **Excess mortality in England and Wales. And in Greater London, during the 1995 heatwave.** *J Epidemiol Community Health* 1998, **52:482-486.**
15. Keatinge WR, Coleshaw SR, Cotter F, Mattock M, Murphy M, Chelliah R: **Increased platelet and red cell counts, blood viscosity, and arterial pressure during mild surface cooling: factors in mortality from coronary and cerebral thrombosis in winter.** *BMJ* 1984, **289:1405-08.**

16. Keatinge WR, Coleshaw SR, Easton JC, Cotter F, Mattock MB, Chelliah R: **Increased Platelet and Red Cell Counts, Blood Viscosity, and Plasma Cholesterol Levels during Heat Stress, and Mortality from Coronary and Cerebral Thrombosis.** *Am J Med* 1986, **81**:795-800.
17. Kilbourne EM: **The Spectrum of Illness During Heat Waves.** *Am J Prev Med* 1999, **6**[4]: 359-360.
18. 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.** *JAMA* 2004, **291**(21):2537-2538.
19. Schwartz J: **Who is sensitive to extremes of temperature? A case-only analysis.** *Epidemiology* 2005, **16**:67-72.
20. Saez M, Sunyer J, Castellsague J, Murillo C, Anto JM: **Relationship between weather temperature and mortality: a time series analysis approach in Barcelona.** *Int J Epidemiol* 1995, **24**:576-582.
21. Braga ALF, Zanobetti A, Schwartz J: **The effect of weather on respiratory and cardiovascular deaths in 12 U.S. cities.** *Environ Health Perspect* 2002, **110**:859-863.
22. Steadman RG: **The assessment of sultriness: Part I: A temperature-humidity index based on human physiology and clothing science.** *J Appl Meteorol* 1979, **18**:861-873.
23. Kalkstein LS, Valimont KM: **An evaluation of summer discomfort in the United States using a relative climatological index.** *Bull Am Meteorolog Soc* 1986, **67**:842-8.
24. Steadman RG: **The assessment of sultriness. Part II: effects of wind, extra radiation and barometric pressure on apparent temperature.** *J Appl Meteorology* 1979, **18**: 874-885.
25. Liang KY, Zeger SL: **Longitudinal analysis using generalized linear models.** *Biometrika* 1986, **73**: 13-22.
26. Chiogna, M, Gaetan G: **Mining epidemiological time series: an approach based on dynamic regression.** *Statistical modelling* 2005, **5**:309-325.
27. Touloumi G, Samoli E, Quenel P, Paldy A, Anderson RH, Zmirou D, Galan I, Forsberg B, Schindler C, Schwartz J, Katsouyanni K: **Short-term effects of air pollution on total and**

- cardiovascular mortality: the confounding effect of influenza epidemics.** *Epidemiology* 2005 Jan 16, **1**:49-57.
28. Muggeo VM: **Estimating regression models with unknown break-points.** *Stat Med* 2003 Oct 15, **22(19)**:3055-71.
29. Samoli E, Touloumi G, Zanobetti A, Le Tertre A, Schindler C, Atkinson R, Vonk J, Rossi G, Saez M, Rabczenko D, Schwartz J, Katsouyanni K: **Investigating the dose-response relation between air pollution and total mortality in the APHEA-2 multicity project.** *Occup Environ Med* 2003 Dec, **60(12)**:977-82.
30. Alberdi JC, Diaz J, Montero JC, Miron I: **Daily mortality in Madrid community 1986-1992: relationship with meteorological variables.** *Eur J Epidemiol.* 1998 Sep, **14(6)**:571-8.
31. 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* 2002, **46**:145-149.
32. Keatinge WR, Donaldson GC, Cordioli E, Martinelli M, Kunst AE, Mackenbach JP, Nayha S, Vuori I: **Heat related mortality in warm and cold regions of Europe: observational study.** *BMJ* 2000, **321**:670-673.
33. Hajat S, Kovats RS, Atkinson RW, Haines A: **Impact of hot temperatures on death in London: a time series approach.** *J Epidemiol Community Health* 2002, **56**:367-372.
34. Michelozzi P, Fano V, Forastiere F, Barca A, Kalkstein LS, Perucci CA: **Weather conditions and elderly mortality in Rome during summer.** *WMO Bulletin* 2000, **49**:348-55.
35. Semenza JC, McCullough JE, Flanders WD, McGeehin MA, Lumpkin JR: **Excess hospital admissions during the July 1995 heat wave in Chicago.** *Am J Prev Med* 1999 May, **16(4)**:269-77.
36. Kalkstein LS, Davis RE: **The development of a weather/mortality model for environmental impact assessment.** *Proceedings of the 7th Conference of Biometeorology and Aerobiology 1985a*, 334-336.

37. Kalkstein LS, Jamason PF, Greene JS, Libby J, Robinson L: **The Philadelphia Hot Weather-Health Watch/Warning System: Development and Application, Summer 1995.** *Bull Am Meteorol Soc* 1996, 1519-28.
38. Kalkstein LS: **A new approach to evaluate the impact of climate on human mortality.** *Environ Health Perspect* 1991, **96**:145-50.
39. Schwartz J: **Air pollution and daily mortality: a review and meta-analysis.** *Environ Research* 1994, **64**:36-52.
40. Schwartz J: **Non-parametric smoothing in the analysis of air pollution and respiratory illness.** *Can J Stat* 1994, **22**:471-87.
41. Hajat S, Armstrong BG, Gouveia N, Wilkinson P: **Mortality displacement of heat-related deaths. A comparison of Delhi, Sao Paulo, and London.** *Epidemiol* 2005, **16**:613-620.
42. Rotton J: **Angry, sad, happy? Blame the weather.** *U.S. News and World Report* 1983, **95**:52-53.
43. Ellis FP: **Mortality from heat illness and heat-aggravated illness in the United States.** *Environ Research* 1972, **15**:504-512.
44. Katsouyanni K, Pantazopoulou A, Touloumi G, Tselepidaki I, Moustiris K, Asimakopoulos D, Pouloupoulou G, Trichopoulos D: **Evidence for Interaction between Air Pollution and High Temperature in the Causation of Excess Mortality.** *Arch Environ Health* 1993, **48(4)**:235-42.
45. Kalkstein LS, Greene JS: **An evaluation of climate/mortality relationships in large U.S. cities and the possible impacts of a climate change.** *Environ Health Perspect* 1997, **105(1)**:84-93.

Table 1. PHEWE cities: characteristics and data series available

City	Characteristics			Health data - Time series used	
	Population	% 75+	Mortality rate (x 100.000)*	Mortality	Hospital Admissions
Athens	3 188 305	6.4	663.6	1992-1996	
Barcelona	1 512 971	10.1	542.5	1992-2000	1994-1997
Budapest	1 797 222	7.3	1093.6	1992-2001	1997-2000
Dublin	481 854	5.3	826.7	1990-2000	1994-2001
Helsinki	955 143	5.0	590.0	1990-2000	
Krakow	741 510	8.9**	805.4	1990-1996	
Ljubljana	263 290	5.9	719.1	1992-1999	1997-1999
London	6 796 900	6.8	584.5	1992-2000	1992-2000
Milan	1 304 942	9.5	439.4	1990-2000	1990-1999
Paris	6 161 393	6.1	554.0	1991-1998	1991-1995
Prague	1 183 900	7.0	779.4	1992-2000	
Rome	2 812 573	7.3	497.4	1992-2000	1998-2000
Stockholm	1 173 183	8.5	576.2	1990-2000	1990-2000
Turin	901 010	9.2	479.5	1991-1999	1995-1999
Valencia	739 004	7.6	595.6	1995-2000	1996-2000
Zurich	990 000	n.a.	n.a.	1990-1996	1990-1996

* adjusted for gender and age
** >=70 years

Table 2. Mortality data: daily mean and standard deviation (sd) by cause and season.

City	Total mortality (ICD-IX < 800.0)				Cardiovascular (ICD-IX: 390-459)				Cerebrovascular (ICD-IX: 430-438)				Sumr
	Summer*		Winter**		Summer*		Winter**		Summer*		Winter**		
	mean	sd	mean	sd	mean	sd	mean	sd	mean	sd	mean	sd	
Athens	67.5	10.8	78.3	13.2	32.6	7.6	39.5	8.4	-	-	-	-	4.2
Barcelona	35.9	6.6	42.8	9.2	13.0	4.0	16.6	5.1	3.6	2.0	4.5	2.1	3.1
Budapest	71.0	11.0	79.8	13.4	34.9	7.3	40.9	8.9	71.0	11.0	79.8	13.4	2.2
Dublin	11.4	3.5	13.6	4.1	4.9	2.2	6.0	2.6	1.0	1.0	1.2	1.1	1.4
Helsinki	17.1	4.2	18.5	4.6	8.2	3.0	8.8	3.1	2.4	1.6	2.7	1.7	1.4
Ljubljana	6.3	2.6	7.1	2.9	2.6	1.6	3.0	1.8	0.6	0.8	0.7	0.9	0.4
London	149.0	16.5	179.2	29.4	61.0	10.5	73.5	13.6	14.1	4.2	16.9	4.7	23.7
Milan	26.3	5.9	31.9	7.2	9.9	3.4	13.2	4.2	2.9	1.8	3.6	2.0	1.7
Paris	115.7	13.8	128.2	16.4	34.8	6.6	40.0	7.9	-	-	-	-	7.7
Prague	34.9	6.5	38.5	7.5	20.3	4.9	22.7	5.6	5.6	2.6	6.2	2.7	1.1
Rome	52.8	9.6	61.7	10.5	20.9	5.5	26.6	6.5	4.9	2.4	5.8	2.6	2.6
Stockholm	27.9	5.4	30.8	6.3	13.5	3.8	14.9	4.3	3.0	1.7	3.3	1.8	2.2
Turin	19.1	4.7	23.2	5.4	7.9	3.0	10.3	3.5	2.7	1.7	3.3	1.9	1.0
Valencia	14.6	4.1	17.9	5.3	5.3	2.4	7.0	2.9	1.6	1.3	1.9	1.5	1.4
Zurich	11.6	3.5	13.5	3.8	5.2	2.4	6.3	2.6	-	-	-	-	0.6

* April-September, ** October-March

Table 3. Hospital admission data: daily mean and standard deviation (sd) by cause and season.

City	Cardiovascular (ICD-IX: 390-459)				Cerebrovascular (ICD-IX: 430-438)				Respiratory (ICD-IX:460-519)			
	Summer*		Winter**		Summer*		Winter**		Summer*		Winter**	
	mean	sd	mean	sd	mean	sd	mean	sd	mean	sd	mean	sd
Barcelona	21.8	6.0	25.9	6.3	5.0	2.3	5.6	2.4	15.9	5.3	23.5	7.6
Budapest	110.8	50.1	119.1	50.0	14.5	7.5	15.2	7.6	25.7	10.0	37.0	15.3
Dublin	25.9	6.4	27.3	6.7	5.1	2.4	5.5	2.4	22.6	5.7	30.3	10.4
Ljubljana	11.2	4.9	12.4	5.4	1.5	1.2	1.6	1.3	6.7	4.4	8.2	4.6
London	163.8	31.8	171.2	34.7	28.3	6.8	30.0	7.5	125.2	25.3	178.6	52.7
Milan	71.2	26.3	81.6	24.7	14.0	5.1	15.2	4.9	25.6	10.4	34.4	11.1
Paris	126.5	45.3	146.5	44.3	n.a.	n.a.	n.a.	n.a.	59.0	19.4	85.0	22.7
Rome	120.3	27.0	133.6	26.1	25.1	6.1	26.7	6.0	43.1	11.4	63.2	18.3
Stockholm	48.0	12.1	50.8	12.2	10.4	3.6	10.9	3.7	18.3	6.1	24.2	7.9
Turin	25.2	6.4	28.5	6.8	7.2	2.8	7.7	2.9	10.1	4.0	15.9	6.4
Valencia	12.4	4.1	13.6	4.6	3.1	1.8	3.2	1.9	9.2	3.6	14.4	5.6
Zurich	8.2	3.4	9.1	4.9	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

* April-September, ** October-March

Table 4. Meteorological data: daily mean values (mean, minimum and maximum)
Summer period (April-September)

CITY	temperature (°C)			relative humidity (%)			sea level pressure (hPa)			wind speed (m/s)			max apparent temperature (°C)		
	mean	min	max	mean	min	max	mean	min	max	mean	min	max	mean	min	max
Athens	23.5	7.6	34.3	57	23	89	1013.0	945.8	1031.3	3.3	0.3	11.6	27.9	7.9	41.6
Barcelona	21.7	8.6	34.2	66	29	99	1015.2	993.7	1030.6	6.7	0.9	22.3	23.3 *	6.5*	36.9*
Budapest	18.2	1.5	29.8	61	30	97	1014.5	992.6	1033.6	2.6	0.7	8.8	21.9	0.2	38.8
Dublin	12.5	1.4	21.0	81	53	100	1014.8	974.7	1038.5	4.7	1.1	12.0	14.7	1.5	28.5
Helsinki	12.0	-6.5	25.4	71	28	98	1012.7	982.9	1035.6	3.6	0.9	9.6	14.3	-3.7	32.8
Krakow	15.0	-1.6	26.6	77	45	98	1015.7	991.1	1033.1	2.3	0.0	10.1	19.1	-2.3	35.8
Ljubljana	15.9	0.6	26.5	75	33	98	970.8	949.2	985.4	1.6	0.2	7.0	20.1	-1.7	35.4
London	15.1	3.2	28.0	71	42	96	1015.5	984.1	1036.3	3.4	0.7	9.3	18.1	1.5	35.2
Milan	20.0	2.5	29.4	72	26	100	1014.2	991.5	1031.9	1.7	0.0	9.4	25.4	2.7	40.8
Paris	16.1	2.1	30.2	72	32	100	1015.9	988.1	1032.9	4.0	1.0	11.9	19.7	1.5	39.4
Prague	15.1	-1.7	28.7	70	31	98	972.5	947.0	990.4	3.8	0.3	12.0	17.8	-3.3	36.3
Rome	20.5	6.1	30.3	72	25	94	1014.2	992.6	1031.8	3.1	0.5	12.5	26.1	5.9	40.5
Stockholm	12.8	-3.2	26.6	72	36	99	1012.9	985.6	1036.1	3.3	0.6	8.1	15.4	-2.1	34.0
Turin	18.5	3.0	27.9	74	32	97	1014.2	993.0	1032.0	1.4	0.0	7.7	23.4	4.2	45.8
Valencia	22.3	10.5	30.0	66	32	92	1015.1	995.1	1030.9	3.3	1.1	9.9	29.5	10.6	44.9
Zurich	15.1	1.4	26.2	73	42	97	1016.4	993.2	1034.6	2.1	0.2	6.0	19.0	0.7	35.2

Winter period (October-March)

CITY	temperature (°C)			relative humidity (%)			sea level pressure (hPa)			wind speed (m/s)			max apparent temperature (°C)		
	mean	min	max	mean	min	max	mean	min	max	mean	min	max	mean	min	max
Athens	13.1	0.7	26.5	70	35	92	1018.2	988.9	1035.7	3.2	0.0	12.8	14.8	0.8	34.1
Barcelona	13.4	1.9	25.2	69	37	100	1018.3	990.2	1038.2	7.0	0.0	22.1	12.3*	0.2*	27.9*
Budapest	4.0	-12.1	19.5	77	36	100	1019.7	988.9	1045.7	2.6	0.5	8.6	5.0	-9.7	25.7
Dublin	7.0	-4.2	17.8	85	54	100	1012.2	971.1	1046.3	6.0	0.6	17.5	7.5	-4.6	19.8
Helsinki	-0.9	-24.1	14.7	85	44	99	1010.8	949.5	1054.4	4.1	0.1	11.5	-0.7	-14.5	14.8
Krakow	2.3	-21.4	17.9	86	53	100	1019.2	987.7	1046.9	2.8	0.0	11.5	3.3	-14.4	25.4
Ljubljana	3.0	-13.3	18.4	83	26	100	973.5	939.8	995.5	1.3	0.0	8.0	4.4	-9.9	24.3
London	7.5	-5.2	18.9	81	52	100	1016.1	978.6	1044.3	3.7	0.4	12.5	8.4	-5.6	24.5
Milan	7.1	-6.5	22.7	81	20	100	1019.1	986.8	1041.0	1.3	0.0	9.4	8.8	-6.3	32.6
Paris	6.9	-10.7	20.0	84	37	100	1018.1	983.3	1044.8	4.8	0.5	14.6	7.7	-9.2	25.4
Prague	2.5	-19.7	19.0	84	42	100	973.8	974.5	996.8	4.6	0.0	16.3	2.6	-13.4	22.5
Rome	10.5	-2.0	25.8	80	34	98	1017.1	990.4	1039.1	3.2	0.3	13.1	13.5	-1.0	41.5
Stockholm	1.3	-16.7	15.8	85	44	99	1010.9	947.9	1049.1	3.7	0.3	10.3	1.3	-12.9	19.4
Turin	6.0	-6.9	20.2	76	25	99	1019.5	989.2	1041.4	1.1	0.0	9.5	8.1	-5.9	29.5
Valencia	13.7	3.4	26.0	69	29	98	1018.7	993.5	1034.8	3.1	0.3	12.2	18.1	3.2	35.9
Zurich	4.0	-11.7	17.0	82	44	98	1020.7	987.2	1044.6	2.4	0.5	10.3	4.8	-9.2	23.5

* for Barcelona the mean apparent temperature is reported