Effects of hot nights on mortality in South Europe

Dominic Royé[1,2]*, Francesco Sera[3], Aurelio Tobías[4,5], Rachel Lowe[6], Antonio Gasparrini[3], Mathilde Pascal[7], Francesca de'Donato[8], Baltazar Nunes[9], Joao Paulo Teixeira[10]

[1]Department of Geography, University of Santiago de Compostela, Santiago de Compostela, Spain
[2]CIBER of Epidemiology and Public Health (CIBERESP), Spain
[3]Department of Public Health Environments and Society, London School of Hygiene & Tropical Medicine, London, United Kingdom
[4]Institute of Environmental Assessment and Water Research (IDAEA), Spanish Council for Scientific Research (CSIC), Barcelona, Spain
[5]School of Tropical Medicine and Global Health, Nagasaki University, Nagasaki, Japan.
[6]Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, United Kingdom
[7]Santé Publique France , Department of Environmental Health, French National Public Health Agency, Saint Maurice, France
[8]Department of Epidemiology, Lazio Regional Health Service, Rome, Italy
[9]Department of Epidemiology, Instituto Nacional de Saúde Dr Ricardo Jorge
[10]Department of Enviromental Health, Instituto Nacional de Saúde Dr Ricardo Jorge

Running title: Effects of hot nights on mortality.

***Corresponding author**:

Dominic Royé
Faculty of Geography and History
University of Santiago de Compostela
Praza Universidade 1
15782 Santiago de Compostela, Spain
Email: dominic.roye@usc.es

The authors declare they have no actual or potential competing financial interests.

ABSTRACT

Background:

There is strong evidence concerning the impact of heat stress on mortality, particularly from high temperatures. However, few studies emphasise the importance of hot nights. In cases of high night temperatures, thermal stress persists and is aggravated by the fact that the human body is prevented from nocturnal rest. The effect of nighttime thermal environment on mortality has been recently explored using different approaches.

Objectives:

In this study, we assess the efficacy of using hot night duration and hot night excess to predict daily cause-specific mortality in summer, using multiple cities in several countries in Southern Europe.

Methods:

We fitted time series regression models to summer cause-specific mortality, including natural, respiratory and cardiovascular causes, in 11 cities across four countries. We included a distributed lag non-linear model with lags up to 7 days for Hot Night duration [HNd] and Hot Night excess [HNe] adjusted by daily mean temperature. City-specific associations were summarised as overall-cumulative exposure-response curves at the country level using meta-analytic techniques.

Results:

We found a positive association between the relative risk of cause-specific mortality and HNd and HNe with a non-linear convex relationship in most cities; the higher the duration or excess, the higher the risk of mortality. The effects of HNd were only significantly associated in Portugal with risks of 1.29 (95% confidence interval [CI], 1.07 to 1.54) for nonaccidental mortality. However, we also found positive effects for Rome and Madrid in specific-city analyses. The HNe showed risks which ranged from 1.12 (95% CI, 1.05 to 1.20) for France to 1.37 (95% CI, 1.26 to 1.48) for Portugal. The risk estimates for HNe were clearly higher than for HNd in all countries and cities.

Conclusions:

This study provides new evidence that, over a wider range of locations, hot night indices are strongly associated with cause-specific deaths. Modelling the impact of thermal characteristics during summer nights on mortality will help to improve decision making for preventive actions in the context of public health strategies.

Keywords: mortality, hot nights, human health, climate change, tropical nights

Introduction

The impact of the thermal environment on human health, comfort and performance is one of the most important public health issues related to global climate change. The effects of heat and heatwaves on population health have been described by numerous studies, which have established clear relationships between high temperatures and mortality[1-3].

During the summer period, heatwaves are a recurrent phenomenon in temperate climates, especially in southern European regions. In the last decade, a considerable increase in the number of heatwaves has been observed on a global and regional scale (4-7). The latest IPCC Working Group II report[8] indicated that the frequency and excess of extreme heat episodes have most probably been increased due to the process of global warming. The IPCC also stated that it is highly likely that there will be more warm days and nights, which may not always be associated with heatwaves. There is also clear statistical evidence of a significant increase in minimum temperatures recorded in 70-75% of continental measurements[9].

Several studies have shown a significant association between an increased risk of mortality and a lower diurnal temperature variability due to increased minimum temperatures[10-12]. High night temperatures, along with high diurnal temperatures, can result in prolonged thermal stress, which is aggravated by the fact that the human body is prevented from nocturnal rest. The most common impact of hot nights on human health is on sleep and rest. Heat can lead to alteration and deprivation of sleep due to the necessary processes of thermoregulation[13-19]. In addition, nighttime exposure may be exacerbated in some areas due to the urban heat island effect or energy poverty, as was seen in Paris during the 2003 heat wave[20].

Most time-series studies have focused on daily maximum temperatures when studying the impact of heatwaves on human health[1,21-22]. Although studies are using the daily mean temperature, which reflects high night temperatures, the focus was on daytime or overall effects over the whole day[1-3]. Recently Murage et al.[18] and Royé[17] quantified the effects of the night thermal environment on mortality using indices based on hourly or sub-hourly temperature data. In particular, the indices developed by Royé[17] focused on the excess and duration of thermal stress, which potentially have synergistic effects. These studies used different analytical approaches and were based on a single population.

This study aimed to quantify the independent effects of nighttime (time between sunset and sunrise) temperatures on mortality in different Southern European cities, characterised by different climate and socioeconomic characteristics. The assessment was made using a common analytical approach that takes into account the complex association between nighttime temperatures and mortality.

Methods

Data collection

The study area included 11 cities from Portugal (Porto, Lisbon), Spain (Bilbao, Madrid, Barcelona, Seville), France (Marseille, Montpellier, Nice, Toulouse) and Italy (Rome) (Table S1). Daily counts of deaths for natural (ICD-10: A00-R99) or all-cause, respiratory (ICD-10: J00-J99) and cardiovascular (ICD-10: I00-I99) causes were assembled from these locations for the period 2000 to 2014 through the MCC Collaborative Research Network (http://mccstudy.lshtm.ac.uk). For Portugal, data was collated for the period 2000 - 2012 and for Italy, between 2001 - 2010. Southern European cities were chosen in climatic terms within the MCC database; in addition, those cities with readily available hourly temperature data were finally selected for this study.

The selection of the period is based on the availability of hourly temperature data, which is available from 2000 onwards. The meteorological data was extracted from a single weather station by city, most of which were located at the main airport, vía the Integrated Surface Global Hourly Dataset for Portugal, Spain and Italy, accessible via the National Oceanic and Atmospheric Administration (NOAA) (https://www.ncdc.noaa.gov/isd), and vía the French national meteorological service (Météo-France) for the French cities. Despite finer temporal resolution in some cities, hourly average air temperatures were calculated for all locations. Missing values (less than 2.4%) were estimated employing linear regression using the nearest weather station . A descriptive data summary of all included locations is presented in Table 1.

Hot night indices

The indicator proposed by Royé[17] relies on hourly air temperature data during hour i in day j, (T_{ij}). The Hot Night duration (HNd) index, which describes the duration of the heat effect, is calculated as the sum of hours during the nighttime (time between sunset and sunrise) for which a temperature threshold (T_{thr}) is exceeded. Subsequently, the value obtained is divided by the total number of night hours, to allow direct comparisons between all nights in the year. Therefore, HNd is expressed as a percentage of night hours exceeding a threshold (Eq. 1):

$$HNd_j = \frac{\sum_{i=1}^{n_j} \mathrm{I}_{Tthr}(t_{ij})}{n_j} \cdot 100 \qquad (1)$$

where: n_j is the number of night hours of day j, t_{ij}: mean temperature during the hour *i* in day *j*, and I_{Tthr} the index function of $\{x \in \mathbb{R} \mid x > T_{thr}\}$, that is:

$$\mathrm{I}_{Tthr}\left(t_{ij}\right) = \begin{cases} 0 \; if \; t_{ij} < Tthr \\ 1 \; if \; t_{ij} \geq Tthr \end{cases}$$

A second index (Eq. 2), Hot Night excess (HNe) in °C, allowing for the evaluation of the excess of nocturnal thermal stress, is obtained through the sum of excess heat during the period with temperatures equal to or greater than Tthr.

$$HNe_j = \sum_{i=1}^{n_j} (t_{ij} - Tthr) \cdot \mathrm{I}_{Tthr}(t_{ij}) \tag{2}$$

We defined T_{thr} as 20°C, which is the threshold used to define tropical nights (minimum temperature greater than or equal to 20°C)[23]. The night is defined as the period between sunset (day t) and sunrise (day t+1). The analysis were carried out with the statistical environment R. The Sun-methods maptools package, which uses the NOAA algorithm, was used to calculate the number of hours between sunset and sunrise.

Statistical analysis

The night heat-mortality relationship was determined using a two-stage time series analysis described in previous studies[1-2]. In the first stage, the city-specific night-index-mortality associations were estimated for each index separately only adjusted by daily mean temperature through quasi-Poisson regression with distributed lag non-linear models (DLNMs)[24-25]. The cross-basis function of HNd and HNe was defined using a natural cubic B-spline function for the night-index dimension, with three internal knots at equally-spaced percentiles of the city-specific index distributions, and a natural spline parametrisation over lag 0-7 with three internal knots placed at equal intervals on the log scale.
The daily mean temperature was considered a confounder and parametrised with a natural cubic B-spline function for the temperature dimension, with three internal knots at equally-spaced percentiles of the location-specific index distributions, and a natural spline parametrisation over lag 0-7 with three internal knots placed at equal intervals on the log scale. To control for long-term trends and residual seasonality, we included interaction terms between a natural cubic B-spline function with 4 degrees of freedom (df) for the day of the year and indicators of year, along with an indicator of the day of the week. The possible effects from air pollution are not included since the effect size is considered small and the cases of adjustment for air pollution in temperature studies are the exceptions[26].

As HNd (> 0%) only occur during the summer months, the analysis was restricted to the period May to October. The selection of the df was made by using the quasi-Akaike Information Criterion (QAIC)[27], and then set for all cities equally. The reference values to calculate relative risks (RR) were 0% for HNd and 0°C for HNe.

In the second stage, we derived the pooled estimates overall across the analysed countries for HNd and HNe applying a multivariate random-effects meta-analysis[28]. We tested the presence of heterogeneity using the I^2 statistic[29]. The main results are presented as overall relative risks calculated at the 95th percentile of the country-specific indicator distribution. All models, statistical analysis and graphic results were performed with the free software environment R, version 3.6.1[30]. The models used in this study have been estimated through {mgcv}, version 1.8-28, and {dlnm} packages, version 2.3.9. For the meta-analysis, the {mixmeta} package, version 1.05, was applied.

Sensitivity Analyses

To examine the robustness of our results, we performed a sensitivity analysis. We modified several features of the city-specific models as follows: 1) changing the number of lagged days from 7 to 5, 10 and 14, 2) checking for non-linearity in the exposure-response association from the DLNM versus linear fit, 3) exploring the predictive ability of the new hot night indices concerning traditional indices without adjustment by another index (daily minimum, mean and maximum temperature, temperature at 00:00, 02:00, 04:00 and 06:00) and 4) evaluating if the hot night indices had an independent effect by adjusting for traditional indices with the same exposure parametrisation.

Results

The analysed cities in the study are characterised by different climate and socioeconomic features (Table S1, Figure S1). Summary statistics of the meteorological variables and mortality counts are shown in Table 1 . The mortality data includes 759,818 nonaccidental deaths, 69,208 respiratory deaths and 236,839 deaths due to cardiovascular causes, occurring during the warmer months (May to October) in the 11 cities. Minimum temperatures (percentile 95%) ranged from 19°C in Bilbao to 23.1°C in Barcelona, reflecting a geographically coherent pattern as it delineates some of the physiographic and landscape units in the affected countries, particularly a north-south gradient (temperate oceanic to Mediterranean climate) and continental influence. The median of daily HNd varies between 55.6% and 100%, with the highest values found in cities on the Mediterranean coast (see Figures S2-3). The highest excess values of HNe were found in Spanish cities. The lowest degree of hot night excess was observed in Porto and Bilbao with less than 5°C; due to their Atlantic coast location. Figure 1 shows the distribution of the thermal night indices for all analysed cities (see Figure S1). It shows a coherent variability expected due to climate differences. Nice and Barcelona clearly stand out in their high median value at 100% of HNd. In both Portuguese cities, a high number of extreme HNe values were observed, which could be related to physiographic factors. Note, a high value of HNd does not necessarily result in high night excess; this is related to small differences between nighttime hours and the threshold.

The impacts of hot nights on mortality relative risk are summarised in Figure 2-4 and Table 2. The country-specific association between mortality and HNe (excess), adjusted for daily mean temperature, was positive with a non-linear convex increase in relative risk (RR).. For nonaccidental causes, the highest risk (95th percentile of the indicator distribution) was observed in Portugal with a RR of 1.37 (95% CI: 1.26-1.48) at 56.5°C of night excess and the lowest risk in France with 1.12 (95% CI: 1.05-1.20) at 47.5°C. For respiratory causes, the mortality increases with regard to HNe showed a different pattern. The highest risk was observed in Italy with a RR of 1.86 (95% CI: 1.52-2.27) at 53.1°C of night excess (95% percentile). Figure 5 reports the relative risk for all analysed cities at the 95th percentile predicted for both hot night indices (see also Figure S4-7). The highest mortality risks were observed in Portuguese cities. The same pattern was found using a fixed excess of 50°C with the exception of respiratory causes, in which high mortality risks were also observed in Nice, France (see Figure S4). A mortality risk for Nice and Toulouse was found in nonaccidental causes with a RR for the HNe index equal to 1.17 (95% CI: 1.03-1.32) and 1.19 (95% CI: 1.05-1.35), respectively. The mortality risks for respiratory diseases appeared to be higher than those of cardiovascular causes. Furthermore, in all analysed cities/countries, RR was greater for the HNe index than of the HNd at the 95% percentile of the indicator distribution (Table 2, Figure 5).

The results for HNd revealed that, after adjusting for daily mean temperature, only Portugal showed significant effects at the 95th percentile with a RR of 1.29 (95% CI: 1.07-1.54) for nonaccidental and 1.49 (95% CI: 1.11-2.00) for respiratory causes (Table 2). Nevertheless, the city-specific results for Rome and Madrid clearly stand out; an overall risk of 1.07 (95% CI: 1.03-1.12) and 1.12 (95% CI: 1.04-1.20) were estimated at the 95th percentile. The maximum effects of HNd were reached with 100%, which is equal to a tropical night in the classical sense, in which the minimum temperature does not fall below the threshold of 20°C. The 95% percentile of HNd was 100% in all analysed cities (see Table 1), which allowed a comparison at the same value.

The lag structure showed at least in half of the citiesimmediate effects between hot night indices and mortality, with the highest risks found on the same day and decreasing steadily up to 3 or 4 days after the exposure in all cities (Figure S8-9). Although the maximum effect was observed three or four days after the exposure event in Portuguese cities, in particular in Lisbon, there was no significant effect on the same day.

The results were robust to changes in the lag structure of 7 days, different lags (5, 10 and 14 days) were analysed (Table S2). In the sensitivity analysis, the check for linearity in the exposure parametrisation resulted in clear evidence of a non-linear association between the hot night indices and the health outcome for all analysed cities (Table S3). Besides, the predictive ability of the hot night indices concerning traditional indices (e.g. Tmin, Tmax, Tmean, Temperature at specific hour) was explored (Table S4). The obtained results showed that in some cities, the proposed indices could fit better than using traditional indices, but in general, no clear pattern of a lower QAIC between the new and traditional indices was found. Finally, the independent effect of hot night indices was evalutated adjusting for usual indices with the same exposure parametrisation as for the night indices (e.g. Tmax, Tmin, Tmean) (Figure S10). For most cities, the results showed an independent effect, particularly for HNe where the model is more stable after adjusting for traditional indices, but the effects seem to disappear in most countries (except for Portugal) for the HNd index. In general, the RR decreased slightly for HNd. However, it is interesting to highlight that with HNe the effects remained similar.

Discussion

The effects of night air temperature on nonaccidental, respiratory and cardiovascular mortality were examined in eleven Southern European cities in four countries using two new thermal indices (Hot Night duration [HNd] and Hot Night excess [HNe]). The study

found strong evidence that daily mortality was associated with HNe and to a lesser extent with HNd in all analysed countries. The results clearly suggest that susceptibility to hot night duration and excess is an essential part of the thermal environment. In particular, high values of HNe proved to be associated with increased cause-specific mortality in some cities. From a physiological standpoint, the results obtained are coherent with the biological mechanisms put forward to explain that changes in the thermal environment at night lead to an increase in cause-specific disorders, which can lead to death.
Air temperatures which are higher than can be considered comfortable can lead to an increase in wakefulness and a decrease in Rapid Eye Movement phases (REM) and Slow-wave Sleep (SWS)[31-33]. Especially the initial stage of sleep, compared with subsequent phases, is described as the most sensitive and can show major alterations due to the accumulative effect of heat stress[32-33]. Nastos and Matzarakis[34] found a statistically significant positive relationship between minimum air temperature and sleep disturbances. Joshi et al.[14] suggested that besides the influence of light and noise, the thermal environment is the most critical parameter that can be modulated to improve sleep quality. Fujii et. al[35] showed that high air temperatures in summer increased fatigue in healthy volunteers. Another study in Cameroon found heat-related headaches, fatigue and negative effects on school performance in a hot indoor environment[36]. Finally, the duration and quality of night sleep are considered to be a risk factor for cardiovascular diseases[37-38]. Palagini et al.[39] made an important connection between sleep loss and the short duration of sleep and increased arterial hypertension, which are very common, often coexisting, phenomena.

Due to the new indices applied as exposure variables and their peculiar characteristics, a comparison with other studies reporting heat effects is limited. The results in this study confirm partially the findings reported in Royé[17], which used the same thermal indices to predict mortality in Barcelona. However, in this study both hot night indices were adjusted by the daily mean temperature, which resulted in a clearly independent effect, particularly for HNe where the model is more stable after adjusting for traditional indices, but the effects seem to disappear in most countries (except for Portugal) for the HNd index. Nevertheless, the results at the country level should be interpreted with caution due to the different number of cities included in the analysis (e.g. Italy includes one city only).

Furthermore, a non-linear convex association between mortality and HNd as well as HNe was observed. This pattern is consistent with findings from previous studies for heat effects on mortality and has been reported in many studies[1,22,40]. Likewise, in our results, a significant proportion of deaths were caused by exposure to moderate hot night duration and excess. The results showed over all countries quasi-direct short-term effects, decreasing risks from the same day of an event of HNd and HNe with a lag of 0-3 days. These findings are in line with the results of heat-related mortality in general[1,3]. However, in this study, higher risks in respiratory diseases are found, which are relevant since the exposure-response association was adjusted by daytime effects. This can be explained by the physiological effects of exposure to heat and, especially, the role of the respiratory system in thermoregulation[41]. Differences between mortality subgroups and even between age groups have been described by several authors[42-43]. The highest mortality risks were found in Portugal. This might be explained by a possible lack of planned or autonomous acclimatisation of the population to hot nights[44], given that the risk in Lisbon was higher than in Porto, which, due to its more southerly location, is characterised by warmer nights. Another possible explanation could be that the outdoor temperature is more representative of real exposure in Portugal than in other countries. In addition, the share of population living in a dwelling not comfortably cool during summertime was higher in Portugal than in other Southern European countries[45]. The growth of cooled floor area per country in the EU between 1990-2010 was observed to be the lowest in Portugal, and the greatest increase was detected in Spain and Italy, which could explain our results partially[46]. The protective effects observed in some cities such as Seville and Barcelona (Spain) could be explained by the psychological or behavioural acclimatisation or, in combination, by the planned adaptation processes since the 2003 heatwave (heat health warning systems, and particularly, air conditioning AC)[44].

In this study, a threshold of 20°C was applied to limit hot night hours, which corresponds to the definition of a tropical night (minimum temperature > 20°C). Royé[17] used the 95th percentile of the minimum temperature as a threshold in the Barcelona study, reaching similar results. Joshi et al.[14] indicated that in several studies, 19°C was found to be the preferred room temperature and deviation from this temperature was accompanied by subjective discomfort. In the case of multicountry studies the main issue is the influence of location on the threshold, using a relative metric could include local acclimation, but at the same time allow low percentile values, which in turn could be in the range of minimum mortality. Another limitation of our study is related to the difference between indoor and outdoor environments, which are important in terms of nighttime thermal environment. For example, in New York, mean nighttime indoor temperatures were higher than the outdoor temperature with AC in summer[47], which could underestimate the relative risk of mortality. In general, the use of AC and thermal balance of buildings are key factors, along with other socioeconomic factors, which could hypothetically influence the metric applied in this study. In Sera et al.[48] an independent association between increased AC prevalence and lower heat-related mortality risk were found, but the increased AC prevalence was responsible only for part of the observed attenuation. Another potential limitation is the location of weather stations. The fact that most monitor stations were located at airports could lead to under or overestimation for certain areas of the city due to the urban heat island effect and other urban factors.

The definition of the night period used in this study (time between sunset and sunrise) could be adapted in such a way that, for example, the twilight phase is excluded. However, we selected sunset and sunrise as the night threshold as they are objective parameters. Therefore, it would be very complex to take into account the time individual people get up or go to bed as this is influenced by many variables, such as cultural aspects, work, age, etc. Further, daily mortality corresponds to deaths occurring in 24 hours of each day, which means that some deaths correspond to the previous night.

Although the proposed hot night indices did not predict better the daily mortality, with a small difference in QAIC performance, they confirm an important nighttime effect. Hence, the findings of this study have important implications for public health, in particular in the context of a changing climate, in which hot nights are becoming more frequent[9]. Obradovich et al.[16] found that climate change may disrupt human sleep with regard to the relationship between sleep and ambient temperature.

Conclusions

Our multicountry time-series analysis provides new evidence that the proposed hot night indices adjusted by daily mean temperature are strongly associated with cause-specific deaths. Hot night excess appears to be the most important thermal variable in all studied cities distributed across a wide geographical area. Encapsulating night heat effects via duration and excess indicators provides a different perspective on heat-related human health impacts. Although apparently, the new indices do not have a greater predictive capacity than the traditional ones, they allow the analysis of the effect of different aspects of exposure (excess and duration) of night heat stress. Another clear advantage as exposure metrics is they more realistically reflect thermal exposure over the entire night period rather than a single-moment temperature, such as minimum temperature. Hence, the use of hourly data allows for a more detailed assessment of the thermal characteristics of summer nights, making it possible to assess the risk of hot nights to population health and wellbeing more accurately. Further research will be necessary to study night heat effects in cities in other climates and examine vulnerable subgroups. In addition, it is also unknown how heat excess and duration relate to one another, when short periods of very high night temperature are more harmful to human health than long high temperatures. In the same sense it would be important to evaluate the optimal predictor of mortality based on night heat in further studies. The results give a better understanding of nighttime effects on health and may help improve decision making for preventive actions, such as refining heatwave warning systems at the population level, in addition to considering individual risk factors.

Acknowledgements: DR was supported by a postdoctoral research followship of the Xunta de Galicia (Spain), RL was supported by a Royal Society Dorothy Hodgkin Fellowship.

|

Table 1. Summary descriptive statistics by city.

Country	City	Period	Number of deaths			P95% Tmin (ºC)	Median HNd (%) [hours]	P95% HNd (ºC)	Median HNe (ºC)	P95% HNe (ºC)
			NA	*RD*	*CVD*					
Spain	Bilbao	2001 - 2014	22,975	1,985	7,042	19.0	62.5 [6]	100	4.5	31.9
	Barcelona	2001 - 2014	99,830	9,478	30,428	23.1	100.0 [8]	100	21.6	57.3
	Madrid	2001 - 2014	170,142	23,746	49,517	20.0	55.6 [5]	100	21.3	67.7
	Seville	2001 - 2014	36,835	2,932	14,541	22.0	66.7 [7]	100	20.1	72.7
Portugal	Lisbon	2000 - 2012	117,880	10,059	44,807	20.0	55.6 [6]	100	6.0	60.5
	Porto	2000 - 2012	79,270	7,660	23,989	17.6	58.3 [5]	100	3.3	45.4
France	Marseille	2000 - 2014	56,552	3,570	16,107	21.3	75.0 [6]	100	12.3	48.6
	Montpellier	2000 - 2014	16,206	942	4,625	21.0	66.7 [6]	100	11.0	44.9
	Nice	2000 - 2014	31,339	1,857	8,882	22.4	100.0 [7]	100	14.3	49.4
	Toulouse	2000 - 2014	30,762	1,573	8,351	19.2	50.0 [4]	100	8.0	45.2
Italy	Rome	2001 - 2010	98,027	5,406	28,550	21.5	80.0 [7]	100	15.3	53.1

NA: nonaccidental; RD: respiratory; CVD: cardiovascular deseases

Table 2. Country-pooled overall cumulative relative risk (95% confidence interval [CI]) of hot nights effect (Hot Night duration [HNd], Hot Night excess [HNe]) on cause-specific mortality for percentile 95% with the inter-country heterogeneity I^2 statistic

	Non-accidental		Respiratory		Cardiovascular	
	HNd [I^2 78.2%]	HNe [I^2 43%]	HNd [I^2 34%]	HNe [I^2 0%]	HN_d [I^2 65%]	HNe [I^2 43%]
Spain	0.98 (0.86-1.12)	**1.16 (1.08-1.25)**	0.99 (0.80-1.23)	**1.30 (1.12-1.51)**	0.91 (0.77-1.07)	1.07 (0.92-1.25)
Portugal	**1.29 (1.07-1.54)**	**1.37 (1.26-1.48)**	**1.49 (1.11-2.00)**	**1.58 (1.27-1.96)**	**1.28 (1.04-1.60)**	**1.41 (1.19-1.66)**
France	1.00 (0.87-1.15)	**1.12 (1.05-1.20)**	1.01 (0.76-1.35)	1.17 (0.92-1.48)	0.97 (0.81-1.15)	1.10 (0.94-1.27)
Italy (Roma)	1.07 (0.84-1.37)	**1.25 (1.13-1.39)**	1.28 (0.88-1.86)	**1.86 (1.52-2.27)**	1.07 (0.80-1.42)	**1.36 (1.07-1.73)**

I^2, the estimated percentage of variation across studies that is due to true heterogeneity rather than chance

References

1. Gasparrini A, Guo Y, Hashizume M, Lavigne E, Zanobetti A, Schwartz J, Tobias A, Tong S, Rocklöv J, Forsberg B, Leone M, De Sario M, Bell ML, Guo YLL, Wu C, Kan H, Yi SM, Coelho M, Saldiva P, Honda Y, Kim H, Armstrong B 2015. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. Lancet 386:369–375. doi 10.1016/S0140-6736(14)62114-0

2. Gasparrini A, Guo Y, Sera F, Vicedo-Cabrera AM, Huber V, Tong S, et al. 2017. Projections of temperature-related excess mortality under climate change scenarios. Lancet Planet Health 1, (9):e360–e367. doi 10.1016/S2542-5196(17)30156-0.

3. Guo Y, Gasparrini A, Armstrong BG, Tawatsupa B, Tobias A, Lavigne E, Coelho MSZS, Pan X, Kim H, Hashizume M, Honda Y, Guo YL, Wu CF, Zanobetti A, Schwartz JD, Bell ML, Scortichini M, Michelozzi P, Punnasiri K, Li S, Tian L, Garcia SDO, Seposo X, Overcenco A, Zeka A, Goodman P, Dang TN, Dung DV, Mayvaneh F, Saldiva PHN, Williams G, Tong S. 2017. Heat Wave and Mortality: A Multicountry, Multicommunity Study. Environmental Health Perspectives, 125, 087006. doi 10.1289/EHP1026.

4. Coumou D, Rahmstorf S 2012. A decade of weather extremes. Nature Climate Change 2:491–496. doi 10.1038/nclimate1452

5. Coumou D, Robinson A 2013. Historic and future increase in the global land area affected by monthly heat extremes. Environ Res Lett 8:034018. doi 10.1088/1748-9326/8/3/034018

6. Guerreiro SB, Dawson RJ, Kilsby C, Lewis E and Ford A 2018. Future heatwaves, droughts and floods in 571 European cities. Environ. Res. Lett. 13:034009. doi 10.1088/1748-9326/aaaad3

7. Guo Y, Gasparrini A, Li S, Sera F, Vicedo-Cabrera AM, de Sousa Zanotti Stagliorio Coelho M, et al. (2018) Quantifying excess deaths related to heatwaves under climate change scenarios: A multicountry time series modelling study. PLoS Med 15(7):e1002629. doi 10.1371/journal.pmed.1002629

8. IPCC (2014) Impacts, adaptation and vulnerability. Tech. rep., Working Group II Contribution to AR5.

9. Smith TT, Zaitchik BF, Gohlke JM 2013. Heat waves in the United States: definitions, patterns and trends. Clim Change 118:811–825. doi 10.1007/s10584-012-0659-2

10. Lim YH, Hong YC, Kim H 2012. Effects of diurnal temperature range on cardiovascular and respiratory hospital admissions in Korea. Sci Total Environ 417-418:55–60. doi 10.1016/j.scitotenv.2011.12.048

11. Luo Y, Zhang Y, Liu T, Rutherford S, Xu Y, Xu X, Wu W, Xiao J, Zeng W, Chu C, Ma W

2013. Lagged effect of diurnal temperature range on mortality in a subtropical megacity of China. PLOS ONE 8(2):e55280. doi 10.1371/journal.pone.0055280

12. Rooney C, McMichael JA, Kovats RS, Coleman MP 1995. Excess mortality in England and Wales, and in Greater London, during the 1995 heatwave. J. Epidemiol. Community Health 52:482–486. doi 10.1136/jech.52.8.482

13. Buguet A 2007. Sleep under extreme environments: Effects of heat and cold exposure, altitude, hyperbaric pressure and microgravity in space. J. Neurol. Sci. 262:145–152. doi 10.1016/j.jns.2007.06.040

14. Joshi SS, Lesser TJ, Olsen JW, O'Hara BF 2016. The importance of temperature and thermoregulation for optimal human sleep. Energy Buildings 131:153–157. doi 10.1016/j.enbuild.2016.09.020

15. Lan L, Tsuzuki K, Liu YF, Lian Z.W 2017. Thermal environment and sleep quality: A review. Energy Buildings 149:101-113. doi 10.1016/j.enbuild.2017.05.043.

16. Obradovich N, Migliorini R, Mednick SC, Fowler JH 2017. Nighttime Temperature And Human Sleep Loss In A Changing Climate. Science Advances 3(5):E1601555. doi 10.1126/sciadv.1601555

17. Royé D. 2017. The effects of hot nights on mortality in Barcelona, Spain. Int J Biometeo. 61(12):2127–2140. doi 10.1007/s00484-017-1416-z

18. Murage P, Hajat S, Kovats RS 2017. Effect of nighttime temperatures on cause and age-specific mortality in London. Environ Epidemiol 1(2):e005. doi 10.1097/EE9.0000000000000005

19. Rifkin DI, Long MW, Perry MJ 2018. Climate change and sleep: A systematic review of the literature and conceptual framework. Sleep Medicine Reviews 42:3-9. doi 10.1016/j.smrv.2018.07.007.

20. Laaidi K, Zeghnoun A, Dousset B, Bretin P, Vandentorren S, Giraudet E, Beaudeau P 2012. The impact of heat islands on mortality in Paris during the August 2003 heat wave. Environ Health Perspect 120:254–259. doi 10.1289/ehp.1103532

21. Díaz J, Carmona R, Miron IJ, Ortiz C, Leon I, Linares C 2015. Geographical variation in relative risks associated with heat: Update of Spain's heat wave prevention plan. Environ. Int. 85:273–283. doi 10.1016/j.envint.2015.09.022

22. Tobías A, García de Olalla P, Linares C, Bleda M, Cayla J, Díaz J 2010. Short-term effects of extreme hot summer temperatures on total daily mortality in Barcelona, Spain. Int J Biometeorol 54:115–117. doi 10.1007/s00484-009-0266-8

23. Alexander LV, Zhang X, Peterson TC, Caesar J, Gleason B, Klein Tank AMG, Haylock M, Collins D, Trewin B, Rahimzadeh F, Tagipour A, Rupa Kumar K, Revadekar J, Griffiths G, Vincent L, Stephenson DB, Burn J, Aguilar E, Brunet M, Taylor M, New M, Zhai P, Rusticucci M, Vazquez-Aguirre JL 2006. Global observed changes in daily climate

extremes of temperature and precipitation. J. Geophys. Res 111:D05, 109. doi 10.1029/2005JD006290

24. Gasparrini A 2011. Distributed lag linear and non-linear models in r: The package dlnm. J Stat Softw 43(8):1–20.

25. Gasparrini A 2014. Modeling exposure-lag-response associations with distributed lag non-linear models. Stat Med 33:881–889. doi 10.1002/sim.5963

26. Gasparrini A, Armstrong B, Kenward MG 2010. Distributed lag non-linear models. Stat Med 29(21):2224–2234, PMID: 20812303, https://doi.org/10.1002/sim.3940.

28. Sera F, Armstrong B, Blangiardo M, Gasparrini A 2019. An extended mixed-effects framework for meta-analysis. Statistics in Medicine 38(29):5429-5444

29. Gasparrini A, Armstrong B, Kenward M 2012. Multivariate meta-analysis for non-linear and other multi-parameter associations. Stat Med, 31:3821-3839

30. R Core Team (2018) R: A language and environment for statistical computing. R Foundation for Statistical Computing.

31. Haskella E, Palcaa J, Walkera J, Bergera R, Hellera H 1981. The effects of high and low ambient temperatures on human sleep stages. Clin. Neurophysiol. 51:494–501.

32. Okamoto-Mizuno K, Mizuno K 2012. Effects of thermal environment on sleep and circadian rhythm. J Physiol Anthropol 31:1:14. doi 10.1186/1880-6805-31-14

33. Okamoto-Mizuno K, Tsuzuki K, Mizuno K 2005. Effects of humid heat exposure in later sleep segments on sleep stages and body temperature in humans. Int J Biometeorol 49:232–237. doi 10.1007/s00484-004-0237-z

34. Nastos PT, Matzarakis A 2008. Human-biometeorological effects on sleep disturbances in Athens, Greece: A preliminary evaluation. Indoor Built Environ 17:535–542. doi 10.1177/1420326X08097706

35. Fujii H, Fukuda S, Narumi D, Ihara T, Watanabe Y 2015. Fatigue and sleep under large summer temperature differences. Environ. Res. 138:17–21. doi 10.1016/j.envres.2015.02.006

36. Dapi LN, Joacim Rocklöv J, Nguefack-Tsague G, Tetanye E, Kjellstrom T 2010. Heat impact on schoolchildren in Cameroon, Africa: potential health threat from climate change. Glob. Health Action 3(1). doi 10.3402/gha.v3i0.5610

37. Nagai M, Hoshide S, Kario K 2010. Sleep duration as a risk factor for cardiovascular disease- a review of the recent literature. Curr Cardiol Rev 6:54–61. doi 10.2174/157340310790231635

38. Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA 2011. Sleep duration

predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. Eur Heart J 32:1484–1492. doi 10.1093/eurheartj/ehr007

39. Palagini L, Bruno R, Gemignani A, Baglioni C, Ghiadoni L, Riemann D 2013. Sleep loss and hypertension: A systematic review. Curr Pharm Des 19(13):2409–2419. doi 10.2174/1381612811319130009

40. Tobías A, Armstrong B, Zuza I, Gasparrini A, Linares C, Diaz J 2012. Mortality on extreme heat days using official thresholds in Spain: A multi-city time series analysis. BMC Public Health 12(133). doi 10.1186/1471-2458-12-133

41. Åström C, Orru H, Rocklöv J, Strandberg G, Ebi K, Forsberg B 2013. Heat-related respiratory hospital admissions in Europe in a changing climate: a health impact assessment. BMJ Open 3:e001842. doi 10.1136/bmjopen-2012- 001842

42. Basagaña X, Sartini C, Barrera-Gómez J, Dadvand P, Cunillera J, Ostro B, Sunyer J, Medina-Ramón M 2011. Heat waves and cause-specific mortality at all ages. Epidemiology 22:765–772. doi 10.1097/EDE.0b013e31823031c5

43. Zhang Y, Li C, Feng R, Zhu Y, Wu K, Tan X, Ma L 2016. The short-term effect of ambient temperature on mortality in Wuhan, China: A time-series study using a distributed lag non-linear model. Int J Environ Res Public Health 2016 13(7):722. doi 10.3390/ijerph13070722

44. Gosling SN, Hondula DM, Bunker A, Ibarreta D, Liu J, Zhang X, Sauerborn R 2017. Adaptation to Climate Change: A Comparative Analysis of Modeling Methods for Heat-Related Mortality. Environmental Health Perspectives 125:8 CID: 087008.

45. Thomson H, Simcock N, Bouzarovski S, Petrova S 2019. Energy poverty and indoor cooling: An overlooked issue in Europe. Energy and Buildings 196 :21-29

46. Pezzutto S, Fazeli R, De Felice M, Sparber W 2016. Future development of the air-conditioning market in Europe: an outlook until 2020. WIREs Energy Environ 5:649-669

47. Quinn A, Kinney P, Shaman J 2017. Predictors of summertime heat index levels in New York City apartments. Indoor Air 27(4):840-851. doi: 10.1111/ina.12367

48. Sera F, Hashizume M, Honda Y, Lavigne E, Schwartz J, Zanobetti A, Tobias A, Iñiguez C, Vicedo-Cabrera AM, Blangiardo M, Armstrong B, Gasparrini A 2020. Air conditioning and heat-related mortality: a multicountry longitudinal study. Epidemiology. In Press.

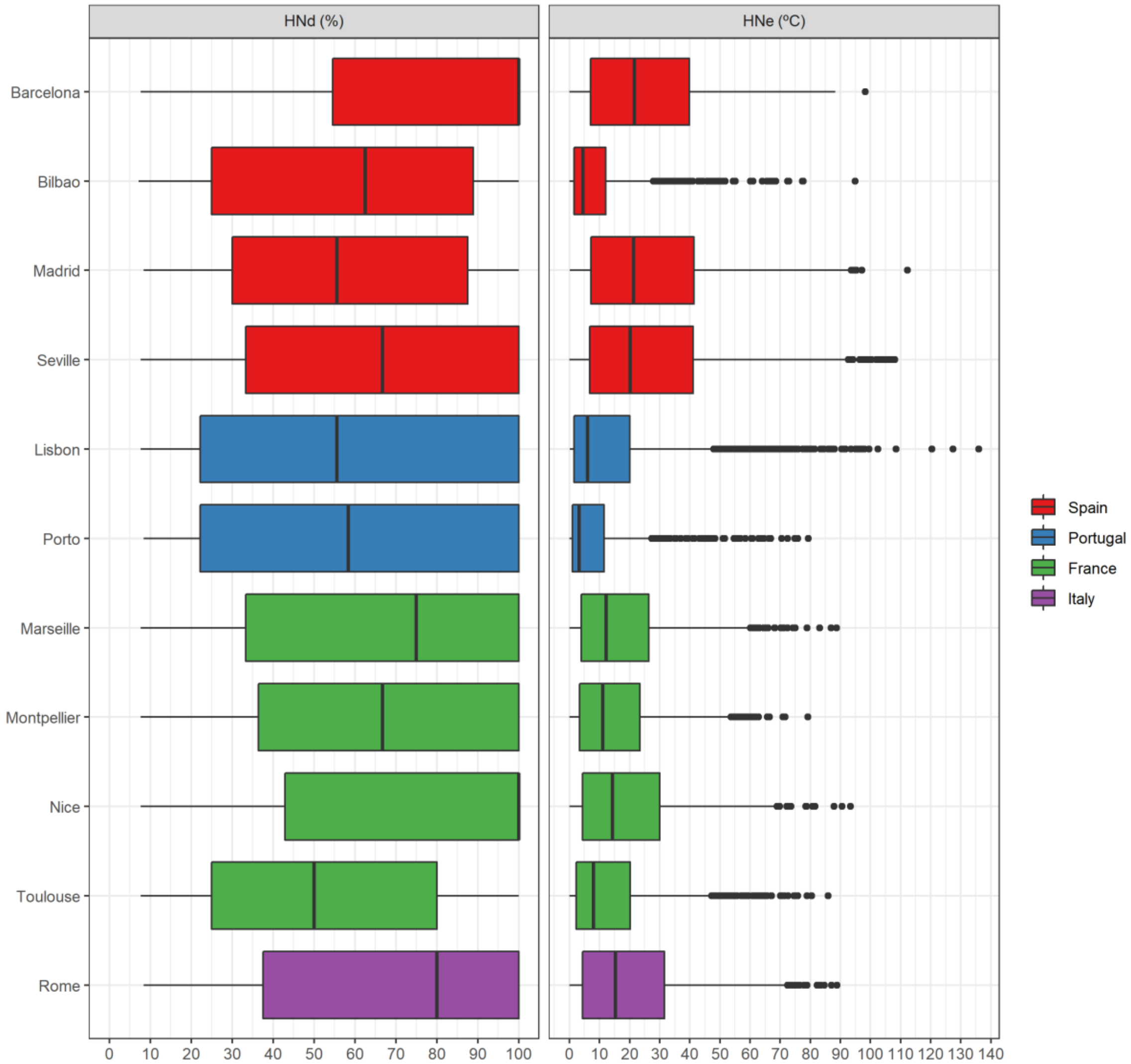


Figure 1. Distribution of HN_d and HNe by city for each study period.

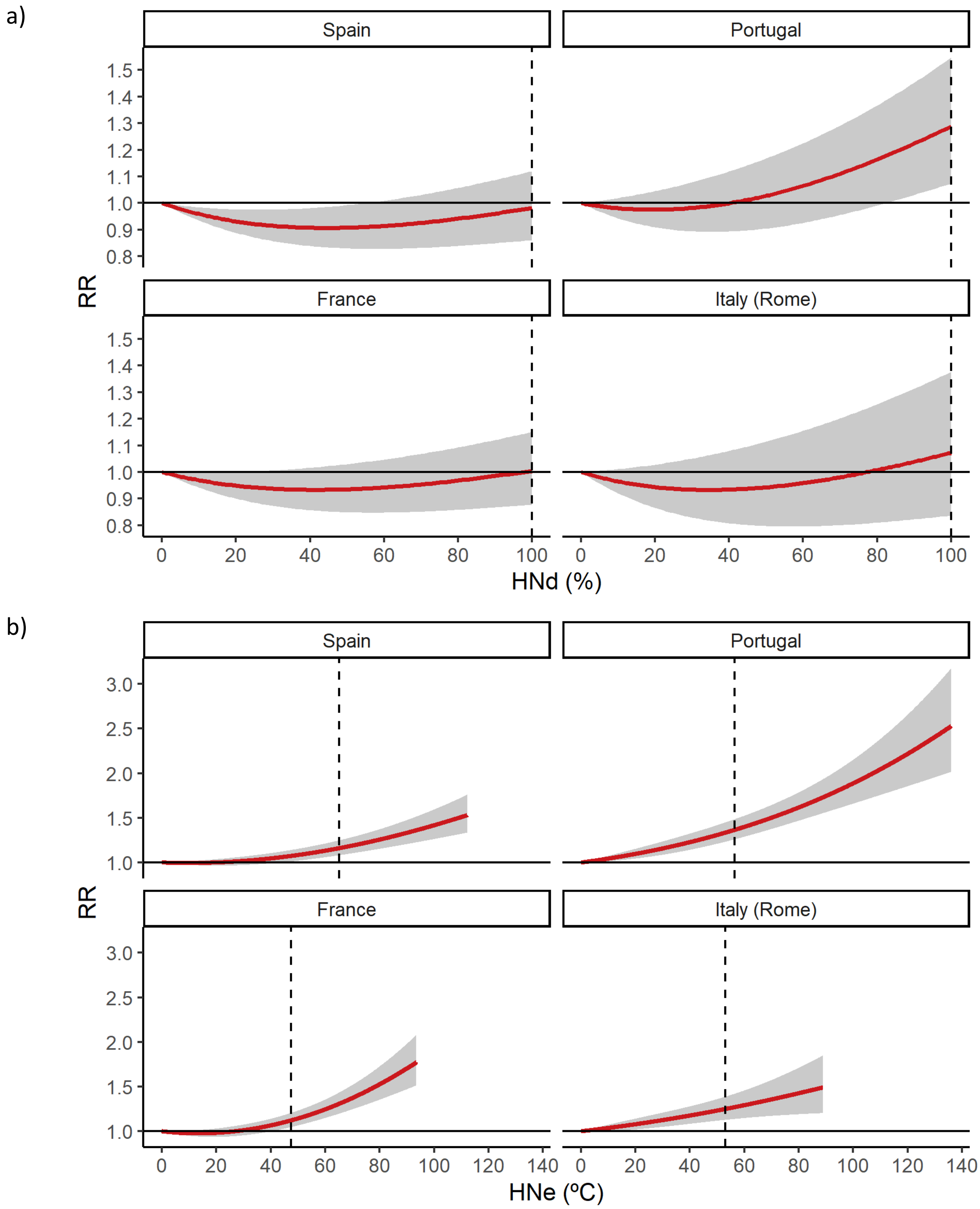


Figure 2. Country-specific overall cumulative exposure-response relationships between hot night indices (a. Hot Night duration [HNd], b. Hot Night excess [HNe]) and nonaccidentalmortality. Dashed vertical line is the 95th percentile.

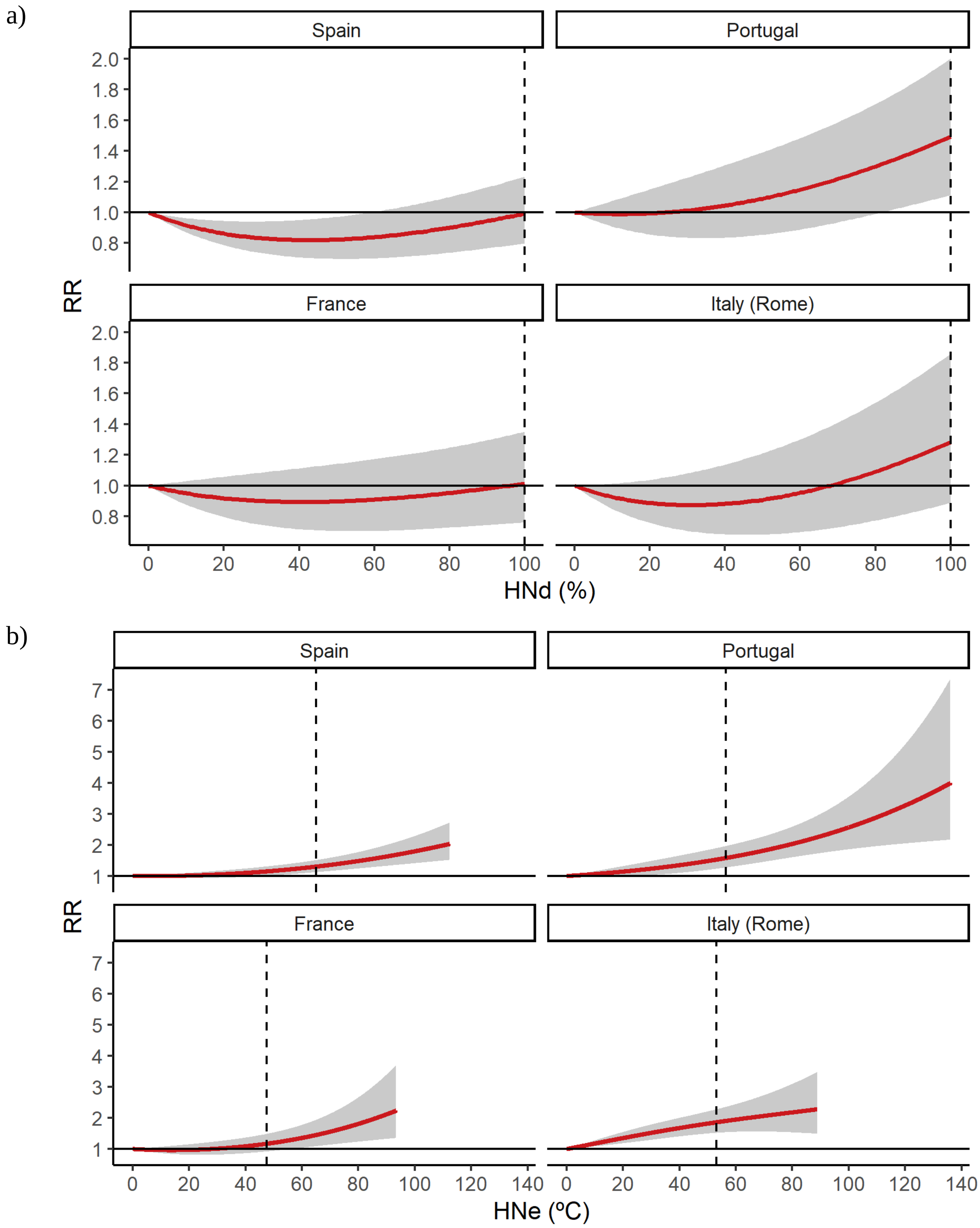


Figure 3. Country-specific overall cumulative exposure-response relationships between hot night indices (a. Hot Night duration [HNd], b. Hot Night excess [HNe]) and respiratory mortality. Dashed vertical line is the 95th percentile.

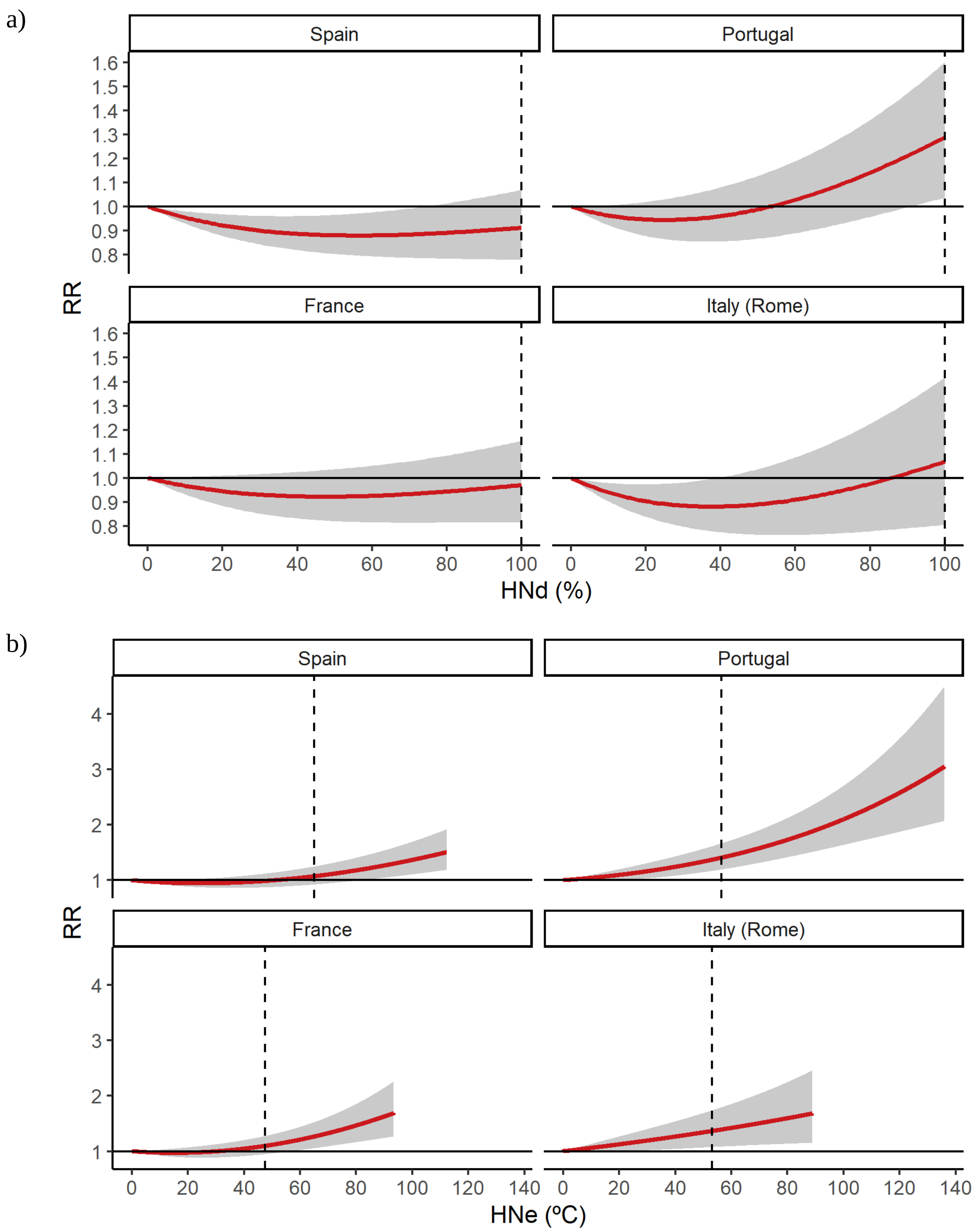


Figure 4. Country-specific overall cumulative exposure-response relationships between hot night indices (a. Hot Night duration [HN_d], b. Hot Night excess [HNe]) and cardiovascular mortality. Dashed vertical line is the 95th percentile.

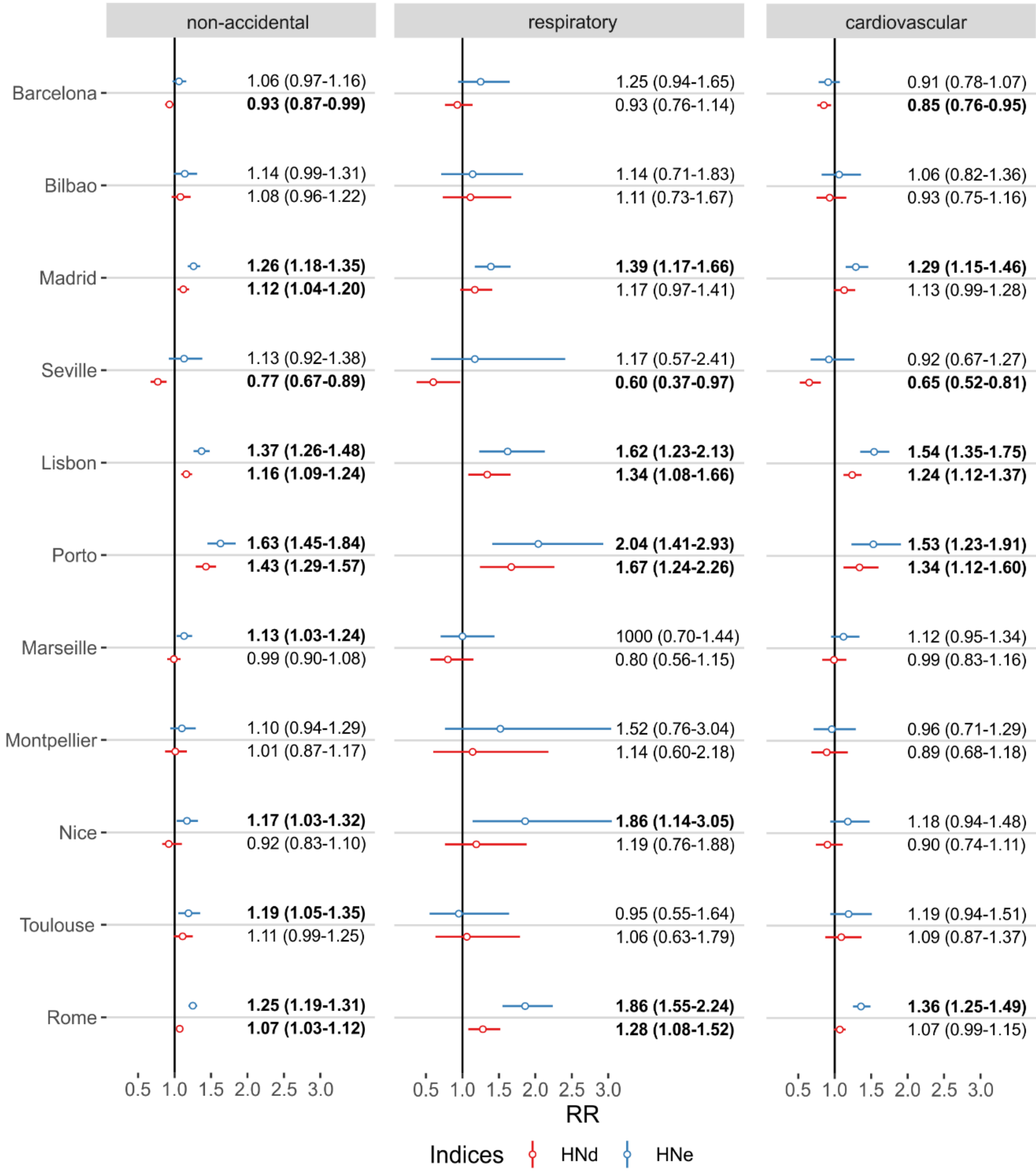


Figure 5. City-specific overall cumulative relative risk (95% confidence interval [CI]) of hot nights effect (Hot Night duration [HNd], Hot Night excess [HNe]) on cause-specific mortality for percentile 95%.

Supplements

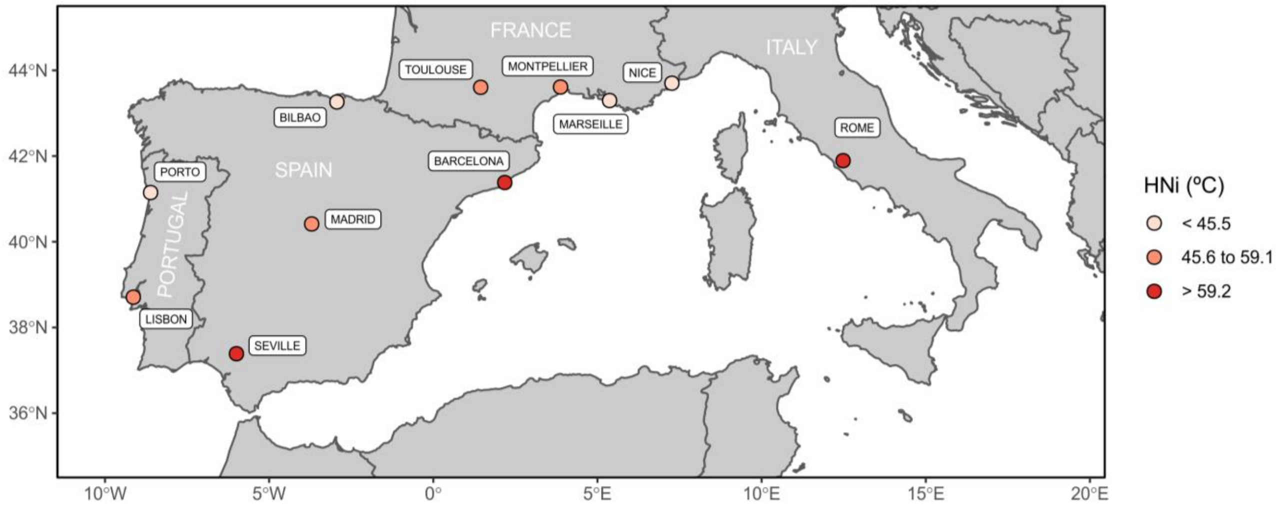


Figure S1. Geographical distribution of city specific Hot Night excess (percentile 95%) of 11 cities of the Multi-City Multi-Country Collaborative Research Network included in the study.

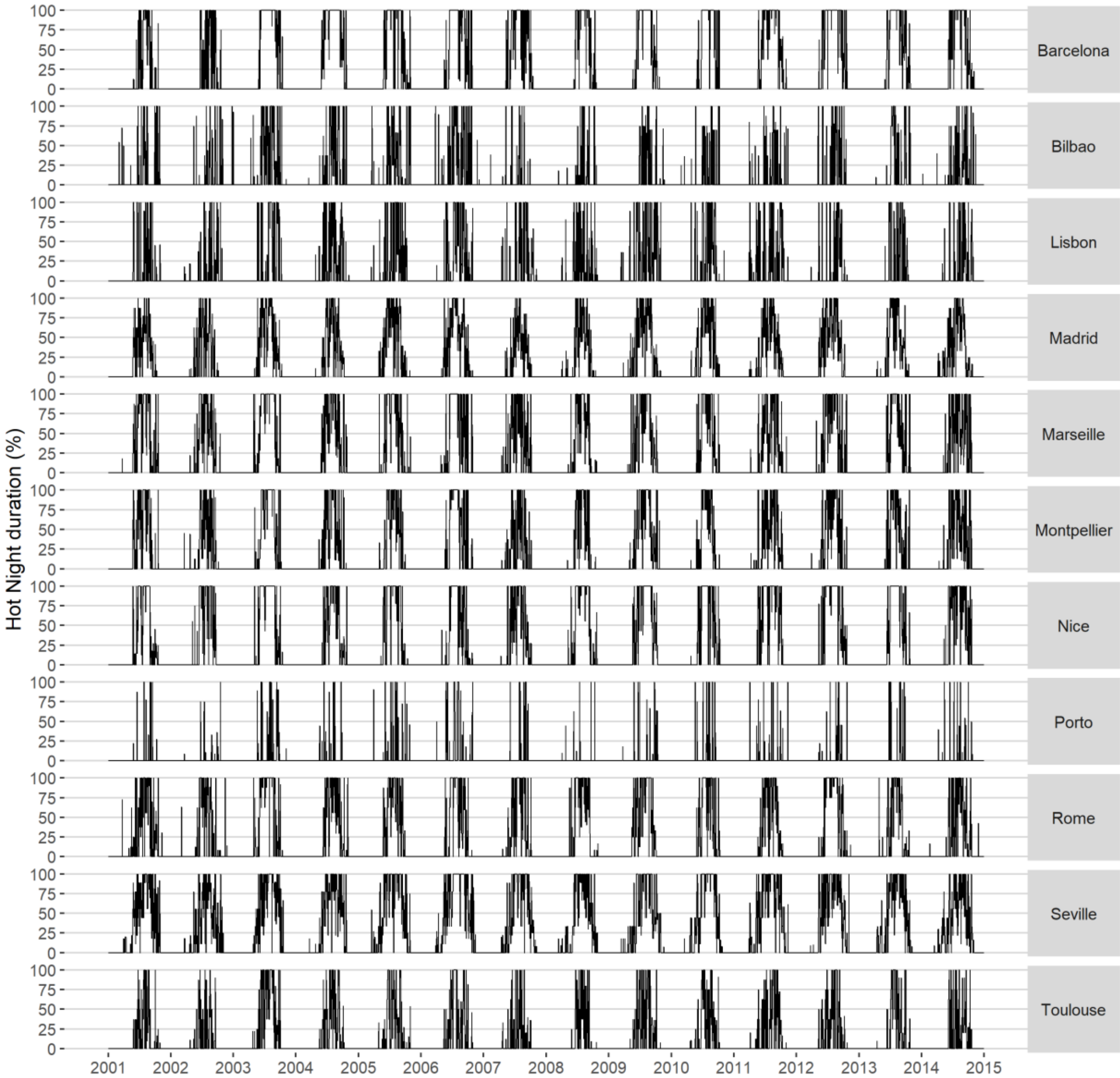


Figure S2. Time series of Hot Night duration for each city.

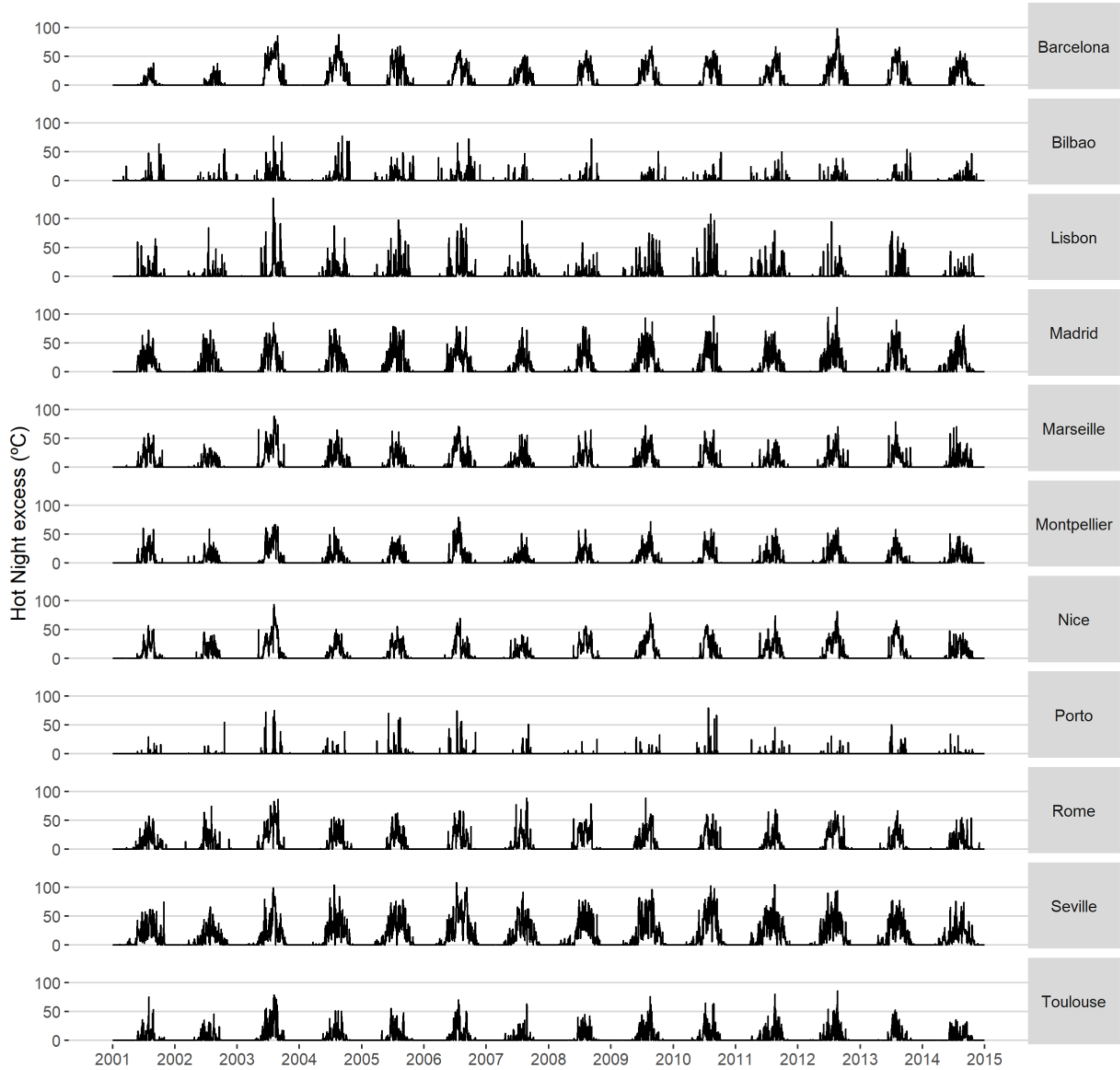


Figure S3. Time series of Hot Night excess for each city.

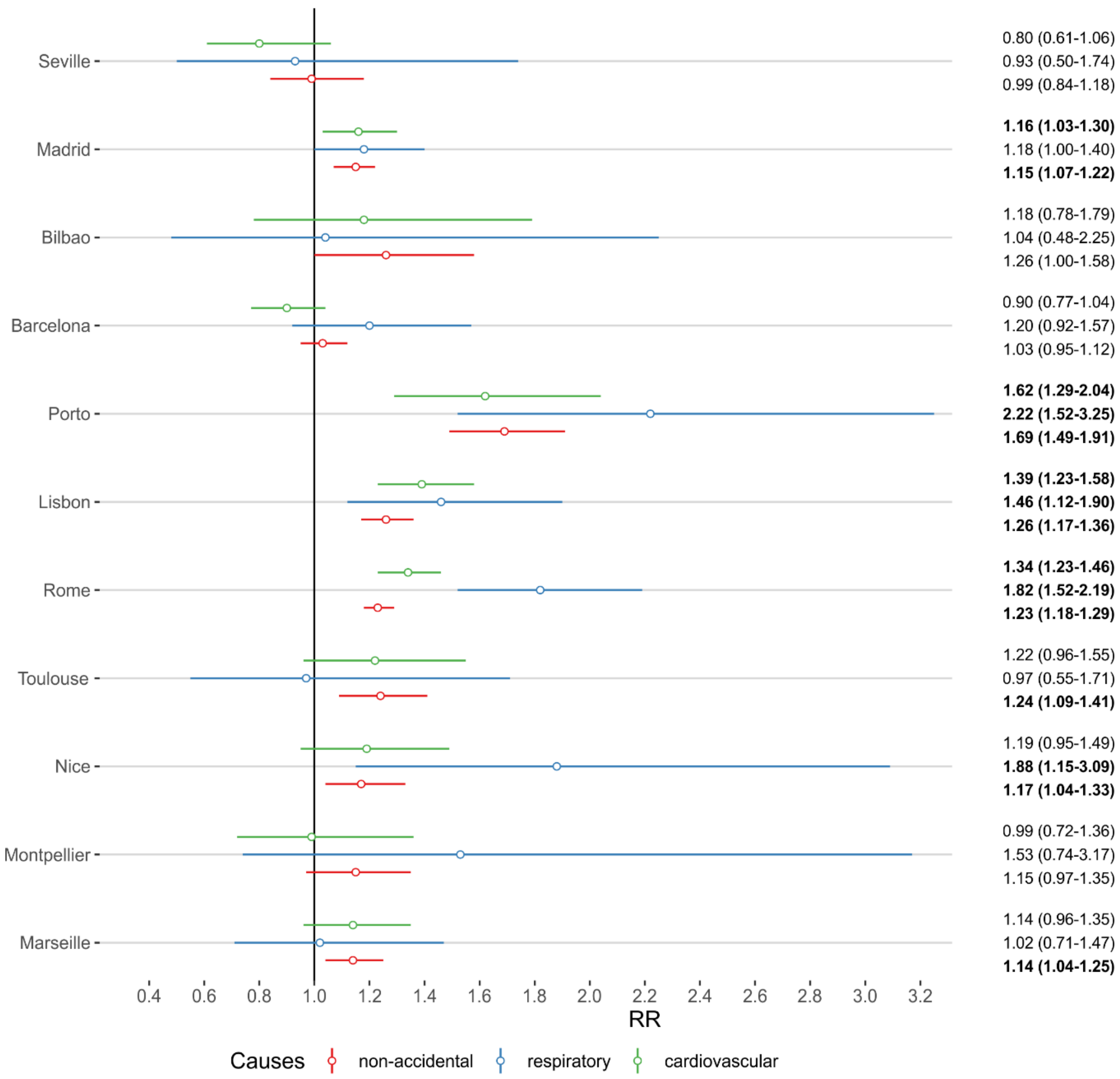
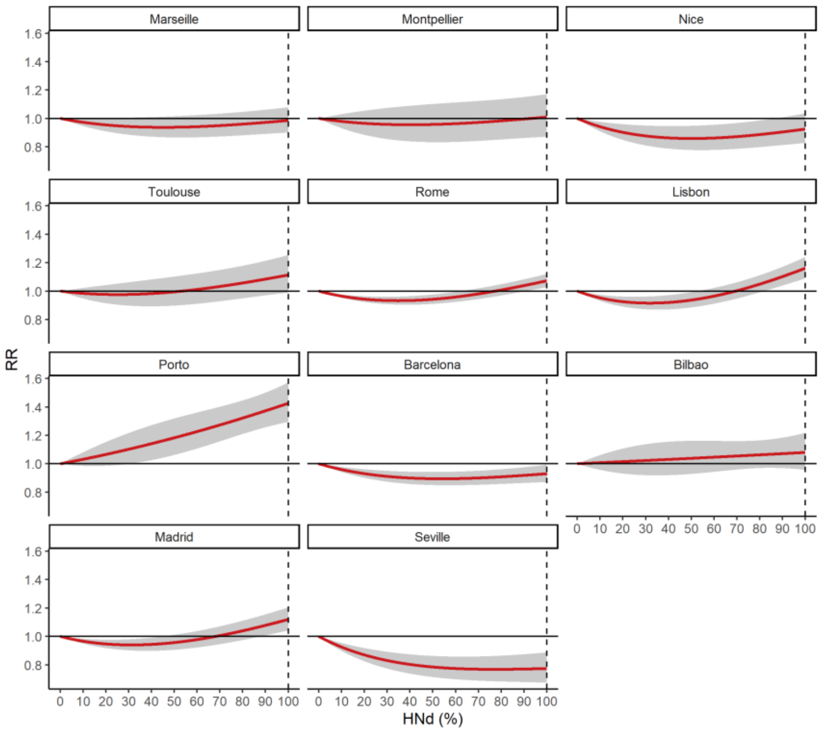


Figure S4. City-specific exposure-response at 50°C of Hot Night excess for cause-specific mortality by city.

a)



b)

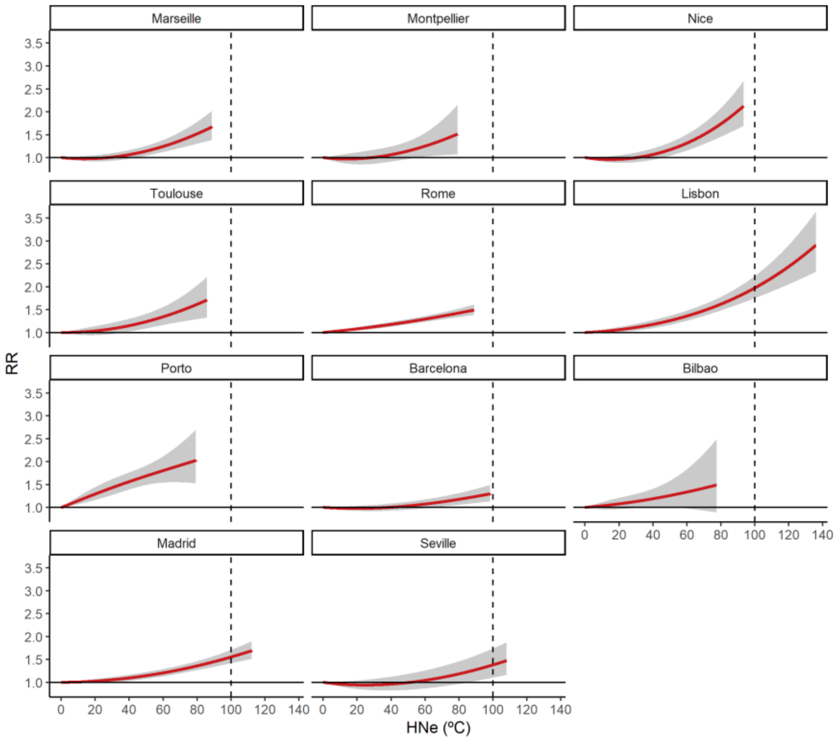
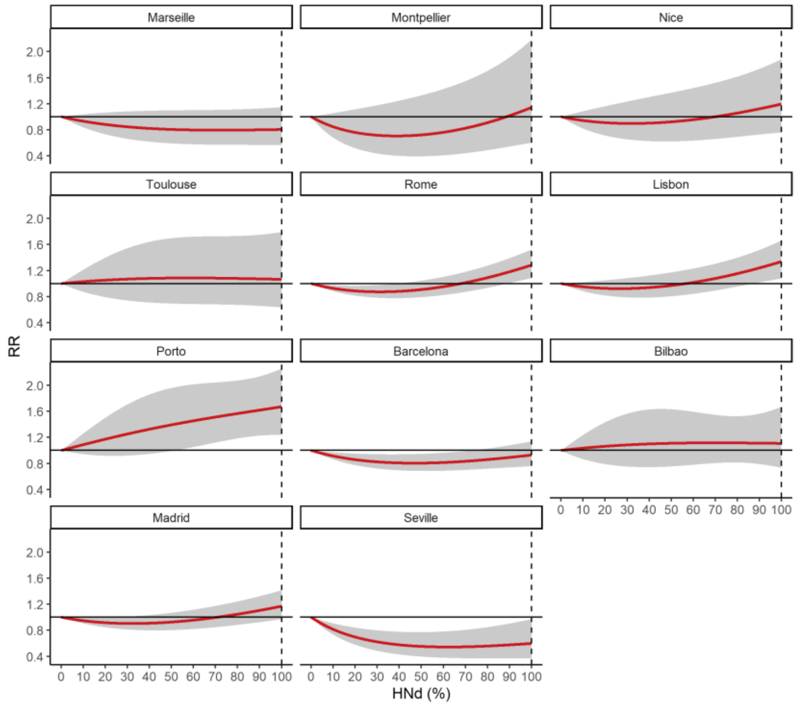


Figure S5. City-specific overall cumulative exposure-response relationships between hot night indices (a. Hot Night duration [HNd], b. Hot Night excess [HNe]) and nonaccidental mortality by city. Dashed vertical line is the 95th percentile.

a)



b)

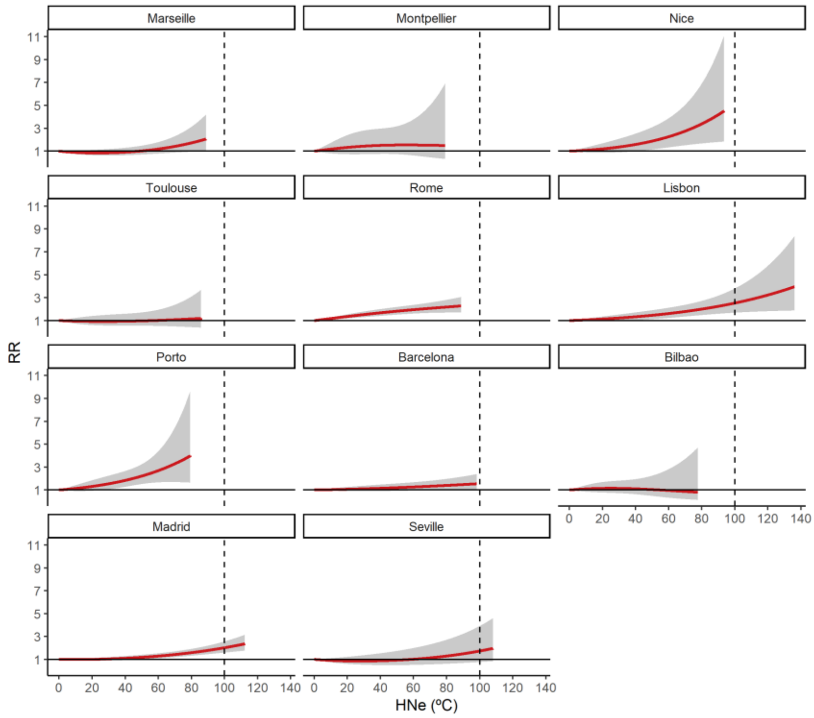


Figure S6. City-specific overall cumulative exposure-response relationships between hot night indices (a. Hot Night duration [HNd], b. Hot Night excess [HNe]) and respiratory mortality by city. Dashed vertical line is the 95th percentile.

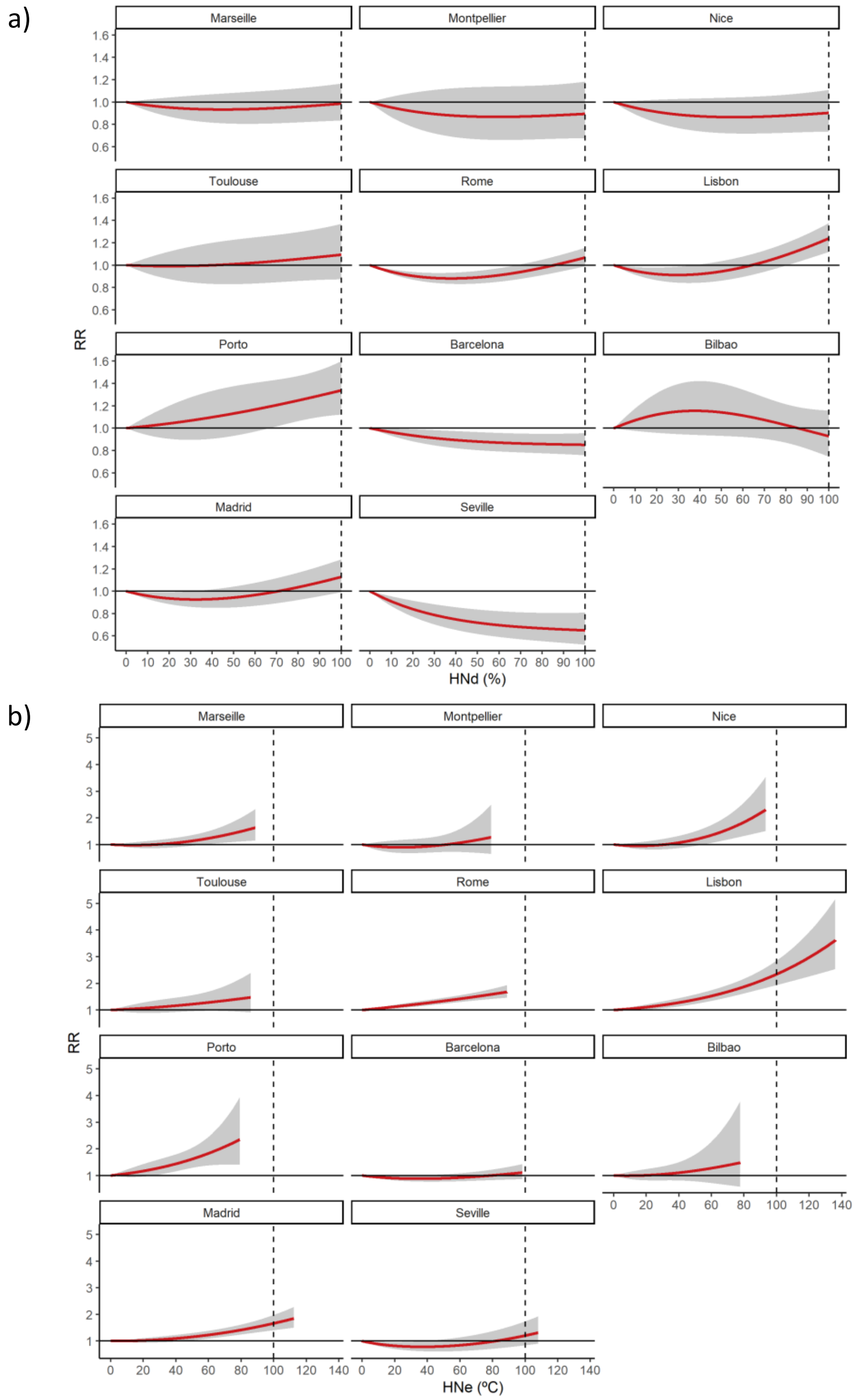


Figure S7. City-specific overall cumulative exposure-response relationships between hot night indices (a. Hot Night duration [HNd], b. Hot Night excess [HNe]) and cardiovascular mortality by city. Dashed vertical line is the 95th percentile.

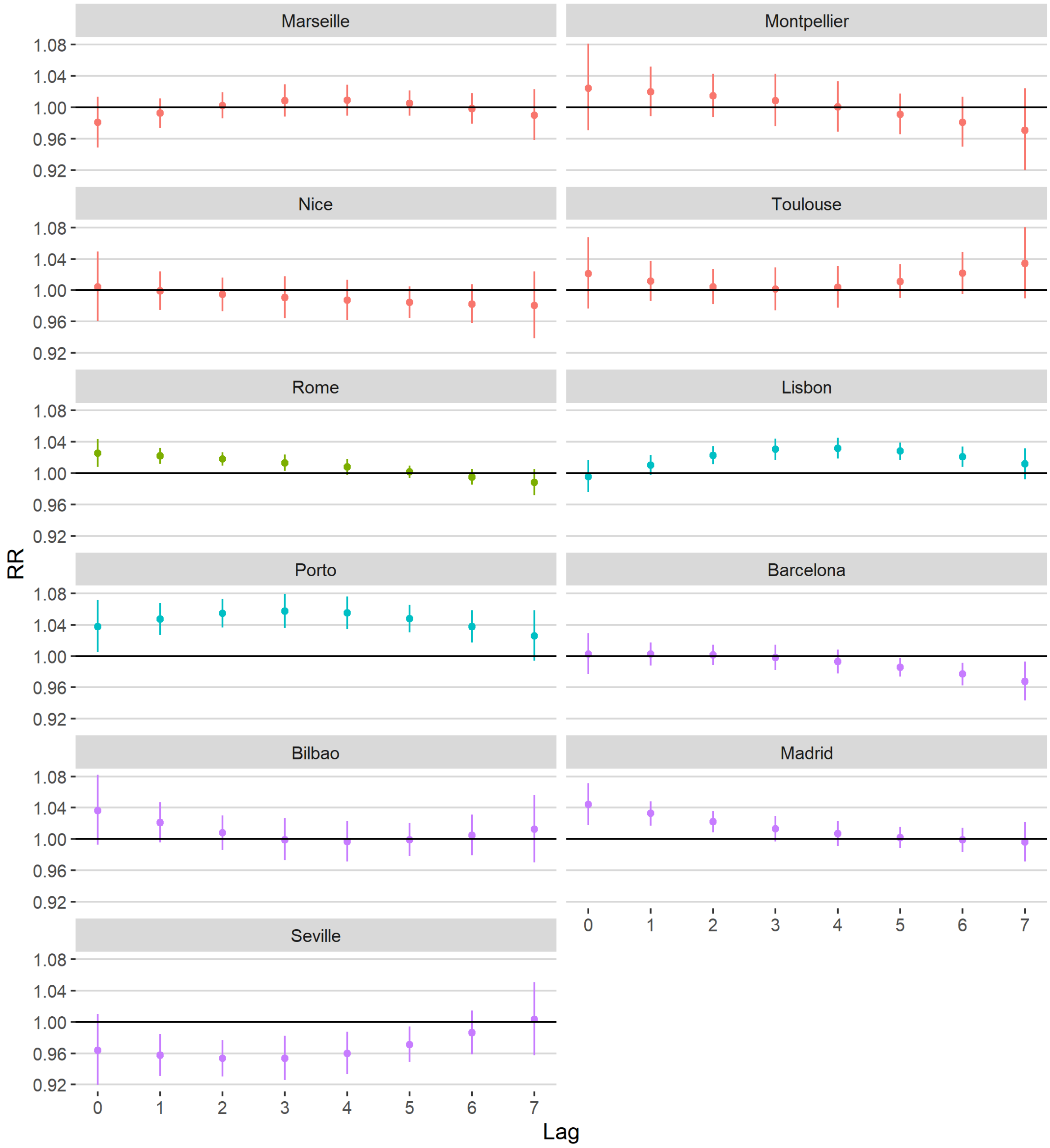


Figure S8. City-specific exposure-response at the 95th percentile of Hot Night duration for nonaccidentalmortality by city and lag.

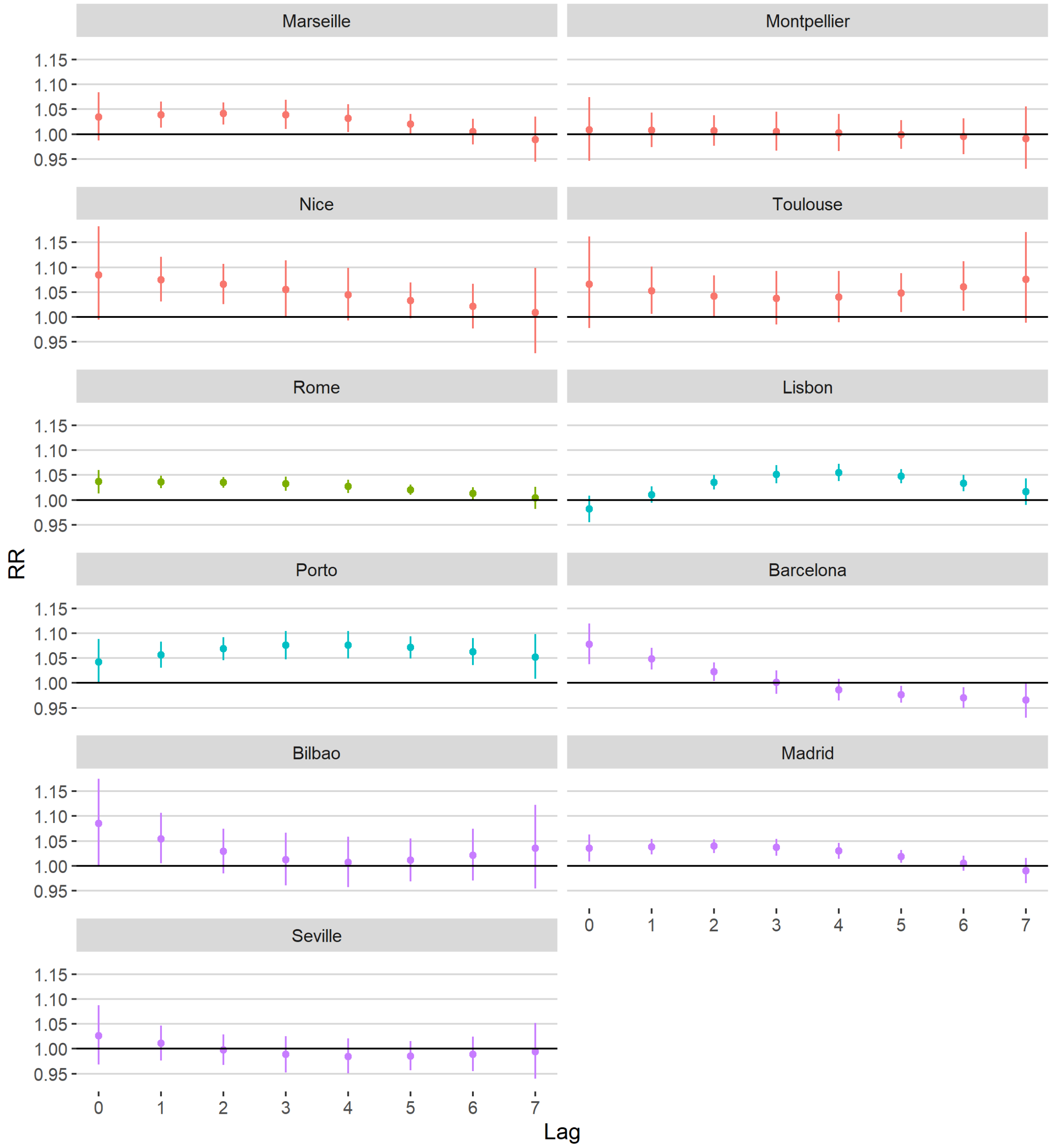


Figure S9. City-specific erxposure-response at the 95th percentile of Hot Night excess for nonaccidental mortality by city and lag.

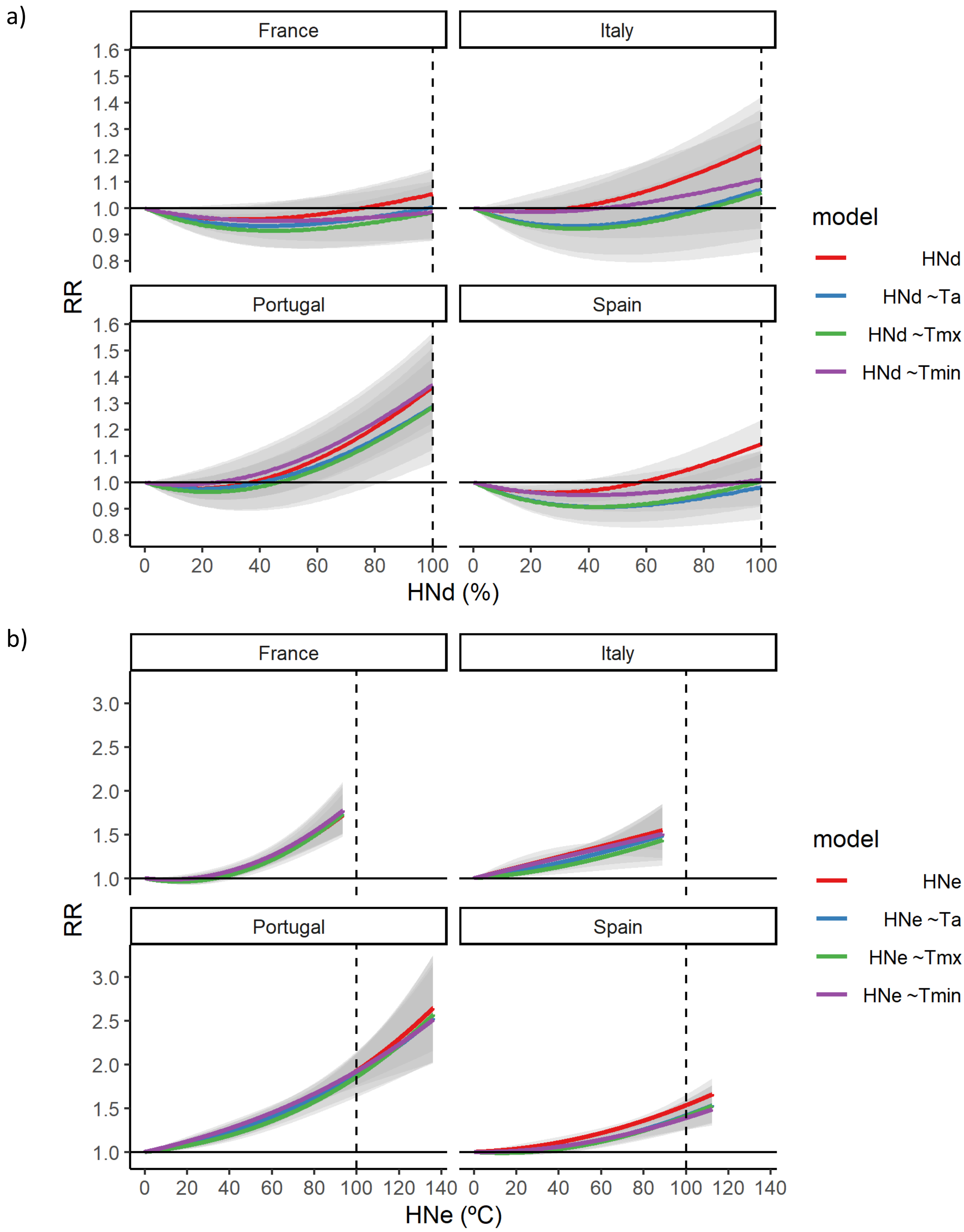


Figure S10. Controled independent effect as pooled results by country for nonaccidental causes (a. Hot Night duration [HNd] without controled independent effects, controlled by daily mean temperature (Ta), maximum temperature (Tmx) and minimum temperature (Tmin), b. Hot Night excess [HNe]). Dashed vertical line is the 95th percentile.

Table S1. Selected Socioeconomic and environmental characteristics by city.

City	Population	Population density	Proportion of old	Life expectancy	Urban area	Green area	Tmx	Tmed	Tmin
Montpellier	554569	248,0	13,0	84,0	8,8	232,6	19,7	15,3	11,0
Marseille	1605188	379,4	15,0	81,1	11,2	51,5	20,3	15,7	11,3
Nice	800168	258,4	19,7	81,1	7,5	244,4	19,5	16,1	12,9
Toulouse	1026947	195,9	12,7	84,7	7,6	212,6	18,4	13,9	9,6
Rome	3702216	651,1	17,6	80,7	11,5	251,9	20,9	16,1	11,6
Lisbon	2638111	661,5	15,3	81,0	13,5	69,6	21,3	16,9	13,5
Porto	1276205	1341,2	12,6	77,4	26,4	68,3	19,0	15,0	11,4
Bilbao	964608	845,4	18,3	81,3	7,5	218,1	19,8	15,0	10,7
Barcelona	3299771	2422,7	17,1	80,3	29,9	2,7	20,2	16,7	13,3
Madrid	5444389	471,9	14,5	83,8	8,0	31,5	21,1	15,0	8,9
Sevilla	1259522	302,5	13,1	78,7	4,9	15,7	25,2	19,0	13,3

Table S2. Evidence of linear against non-linear relationship for hot night indices (QAIC) [nonaccidental causes]

	HNd		**HNe**	
City	*non-linear*	*linear*	*non-linear*	*linear*
Marseille	15637.44	15647.04	15606.78	15620.44
Montpellier	12097.83	12104.07	12098.83	12102.70
Nice	14197.64	14220.17	14171.26	14188.49
Toulouse	14103.61	14107.81	14090.40	14094.35
Rome	25159.57	25252.75	25149.00	25157.89
Lisbon	15771.03	15796.99	15755.20	15760.06
Porto	13608.22	13618.21	13604.59	13605.94
Barcelona	16401.80	16405.14	16375.30	16383.45
Bilbao	12510.07	12511.51	12508.95	12510.88
Madrid	17662.25	17689.61	17654.33	17666.72
Seville	13690.48	13695.82	13691.28	13696.75

Table S3. Overall exposure-response at the 95th percentile of Hot Night indices for nonaccidental mortality by city and different fitted lag structure.

		HNe		
City	**Lag 5**	**Lag 7**	**Lag 10**	**Lag 14**
Marseille	1.16 (1.07-1.26)	1.13 (1.03-1.24)	1.10 (0.99-1.22)	1.07 (0.94-1.22)
Montpellier	1.09 (0.94-1.25)	1.10 (0.94-1.29)	1.21 (1.01-1.45)	1.15 (0.93-1.42)
Nice	1.18 (1.06-1.32)	1.17 (1.03-1.32)	1.13 (0.98-1.30)	1.04 (0.88-1.22)
Toulouse	0.99 (0.80-1.21)	1.06 (0.83-1.34)	1.26 (0.94-1.68)	1.37 (0.96-1.95)
Rome	1.24 (1.18-1.29)	1.25 (1.19-1.31)	1.25 (1.19-1.32)	1.25 (1.18-1.32)
Lisbon	1.19 (1.09-1.31)	1.26 (1.13-1.41)	1.43 (1.24-1.66)	1.63 (1.31-2.03)
Porto	1.31 (1.15-1.49)	1.40 (1.20-1.64)	1.65 (1.34-2.02)	2.31 (1.70-3.12)
Barcelona	1.03 (0.93-1.14)	0.94 (0.83-1.06)	0.95 (0.82-1.10)	0.95 (0.79-1.14)
Bilbao	1.09 (0.94-1.26)	1.03 (0.87-1.23)	1.12 (0.90-1.38)	0.91 (0.69-1.21)
Madrid	1.13 (1.05-1.22)	1.13 (1.04-1.22)	1.15 (1.03-1.27)	1.16 (1.02-1.33)
Seville	1.07 (0.87-1.30)	1.10 (0.87-1.39)	1.44 (1.09-1.92)	1.60 (1.10-2.32)
		HNd		
Marseille	1.01 (0.94-1.10)	0.99 (0.90-1.08)	1.00 (0.90-1.11)	0.98 (0.86-1.12)
Montpellier	1.06 (0.93-1.21)	1.01 (0.87-1.17)	1.12 (0.94-1.34)	1.11 (0.89-1.37)
Nice	0.97 (0.88-1.07)	0.92 (0.83-1.03)	0.94 (0.82-1.07)	0.90 (0.77-1.05)
Toulouse	1.08 (0.97-1.20)	1.11 (0.99-1.25)	1.15 (1.00-1.32)	1.11 (0.94-1.33)
Rome	1.08 (1.04-1.12)	1.07 (1.03-1.12)	1.06 (1.01-1.11)	1.06 (1.01-1.13)
Lisbon	1.06 (0.99-1.13)	1.08 (0.99-1.17)	1.14 (1.02-1.28)	1.26 (1.07-1.48)
Porto	1.19 (1.07-1.32)	1.23 (1.09-1.41)	1.39 (1.17-1.65)	1.76 (1.36-2.28)
Barcelona	1.00 (0.94-1.07)	0.95 (0.87-1.02)	1.02 (0.92-1.12)	1.01 (0.89-1.15)
Bilbao	1.05 (0.93-1.18)	1.00 (0.86-1.15)	1.01 (0.84-1.21)	0.85 (0.67-1.08)
Madrid	1.05 (0.97-1.12)	1.03 (0.95-1.13)	1.06 (0.95-1.18)	1.07 (0.92-1.23)
Seville	0.83 (0.72-0.95)	0.83 (0.70-0.98)	0.84 (0.68-1.04)	0.84 (0.63-1.12)

Table S4. Predictive abaility of the hot night indices with respect to traditional indices (QAIC) [nonaccidentalcauses]

City	HNe	HNd	Tmx	Tmin	Tmed	TH0	TH2	TH4	TH6
Marseille	15866.69	15903.77	15854.74	15833.65	15849.06	15791.39	15829.85	15832.26	15749.20
Montpellier	12233.85	12231.53	12237.58	12234.45	12236.31	12233.84	12231.89	12231.62	12232.39
Nice	14355.69	14388.26	14403.43	14403.13	14403.33	14360.32	14360.15	14327.08	14327.19
Toulouse	14256.07	14266.87	14248.96	14262.77	14260.60	14224.74	14229.56	14203.14	14225.80
Rome	25366.13	25466.36	25459.64	25435.15	25483.25	25044.95	24225.98	24894.92	25195.51
Lisbon	15981.60	16028.23	16007.00	16030.61	15976.09	15901.39	15658.29	15643.57	15859.83
Porto	13814.62	13815.97	13811.53	13882.93	13797.22	13774.96	13580.87	13618.48	13756.94
Barcelona	16589.47	16631.36	16574.33	16626.27	16584.28	16548.86	15984.29	16168.52	16485.29
Bilbao	12662.01	12663.57	12649.23	12649.76	12651.09	11435.98	11194.93	12409.78	12544.01
Madrid	17892.36	17914.45	17924.70	17917.46	17912.91	17750.64	17287.56	17443.44	17726.51
Seville	13849.97	13891.15	13856.67	13880.95	13854.82	13649.21	13188.70	13636.33	13736.56

Tmx: Maximum temperature; Tmin: Minimum Temperature; Tmed: Mean temperature; TH0-6: Temperature at 0 to 6 hour