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The evolution of minimum mortality temperatures as an indicator of heat adaptation: The cases of Madrid and Seville (Spain).

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- 1 The Evolution of Minimum Mortality Temperatures as an Indicator of Heat Adaptation: The
- 2 Cases of Madrid and Seville (Spain)
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9 Abstract

The increase in the frequency and intensity of heat waves is one of the most unquestionable effects of climate change. Therefore, the progressive increase in maximum temperatures will have a clear incidence on the increase in mortality, especially in countries that are vulnerable due to geographical location or their socioeconomic characteristics. Different research studies show that the mortality attributable to heat is decreasing globally, and research is centred on future scenarios. One way of detecting the existence of a lesser impact of heat is through the increase in the so-called temperature of minimum mortality (TMM). The objective of this study is to determine the temporal evolution of TMM in two Spanish provinces (Seville and Madrid) during the 1983-2018 period and to evaluate whether the rate of adaptation to heat is appropriate. We used the gross rate of daily mortality due to natural causes (CIEX: A00-R99) and the maximum daily temperature (°C) to determine the quinquennial TMM using dispersion diagrams and realizing fit using quadratic and cubic curvilinear estimation. The same analysis was carried out at the annual level, by fitting an equation to the line of TMM for each province, whose slope, if significant (p<0.05) represents the annual rate of variation in TMM. The results observed in this quinquennial analysis showed that the TMM is higher in Seville than in Madrid and that it is higher among men than women in the two provinces.

Furthermore, there was an increase in TMM in all of the quinquennium and a clear decrease in the final period. At the annual level, the linear fit was significant for Madrid for the whole population and corresponds to an increase in the TMM of 0.58 °C per decade. For Seville the linear fits were significant and the slopes of the fitted lines was 1.1°C/decade. Both Madrid and Seville are adapting to the increase in temperatures observed over the past 36 years, and women are the group that is more susceptible to heat, compared to men. The implementation of improvements and evaluation of prevention plans to address the impact of heat waves should continue in order to ensure adequate adaptation in the future.

Introduction

One of the effects that is directly related to the impacts of climate change on health is the increase in maximum daily temperatures, and therefore, the increase in the frequency and intensity of heat waves (IPCC, 2013). Different studies indicate that these heat waves are going to have a clear incidence in the increase in daily mortality associated with the high temperatures that are projected to occur in the future, along with their associated economic impact (Hajat et al., 2014; Guo et al., 2018; Díaz et al., 2019).

Much of this research begins with the assumption of a constant impact of mortality

attributable to heat over time. This is to say that the increase in mortality due to each degree of increase in temperature during a heat wave is constant. It also supposes a heat wave definition temperature that remains constant over time (Roldán et al., 2016; Guo et al., 2018; Díaz et al., 2019). However, the assumption of a constant impact of heat on mortality is not realistic. Studies show that the impact of mortality attributable to heat is decreasing globally (Coates et al., 2014; Barreca et al., 2016; Vicedo-Cabrera et al., 2018; Díaz et al., 2018), which causes us to believe in the existence of possible adaptation to heat, due to multiple factors related both to the existence of prevention plans (Ebi and Rocklow 2014; Martínez et al.,

2019) as well as social, cultural (Bobb et al., 2014), health, and economic factors and infrastructure improvements (Sheridan et al.2018; Linares et al., 202**0a**).

Another way of detecting that existence of a lower impact of heat on mortality is through the increase in the threshold temperature that gives way to an increase in heat-related mortality, which is to say that in each place, a higher and higher temperature would be needed to produce fatalities due to high temperatures. This temperature is referred to as the temperature of minimum mortality (TMM) (Astrom et al., 2016), and it corresponds to the vertex of the traditional V form detected epidemiologically for the relationship between temperature and mortality (Alberdi et al., 1998; Montero et al., 2012; Díaz et al., 2002a).

From the point of view of the evaluation of existing prevention plans in different locations in Europe, evaluation lies in the decrease in mortality in specific places (Fouillet et al., 2008; de 'Donato et al., 2018; Linares et al., 2015) and in determined age groups, especially the elderly (de 'Donato et al., 2018; Pascal et al., 2019) using diverse methodologies with results that are difficult to compare. This complicates the development of measures for improvement of prevention plans (Martínez et al., 2019).

Therefore, another way to evaluate the adaptation to heat and the effectiveness of institutional measures adopted (such as those adopted autonomously by the population) is to look at whether the temporal evolution of the TMM has occurred at the same rate as other climate models in which different scenarios and time horizons estimate an increase in daily temperature as a consequence of global warming (Martínez et al., 2019; Linares et al., 2020a). Thus, "complete adaptation" would occur when the percentile that corresponds to TMM in relation to the series of maximum daily temperatures of the summer months remains constant over time (Martínez et al., 2017; 2018; Díaz et al., 2019a). This would suppose, for example, that for the period 2031-2080 the TMM must increase by at least 1.4 °C in Spain and 1.7 °C in Finland in a RCP4.5 scenario and 2.2 °C in Iceland or 3.3 in Moldova in a RCP 8.5 scenario,

according to data from Guo et al. (Guo et al., 2018). In this sense, the determination of the temporal evolution of the TMM seems a key point to the evaluation of these current prevention plans.

Despite the importance of TMM as an indicator of processes of adaptation to heat, its evolution has been studied infrequently. Studies carried out in Stockholm during the 1901-2009 period are worth highlighting (Astrom et al., 2016); as well as the study carried out in various Spanish cities during 1975-2003 (Mirón et al., 2008), the country-wide study in Japan during 1972-2012 (Chung et al., 2018) and in France during 1968-2009 (Todd and Valeron, 2015). All of these studies found an increase in TMM that authors explain according to the incidence of different demographic (Mirón et al., 2008) or socioeconomic factors (Sheridan et al., 2018) and adaptation (Bobb et al., 2014; Todd and Valerón, 2015). In these studies, the analyses were carried out at the general population level and for all causes of mortality, without consideration of the differences that might exist between the sexes.

However, an analysis at a smaller than state level of the mortality associated with high temperatures is also called for. This is because of factors like population age (Montero et al., 2012), geographic location (Allen and Sheridan, 2018), socioeconomic level (Paz and Semenza 2013), level of acclimatization (Van Loenhout el tal., 2016), and even factors related to urban character such as the existence of the thermal island effect (Burkart et al., 2016) and the age of the building structures (López-Bueno et al., 2019).

The objective of this study was to determine the temporal evolution of TMM in two Spanish cities in which there has been a sudden decrease in the impact of heat, such as the case of Seville, and in other where this decrease has been much more moderate, such as the case of the city of Madrid, for the period 1983-2018 (Díaz et al., 2018). Comparing the rate of variation in TMM with the rate of increase in maximum temperature foreseen for these cities in other studies for the horizon 2050-2100 for an RCP 8.5 scenario (Díaz et al., 2019a) serves to

evaluate whether the rate of adaptation to heat in these provinces is that which is necessary to avoid an increase in the number of heat waves during the period, and thus, in the associated mortality due to heat waves. This study provides for differences in sex, given that women are especially susceptible to heat, as mentioned earlier (Gagnon et al., 2013).

Methodology

Variables:

The dependent variable in this study was daily mortality due to natural causes (CIEX: A00-R99) that took place in the province of Madrid and Seville during the 1983-2018 period. Mortality refers to the morality in municipalities of more than 10,000 inhabitants in these provinces. These data were provided by the National Statistics Institute (INE). The daily population at the province level was calculated based on annual population data (also provided by INE), using linear interpolation. Mortality data and population data were used to obtain the gross mortality rate per 100,000 inhabitants for each province and for each of the specific causes already described. The data were disaggregated by sex.

The independent variable was maximum daily temperature (Tmax) in degrees Celsius (°C) during the period mentioned, measured in the observatories of reference in Madrid and Seville, established by the State Meteorological Agency (AEMET), which also provided these data.

Determination of the maximum daily temperature of minimum mortality (TMM)

The determination of TMM was made along two scales for the data of the two provinces analysed. The first five year scale grouped mortality rates and maximum daily temperatures during the periods: 1983-1988 (first quinquennium); 1989-1993 (second quinquennium); 1994-

1998 (third quinquennium); 1999-2003 (fourth quinquennium); 2004-2008 (fifth quinquennium); 2009-2013 (sixth quinquennium) y 2014-2018 (seventh quinquennium). Based on the daily values of Tmax and daily mortality rates, we analysed the functional relationship through dispersion diagrams, which situated Tmax on the X axis in intervals of ^oC and average daily mortality on the Y axis.

Later adjustment was made by means of a quadratic and cubic curvilinear estimation choosing the curve with the best fit. The temperature of minimum mortality is the minimum point on the fitted curves. In this way, a maximum daily temperature of minimum mortality was obtained for each quinquennium and province, representing the temporal evolution each five years. This same analysis was carried out at the annual level, and the evolution of the TMM for each province from 1983 to 2018 was represented by fitting the evolution to the equation of a line, whose slope, if significant (p<0.05), represents the annual rate of variation in TMM.

Results

Descriptive statistics of the dependent and independent variables for the provinces of Madrid and Seville are shown in Tables 1 and 2, respectively. In these tables it should be noted that the average maximum daily temperature in the first quinquennium in Madrid rose from 19.7 °C (IC95% 19.3 20.1) to 21.3 °C (IC95% 20.9 21.7) in the last, representing an increase of 1.6 °C, which is a statistically significant difference. In the case of Seville the average maximum daily temperature rose from 24.8 °C in the first quinquennium (IC95% 24.1 25.1) to 26.0 °C (IC95% 25.6 26.4) in the last, with a statistically significant difference of 1.2 °C (p<0.05).

In terms of TMM at the quinquennium level, in all cases the best curvilinear fit was that of a third degree polynomial. At the annual level and for the general population, the best curvilinear fit was for a third degree polynomial except for the years 2000 and 2016, in which

case the best fit was a quadratic function. For the case of men, the cubic fit was the best, except for the years 1989 and 2009, in which the quadratic was best. In the case of women, only in the year 2016 was the cubic fit substituted for the quadratic fit.

Figures 1a and 1b show the temporal evolution of TMM for the provinces of Madrid and Seville, both for the general population as well as disaggregated for men and women. These figures show that the TMM was higher Seville than in Madrid, and furthermore, it was more elevated in men than in women. Also, there is was increase in this TMM in all of the quinquennium, with a clear decrease in TMM in the last quinquennium, especially in the case of Madrid.

Figure 2 shows the annual change for the city of Madrid, both in terms of TMM and in the annual rates of mortality in winter (the months of November to May) and summer (the months of June to September). The Pearson's correlation coefficients among the series of TMM and the rates in summer and winter for the total of the series were -0.27 and -0.13, respectively, but not statistically significant. For the case of the periods of 1999-2003 and 2014 2018, the correlation coefficient between TMM and the mortality rate in summer was -0.658, which is significant at p<0.05.

Figures 3a and 3b show the temporal evolution in the TMM corresponding to mortality due to natural causes with more detail for Madrid and Seville, respectively. They show the TMM for each year, both for men and for women as well as the slope of the corresponding linear fit.

For the case of Madrid for the general population for both men and women, the linear fit is significant at p<0.05. The case of the whole population corresponds to the slope of a line of 0.0577 °C/year, or an increase in the TMM of 0.58 °C/decade. For the case of men, the slope of the fitted line is 0.65 °C/decade, and for women it is 0.56 °C/decade.

Figure 3b shows the results of the province of Seville, for which the fitted lines are significant at p<0.05. The slopes of the lines of TMM both for the general population as well as for men and women were greater than those found in the province of Madrid. Specifically, in the case of the whole population the slope of the fitted line was 1.1°C/decade, greater than the result obtained for Madrid. In the case of men, in the same way as for Madrid, the slope of the fitted line of 1.2 °C/decade was greater than that of women at 1.0 °C/decade.

Discussion

The countries in the Mediterranean basin are those that are most affected by climate change (Negev et al., 2015). The current average annual increase in temperatures compared to those of the nineteenth century, is 1.4 °C, which is higher than the global warming of the planet (Cramer et al., 2018). In our case, the increases in the average maximum daily temperatures found between the quinquennia 1983-1988 and 2014-2018 of 1.6 °C in the case of Madrid and 1.2 °C in the case of Seville are similar to the increases described for the Mediterranean (Cramer et al., 2018). However, it should be taken into account that our case is not compared with the average of the whole century, and our data refer to the maximum daily temperatures and not the average temperatures.

Figures 1a and 1b show clearly that the TMM for men is greater than that of women, which indicates greater vulnerability to the impact of heat among women compared to men. These results agree with results found in other studies carried out in Madrid (Díaz et al., 2002a) and Seville (Díaz et al., 2002b). According to these studies, the percentage increase in mortality for each degree above the temperature definition of a heat wave was 12.6 percent for men over age 75, while for women it reached 28.4 percent. In Seville, the impact per degree for men

over age 65 was 29 percent, while for women it reached 46 percent. These results also

coincide with those found in other locations and establish that, in general, the risk of death due to heat in women is greater than it is in men (Kovats **and** Hajat, 2008).

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In addition to health differences in the context of gender, there are physiological differences in thermoregulatory function between men and women that could explain the greater impact of heat in women, including: body size, physical condition and/or state of adaptation (Gagnon and Kenny, 2012). There are also added factors such as greater body fat among women and the role played by sexual hormones in thermoregulatory mechanisms (Guyton and Hall, 2011). In general, the most noteworthy results of the quinquennial analysis of the evolution of TMM shown in Figures 4a and 4b is the decrease in TMM found in the quinquennium of 1999-2003, and especially during 2014-2018, thanks to the low TMM in the year 2015, especially in the case of Madrid. Figure 2 shows this behavior, showing the temporal evolution of TMM versus the mortality rate in winter periods (the months of November to March) and summer periods (months of June to September) for Madrid. A negative correlation coefficient between TMM and the mortality rate in summer indicates a high summer mortality related to lower minimum mortality temperatures. Therefore, the decrease in TMM found in these periods is related to the high rate of mortality produced in those years due to circulatory causes but not for mortality due to respiratory causes, which agrees with the results found in Madrid and in other places in Spain that show that it is circulatory causes that have the greatest association with summer mortality (Díaz et al., 2002a; Díaz et al., 2002b; Montero et al., 2012; Mirón et al.,

Another of the results obtained in this study is that a better fit in the dispersion diagrams of maximum daily temperature-mortality rate is, in the majority of cases, a third degree polynomial. A fit of a third degree polynomial supposes the existence of a maximum and minimum value in the fitted curve. The maximum value in the mortality rate corresponds to a low temperature, thus there is a relationship with winter mortality, while the minimum value

of the mortality rate corresponds to the TMM value that is the concern of this study. Therefore, the fit of the third degree polynomial indicates that maximum mortality continues to occur in the winter, despite the increase in the maximum daily temperature seen in this study. These result agrees with the results found in other studies, which show that winter mortality does not decrease in a significant way, despite global warming (Ebi and Mills; 2013; Staddom et al., 2014; Martínez et al., 2018; Díaz et al., 2019a), probably due to the fact that a better adaptation to high temperatures is accompanied by a "de-adaptation" to low ones, and what currently does not constitute a cold wave will probably do so in the near term future (Díaz et al., 2019b).

The slope of the line that corresponds to the fit of TMM across the 2983-2018 period indicates that that minimum mortality temperature is increasing at a rate of 0.58 °C/decade for Madrid and 1.1°C for Seville. The value for Madrid was less than that of the city of Stockholm, which established this increase of 0.8 °C/decade in TMM (Astrom et al., 2016) and that of Japan of 1.4 °C/decade (Chung et al., 2018), but similar to that obtained for other places in the Mediterranean part of Europe such as some French cities, at 0.53 °C/decade (Todd and Valleron, 2015). According to studies carried out in Madrid (Díaz et al., 2019a), in an RCP8.5 scenario, the average maximum daily temperatures will rise from 29.9°C in the 2000-2009 period to 34.8 in 2050-2100. This represents an increase of 0.54 °C/decade, which means going from 22 heat waves/year with an associated mortality of 230 deaths/year in 2000-2009 to 74 heat waves/year in the 2050-2100 period and an associated mortality of 2250 deaths/year. Therefore, the rate at which TMM would need to increase in order to avoid an increase in mortality is very similar to that which currently exists. It is also true that this rate would have been 0.78 °C/decade, if the behavior of the anomalous years of 2015 and 2018 was eliminated.

For the case of Seville, the rate of increase in TMM for both sexes was 1.14 °C/decade, much higher than Madrid, France (Todd and Valleron, 2015) and Stockholm (Astrom et al., 2016) and similar to that of Japan (Chung et al., 2018). The average of the maximum daily temperatures in Seville in the 2000-2009 period was 34.4 °C with 7 heat waves/year and an associated mortality of 63 deaths/year. In 2050-2100 it will increase to 39.8 °C, which represents an increase of 0.6 °C/ decade. On this time horizon there will be 64 heat waves/year with 1050 deaths/year. In this case, the rate of increase in TMM is greater than that which is needed to avoid an increase in mortality due to heat in Seville.

A greater rate of increase in TMM than rate of increase in the temperature results in an increase in the percentile values of TMM related to the series of maximum daily temperatures. This is especially clear in the case of Seville, in which the average maximum temperature has increased at a rate of 0.3°C/decade, while TMM have increased by 1.1 °C/decade, and therefore the TMM percentiles have increased over the time of study.

The fact that the rate of evolution of TMM for Seville was higher than for Madrid indicates that the places with high temperatures are less vulnerable to heat than those with more temperate climates, which is consistent with other studies carried out in different locations (Chung et al., 2015, 2017; Gasparrini et al., 2015; Linares et al., 2015b; Montero et al., 2012), and the adaptation to high temperatures is greater (Chung et al., 2018). The same result was observed by sex, thus, the rate of increase in TMM in the case of women, a more vulnerable population, was lower than that of men, which agrees with the gender and physiological differences already described (Gagnon et al., 2013).

As limitations of this study, it should be noted that from a methodological point of view, the causality between daily mortality and daily maximum temperature cannot be inferred with the scatter plots performed. The objective in this study, is to see how the temperature of minimum mortality (TMM) evolves and not to observe changes in daily mortality attributable

to heat. This last analysis can be reach with a process of pre-whitening of the series and the representation of the residuals of the daily mortality data against temperature to speak strictly about mortality attributable to heat. In addition, this methodology to calculate TMM has been used previously in other studies (Miron et al., 2007; Mirón et al., 2008, Alberdi et al., 1998). On the other hand, the possible effect on daily mortality of other variables such as: Relative humidity (Díaz et al., 2015), chemical atmospheric pollution by ozone (Díaz et al., 2002), an increase in particulate material, caused by anthropogenic origin (Ortíz et al., 2017) or caused by advection of dust from the Sahara (Díaz et al., 2017) seems to have few relevant effect in the different analysis conducted in Spain. To finish, in all of the studies that analyze the effect of environmental variables on health variables, there is a problem of misalignment (Gelfand AE, 2010; Barceló et al., 2016).

It can be concluded from the results of this study in terms of the evolution of TMM that both Madrid and Seville are adapting to the increase in temperatures that has been observed in the past 36 years. This had already been detected through the decrease in RA attributable to mortality due to heat waves that was especially important in the case of Seville (Díaz et al., 2018). This supports the evolution of TMM shown in this work. The results of this study show that women are a group that is more susceptible to heat, compared to men, and therefore measures for adaptation should be aimed especially at women.

On the other hand, that the rate of adaptation that was obtained in the studied period has helped avoid greater mortality due to heat as a consequence of registered temperature increases does not guarantee that the same will occur in the future. Therefore, the challenge lies in continuing with adaptation. From the perspective of "planned" adaptation (that is to say, institutional adaptation), this includes continuing to progress in terms of implementation, evaluation and improvement in prevention plans (Linares et al., 2020b), greater governance

and stakeholder involvement (Martinez et al., 2019), interventions at the urban and healthcare level, and improvements in infrastructure and population education.

Disclaimer

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References:

- Alberdi JC, Díaz J, Montero JC, Mirón I. Daily mortality in Madrid community (Spain)
 1986-1992: Relationship with meteorological variables. Eur J Epidemiol 1998; 14: 571 8.
- Allen MJ & Sheridan SC. Mortality risks during extreme temperature events (ETEs)
 using a distributed lag non-linear model. Int J Biometeorol. 2018; 62(1), 57–67.
- Åström DO, Tornevi A, Ebi KL, Rocklöv J, Forsberg B. Evolution of Minimum Mortality
 Temperature in Stockholm, Sweden, 1901-2009. Environ Health Perspect. 2016
 Jun;124(6):740-4.
- Barceló MA, Varga D, Tobias A, Díaz J, Linares C, Saez M. Long term effects of traffic
 noise on mortality in the city of Barcelona, 2004-2007. Environ. Res. 2016, 147, 193 206.
- Barreca A, Clay K, Deschenes O, Greenstone M, Shapiro JS. Adapting to Climate
 Change: The Remarkable Decline in the US Temperature-Mortality Relationship over
 the Twentieth Century. J Politic Economic 2016; 124(1):105-109.
- Bobb JF, Peng RD, Bell ML & Dominici F. Heat-related mortality} and adaptation to heat
 in the United States. Environ Health Perspect 2014; 122(8), 811–816.
- Burkart K, Meier F, Schneider A, Breitner S, Canário P, Alcoforado MJ, et al.
 Modification of Heat-Related Mortality in an Elderly Urban Population by Vegetation
 (Urban Green) and Proximity to Water (Urban Blue): Evidence from Lisbon, Portugal.
 Environ Health Perspect 2016; 24(7):927-34.
- Chung Y, Lim YH, Honda Y, Guo YL, Hashizume M, Bell ML, Chen BY, Kim H. Mortality
 related to extreme temperature for 15 cities in northeast Asia Epidemiology. 2015
 Mar;26(2):255-62.

- Chung Y, Noh H, Honda Y, Hashizume M, Bell ML, Guo YL, Kim H. Temporal Changes in
 Mortality Related to Extreme Temperatures for 15 Cities in Northeast Asia: Adaptation
 to Heat and Mal adaptation to Cold.Am J Epidemiol. 2017 May 15;185(10):907-913
- Chung Y, Yang D, Gasparrini A, Vicedo-Cabrera AM, Fook Sheng Ng C, Kim Y, et al.

 Changing Susceptibility to Non-Optimum Temperatures in Japan, 1972-2012: The Role

 of Climate, Demographic, and Socioeconomic Factors. Environ Health Perspect

 2018;126(5):057002.
- Coates L, Haynes K, O'Brien J, McAneney J, De Oliveira FM. Exploring 167 years of vulnerability: An examination of extreme heat events in Australia 1844-2010. Environ Science& Policy 2014; 42: 33-44.
- Cramer, W., Guiot J., Fader M., Garrabou J., Gattuso J.-P., Iglesias A., et al., 2018.

 Climate change and interconnected risks to sustainable development in the Mediterranean, Nature Climate Change 8, 972-980.
- de'Donato F, Scortichini M, De Sario M, de Martino A, Michelozzi P. Temporal variation
 in the effect of heat and the role of the Italian heat prevention plan. Publ Health
 2018;161, 154–162.
- Díaz J, López C, Jordán A, Alberdi JC, García R, Hernández E, Otero A. Heat waves in
 Madrid, 1986-1997: effects on the health of the elderly. International Archives
 Occupational and Environmental Health. 2002a; 75:163-170.
- Díaz J, García R, Velázquez F, López C, Hernández E, Otero A. Effects of Extremaly Hot
 Days on People older than 65 in Seville (Spain) from 1986 to 1997. International
 Journal of Biometeorology. 2002b; 46:145-149.
- Díaz J, Carmona R, Mirón IJ, Ortiz C, León I, and Linares C. Geographical variation in
 relative risks associated with heat: update of Spain's Heat Wave Prevention Plan.
 Environment International. 2015; 85:273-283.

- Díaz J, Linares C, Carmona R, Russo A, Ortiz C, Salvador P,Trigo RM. Saharan dust
 intrusions in Spain: health impacts and associated synoptic conditions. Environmental
 Research 2017; 156:455-467.
- Díaz J, Carmona R, Mirón IJ, Luna MY, Linares C. Time trend in the impact of heat
 waves on daily mortality in Spain for a period of over thirty years (1983-2013).
 Environment International 2018; 116:10-17.
- Díaz J, Sáez M, Carmona R, Mirón IJ, Barceló MA, Luna MY, Linares C. Mortality
 attributable to high temperatures over the 2021-2050 and 2051-2100 time horizons in
 Spain: adaptation and economic estimate. Environmental Research. 2019a; 172:475 485.
- Díaz J, López-Bueno JA, Sáez M, Carmona R, Mirón IJ, Barceló MA, Luna MY, Linares C.
 Will there be cold-related mortality in Spain over the 2021-2050 and 2051-2100 time
 horizons despite the increase in temperatures as a consequence of climate change?
 Environmental Research 2019b Jun 19; 176:108557.
- Ebi KL, Mills D. Winter mortality in a warming climate: A reassessment. Wiley

 Interdiscp Rev Clim Change 2013; 4:203-212.
- Ebi KL, Rocklöv J. 2014. Climate change and health modeling: horses for courses. Glob
 Health Action 7:24154.
- Fouillet A, Rey G, Wagner V, Laaidi K, Empereur-Bissonnet P, Le Tertre A, Frayssinet P,

 Bessemoulin P, Laurent F, De Crouy-Chanel P, Jougla E, Hémon D. Has the impact of

 heat waves on mortality changed in France since the European heat wave of summer

 2003? A study of the 2006 heat wave. Int J Epidemiol 2008; 37: 309–317.
- Gagnon D, Kenny GP. Does sex have an independent effect on thermal effect or responses during exercise in the heat? J Physiol 2012; 590: 5963-5973, 2012.
- Gagnon D, Crandall C G, Kenny GP. Sex differences in postsynaptic sweating and
 cutaneous vasodilation. J Appl Physiol 2013;114(3), 394–401.

- Gasparrini A, Guo Y, Hashizume M, Kinney PL, Petkova EP, Lavigne E, Zanobetti A,

 Schwartz JD, Tobias A, Leone M, Tong S, Honda Y, Kim H, Armstrong BG. Temporal

 Variation in Heat-Mortality Associations: A Multicountry Study. Environ Health

 Perspect. 2015 Nov; 123(11):1200-7.
- Gelfand AE. Misaligned spatial data: The change of support problem. Handbook of
 Spatial Statistics; Gelfand AE, Diggle PJ, Fuentes M, Guttorp P, Eds.; Taylor & Francis:
 Boca Raton, FL, USA, 2010.
- Guo Y, Gasparrini A, Li S, Sera F, Vicedo-Cabrera AM, de Sousa Zanotti Stagliorio
 Coelho M, Saldiva PHN, et al. Quantifying excess deaths related to heatwaves under
 climate change scenarios: A multicountry time series modelling study. PLoS Med. 2018
 Jul 31; 15(7):e1002629.
- Guyton AC y Hall JE. Tratado de Fisiología Médica. 12ª Ed. Madrid. Ed. Elsevier; 2011.
- Hajat S, Vardoulakis S, Heaviside C & Eggen B. Climate change effects on human
 health: projections 541 of temperature-related mortality for the UK during the 2020s,
 2050s and 2080s. Journal of Epidemiology 542 and Community Health 2014; 68(7),
 641–648.

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397

398

399

- IPCC. Climate Change 2013: The Physical Science Basis. Contribution of Working Group
 I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change
 [Stocker TF, Qin D, Plattner GK, Tignor M, Allen SK, Boschung J, Nauels A, Xia Y, Bex V,
 Midgley PM (eds.)]. 2013. Cambridge University Press, Cambridge, United Kingdom and New York, NY, USA, 1535 pp. http://www.ipcc.ch/report/ar5/2.
- Kovats RS, Hajat S. Heat stress and public health: a critical review. Annu Rev Public

 Health. 2008;29:41-55.
- Linares C, Sánchez R, Mirón IJ, DíazJ. Has there been a decrease in mortality due to
 heat waves in Spain? Findings from a multicity case study. J Integr EnvironSci 2015a;
 12, 153–163.

- Linares C, Diaz J, Tobias A, Carmona R, Mirón IJ. Impact of heat and cold waves on
 circulatory-cause and respiratory-cause mortality in Spain: 1975-2008. Stochastic
 Environmental Research and Risk Assessment. 2015b; 29:2037-2046.
- Linares C, Díaz J, Negev M, Sánchez-Martínez G, Debono R, Paz S. Impacts of Climate
 Change on the Public Health of the Mediterranean Basin Population Current
 Situation, Projections, Preparedness and Adaptation. Environmental Research 2020a;
 182, 109107.
- Linares C, Sánchez-Martínez G, Kendrovski V, Díaz J. A New Integrative Perspective on
 Early Warning Systems for Health in the Context of Climate Change. Environmental
 Research 2020b; 187, 109623.
- Lopez-Bueno JA, Diaz J, Linares C. Differences in the impact of heat waves according to
 urban and peri-urban factors in Madrid. Int J Biometeorol 2019; 63(3), 371-380.
- Martinez GS, Hooyberghs H, Bekker-Nielsen Dunbar, M, Linares C, Kendrovski V. Aerts
 R. Van Nieuwenhuyse A, Carmona R, Diaz J, De Ridder K, Lauwaet D,OrtizC Heat and
 health in Antwerp under climate change: projected impacts and implications for
 prevention. Environ Int 2017;111: 135–143.

422

423

424

- Martínez GS, Diaz J, Hooyberghs H, Lauwaet D, De Ridder K, Linares C, Carmona R,
 Ortiz C, Kendrovski V, Adamonyte D. Will a decrease in cold-related deaths
 compensate for an increase in heat-related mortality? A case study in Vilnius
 (Lithuania). Environment Research.2018; 166:384-393.
- Martínez GS, Linares C, Ayuso A, Kendrovski V, Boeckmann M, Díaz J. Heat-Health
 Action Plans in Europe: challenges ahead and how to tackle them. Environmental
 Research 2019 Jun 19; 176:108548.
- Mirón IJ, Montero JC, Criado-Álvarez JJ, Mayoral S, Díaz J, Linares C. Evolución de los
 efectos de las temperaturas máximas sobre la mortalidad por causas orgánicas en

- Castilla- La Mancha de 1975 a 2003. Revista Española de Salud Pública. 2007;81:375-432 385.
- Mirón IJ, Criado-Álvarez JJ, Díaz J, Linares C, Mayoral S, Montero JC. Time trends in
 minimum mortality temperatures in Castile- La Mancha (Central Spain): 1975 2003.
 International Journal of Biometeorology. 2008; 52:291-299.
- Miron IJ, Linares C, Montero JC, Criado-Alvarez JJ, Díaz J., 2015. Changes in cause specific mortality during heat waves in central Spain, 1975-2008. Int J Biometeorol
 59(9):1213-22.
- Montero JC, Miron IJ, Criado-Alvarez JJ, Linares C, Diaz J. Influence of local factors in
 the relationship between mortality and heat waves: castile-La Mancha (1975-2003). Sci
 Total Environ 2012; 414: 73–80.
- Negev, M., Paz, S., Clermont, A., Pri-Or, N., Shalom, U., Yeger, T. Green, M., 2015.

 Impacts of climate change on vector borne diseases in the Mediterranean Basin—

 implications for preparedness and adaptation policy. Int. J. Environ. Res. Pub. Heal.

 12(6), 6745-6770.
- Ortiz C, Linares C, Carmona R, Díaz J. Evaluation of short-term mortality attributable to
 particulate matter pollution in Spain. Environmental Pollution.2017; 224:541-551.
- Pascal M, Wagner V, Corso M, Laaidi K, Le Tertre A. Évolution de l'exposition aux
 canicules et de la mortalité associée en France métropolitaine entre 1970 et 2013.
 Santé Publique Française.2019. 69 P.
- Paz S, Semenza J. Environmental drivers of West Nile fever epidemiology in Europe and Western Asia—a review. Int J Env Res Pub Health 2013;10(8):3543-3562.
- Roldán E, Gómez M, Pino MR, Pórtoles J, Linares C, Díaz J. The effect of climatechange-related heat waves on mortality in Spain: Uncertainties in health on a local scale. Stochastic Research and Risk Assessment. 2016;30:831-839.

- Sheridan SC, Allen MJ. Temporal Trends in human vulnerability to excesssive heat.
 Environl Res Letters 2018; 13(4)1-12.
- Staddon PL, Montgomery HE, Depledge MH. Climate warming will not decrease winter

 mortality. Nat Clim Change 2014; 4:190-194.
- Todd N, Valleron A-J. Space-Time Covariation of Mortality with Temperature: A
 Systematic Study of Deaths in France, 1968-2009. Environ Health Perspect.
 2015;123(7):659-64.
- Van Loenhout, J., Rodriguez-Llanes, J., Guha-Sapir, D., van Loenhout, J. A. F.,
 Rodriguez-Llanes, J. M., Guha-Sapir, D.,2016. Stakeholders' Perception on National
 Heatwave Plans and Their Local Implementation in Belgium and The Netherlands. Int.
 J. Env. Res. Pub. Health 13(11), 1120.
- Vicedo-Cabrera AM, Sera F, Guo Y, Chung Y, Arbuthnott K, Tong S, et al. A multi country analysis on potential adaptive mechanisms to cold and heat in a changing
 climate. Environ Int. 2018 Feb; 111:239-246.