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Temporal changes in temperature-related mortality in Spain and effect of the implementation of a Heat Health Prevention Plan

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ABSTRACT

Exposure to extreme ambient temperatures has been widely described to increase mortality. Exploring changes in susceptibility to temperatures over time can provide useful information for policy planning and can provide insights on the effectiveness of health preventive plans. The aims of this study were i) to compare changes in temperature-related mortality in Spain during a 20-year period and ii) to assess whether the number of actions implemented in each region as part of a Heat Health Prevention Plan (HHPP) was associated with the temporal changes in heat-related mortality. Daily counts of deaths and daily maximum temperature were obtained for each Spanish province (1993–2013). We used time-varying distributed lag non-linear models to estimate the relationship between temperature and mortality. We compared the risk of death due to extreme temperatures (cold and heat) in the two periods (1993–2002 and 2004–2013), assuming a constant temperature distribution and different temperature-mortality function. Results were reported as mortality attributable fraction (%) (AF). Overall, there was a decrease in mortality attributable to temperature in period 2, more remarkable for extreme cold (from 1.01% to 0.52%), while for moderate heat there was an increase (from 0.38% to 1.21%). Provinces with more actions implemented in their HHPP showed stronger decreases in mortality attributable to extreme heat. Other variables (e.g. average temperature) could explain this association. The highest mortality-AF reductions were detected among the elderly, in mortality for cardiovascular causes and in towns with high socioeconomic vulnerability. Our results suggest that the implementation of the Spanish HHPP could help reduce heat-related mortality.

1. Introduction

Extreme heat, but also extreme cold, represents an important public health risk, especially for their effects on mortality. The percent of total deaths attributed to temperatures was quantified to be around 8% in a large multi-country study, with cold accounting for more deaths than heat (Gasparrini et al., 2015b). In Spain, 6.5% of registered mortality can be attributed to extreme ambient temperatures, being cold more harmful (5.5% due to cold and 1.1% due to heat). This may differ in the future, with the predicted increases in worldwide surface temperature of between 1 °C and 4 °C because of climate change (IPCC, 2014), although this will also depend on population adaptation (Guo et al., 2018).

Comparisons of the effects of temperature in different periods are useful to assess changes in susceptibility over time (Arbuthnott et al., 2016; Barreca et al., 2016; Vicedo-Cabrera et al., 2018). Such comparisons between periods can also be useful in assessing the effects of interventions. Many European countries, including Spain, introduced heat-health prevention plans (HHPP) in 2004, after the devastating effects of the 2003 European heat wave (Robine et al., 2008). Indeed, the WHO elaborated a guide that encourages all countries in Europe to develop HHPP and makes recommendations about the core elements and general principles that they should include (Matthies, 2008). A limited number of before-after studies have been conducted to evaluate those plans (Boeckmann and Rohn, 2014; de' Donato et al., 2015; Díaz et al., 2018; Linares et al., 2015; Schifano et al., 2012; Toloo et al., 2013). A reduction of the effect of high temperatures on mortality was observed in countries such as Italy (Schifano et al., 2012), and in cities like Montreal (Benmarhnia et al., 2016), Rome or Paris (de' Donato et al., 2015) after the implementation of prevention programs. However, a common characteristic of all these studies is the difficulty of evaluating whether the reduction in weather-related mortality is due to

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the intervention programs or to other factors such as biological adaptation, improvements of healthcare system, technological advancements, changes in urban built environment or social progress (Boeckmann and Rohn, 2014).

Before-after comparisons provide stronger results when the study includes an appropriate control region. However, in practice, good control regions often do not exist. Despite the Spanish HHPP works at a national level, each region (Autonomous Communities) can incorporate additional interventions. This study provides a good opportunity to evaluate the changes in temperature-mortality associations across different regions of the same country with common health services, and to test whether changes over time are associated with the number of actions implemented in each region. Additionally, our research contributes to understand changes in cold-related mortality over the last decades, only reported in very few previous studies.

Spain has experienced an increase in the average temperature in the last decades, around 0.5 degrees per decade. As the Intergovernmental Panel on Climate Change (IPCC) has pointed out in its last assessment report (IPCC, 2014), temperatures will be increasing in the coming years. It is expected that the Mediterranean area will be one of the most affected regions. Despite this, episodes of cold (cold spells and frost days) are still present in Spain, and as predicted, will continue to happen (IPCC, 2014), but less frequently.

The objectives of this study were to compare the temporal changes in the effects of cold, heat and heat waves on mortality over a 20-year period in Spain. Studies on the relationship between temperature and mortality are often based on large cities. Importantly, here we included small municipalities of less than 10,000 inhabitants and can compare results in urban and rural areas. Additionally, we assessed whether the effect of extreme heat, which was targeted by the HHPP introduced in the middle of the period, changed according to the number of actions implemented in each region's preventive plan.

2. Methods

2.1. Setting

This study was performed in Spain, with a population of 46.5 million living in 50 provinces (excluding Ceuta and Melilla in North Africa). The predominant climate of Spain is Mediterranean, with dry, hot summers and winters with balanced temperatures and low rainfall. However, other climates are present, such as oceanic (north-western region), arid and semi-arid (south-western region), subtropical (Canary Islands) and continental climate (mountain ranges). The study period covered 21 years from 1993 to 2013.

2.2. Data

2.2.1. Mortality

We obtained individual records for all deaths older than 15 years occurred in the study period from the Spanish National Statistics Institute (Instituto Nacional de Estadística - España, 2018), with information on date of death, sex, age, cause of death and municipality. From these data, we obtained total daily counts by province. Additionally, we obtained counts by sex; age group (16–64, 65–74, 75–85, 85 or more); selected causes of death based on previous research (Basagaña et al., 2011) (Diabetes: ICD codes E10-E14; Mental and nervous system disorders: ICD codes F00-H95; Cardiovascular diseases: ICD codes I00-I99; Respiratory Diseases, ICD codes: J00-J99; and External causes, ICD codes: V01-Y89); urban or rural environment, based on the number of inhabitants of the municipality being higher or lower than 10,000; and according to the economic vulnerability index of the municipality, divided into low, medium and high based on tertiles. The economic vulnerability index was based on data from the 2001 Spanish census and was computed using five variables, namely % of unemployment, % of youth unemployment, % of temporary workers, % of unskilled workers and % of illiterate population (Ministerio de Fomento, 2018). We also obtained the percentage of air conditioning of each municipality from the 2001 census.

2.2.2. Weather

Data on daily maximum temperature were obtained for each provincial capital from the European Climate Assessment & Dataset (European Climate Assessment and Dataset, 2016.). Temperature data of a single weather station, located in the province capital, were assigned to all municipalities in the province. Missing values in temperature variables (0.01% of the data) were imputed considering: 1) the mean temperature registered on the day after and before the missing day, if only one value was omitted; or 2) the temperature registered in the most correlated station for the same day-month-year, if more than two consecutive days were missing. Our main results did not change if missing values were excluded (data not shown).

In order to evaluate the effectiveness of the HHPP, we used the definition of heat wave used to activate levels 1–3 of the HHPP. The activation of the plan was based on exceeding province-specific thresholds for both maximum and minimum temperature (Ministerio de Sanidad, Consumo y Bienestar Social, 2004). However, a previous study conducted in Spain found that mortality-related temperature during the summer months increased at temperatures below the thresholds used in the Spanish HHPP (Díaz et al., 2015a). Thus, we also conducted the analyses using other definitions of heat waves based on relative thresholds of historical series of daily maximum temperature. In particular, we defined heat waves as periods of ≥ 2, ≥ 3 or ≥ 4 consecutive days with maximum temperature exceeding the 90th, 92.5th, 95th or 97.5th percentile of the province, as used in previous papers (Gasparrini and Armstrong, 2011; Guo et al., 2017).

2.2.3. Heat-health prevention plan implementation

In 2004, Spain introduced its national HHPP, “National plan for preventive actions against the effects of excess temperatures on health" (Ministerio de Sanidad, Consumo y Bienestar Social, 2004). Its main objective was to coordinate the different institutions involved in the execution of the plan and also to establish actions and strategies to reduce the health effects of heat waves. The Spanish HHPP includes weather forecasts by the State Meteorology Agency, which establishes thresholds to activate different actions of the plan. Four levels of risk were defined depending on the number of forecasted days exceeding the threshold in the next 5 days (level 0: no exceedances; level 1: 1–2 days; level 2: 3–4 days; level 3: 5 days). Actions include dissemination of preventive information to the general population and specific high-risk groups and activation of a general hotline and emergency services. It is important to highlight that Spanish regions (Autonomous Communities) may incorporate additional specific heat-related interventions, and this resulted in different actions being implemented by region.

Here, we reviewed the regional plans and evaluated how many of the elements suggested by WHO within the EuroHEAT project (Matthies, 2008) were incorporated in their plans. The eight essential core elements identified include: 1) agreement on a lead body and clear definition of actors' responsibilities; 2) accurate and timely alert systems (determine the thresholds for action); 3) a health information plan (regarding the information, time and channels of communication); 4) a reduction in indoor heat exposure (to protect the most vulnerable); 5) particular care for vulnerable groups (identification and actions to protect the most vulnerable groups); 6) preparedness of the health and social care system; 7) long-term urban planning (in order to reduce heat exposure); and 8) real-time surveillance and evaluation. The scores of some Autonomous Communities have to be taken cautiously, as specific details were not available from public web pages. We considered that these regions did not have specific plans and relied on the national one.

2.3. Statistical analysis

Daily mortality counts were linked with temperature using quasi-Poisson regression and the distributed lag non-linear model (dlnm) framework (Gasparrini, 2014). This methodology allows capturing non-linear and lagged associations using basis functions. Although dlnm is a common option to analyse the effects of temperatures on mortality, other studies have used other methodologies such as difference-in-differences (Benmarhnia et al., 2016; Morabito et al., 2012). We excluded year 2003 from the analysis because of the unusually high temperatures registered in that summer, and conducted the analyses separately for two 10-year periods, period 1 (1993–2002) and period 2 (2004–2013). The HHPP was in place during the entire period 2. Modelling was done in a two-stage process. First, analyses were conducted in each province. In a second stage, province-specific results were combined using multivariate meta-analysis (Gasparrini, 2014).

2.3.1. First stage: models for province

The exposure-response association was modelled using a quadratic B-spline with 3 internal knots placed at the 10th, 75th and 90th percentiles of location-specific temperature distribution (Gasparrini et al., 2015b). We controlled for seasonality by including a natural cubic B-spline of day of the year with equally spaced knots and 8 degrees of freedom per year. An interaction between this spline function and indicator of year was specified to relax the assumption of a constant seasonal trend. Long-term trends were controlled by including a linear term for year. In addition, we included indicator variables for day of the week, holidays and the number of hospitalizations due to influenza (except for respiratory diseases). The lag-response association was modelled using a natural cubic B-spline with an intercept and three internal knots placed at equally spaced values in the log scale. The lag period was extended up to 21 days in order to include possible long delays in the effects of temperature. Finally, the results of this stage were cumulated over all lags to obtain the overall temperature-mortality association curve. Sensitivity analyses were carried out to test all these modelling choices (Supplementary Material Table S9).

2.3.2. Second stage: meta-analysis

The estimated location-specific associations were pooled using a multivariate meta-regression model. Then, we derived the best linear unbiased prediction of the overall cumulative exposure-response association in each province. This approach allows areas with small daily mortality counts, usually characterised by very imprecise estimates, to borrow information from larger populations that share similar characteristics (Gasparrini et al., 2015a, 2015b). The pooled curve was used to define the temperature percentile of minimum mortality (MMP).

2.3.3. Comparison of the two periods

To compare the two periods, we calculated the fraction of deaths attributable to temperature in each of the periods considering a scenario in which both periods had the same temperatures and population (those of period 2) but had their own exposure-response function. This approach has been used previously (Vicedo-Cabrera et al., 2018). To calculate the attributable fractions, we used the methods described elsewhere (Gasparrini and Armstrong, 2013). We calculated the fraction due to cold and heat by considering days with temperatures below and above the MMP, respectively. We also calculated the fractions attributable to extreme cold and heat by considering days with temperatures below the 2.5th and above the 97.5th percentiles, respectively (Gasparrini et al., 2015a, 2015b). Empirical confidence intervals were reported using Monte Carlo simulations (Gasparrini et al., 2015a, 2015b). Wald test was used to test differences between temperature-related mortality in period 1 and period 2 (Gasparrini et al., 2015a).

As the HHPP targeted the effects of extreme heat, we calculated the differences in attributable fractions due to extreme heat in the two periods for each of the provinces and assessed whether those differences were related with the number of elements implemented in the regional plans. This was done using a meta-regression model. Additionally, we also tested with meta-regression the effects of the average maximum temperature, the average of the vulnerability index and the percentage of air conditioning of the province.

Since the plan paid particular attention to heat wave periods, we calculated the fraction of deaths attributable to heat waves, according to the definition used in the HHPP. The analyses on heat waves were restricted to the period in which the plan was active, June 1st to September 15th. Attributable fractions for heat waves were based on the same models described above, i.e. models with a cross-basis function of maximum temperature, but with the addition of a heat wave indicator to capture the added effects of heat waves (Gasparrini and Armstrong, 2011).

All analyses were performed with R software (version 3.3.3). The code used for the analyses is available at https://github.com/ericamartinez/Temperatures_mortality.

3. Results

The study included 7,378,435 deaths occurred between 1993 and 2013 (excluding 2003). The average number of daily deaths was around 1,000, with more deaths registered in period 2, reflecting an increase in both total population (increase of around 8 million inhabitants during the study period) and proportion of elderly (increase from 13% to 17% in the percent of inhabitants > 65 years) (Instituto Nacional de Estadística - España, 2018) (Supplementary Material Table S1). The mortality-sex ratio was similar in the two periods, while in terms of age, period 2 registered smaller percentages of deaths in the younger groups that was shifted to the oldest ones (Supplementary Material Table S1). In terms of the selected causes of death, the percentage due to cardiovascular causes doubled in period 2 compared to period 1, while an opposite trend was observed for respiratory diseases. Increases in deaths by diabetes and mental and nervous system disorders were also observed in period 2, while the percent due to external causes decreased (Supplementary material Table S1). Period 2 registered a slight increase in the percent of deaths occurred in urban areas, while the distribution in terms of the economic vulnerability index of the municipality and the air conditioning ownership was similar in the two periods (around 12% and 4% of the deaths occurred in the provinces with high vulnerability and low air conditioning ownership, respectively). Maximum temperature registered in Spain was higher in period 2, especially during the warm period (May-October) (Fig. 1). While only two years in period 1 had maximum temperature above 35 °C (1993 and 1995), period 2 registered six years (2004, 2006, 2007, 2010–2012) (Supplementary material Table S2). Climate in Spain presents some variability. The daily average maximum temperature ranged from 16.8 °C in Leon to 25.7 °C in Seville (Supplementary material Table S3). The coldest provinces in Spain registered minimum values below 0 °C (e.g., Albacete, Huesca, Teruel, Soria, and Lleida).

3.1. Temperature-mortality association in the two periods

The relationship between maximum ambient temperature and the risk of death in the two periods is represented by the pooled overall cumulative curve shown in Fig. 2. For both periods, the curve had a U-shape, showing that the risk of death (for all causes) increased for both cold and hot temperatures. The temperature percentile of minimum mortality was the 66th in period 1 and the 76th in period 2. The risk of death associated with cold temperatures reduced substantially in period 2 compared to period 1 (Percent change-%- and 95% CI; period 1: 33.6 (28.7–38.6); period 2: 14.7 (10.6–19.0); Supplementary material Table S4). In terms of the risk of death associated with heat, the confidence intervals for the two periods overlapped, although for temperatures above the 99th percentile period 2 showed lower risks (Percent change-%- and 95% CI; period 1: 28.0 (22.4–33.9); period 2: 24.9 (21.4–28.6);

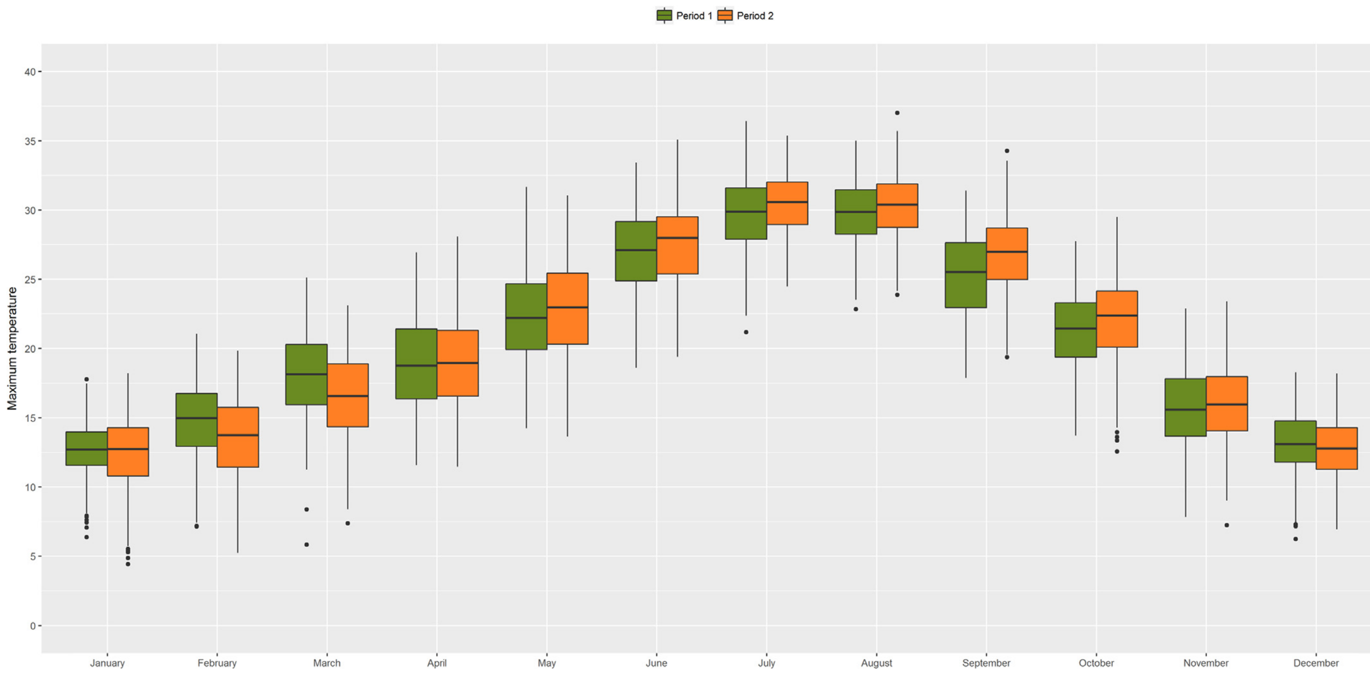

Fig. 1. Maximum monthly temperature distribution for the two study periods (1993–2002 and 2004–2013).

Supplementary material Table S4). The differences in the temperature-mortality curves from the two periods were significant ($p < 0.001$). Different patterns were seen comparing the curves for each Spanish province (Supplementary material Fig. S1). The vast majority showed the same national pattern, with a reduction in the risk associated with cold temperatures. However, there was a group of provinces in which the risk of death associated with heat was higher in period 2 than in period 1 (e.g. Guipuzcoa, Lugo, Asturias).

Table 1 shows the estimation of the fraction of total mortality attributable to temperature in the two periods in the hypothetical case in which period 1 registered exactly the same temperatures than period 2 and had the same population, but had different risk curves as illustrated in Fig. 1. Mortality attributable to temperature reduced in period 2, mainly because of a reduction in mortality attributable to cold temperatures. For heat, there was a small decrease in mortality attributable to extreme heat (from 0.67% to 0.56% in periods 1 and 2, respectively), which was offset by an increase in mortality attributable to moderate heat (from 0.38% to 1.21% in periods 1 and 2, respectively). The reduction of the effects of extreme cold in period 2 was most noticeable among those older than 85 years, on deaths for respiratory causes and in rural areas, while few differences were observed by sex and socioeconomic vulnerability of the town of residence (Fig. 3). The small reduction of the effects of extreme heat in the second period was most noticeable in the older age groups, in mortality by cardiovascular causes and in towns with high socioeconomic vulnerability (Fig. 3).

The distribution of the mortality attributable fraction for cold and extreme heat and its difference in the two study periods by Spanish provinces is represented in Figs. 4 and 5 (Supplementary material Table

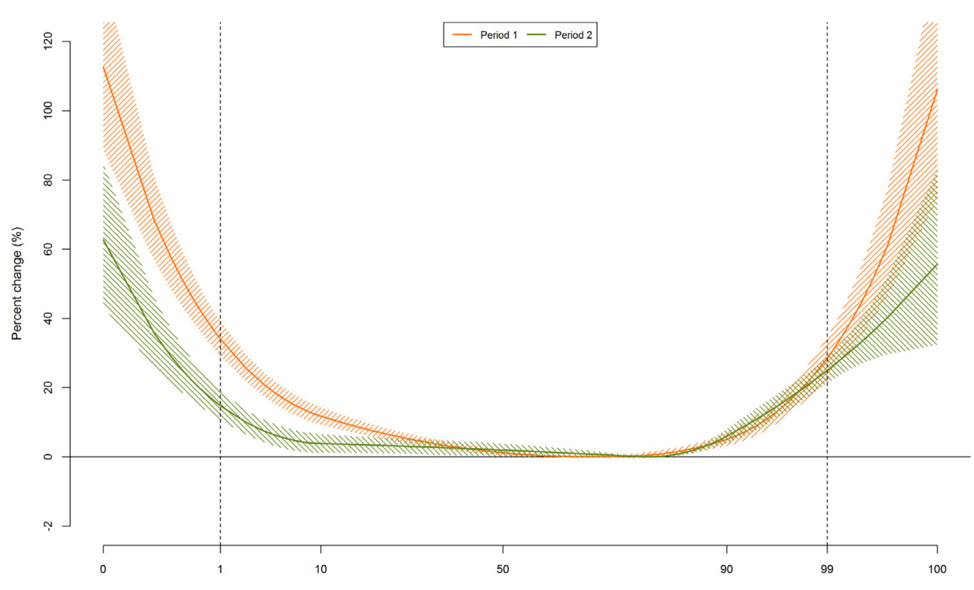

Fig. 2. Overall cumulative temperature-mortality relationship for the two study periods (1993–2002 and 2004–2013). Shaded areas correspond to 95% confidence intervals.

Table 1
Mortality attributable fraction (%) and 95% confidence intervals for components of cold and heat in the two study periods (1993–2002 and 2004–2013).

	Period 1 (1993–2002)	Period 2 (2004–2013)
Global	5.25 (4.67–5.77)	4.59 (3.99–5.11)
Cold	4.26 (3.78–4.71)	2.88 (2.26–3.37)
Heat	0.99 (0.69–1.24)	1.73 (1.47–1.96)
Extreme cold	1.01 (1.03–1.16)	0.52 (0.46–0.57)
Moderate cold	3.27 (2.83–3.71)	2.39 (1.79–2.87)
Moderate heat	0.38 (0.12–0.62)	1.21 (0.98–1.44)
Extreme heat	0.67 (0.61–0.72)	0.56 (0.52–0.59)

Mortality attributable fraction due to cold and heat was calculated by considering days with temperatures below and above the minimum mortality percentile, respectively. The fractions attributable to extreme cold and heat correspond to days with temperatures below the 2.5th and above the 97.5th percentiles, respectively.

S6 and Table S7). Cold-related mortality was higher mainly in provinces in the south Spain and the Mediterranean basin (Fig. 4a). In general, lower values of cold mortality attributable fraction were registered in period 2 (Fig. 4b). Specifically, the majority of the Spanish provinces showed a reduction in cold-related mortality, except in areas like Madrid, Asturias in the north and Murcia in the south (Fig. 4c). Extreme heat had less impact than cold in terms of mortality in Spain (attributable fraction between 0% and 1.2%). In terms of the geographical pattern, provinces in the south and centre Spain were the most effected by extreme heat (Fig. 5a). A general reduction in extreme-heat mortality fraction was observed in period 2 (Fig. 5b). More precisely, when looking at the differences for the periods, only a slight increase was observed in period 2 in a few provinces (i.g. Avila, Lleida, Navarra) (Fig. 5c).

3.2. Heat waves and mortality

Table 2 displays the number of days the Spanish HHPP would have been activated in the two periods according to the criteria outlined in the plan. In period 1 (in which the plan was not active), this resulted in 1,711 days (ranging from 0 –e.g. Asturias, Cantabria, Ávila– to 232 –Ciudad Real), while in period 2, there were 2,876 days exceeding the official thresholds (ranging from 0 –e.g Guipuzcoa, Lugo, Ávila- to 240 –Ciudad Real). High variability was detected according to the different Spanish provinces (Supplementary material Fig. S3 and Table S5). Provinces in the south (e.g. Almeria, Ciudad Real, Malaga, Sevilla, Toledo) registered the highest number of days exceeding the thresholds establish in the Plan in the two study periods. It is important to note that period 2 was hotter and this was reflected with a general increase in the number of days when the plan was activated but also for the different definitions of heat wave used (Supplementary material Fig. S3 and Table S5). For comparison, results for other definitions of heat wave were also provided.

Attributable mortality during the days of potential activation of the plan was smaller in period 2 (0.47%, 95% CI: 0.34, 0.58) than in period 1 (0.69%, 95% CI: 0.56, 0.80). Reductions were also observed for definitions of heat wave based on temperatures greater than the 90th percentile, except for heat waves with a duration of 4 or more days, which had similar effects in both periods. Considering the official thresholds used in the plan, a different mortality geographical pattern was observed. The provinces where heat had more impact in mortality were located in the south (period 1) and centre (period 2) of the country (Supplementary material Fig. S2). We observed a general reduction for heat-mortality in all provinces, using the definition of the plan. The changes in period 2 ranged from − 2.28% to − 0.01% (Supplementary material Table S8). Only six provinces (Albacete, Madrid, Badajoz, Barcelona, Las Palmas and Huesca) experienced an increase in mortality attributable to heat (Supplementary Material Fig. S2c and Table S8).

3.3. Characteristics of the heat-health prevention plan

Table 3 shows the elements implemented in the plan of each Autonomous Community. All of them included elements related with alert systems and cross-border collaboration, but there were differences in the implementation of other elements. None of the plans incorporated long-term urban planning measures. Adding all the elements, the distribution varied from 6 to 31 elements included. In a regression model for the number of elements implemented in the plan, the average

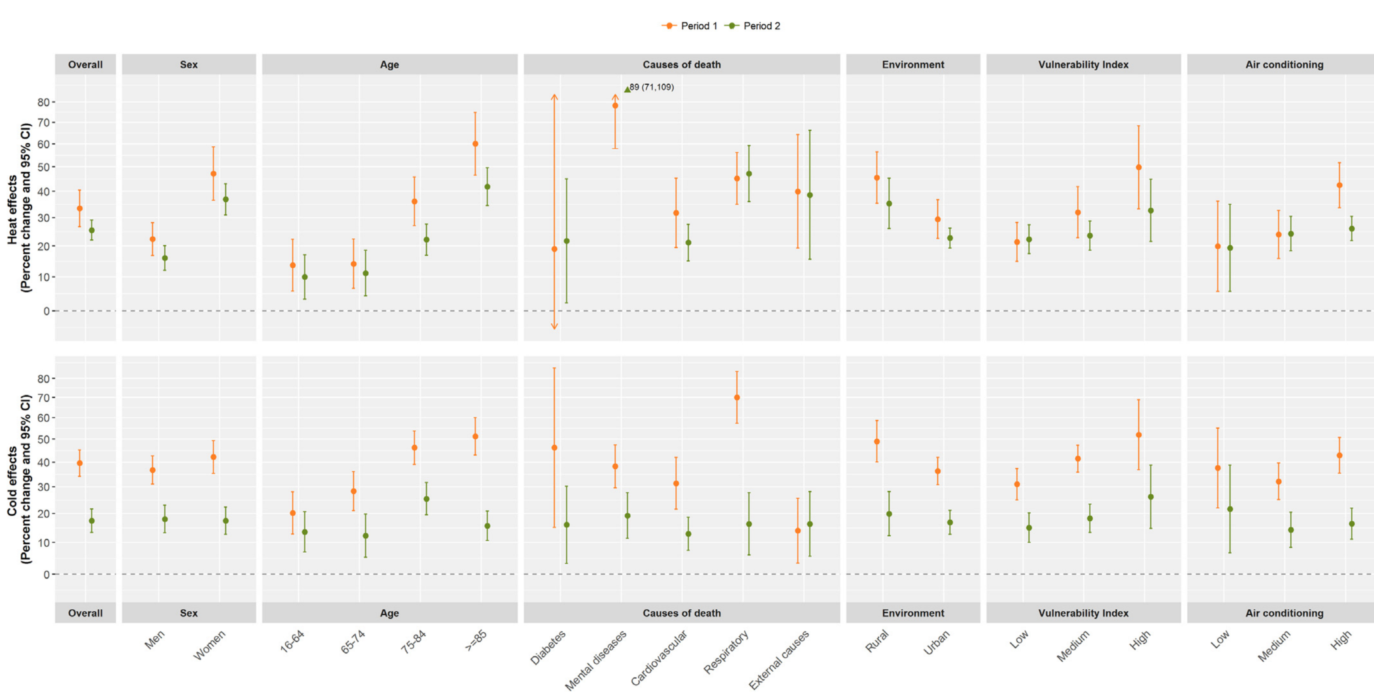

Fig. 3. Percent change (95% CI) for the relationship between extremely cold - hot ambient temperatures and mortality in Spain for the two study periods (1993–2002 and 2004–2013).

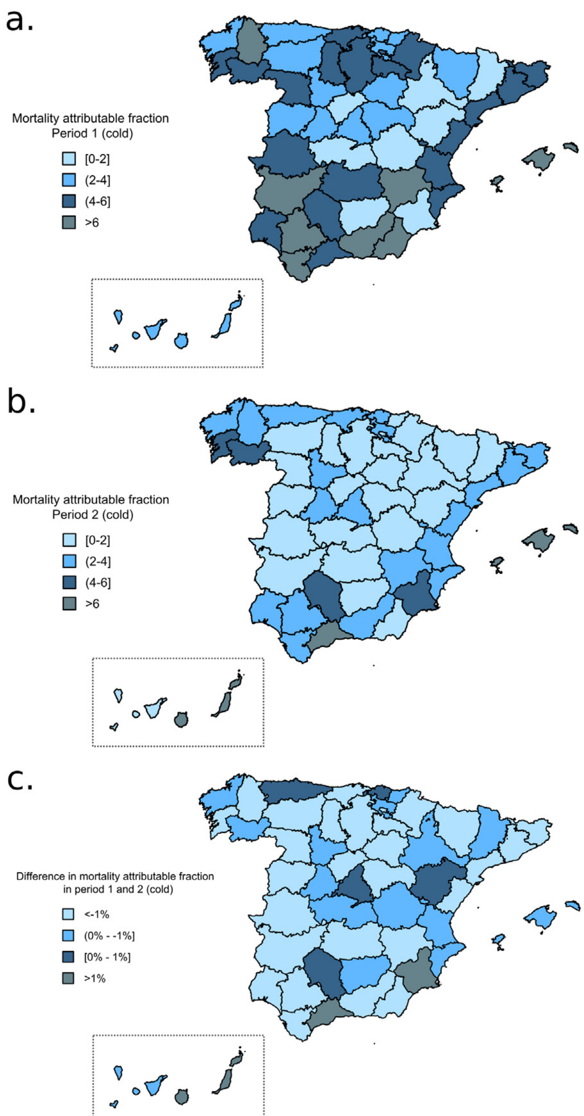

Fig. 4. Cold-mortality attributable fraction (%) computed for period 1 (a), period 2 (b) and the difference between period 2 and period 1 (c) by Spanish provinces. Mortality attributable fraction due to cold was calculated by considering days with temperatures below the minimum mortality percentile. The attributable fraction corresponds to the ratio between the attributable and total number of deaths. The map of Spain and the province borders were downloaded from https://gadm.org, which allows using the data for academic publishing. The final maps were created with the sp library from the R software (version 3.3.3; R Development Core Team).

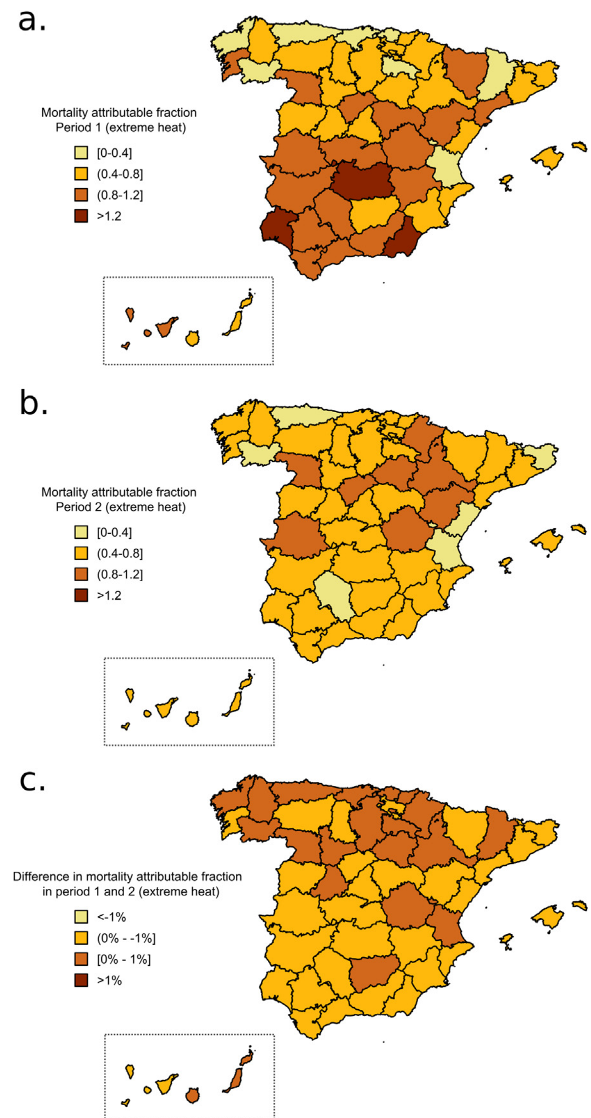

Fig. 5. Extreme heat-mortality attributable fraction (%) computed for period 1 (a), period 2 (b) and the difference between period 2 and period 1 (c) by Spanish provinces. Mortality attributable fraction due to extreme heat was calculated by considering days with temperatures above the 97.5th percentile. The attributable fraction corresponds to the ratio between the attributable and total number of deaths. The map of Spain and the province borders were downloaded from https://gadm.org, which allows using the data for academic publishing. The final maps were created with the sp library from the R software (version 3.3.3; R Development Core Team).

maximum temperature of the province was significant predictor but the vulnerability index of the province was not (data not shown). In particular, hotter regions (e.g. Andalucia, Comunidad Valenciana) implemented more elements.

Fig. 6 shows the relationship between the difference in the fraction of deaths attributable to extreme heat in the two periods against the number of elements included in the HHPP in each province. The provinces that implemented more elements in the plan achieved significantly greater reductions in mortality attributable to extreme heat in period 2 compared to period 1. This relationship was also observed when considering days in which the criteria for activation of the HHPP were met (Table 4). Other characteristics of the provinces were also associated with the reduction of the effects of heat in period 2 (Table 4). In particular, for extreme heat, hotter provinces, provinces with more air conditioning in 2001 and more deprived provinces had larger reductions. When one of these variables was introduced in the model along with the number of elements in the HHPP, the association with the number of elements of the plan attenuated and in most cases it lost statistical significance, presumably due to the correlation between variables (>0.45) (data not shown). Average maximum temperature of the province was the strongest predictor of the reduction in the second period. The models for activation of the plan had lower precision. Apart from the number of elements in the plan, the percentage of air conditioning was also significantly associated with the reduction in period 2, but none of them were significant when included together (Table 4).

3.4. Sensitivity analyses

Our results showed some variations in results when modelling choices were tested (lag structure and degrees of freedom for day of season; Supplementary material Table S9). Using shorter lag periods led

Table 2
Number of days and mortality attributable fraction (%) for the activation of the Spanish Heat Health Prevention Plan and for different definitions of heat waves in the two study periods (1993–2002 and 2004–2013).

	No. days[a]		Attributable fraction (%)[b] and 95% confidence intervals	
	PERIOD 1	PERIOD 2	PERIOD 1	PERIOD 2
Activation HHPP	1711	2876	0.686 (0.556, 0.800)	0.472 (0.343, 0.577)
≥ 2 days + 90th percentile	2242	3067	0.798 (0.679, 0.896)	0.839 (0.739, 0.934)
≥ 2 days + 92.5th percentile	1513	2162	0.608 (0.511, 0.685)	0.509 (0.423, 0.580)
≥ 2 days + 95th percentile	850	1269	0.416 (0.341, 0.476)	0.259 (0.188, 0.321)
≥ 2 days + 97.5th percentile	371	531	0.191 (0.146, 0.232)	0.078 (0.036, 0.116)
≥ 3 days + 90th percentile	1020	1524	0.416 (0.351, 0.471)	0.459 (0.410, 0.510)
≥ 3 days + 92.5th percentile	635	971	0.287 (0.238, 0.329)	0.264 (0.219, 0.302)
≥ 3 days + 95th percentile	346	481	0.171 (0.136, 0.204)	0.128 (0.100, 0.156)
≥ 3 days + 97.5th percentile	146	162	0.061 (0.043, 0.077)	0.036 (0.021, 0.049)
≥ 4 days + 90th percentile	472	752	0.203 (0.167, 0.235)	0.246 (0.215, 0.274)
≥ 4 days + 92.5th percentile	286	432	0.121 (0.098, 0.142)	0.136 (0.116, 0.154)
≥ 4 days + 95th percentile	162	166	0.062 (0.045, 0.077)	0.060 (0.045, 0.073)
≥ 4 days + 97.5th percentile	72	47	0.017 (0.010, 0.023)	0.014 (0.008, 0.019)

Activation HHPP: thresholds established in each province to activate the Spanish Heat Health Prevention Plan.
Results obtained from a model including added effects.

[a] Number of days in which the Spanish Heat Health Prevention Plan was activated and number of days considered heat wave, according to the different definitions.

[b] Mortality attributable fraction was calculated with the risk mortality-related temperature function in each period and maintaining constant the temperature distribution (using temperatures in the after period).

to smaller effects, while longer lag periods basically reduced the effect of heat in period 1. Less stringent control for seasonality led to smaller effects in period 1, and fewer changes were observed when using more degrees of freedom for seasonality.

4. Discussion

This study examined the association between extreme ambient temperatures and mortality in Spain over two 10-year periods. A HHPP was in place in the second period but not on the first. Our results were obtained for a counterfactual scenario in which temperatures were assumed to be the same in the two periods. Overall, we found a strong decrease in cold-related mortality in the second period, and a decrease in mortality attributable to extreme (but not moderate) heat. The provinces that incorporated more elements in the Heat Health Prevention Plan experienced stronger decreases in mortality attributable to extreme heat, although other characteristics of the provinces such as average temperature or percent of air conditioning ownership could confound this association. Municipalities with less than 10,000 inhabitants were more sensitive to both cold and heat than larger municipalities, but they also experience greater reductions in the second period, especially for cold-related mortality. The elderly also experienced greater reductions in both cold- and heat-related mortality.

Previous studies in Spain have examined temporal changes in the temperature-mortality associations. In general, we found similar results that those reported elsewhere when restricting to the same geographical areas. One study including only five province capitals from a specific region (Castilla La Mancha) found that the effect of extreme heat was in general lower after the implementation of the preventive plan (Linares et al., 2015). We also reported a decrease in extreme heat-related mortality in these provinces, although in one of them (Cuenca) we found a decrease. Additionally, in the same region but for cold-related mortality, we obtained consistent findings with those reported in a study covering three decades (a strong decrease during the last decade) (Linares et al., 2016). Moreover, our results were also consistent with a study conducted only in the city of Madrid (Díaz et al., 2015b). They also found a small reduction in the effect of extreme heat but an increase in the effect of extreme cold in the last period of study. Another study on the effects of heat waves included all municipalities with more than 10,000 inhabitants of 10 out of the 50 Spanish provinces (Díaz et al., 2018). Contrary to the slight reduction that we observed, that study found a sharp decrease in the effect of heat waves in the period after the introduction of the preventive plan. A wider range in the study period or the restriction of the analyses to the more-populated municipalities in only ten Spanish provinces could explain the differences observed in the results. Despite we reported similar results than previous research, the studies mentioned had a limited spatial coverage and did not examine the effect of temperature across the entire range; they only considered the effect of extreme weather. The most comprehensive study published so far included the 50 province capitals of Spain as part of a multi-country assessment (Vicedo-Cabrera et al., 2018). For Spain, they reported a decrease in cold-related mortality and a less obvious decrease in heat-related mortality, although the periods considered differed. However, the majority of previous studies included province capitals only, and none of them included municipalities with fewer than 10,000 inhabitants.

Several studies have assessed temporal changes outside of Spain. The aforementioned multi-country study, including 305 locations in 10 countries, found consistent reductions in heat-related mortality, except in Australia and Brazil (Vicedo-Cabrera et al., 2018). These reductions were explained mainly by a reduction in susceptibility to heat, as observed when keeping temperatures constant in the different periods. Instead, the trends for the effects of cold were heterogeneous across countries. A review paper also reported that most of the studies that assessed temporal changes in heat-related mortality found decreases with time, while results for cold were not consistent (Arbuthnott et al., 2016). One of the previous studies in one region of Spain reported as a potential reason for the decrease in cold-related mortality an increase in the number of homes with heating systems (Linares et al., 2016).

Some studies have specifically compared periods before and after the implementation of heat-health prevention plans. Overall, our results showing a decrease in heat-related mortality were consistent with previous research. For instance, a study conducted in Italy has documented decreasing effects of heat on mortality due to the introduction of adaptation measures and also to variations in summer temperature distribution (Schifano et al., 2012). Similar findings were reported in Quebec, where authors found evidence that heat action plans contributed to reduce mortality during hot days (Benmarhnia et al., 2016). A review study reported that in general, the effects of extreme heat reduced when preventive measures were implemented (Boeckmann and Rohn, 2014). A study conducted in nine European cities detected a reduction in heat-mortality risk in Rome and Paris, which implemented

Table 3
Characteristics of the specific plans to prevent the health effects of high temperatures in each Spanish region. Based on the WHO guidance "Heat-Health Action Plans", eight core elements were evaluated for each Autonomous Community.

Elements	Andalucia	Aragón	Asturias	Cantabria	Castilla y León	Castilla La Mancha	Catalunya	C. Valenciana	Extremadura	Galicia	Islas Baleares	Islas Canarias	La Rioja	Madrid	Murcia	Navarra	País Vasco
1. Agreement on a lead body and clear definition of actors' responsibilities																	
Clearly defined lead body	x			x		x	x	x	x	x	x		x	x	x	x	
Involvement of > 1 other agencies	x		x	x		x	x	x	x	x	x		x	x	x	x	
Regular meetings and/or reviews	x			x		x	x	x	x	x			x	x	x		
Inclusion in national disaster preparedness	x		x	x		x	x	x	x	x	x		x	x	x		
Cross-border cooperation	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
2. Accurate and timely alert systems																	
Threshold definition scientifically sound	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Regionally adapted definitions	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Warning is issued well in advance	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Different alert levels for different levels of action	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Alert is communicated following a clear plan	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3. Health information plan																	
Clearly defined actors/ recipients/contents	x			x	x	x	x	x	x	x	x	x	x	x			
Effective dissemination of information (> 1 channel)	x		x	x		x	x	x	x	x			x	x			
Quality of advice	x			x		x	x	x	x	x	x		x	x			
Public & professionals addressed	x			x			x	x	x	x			x	x			
Appropriate timing of information campaign	x			x			x	x	x	x	x		x	x		x	
4. Reduction in indoor heat exposure																	
Giving advice	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Providing cool rooms/ spaces								x									
Provision or use of mobile coolers																	
Planning or support for increased albedo or shading																	
Planning or support for better insulation																	
5. Particular care for vulnerable groups																	
Identification of relevant groups (> 1)	x			x	x	x	x	x	x	x		x	x	x		x	x
Activation of a telephone service	x			x		x	x	x		x			x	x			

(continued on next page)

Table 3 (*continued*)

Elements	Andalucia	Aragón	Asturias	Cantabria	Castilla y León	Castilla La Mancha	Catalunya	C. Valenciana	Extremadura	Galicia	Islas Baleares	Islas Canarias	La Rioja	Madrid	Murcia	Navarra	País Vasco
Specific measures (buddies, neighbours …)																	
Regular re-assessment of vulnerable population groups	x			x		x	x	x	x	x			x	x			
Information and training for caregivers	x			x		x	x	x		x			x	x			
6. Preparedness of the health/ social care system																	
Increase of capacity of health services	x			x		x	x	x		x				x			
Heat reduction in healthcare facilities	x			x			x	x	x	x				x			
Special precautions in nursing homes	x			x		x	x	x		x			x	x			
Special resources for patients/public	x			x		x	x	x		x			x	x			
Improving health-care networks	x			x		x	x	x		x			x	x			
7. Long-term urban planning																	
Increased green & blue spaces																	
Changes in building design (albedo, insulation, passive cooling)																	
Changes in land-use decisions																	
Energy consumption reduction																	
Individual and public transport policies																	
8. Real-time surveillance and evaluation																	
Less than 48-h interval	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Involving data from > 1 region/city	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Involving data from > 1 health effect	x		x	x		x	x	x	x	x			x	x	x	x	
Use for adjustment of measures	x			x		x	x	x	x	x			x	x	x		
Use for evaluation of effectiveness	x			x		x	x	x	x	x			x	x	x		
TOTAL POINTS (WHO)	**13**	**3**	**8**	**13**	**8**	**13**	**13**	**14**	**12**	**13**	**8**	**8**	**13**	**13**	**6**	**9**	**6**
TOTAL POINTS (subelements)	**30**	**6**	**13**	**30**	**11**	**27**	**30**	**31**	**24**	**30**	**15**	**11**	**28**	**30**	**16**	**14**	**10**

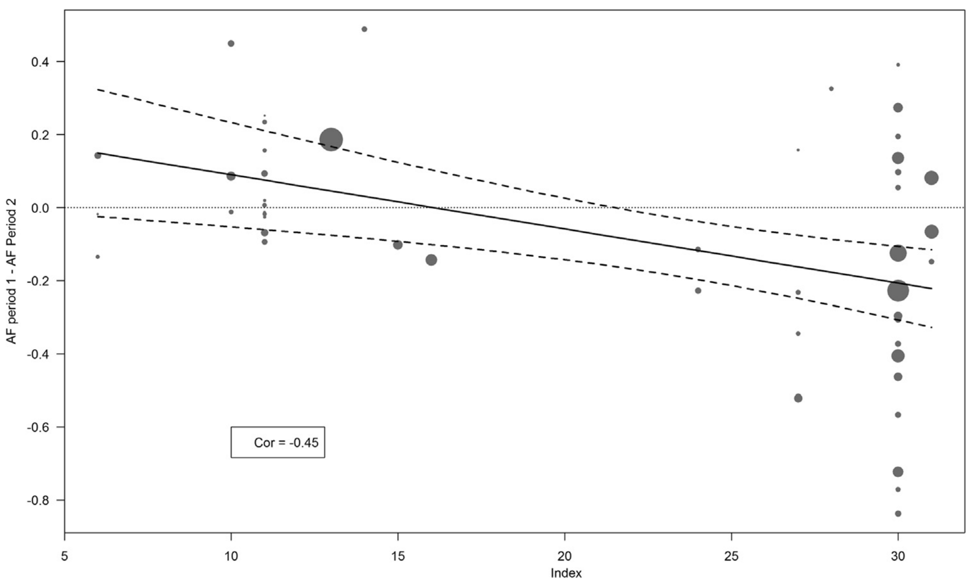

Fig. 6. Relationship between the difference in extreme heat-related mortality attributable fraction (%) in period 1 and 2 and the number of elements included in the Heat Health Prevention Plan in each Spanish Province (index). The index was calculated considering the eight core elements of heat-health action plans and their sub-elements, reported in “Are European countries prepared for the next big heat-wave?” (Eur J Public Health. 2014 Aug;24(4):615–9). The size of the points is proportional to the inverse of variance of the measure in the Y axis. Dashed lines indicate 95% confidence intervals.

preventive plans, but also in Athens, which did not have a preventive plan (de’ Donato et al., 2015, p. 20). Likewise, other cities with a preventive plan did not show a reduction. This illustrates the difficulty to assess the effectiveness of plans, as many other temporal changes occur in parallel to the plan implementation. They include demographic changes, biological adaptation, changes in healthcare systems, social progress or increased use of air conditioning (Boeckmann and Rohn, 2014). Having control regions, i.e. regions that have not implemented preventive plans, can be useful to assess effectiveness, but when control regions are too different and have different temporal trends with regards to other relevant variables, they may be of little help, as exemplified in the aforementioned study.

Unexpectedly, the highest mortality reduction was observed for cold temperatures even though the Spanish HHPP was activated only during heat wave periods. Different causes of the decline in cold-related mortality should be named. Firstly, some studies pointed out a possible biological adaptation to extreme ambient temperatures (Boeckmann and Rohn, 2014) which may help to reduce weather- related mortality. Recently, a study highlighted a possible modification in susceptibility to temperature (Vicedo-Cabrera et al., 2018). Indeed, they found a decreased in heat-related mortality in the past decades in several countries, including Spain, but for cold, the pattern was not clear. Even though in some countries cold mortality decreased (i.e. Spain), in some others there was an increasing (USA) or stable trend (UK and Canada). Secondly, the inclusion of adaptation measures specifically for heat may change also people's behaviour when they are exposed to cold temperatures. Moreover, other factors may contribute of changes in susceptibility to temperatures, such us the ageing population, improvements in healthcare system, technological advancements, better living conditions, adjustments to the urban built environment and social progress (Boeckmann and Rohn, 2014; Toloo et al., 2013).

Our study was conducted in a homogeneous area, the country of Spain, with a universal health care system and a national HHPP that covered several aspects. However, each region could have additional measures implemented. This provided the possibility to use certain regions as controls, or more generally to assess whether the number of actions implemented correlated with a decrease in the effect of extreme heat. We did observe our hypothesised correlation, i.e. areas with more complete plans showed stronger reductions in the effects of extreme heat. Still, even if areas within the same country can be more homogeneous, each area can have different trends on other relevant variables that explain the temporal changes. For example, we also observed correlations between a decrease in effects and the percentage of air conditioning ownership or the socioeconomic vulnerability of the area, although the variable that better predicted the reduction in the effects of extreme heat was the average temperature of the region. This variable was strongly associated with the number of elements incorporated in the preventive plan, i.e. hotter regions implemented more complete plans, and it could be associated with greater awareness of the risks of heat in those regions. Thus, it is still very difficult to attribute those observed changes to the effectiveness of the plan, as observed by others (Boeckmann and Rohn, 2014).

Air conditioning ownership was associated with the reduction in the effects of extreme heat. Even though the use of air conditioning was not a measure included in the Spanish plan, its ownership has been increased in the last decades. This justifies the inclusion of this indicator to better interpret the reduction in heat-related mortality. Others have also highlighted the potential effect of air conditioning (Bobb et al., 2014; Petkova et al., 2014). In our case, we only could assess that in a single point, and were not able to quantify trends in air conditioning use, which could be more relevant. Studies in the U.S. did not find significant associations between temporal reductions in heat effects and air conditioning prevalence (Arbuthnott et al., 2016), although this could be due to the very high prevalence of air conditioning in that country.

The comparison of the number of elements incorporated in the HHPP included in this analysis is observational in nature and therefore it has some limitations, such as being subject to the actual implementations in each region. Several aspects were incorporated in the national plan and therefore implemented in all regions. This was the case for cross-border cooperation and the aspects related to early warning systems, which in consequence are not evaluated in our study. A recent study in the U.S. used an original design to assess the effectiveness of early warnings taking advantage of the fact that they are issued based on predictions and not on actual temperatures (Weinberger et al., 2018). This allowed comparing days with similar real temperatures in which a warning was or was not issued. They found little support for the effectiveness of the warnings. Likewise, we could not evaluate measures that were not incorporated in any of the regions, such as those related to urban planning.

This study included rural areas, which are often not included in studies on the health effects of temperature. We detected higher temperature-related mortality in rural areas, for both heat and cold, and a greater decline in cold-related mortality in the second period. Even though only data from the capital of the province was used, potentially leading to misclassification, we observed in a previous study that the

Table 4
Relationship between the difference in mortality attributable fraction (%) in period 1 and 2 and the province level variable. Results (regressions coefficients (coef) and 95% confidence intervals (CI)) obtained from meta-regression models. Number of elements in the Heat Health Prevention Plan in each Spanish Province.

	Single variable models		Two variable models					
	Coef (95% CI)	p-value	Coef (95% CI)	p-value	Coef (95% CI)	p-value	Coef (95% CI)	p-value
Models for extreme heat								
Number of elements in HHPP	− 0.015 (− 0.024, − 0.006)	0.0013	− 0.008 (− 0.018, 0.002)	0.0994	− 0.010 (− 0.020, 0.000)	0.0590	− 0.011 (− 0.020, − 0.001)	0.0359
Avg. max. temperature	− 0.064 (− 0.094, − 0.033)	< 0.0001	− 0.051 (− 0.085, − 0.017)	0.0032				
% air conditioning	− 0.012 (− 0.019, − 0.006)	0.0004			− 0.009 (− 0.016, − 0.002)	0.0188		
Vulnerability index	− 1.056 (− 1.629, − 0.485)	0.0003					− 0.850 (− 1.441, − 0.259)	0.0048
Models for activation of the plan								
Number of elements in HHPP	− 0.005 (− 0.009, − 0.006)	0.0274	− 0.004 (− 0.009, 0.001)	0.1261	− 0.003 (− 0.008, 0.002)	0.2574	− 0.005 (− 0.009, − 0.000)	0.0434
Avg. max. temperature	− 0.021 (− 0.042, 0.001)	0.0648	− 0.011 (− 0.035, 0.012)	0.3479				
% air conditioning	− 0.007 (− 0.013, − 0.001)	0.0208			− 0.005 (− 0.012, 0.002)	0.1841		
Vulnerability index	− 0.293 (− 0.841, 0.255)	0.2942					− 0.157 (− 0.701, 0.387)	0.5720

HHPP: heat-health prevention plan.

correlation between temperatures in rural and urban areas from the same province was high (> 0.87) (Martínez-Solanas et al., 2018). Thus, we expect the potential bias introduced by this fact to be low. A study in the U.S. found higher risk for heat-related mortality in rural areas, but the opposite for cold (Shi, Kloog et al., 2015). Another study in Australia found stronger effects of cold on mortality and emergency department visits in rural areas, while the effect of heat on mortality was higher in major cities (Jegasothy et al., 2017). A study on the effect of heat on acute heat illness in the entire U.S. found higher effects in metropolitan areas than in rural areas (Hess et al., 2014), while a similar study conducted in the state of North Carolina (U.S.) reported higher risks in rural counties (Lippmann et al., 2013). Overall, results are not consistent and can be location-dependent, depending on, for example, working patterns (e.g. agricultural work outdoors), age structure, housing conditions or air conditioning prevalence, among others. However, regardless of where the effects of temperature are stronger, it should be clear that both urban and rural areas are at risk for temperature-related mortality.

This study has some limitations. First, our analysis was based on maximum temperature registered from a single monitoring station in each province (located in the province capital), leading to misclassification. The exposure misclassification is expected to be stronger in rural areas that are far from the province capital. Those rural areas often account for a small proportion of the population in the province, therefore any potential bias in overall estimates is expected to be small. However, our estimates for rural areas should be interpreted with caution. Moreover, it is important to highlight that, although temperature from different monitoring stations in a province, including rural and urban areas, had correlations above 0.87 (Martínez-Solanas et al., 2018), in cities temperature can be affected by factors such as the urban heat island (CalEPA, 2017). It is hard to anticipate the direction of the bias caused by this exposure misclassification in rural areas, as this can vary with time. For example, temperature differences between rural areas and cities may be wider (or smaller) in the hottest days, which are also the ones that register more deaths. Second, when applying the exposure-response function from period 1 to the temperatures in period 2, we were extrapolating the values at the extreme temperatures not registered in period 1. Third, the design of our study does not allow establishing causality because we cannot evaluate whether other changes occur during the study period. Fourth, we did not include data on air pollution as this was not available. Nevertheless, as argued by Buckley et al. (2014), air pollution should not confound the effects of temperature. However, some studies have reported interactions between temperature and air pollution. The role of such interactions on temporal changes is an interesting topic for future studies. Fifth, our study accounted for short-term mortality displacement of up to three weeks. However, mortality displacement at longer scales was not considered. One study including data from Spain (Armstrong et al., 2017) reported that the effects of having low winter mortality on the following summer were low.

5. Conclusions

Our nationwide study reported a decrease in cold-related mortality in the last years, and also a decrease in mortality attributable to extreme but not moderate heat. The effect of extreme heat decreased more in the regions that implemented more actions in the heat-health prevention plan, although other characteristics of the regions could explain this reduction. Further public health actions are needed to reduce the burden of heat-related mortality in Spain.

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Declarations of interest

There are no conflicts of interest to declare.

Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.envres.2018.11.006.

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