

# High Temperature and Hospitalizations for Cardiovascular and Respiratory Causes in 12 European Cities

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**Rationale:** Episode analyses of heat waves have documented a comparatively higher impact on mortality than on morbidity (hospital admissions) in European cities. The evidence from daily time series studies is scarce and inconsistent.

**Objectives:** To evaluate the impact of high environmental temperatures on hospital admissions during April to September in 12 European cities participating in the Assessment and Prevention of Acute Health Effects of Weather Conditions in Europe (PHEWE) project.

**Methods:** For each city, time series analysis was used to model the relationship between maximum apparent temperature (lag 0–3 days) and daily hospital admissions for cardiovascular, cerebrovascular, and respiratory causes by age (all ages, 65–74 age group, and 75+ age group), and the city-specific estimates were pooled for two geographical groupings of cities.

**Measurements and Main Results:** For respiratory admissions, there was a positive association that was heterogeneous between cities. For a 1°C increase in maximum apparent temperature above a threshold, respiratory admissions increased by +4.5% (95% confidence interval, 1.9–7.3) and +3.1% (95% confidence interval, 0.8–5.5) in the 75+ age group in Mediterranean and North-Continental cities, respectively. In contrast, the association between temperature and cardiovascular and cerebrovascular admissions tended to be negative and did not reach statistical significance.

**Conclusions:** High temperatures have a specific impact on respiratory admissions, particularly in the elderly population, but the underlying mechanisms are poorly understood. Why high temperature increases cardiovascular mortality but not cardiovascular admissions is also unclear. The impact of extreme heat events on respiratory admissions is expected to increase in European cities as a result of global warming and progressive population aging.

**Keywords:** heat; hospital admissions; elderly; respiratory diseases; cardiovascular diseases

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## AT A GLANCE COMMENTARY

### Scientific Knowledge on the Subject

It is known that high temperatures increase mortality from cardiovascular and respiratory causes, but there is limited information about the effects of high temperatures on morbidity.

### What This Study Adds to the Field

High temperatures increase the risk of hospitalization for respiratory diseases, with geographical heterogeneity. Although previous research showed that high temperatures increase cardiovascular mortality, this was not observed for admissions.

Climate change scenarios presented in the latest Intergovernmental Panel on Climate Change Assessment Report predict an increase in average surface temperature at a global level (1). In Europe, an increase in the frequency and intensity of summer heat waves is expected, especially in central, southern, and eastern countries (1). These changes will contribute to the burden of diseases and premature deaths, particularly in population subgroups with limited adaptive capacity. 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, further increasing the health impact of heat waves.

Although the short-term effects of high environmental temperatures on mortality have been well documented (2), there is much less evidence about the effects of high temperature on morbidity. Studies of heat waves tend to show comparatively smaller increases in hospital admissions than in mortality (3, 4), but the results of time series studies are not consistent. In 12 US cities, there was an association between hot weather and a rise in admissions for heart diseases in the 65+ age group (5). In Denver, Colorado, high temperatures were associated with an increase in admissions for acute myocardial infarction and congestive heart failure (6). However, studies performed in London and Madrid found no association between high temperatures and emergency hospital admissions for cardiovascular diseases and only a modest

increase in admissions for respiratory diseases among the elderly population (4, 7). Given the limited and contradictory evidence, further research is needed to increase our understanding of the impact of heat on morbidity outcomes and to clarify the mechanisms that underlie such associations.

The European Union–funded project “Assessment and Prevention of Acute Health Effects of Weather Conditions in Europe” (PHEWE) is a multicenter collaboration designed to investigate the short-term health effects of weather during the hot and cold seasons in European cities using a time series approach (8). In the PHEWE study, the health outcomes analyzed were total and cause-specific mortality and hospital admissions for cardiovascular, cerebrovascular, and respiratory causes. These outcomes were chosen because mortality has been observed to increase during heat waves and days of high ambient temperature (2). The study results will guide health care providers in preventing or reducing the adverse effects of hot weather on health. City-specific and pooled estimates of the effects of heat on morbidity and mortality from the PHEWE project, as well as results from other large studies, can provide a sound basis for estimating the future impacts of climate change in Europe.

This article evaluates the impact of high temperatures on hospital admissions for cardiovascular, cerebrovascular, and respiratory causes during the warm period, with a focus on elderly persons, who are more vulnerable because of pre-existing chronic diseases and a less effective thermoregulatory system (9). This study will enable the effects of high temperatures on hospital admissions, an indicator of morbidity, to be compared with those obtained by the PHEWE project for mortality in the same cities (10).

## METHODS

Twelve cities were included in the analysis (Barcelona, Budapest, Dublin, Ljubljana, London, Milan, Paris, Rome, Stockholm, Turin, Valencia, and Zurich). Each city provided hospital admission, meteorological, and air pollution data for at least 3 years within the period 1990 to 2001. Information on the study area, the population, and the dataset has been published recently (8).

Hospital admissions referred to the daily counts for cardiovascular (ICD-9: 390–459), cerebrovascular (ICD-9: 430–438), and respiratory causes (ICD-9, 460–519) by age (all ages, 65–74 age group, and 75+ age group) in the resident population. The main discharge diagnosis was considered, and only acute conditions were selected. A code for acute admissions was available for eight cities, and for the others a common procedure was adopted to exclude elective reasons for admissions (e.g., admission for rehabilitation, surgery, or psychiatric and dermatological conditions) and transfers from other hospitals.

Maximum apparent temperature ( $T_{\text{appmax}}$ ; °C) was used as the exposure variable of interest in the PHEWE project (8); this is an index of thermal discomfort based on air temperature ( $T_{\text{air}}$ ; °C) and dew point temperature ( $T_{\text{dewpt}}$ ; °C) according to the following formula (11, 12):

$$T_{\text{app}} = -2.653 + 0.994(T_{\text{air}}) + 0.0153(T_{\text{dewpt}})^2$$

This simple indicator accounts for the combined effect of temperature and humidity, which, especially during hot days, can influence the body's ability to cool itself by evaporation and perspiration. Furthermore, it was chosen on the basis of data quality and availability in all the European cities considered. The analysis was restricted to the warm period of the year (April–September) and comprised two stages. In the first stage, city-specific effects were estimated; in the second stage, the results were combined to obtain pooled estimates. Generalized estimating equations (13) were used to model the relationship between daily hospital admission counts and  $T_{\text{appmax}}$ . The observations among

summers of different years were assumed to be independent, whereas daily counts of hospitalizations within each summer were considered to be correlated. On the basis of an exploratory analysis (14, 15), we specified a first-order autoregressive structure (16), where observations close in time tend to be more correlated than distant observations, to take into account the intrasummer correlation. We used the model-based variance estimator for the standard errors because this has been recommended for use in the presence of few large clusters (17).

A common city-specific model was used. A Poisson distribution of the outcome variable was assumed, including the following potential confounders: holidays, day of the week and calendar month, linear terms for barometric pressure (lag 0–3) and wind speed, and linear and quadratic terms for time and maximum 1-hour daily value of nitrogen dioxide ( $\text{NO}_2$ ) (lag 0–1).  $\text{NO}_2$  was chosen as an indicator of traffic-related pollution, which is the most important source of ambient pollution in the PHEWE cities.  $\text{NO}_2$  data were complete in all cities except for Dublin and Ljubljana, where the daily average of black smoke and  $\text{SO}_2$  were used, respectively. To take into account the possible additional confounding by ozone, we ran a sensitivity analysis for the cities with available data by including  $\text{NO}_2$  and ozone in the model. To control for a short-term population decrease and a reduction of hospital services during summer holiday periods, a 7-day moving average value of total admissions was included as an offset variable. Based on the exploratory analysis, a delayed effect of temperature on hospitalization up to 3 days was chosen (lag 0–3). Sensitivity analyses using the mean and minimum  $T_{\text{app}}$  were performed.

Two models were used to describe the  $T_{\text{appmax}}$ –admission relationship. In the first model, a semiparametric approach that includes penalized cubic regression splines for temperature was applied to describe the exposure–response relationship. This approach allows to model the data in a flexible way without imposing a specific shape of the exposure–response curve (18). The relationship was modeled using piece-wise polynomials between equally spaced breakpoints.

Because no threshold of  $T_{\text{appmax}}$  value was identified in the exposure–response curves, to estimate the impact of  $T_{\text{appmax}}$  on admissions we applied a second model, assuming a log-linear increase in risk above the 90th percentile of the distribution of  $T_{\text{appmax}}$  (lag 0–3) in each city. The effect was expressed as percent variation in daily hospital admissions for 1°C increase in  $T_{\text{appmax}}$  above this value.

To provide summary estimates and to reduce heterogeneity, cities were grouped into “Mediterranean” (Barcelona, Ljubljana, Milan, Rome, Turin, and Valencia) and “North-Continental” (Budapest, Dublin, London, Paris, Stockholm, and Zurich) according to geographical and climatic criteria. City-specific effect estimates were combined using random effect meta-analysis with the method described by DerSimonian and Laird (19). To describe the overall exposure–response curves, a generalized estimating equations model was used, similar to the city-specific one, adding a city indicator variable and interaction terms of the exposure variable with the confounders.

## RESULTS

Table 1 summarizes the study period, mean values of  $T_{\text{appmax}}$ , population size, and daily mean number of cause-specific hospital admissions during the warm period for the 12 cities. There is considerable variability, with mean  $T_{\text{appmax}}$  values ranging from 14.7°C in Dublin to 29.5°C in Valencia. The proportion of people in the 75+ age group is heterogeneous, ranging from 5 to 6% in Dublin, Ljubljana, and Paris to around 10% in Barcelona, Milan, and Turin. More detailed information on the meteorological variables and health outcomes are available in Michelozzi and colleagues (8).

The exposure–response curves of the relationship between  $T_{\text{appmax}}$  and admissions (not shown) were heterogeneous between cities. For cardiovascular and cerebrovascular causes, no association was present in most cities, whereas a negative linear trend was found in some Mediterranean cities (Barcelona, Milan, and Valencia). For respiratory causes, an increase in hospital admissions with increasing temperatures was observed in most cities, particularly in the older age groups.

**TABLE 1. STUDY PERIOD, MEAN OF DAILY MAXIMUM APPARENT TEMPERATURE, POPULATION SIZE, AND DAILY MEAN NUMBER OF HOSPITAL ADMISSIONS FOR CARDIOVASCULAR, CEREBROVASCULAR, AND RESPIRATORY CAUSES BY AGE GROUP**

City	Study period	T <sub>appmax</sub> (°C) (daily mean)	Population size*		Cardiovascular causes (daily mean HA)		Cerebrovascular causes (daily mean HA)		Respiratory causes (daily mean HA)	
			All ages (n)	75+ age group (%)	All ages (n)	75+ age group (%)	All ages (n)	75+ age group (%)	All ages (n)	75+ age group (%)
Barcelona	1994–1997	23.3 <sup>†</sup>	1,512,971	10.1	22	9	5	2	16	6
Budapest	1997–2000	21.9	1,797,222	7.3	111	50	15	6	26	5
Dublin	1994–2001	14.7	481,854	5.3	26	9	5	2	23	5
Ljubljana	1997–1999	20.1	263,290	5.9	11	3	2	1	7	1
London	1992–2000	18.1	6,796,900	6.8	164	68	28	15	125	33
Milan	1990–1999	25.4	1,304,942	9.5	71	25	14	8	26	6
Paris	1991–1995	19.7	6,161,923	6.1	127	29	n.a.	n.a.	59	11
Rome	1998–2000	26.1	2,812,573	7.3	120	50	25	14	43	11
Stockholm	1990–2000	15.4	1,173,183	8.5	48	25	10	6	18	6
Turin	1995–1999	23.4	901,010	9.2	25	11	7	4	10	3
Valencia	1996–2000	29.5	739,004	7.6	12	5	3	1	9	3
Zurich	1990–1996	19.0	990,000	n.a.	8	5 <sup>‡</sup>	n.a.	1 <sup>‡</sup>	n.a.	n.a.

Definition of abbreviations: HA = hospital admissions; n.a. = not available; T<sub>appmax</sub> = maximum apparent temperature.

\* 1996 population in Dublin; 1999 population in Paris; 2000 population in Barcelona, Budapest, Ljubljana, Rome, Stockholm, Turin, and Valencia; 2001 population in London and Milan; 1990 population in the canton of Zurich.

<sup>†</sup> Mean apparent temperature.

<sup>‡</sup> Daily number of hospital admissions for the 65+ age group.

City-specific and pooled estimates of the effect of high temperatures on cardiovascular, cerebrovascular, and respiratory hospital admissions in the total population and in the 75+ age group are summarized in Figure 1. In most cities no association between high temperatures and cardiovascular and cerebrovascular hospital admissions was found, whereas in some cities negative coefficients were observed. The pooled estimates for Mediterranean and North-Continental cities were negative for all ages and for the 75+ age group. For respiratory causes, a positive association between temperature and hospital admissions was observed in most cities for all ages and the 75+ age group, with a heterogeneous effect among cities. The pooled estimates for Mediterranean and North-Continental cities were positive for all ages and for the 75+ age group.

For respiratory hospital admissions, city-specific results in terms of percent change of the effect of temperatures above the 90th percentile are shown in Table 2. In several cities the estimated effect increases with age (London, Milan, Paris, Rome, and Valencia). In these cities, the highest effect was observed in the 75+ age group; whereas in Barcelona, Ljubljana, and Stockholm, the highest increase was observed in the 65 to 74 age group.

The results of the pooled analysis (Mediterranean and North-Continental cities) are reported in Figure 2 and Table 3. The pooled exposure–response curves are shown only for respiratory admissions and illustrate a positive association for all ages and the 75+ age group, whereas in the 65 to 74 age group the positive association was found only in North-Continental cities. The results of the pooled analysis for cardiovascular and cerebrovascular causes (Table 3) show that hospital admissions decrease as temperature increases. In contrast, for respiratory causes, the association between temperature and hospital admissions was positive. Estimates for the 75+ age group were twice that of all ages (+4.5 vs. +2.1% and +3.1 vs. +1.2% in Mediterranean and North-Continental cities, respectively).

For respiratory causes, the analyses were performed also for the 0 to 14 and 15 to 64 age groups; counts were generally small, and no clear association was found (data not shown).

Results from the sensitivity analysis on the role of additional confounding by ozone show that the risk estimates for the six cities with available ozone data did not substantially differ from those adjusted for NO<sub>2</sub> alone (data not shown).

## DISCUSSION

The PHEWE project represents the first attempt to evaluate the effect of temperature on several morbidity outcomes using a standardized methodology in a multi-center European study (8). The study presents results on the effect of heat on hospital admissions for cardiovascular, cerebrovascular, and respiratory causes in 12 cities, with a total population of about 25 million people, which varies greatly by climatic and socio-demographic characteristics.

In most cities, only an effect of high temperatures on hospital admissions for respiratory causes in the 75+ age group was observed, whereas the association with admissions for cardiovascular and cerebrovascular causes tended to be negative but not statistically significant at the 5% level. These findings provide further insight into the PHEWE project results on mortality based on the same methodologic approach, which showed an increase for cardiovascular and respiratory causes of death (10). Moreover, the effects observed on respiratory admissions were lower than those observed on respiratory mortality (+4.5 and +8.1% in Mediterranean cities and +3.1 and +6.6% in North-Continental cities, respectively, for a 1°C increase in the 75+ age group) (10).

The absence of an effect of heat on cardiovascular admissions agrees with results from studies performed in London and Madrid where no effect on heart disease admissions was observed (4, 7). Furthermore, the lower impact of heat on hospital admissions than on mortality for respiratory causes agrees with findings from the London and Madrid studies (4, 7) and with results from studies on heat wave episodes that showed a greater impact on mortality than on hospitalizations (3). These results suggest that, during periods of high temperature, many deaths occur rapidly before the patient receives medical treatment or is admitted to a hospital (4, 7, 20), and this may be particularly true for acute events, which are more common within the cardiovascular diagnostic group (21). This explanation is supported by previous reports of a greater burden in terms of out-of-hospital deaths compared with in-hospital deaths (12, 22, 23) and of an increased mortality for cardiovascular causes among those dying out of hospital during extreme heat events (23). Results from an additional analysis performed in the city of Rome support this hypothesis: An increase in out-

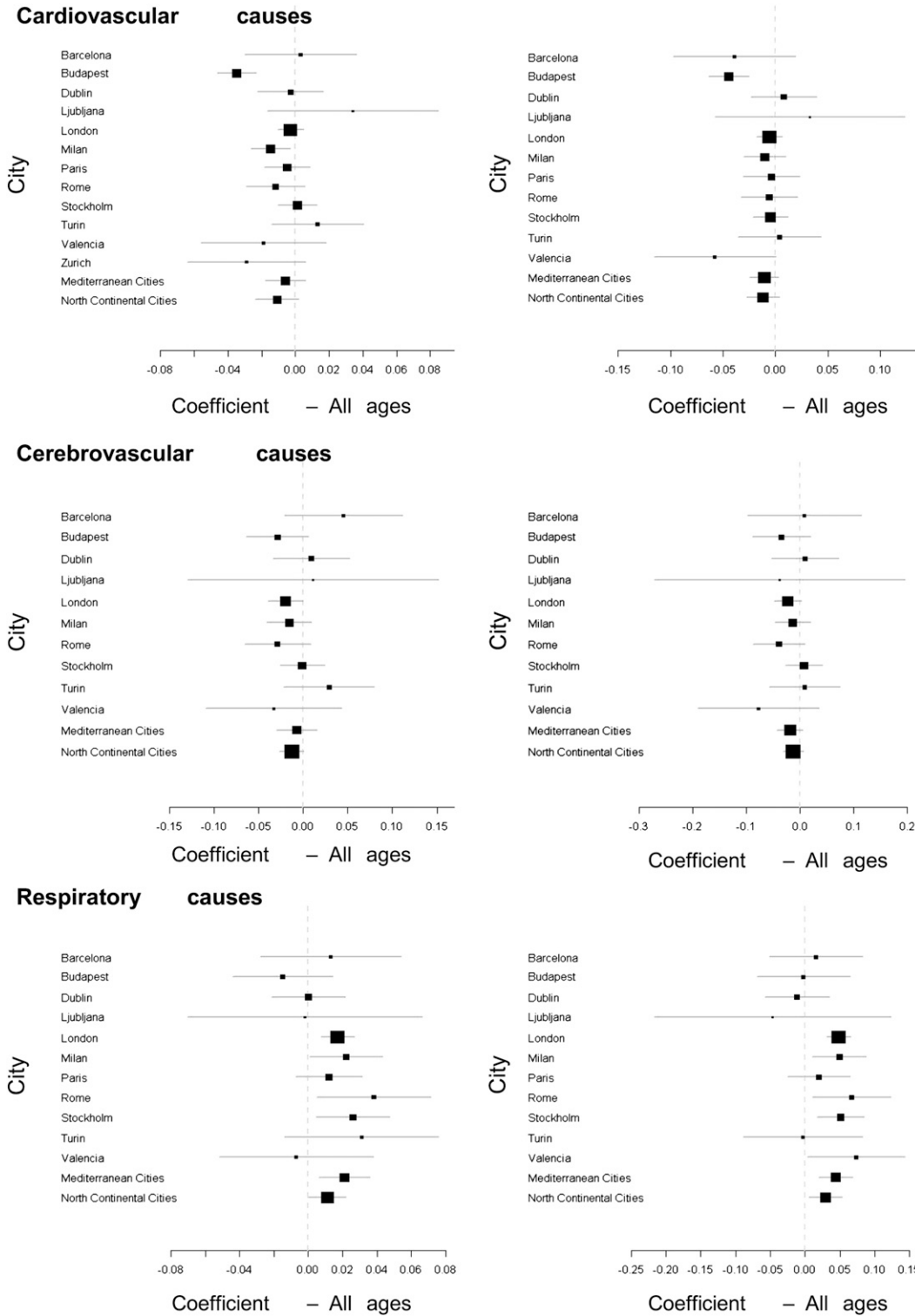


Figure 1. City-specific and pooled estimates (regression coefficients and 95% confidence intervals) of the effect of maximum apparent temperature on daily hospital admissions for cardiovascular, cerebrovascular, and respiratory causes by age group.

of-hospital mortality for cardiovascular causes during heat waves episodes was observed (+12.4%), whereas during the same days a decrease for hospital admissions was observed (-1.2%).

The contrasting pattern between admissions and mortality could also be related to differences in physiopathologic mechanisms, which might be reflected in differences in the lag between heat exposure and the outcome. Time series studies on mortality have demonstrated an immediate impact of high temperature on cardiovascular causes, followed by a compensa-

tory low risk at longer lags (24), suggesting that cardiovascular deaths during hot days tend to occur suddenly in persons whose health is compromised. Respiratory mortality, on the contrary, tends to peak later than cardiovascular mortality, with effects observed up to 3 weeks after exposure without evidence of harvesting (24). Several physiopathologic mechanisms connect heat stress and cardiovascular disease, including the release of platelets into circulation and increases in red and white cell counts, blood viscosity, and plasma cholesterol due to water loss and reduced plasma volume (25). The reasons why such mechanisms

**TABLE 2. CITY-SPECIFIC ESTIMATES OF THE EFFECT OF MAXIMUM APPARENT TEMPERATURE ON DAILY HOSPITAL ADMISSIONS FOR RESPIRATORY CAUSES BY AGE GROUP**

City	90th percentile of T <sub>appmax</sub> (°C)	% Change (95% CI)*		
		All ages	65–74 age group	75+ age group
Barcelona	30.8	1.3 (–2.7 to 5.5)	2.6 (–5.9 to 11.8)	1.6 (–5.0 to 8.6)
Budapest	28.9	–1.4 (–4.4 to 1.6)	–0.3 (–7.3 to 7.3)	–0.6 (–6.1 to 7.9)
Dublin	19.7	0.0 (–2.2 to 2.2)	0.5 (–4.8 to 6.1)	–1.2 (–5.7 to 3.6)
Ljubljana	27.3	–0.2 (–6.8 to 6.9)	3.8 (–13.5 to 24.5)	–4.6 (–19.6 to 13.2)
London	24.6	1.7 (0.7 to 2.8)	3.6 (1.2 to 6.1)	4.9 (3.1 to 6.8)
Milan	33.8	2.2 (0.1 to 4.4)	3.6 (–1.4 to 8.9)	5.1 (1.0 to 9.2)
Paris	27.8	1.3 (–0.7 to 3.2)	–0.9 (–6.1 to 4.6)	1.9 (–2.6 to 6.7)
Rome	34.5	3.9 (0.5 to 7.4)	–5.0 (–11.4 to 1.9)	6.9 (1.0 to 13.2)
Stockholm	22.8	2.7 (0.5 to 4.9)	8.4 (3.7 to 13.2)	5.2 (1.7 to 8.9)
Turin	31.2	3.1 (–1.4 to 7.9)	–2.4 (–12.6 to 9.0)	–0.4 (–8.6 to 8.6)
Valencia	36.4	–0.7 (–5.2 to 3.9)	–6.2 (–15.5 to 4.1)	7.6 (0.2 to 15.5)

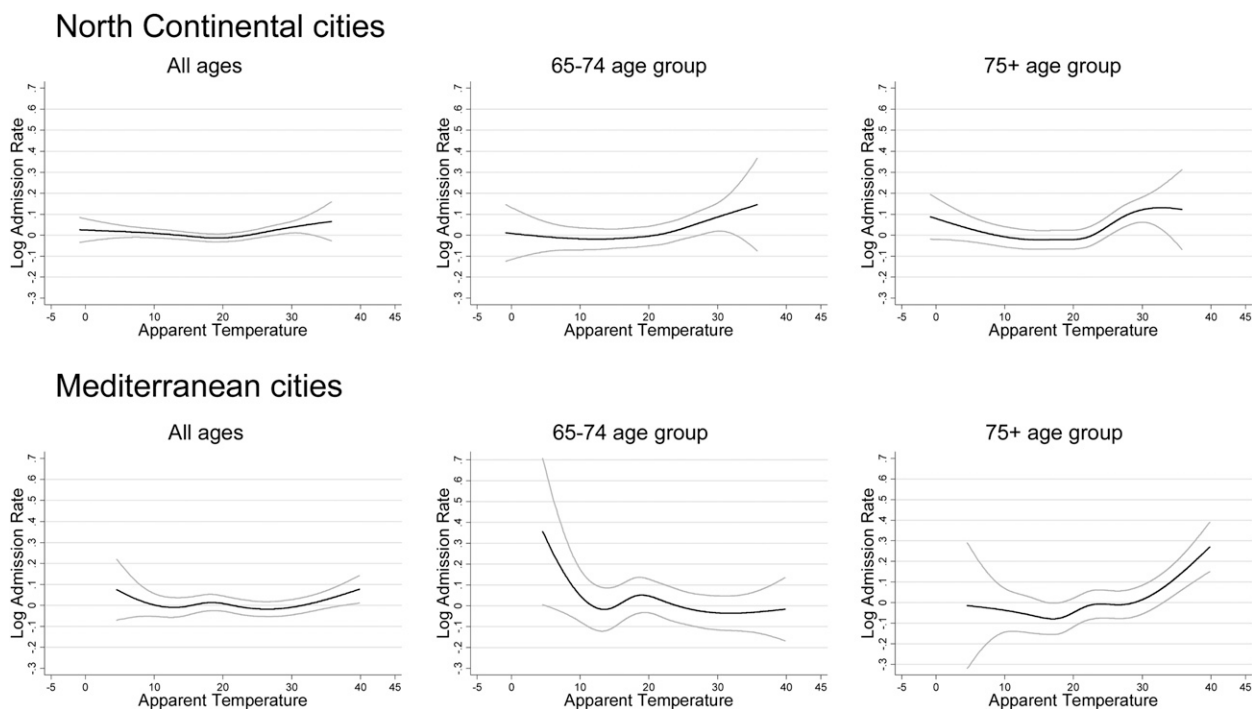
Definition of abbreviations: CI = confidence interval; T<sub>appmax</sub> = maximum apparent temperature.

\* Percentage change in hospital admissions for 1°C increase over the 90th city-specific percentile of T<sub>appmax</sub> (°C) (lag 0–3).

may rapidly lead to death from cardiovascular diseases should be investigated further. One hypothesis is that most of these sudden deaths are due to congestive heart failure, which has been identified as a major prognostic factor in patients with heatstroke (26) and as a strong determinant for in-hospital mortality during hot days (27). Patients with heart failure may be particularly vulnerable to heat stress due to their attenuated cutaneous vasodilator response (28).

Overall, the PHEWE results indicate an effect of heat on respiratory but not cardiovascular admissions. The underlying mechanisms through which high temperatures may increase the risk of hospitalization for respiratory diseases are unclear. To clarify this point, exacerbations of chronic obstructive pulmonary disease (COPD) are one of the most common reasons for hospital admissions for respiratory causes in the elderly population (29). These acute episodes are associated with airways

and systemic inflammation as well as cardiovascular comorbidity and may be triggered by exposures to heat. During an extreme heat event, subjects with COPD may hyperventilate (30), thus increasing the possibility of dynamic hyperinflation, leading to dyspnea and to mechanical and cardiovascular effects. In addition, elderly patients with COPD may be unable to dissipate excess heat through circulatory adjustment, and exposure to extreme temperatures increases their risk of developing pulmonary vascular resistance secondary to peripheral pooling of blood or hypovolemia (30). Understanding the pathophysiology and clinical course of heat-related illnesses such as heatstroke is also relevant (31). The hypothesized pathway is that patients with heatstroke may develop an intravascular coagulation due to the heat-induced release of IL-1 or IL-6 into the systemic circulation. This results in damage to the vascular endothelium and in a diffuse microvascular



**Figure 2.** Pooled exposure-response curves (asterisk) and 95% confidence intervals between maximum apparent temperature and daily hospital admissions for respiratory causes by age group in North-Continental (top row) and Mediterranean (bottom row) cities. The x-axes show maximum apparent temperature (°C) (lag 0–3). The y-axes represent natural logarithm of the absolute risk of admissions, centered at 0.

**TABLE 3. POOLED ESTIMATES OF THE EFFECT OF MAXIMUM APPARENT TEMPERATURE ON HOSPITAL ADMISSIONS FOR CARDIOVASCULAR, CEREBROVASCULAR, AND RESPIRATORY CAUSES BY AGE GROUP. MEDITERRANEAN AND NORTH-CONTINENTAL CITIES**

	% Change (95% CI)*	
	Mediterranean cities	North-Continental cities
<b>Cardiovascular causes</b>		
All ages	-0.6 (-1.8 to 0.5)	-0.6 (-1.2 to 0.1)
65-74 age group	-0.5 (-2.7 to 1.7)	-1.1 (-2.3 to 0.1)
75+ age group	-1.1 (-2.5 to 0.3)	-0.6 (-1.4 to 0.3)
<b>Cerebrovascular causes</b>		
All ages	-0.7 (-3.0 to 1.6)	-1.1 (-2.5 to 0.2)
65-74 age group	0.4 (-3.1 to 4.0)	-1.6 (-4.2 to 1.1)
75+ age group	-1.9 (-4.2 to 0.5)	-1.3 (-3.1 to 0.6)
<b>Respiratory causes</b>		
All ages	2.1 (0.6 to 3.6)	1.2 (0.1 to 2.2)
65-74 age group	-0.3 (-4.1 to 3.6)	2.7 (-0.3 to 6.0)
75+ age group	4.5 (1.9 to 7.3)	3.1 (0.8 to 5.5)

Definition of abbreviation: CI = confidence interval.

\* Percentage change in hospital admissions for 1°C increase over the 90th percentile of maximum apparent temperature (°C) (lag 0-3).

thrombosis through the hyperactivation of endothelial cells and leukocytes and the activation of coagulation and inhibition of fibrinolysis; these vascular changes may trigger a respiratory distress syndrome through the activation of the complement system (32). Because chronic respiratory disease has been found to be an important risk indicator of increases in mortality among in-hospital patients during hot days (27), this is an area where further research and development are clearly needed, especially because the burden of such diseases is expected to grow in developed countries as a consequence of population aging (33).

Our estimates of the effect of heat on respiratory admissions show considerable geographical variability in European cities. Overall, a greater heat impact was observed in the Mediterranean cities, suggesting that even in cities where hot temperatures occur frequently and where populations and health care providers are more capable of adapting to these conditions, heat can cause a considerable burden in admissions or deaths in the elderly population. Heterogeneity in the effect of heat on mortality and morbidity outcomes has been described (12, 27, 34, 35) and may be explained by differences in the intensity of exposure, by a different susceptibility of the populations under study, or by heterogeneity in health and social care services. Across European countries, there is wide variation in systems for the delivery of health care, such as admission policies, availability of hospital beds, and the classification of the diagnoses. For a specific disease, the probability of being admitted to a hospital may vary for a number of reasons, including the availability of primary care and out-patient services, social care arrangements, levels of socioeconomic deprivation, and customs of clinical management.

The aim of this study was to evaluate the effect of heat on acute hospital admissions; however, a specific code identifying acute admissions was available in only eight cities. The selection procedure adopted in the other cities might have increased the heterogeneity. Moreover, in accordance with the study protocol, only the main discharge diagnosis was considered, and this could have influenced our results. The hospitalization rates obtained for the first-listed diagnosis may under-represent the actual number of admissions associated with a specific disease. This might have been more completely assessed by including other recorded diagnoses in the analysis. In the Chicago 1995 heat wave study, researchers found only a small increase in cardiovascular and respiratory disease as a primary discharge

diagnosis, but when all discharge diagnoses were considered, they detected significant heat wave related increases in cardiovascular and respiratory causes (3). A further point of discussion is about the exposure indicator. In the present study,  $T_{appmax}$ , with a lag of up to 3 days, was used, and sensitivity analysis with mean and minimum apparent temperature did not substantially alter our results (data not shown). Apparent temperature has been used in other studies assessing the effect of heat (12, 22, 27, 34). However, time series analyses have considered a range of different exposure variables, including temperature alone (i.e., minimum, mean, and maximum) (5-7) or combined indexes (19). An important issue in our study is the control of the confounding effect of air pollution. We added a linear term for maximum 1-hour daily value of  $NO_2$  (lag 0-1) to the model because it was available in a greater number of cities and is a good indicator of traffic pollution. In a sensitivity analysis for the six cities with available data, risk estimates based on adjustment for ozone in addition to  $NO_2$  did not substantially differ from those adjusted for  $NO_2$  alone (results available upon request).

In conclusion, the results of this multicenter European PHEWE project strengthen the evidence that high temperatures have an impact on hospital admissions for respiratory causes. This effect is more evident in the elderly population, which is consistent with their reduced capacity for coping with heat stress. The mechanisms underlying the rapid deterioration of the respiratory health in people with chronic respiratory diseases during hot weather are not well understood. These findings are important for public health because the prevalence of chronic diseases, such as COPD, is expected to increase in developed countries as a result of population aging (33). Under climate change scenarios, the increase in extreme weather events and certain air pollutants, especially ozone (1), are likely to further aggravate chronic respiratory diseases. Public health interventions should be directed at preventing this additional burden of disease during the summer season. The observed heterogeneity of the health effect among cities indicates a need to tailor programs for individual cities.

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