Effectiveness of the Spanish plan to prevent the health effects of high temperatures

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A en Quim, per ensenyar-me cada dia,
a l’Eloi, per compartir la vida amb mi,
als meus pares, per guiar-me fins aquí

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Aquest és el moment i el lloc per agrair a totes les persones que m'han ensenyat, guiat, ajudat i recolzat durant tot aquest llarg camí. I és que els agraïments és una de les parts més importants d'una tesi. A través de la seva lectura, un es pots fer una idea de l'esforç i de les persones que han contribuït a aquest treball d'investigació. Aquesta tesi doctoral és fruit de moltes persones. És més que un projecte professional, és un repte personal, un projecte familiar.

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Abstract

Exposure to ambient temperatures has been widely described as an important health hazard. The most studied effect of temperatures is an increase on mortality; however, there is less evidence on other health impacts. In response to climate change and associated extreme events, public health adaptation has become imperative. The Spanish Government implemented in 2004 a heat health prevention plan (HHPP). This thesis aimed to evaluate the effectiveness of the Spanish HHPP in terms of reductions in mortality and cause-specific hospitalizations, and to assess the effects of weather factors on gastroenteritis and on occupational injuries. Daily maximum and average temperature, and daily precipitation in each capital of province were used as exposure measures. Daily counts of deaths, hospitalizations for cardiovascular, cerebrovascular and respiratory diseases, hospitalizations for infectious gastroenteritis and occupational injuries registered in Spain were included as health outcomes. Our results suggested that the implementation of the HHPP has reduced extreme heat-related mortality and respiratory admissions. By contrast, an increment of moderate heat-related mortality was observed. We also found that the effects of cold temperatures on mortality and respiratory admissions experienced a decrease in the second period, although this was not observed for cardiovascular and cerebrovascular admissions. Cold and heat were also associated with higher risk of gastroenteritis admissions and occupational injuries. An important economic impact of working at non-optimum temperatures has been estimated in this thesis. We observed a protective effect of heavy precipitation on gastroenteritis admissions. This thesis showed some improvements on health outcomes after the implementation of the HHPP. Nonetheless, ambient temperatures still have an important role in increasing health hazards. Public health prevention measures should consider all range of temperatures as well as target specific actions for some vulnerable groups, such as workers or children.

Resum

L'exposició a temperatures ambient ha estat àmpliament descrita com un important perill per a la salut. L'efecte més estudiat de les temperatures és un augment de la mortalitat, no obstant, l’evidència sobre altres impactes en salut és més escassa. Com a resposta al canvi climàtic i als seus esdeveniments extrems associats, mesures d'adaptació en salut pública són indispensables. El Govern espanyol va implementar el 2004 un pla de prevenció dels efectes en salut de la calor (HHPP). L’objectiu d’aquesta tesi era avaluar l'efectivitat del HHPP en quant a reducció de la mortalitat i de determinades causes específiques d’hospitalitzacions, així com avaluar els efectes dels factors climatològics en les gastroenteritis i les lesions laborals. Com a mesures d’exposició es van utilitzar la temperatura màxima i mitjana diària i la precipitació diària a cada capital de província. Es van incloure, com a indicadors de salut, el nombre diari de defuncions, hospitalitzacions per malalties cardiovasculars, cerebrovasculars i respiratòries, hospitalitzacions per gastroenteritis infeccioses i lesions laborals registrades a Espanya. Els nostres resultats van suggerir que la implementació del HHPP va reduir la mortalitat i també els ingressos hospitalaris per malalties respiratòries relacionats amb la calor extrema. Per contra, es va observar un increment de la mortalitat relacionada amb la calor moderada. També es va constatar que els efectes de les temperatures fredes sobre la mortalitat i ingressos respiratoris van experimentar una disminució en el segon període, mentre que aquesta reducció no es va observar en els ingressos cardiovasculars i cerebrovasculars.

El fred i la calor també es van associar amb un major risc d'ingressos per gastroenteritis així com de les lesions laborals. En aquesta tesi es va estimar un important impacte econòmic de treballar amb temperatures no òptimes. Es va observar un efecte protector de les precipitacions intenses en els ingressos per gastroenteritis. A més, aquesta tesi va mostrar algunes millores en salut després de la implementació del HHPP. De totes maneres, actualment les temperatures ambient suposen un perill per la salut. És necessari, per tant, que les mesures de prevenció en salut pública cobreixin tot el rang de temperatures, així com que s’estableixin accions específiques per a determinats grups vulnerables de població, com ara els/les treballadors/es o els infants.

Preface

This thesis has been conducted between 2015 and 2018 at ISGlobal (Barcelona Institute for Global Health) under the supervision of Dr. Xavier Basagaña and according to the Biomedicine PhD Program of the Department of Experimental and Health Sciences of Pompeu Fabra University. The research presented in this thesis has been funded by Instituto de Salud Carlos III and co-funded by European Union (ERDF, “A way to make Europe”), project “PI14/00421".

Climate change has important consequences on human’s health. Rising temperatures, one of the direct effects of climate change, have been associated with increases in mortality and morbidity. Public adaptation strategies, like heat health prevention plans, are useful tools to reduce the burden of disease produced by high temperatures. This thesis provides an assessment of the effectiveness of a heat health prevention plan introduced in Spain in 2004. It also gives insight into the potential effects of weather factors (temperatures and precipitation) on hospital admissions and occupational injuries. The book here presented is structured into seven sections, including a general introduction with a review of the relevant literature, the thesis’s rationale and objectives, the research results (four original papers, three of them published), a global discussion, final conclusions and several annexes.

Apart from the scientific publications included in this thesis, the PhD candidate has contributed in other scientific papers and in the

Health chapter of the *Third Report on Climate Change in Catalonia*, commissioned by the Catalan government. Her main work during this research consisted on data request, data cleaning, statistical analyses and writing the articles. The PhD candidate has also participated in writing project reports and communication of results at a local level, but also in international conferences as well as in activities address to the community. As a part of her training, she did a short scientific stay in the London School of Hygiene and Tropical Medicine (Department of Social & Environmental Health Research), under the supervision of Dr. Antonio Gasparrini.

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1. INTRODUCTION

1.1. Climate Change

Throughout history, climate has experienced alterations caused by several natural factors, such as ocean currents, the direction of prevailing winds or the *El Niño* phenomenon. However, in the last Century human activity has influenced our climate. Indeed, the Intergovernmental Panel on Climate Change (IPCC) in its last assessment report concluded that climate change is unequivocal and it has been forced by the human activity, through greenhouse gas (GHG) emissions in the atmosphere (IPCC, 2013). Concentrations of different pollutants, mainly carbon dioxide (CO_2), have grown in the last decades. This increase basically comes from emissions derived from fossil fuels combustion (oil, carbon and natural gas) (IPCC, 2013). CO_2 concentrations in the atmosphere have increased by 40% since 1750, when the industrial revolution began. Linked to this, global surface temperature has risen since the beginning of the last Century. Figure 1 shows the temporal trends in CO_2 emissions and global average surface temperature. As it can be observed, greenhouse gas emissions have increased at the same rate as temperature. Thus, for the first time, in 2015 global mean surface temperature was 1ºC higher than in pre-industrial era (MacGregor and WMO, 2015).

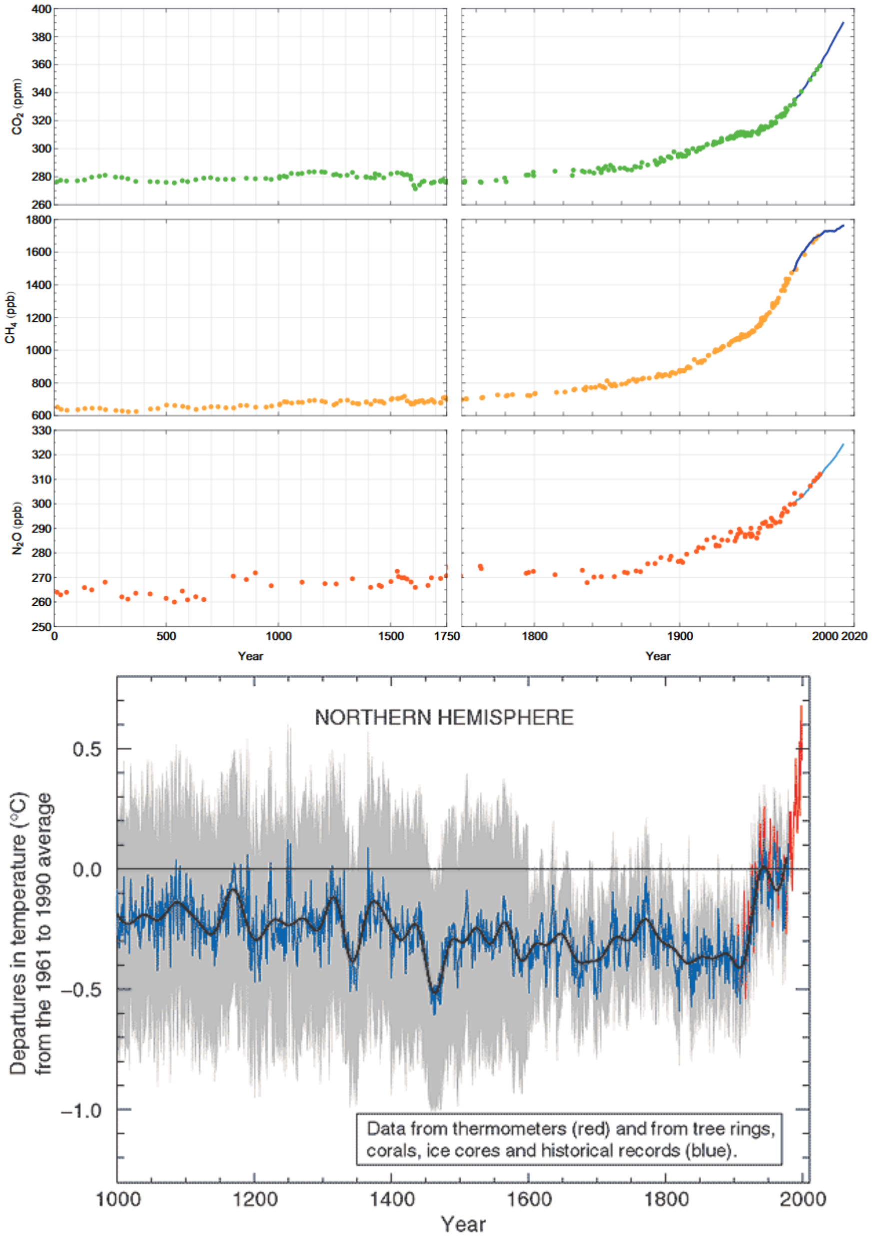


Figure 1: On top, atmospheric CO_2 concentration history over the industrial era (right) and from year 0 to the year 1750 (left). Below, variations of the global surface temperature over the last millennium.

Source: Adapted from the IPCC, 2013.

Projections indicate that the average surface temperature will keep increasing in the upcoming decades. In the Fifth Assessment Report, the IPCC includes temperature projections, according to four different scenarios (IPCC, 2014). These scenarios, defined as *Radiative Concentration Pathways* (RCP), take into account future trends in GHG emissions. For each of them, there is a projected temperature by the end of this Century (Figure 2). For instance, the most conservative scenario (RCP2.6), which predicts a reduction in global emissions, is associated with an increment between 0.9 and 2.3°C in global surface temperature. By contrast, in the most extreme scenario (RCP8.5), where it is considered that emissions will continue to increase at the current rate throughout the Century, global surface temperature will become 3.2 to 5.4°C hotter than that registered in the period 1850-1900.

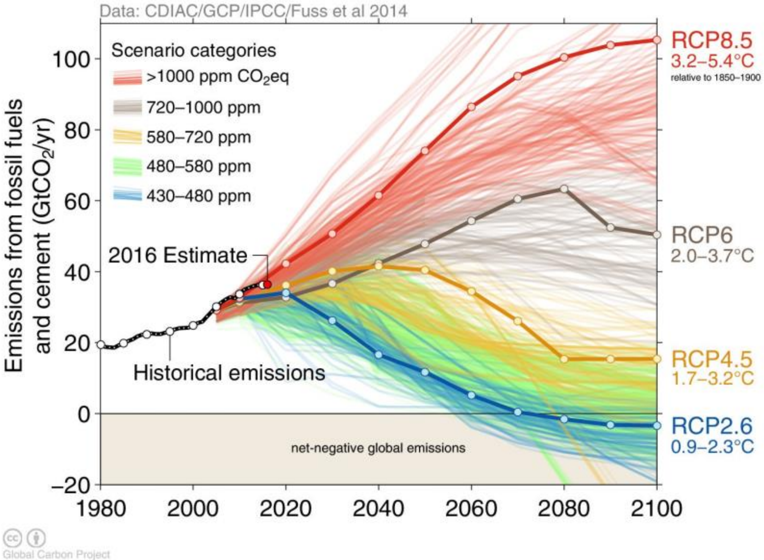


Figure 2: Trajectories of CO_2 emissions used in the IPCC Fifth assessment report (2013-2014).

Source: IPCC, 2014

Apart from a generalized increase in temperatures, predictions also indicate that heat waves will increase in frequency, intensity and duration. Furthermore, other meteorological extreme events are likely to occur in the upcoming decades, such us heavy rainfall and floods (IPCC, 2014). Floods can be caused by intense and/or long-lasting precipitation, among other factors.

The effects of climate change vary depending on the region. Some areas are more vulnerable to suffer the highest impacts of changes in climate (Watson et al., 2001). Coastal zones, the Pacific islands and some regions in Africa will be among the most affected by rising temperatures and sea level. Europe will also suffer the effects of climate change, even though differently depending on the region.

Climate models indicate a generalized warming all over Europe, particularly during summers in Southern Europe. It is expected that the Mediterranean area will be one of the most damaged areas in terms of the increasing frequency and intensity of heat waves, but also droughts, floods and heavy precipitation events, although less common (IPCC, 2014).

1.1.1. The case of Spain

Spain, located in the Mediterranean base, has experienced an increase in the average temperature in the last decades, resulting in around 0.33 degrees hotter temperatures in summer every decade (Achebak et al., 2018). According to the *Agencia Estatal de Meteorología* (Aemet) temperature in Spain has raisin around 0.6°C between 1960 and 2010. Moreover, 2017 was the warmest year since the beginning of the registry, in 1965 (Aemet, 2017). Seven of the ten hottest years during the last 50 years have occurred during the current Century, and five of them are from the current decade. All these facts highlight that climate change is already being experienced in Spain.

There is no clear trend in precipitations in Spain. In the last decades, precipitation amount has varied between years. While 2017 was one of the driest years ever registered, 2009 was one with more precipitation recorded (Aemet, 2017). Within Spain, differences in precipitation patterns are observed. North-western regions are more humid, whilst the Mediterranean coast and mainly the south register less amount of rainfall.

In this Century the warming is projected to continue in Spain. Indeed, projections indicate an increase in annual maximum temperature in Spain between 1° and 3°C, if we consider a moderate scenario of GHG emissions (RCP4.5) and up to 6°C if emissions will continue increasing at the same current rate (RCP8.5) (Aemet, 2018). This increment might vary depending on the regions. The warming is likely to be largest in summer, with an expected increase of maximum temperature that in some areas could exceed 7°C. In terms of precipitation, climate predictions are more uncertain. Generally, in Spain is projected a reduced annual mean precipitation, more accentuated in summer (Aemet, 2018). However, extreme flash floods may increase due to the increased water vapour content of a warmer atmosphere (Fundación Biodiversidad et al., 2013). In addition, the risk of droughts is likely to increase in southern and central Europe (IPCC, 2007).

1.2. Climate change and its impact on health

According to the *2015 Lancet Commission on Health and Climate Change*, climate change has been considered one of the greatest threats for human health in this Century (Watts et al., 2015). Climate change can affect human health in different ways. There are direct effects, resulting from extreme weather and hazards (droughts, floods, heat waves), but also indirect effects, which are mediated through the impacts of climate change on the atmosphere (e.g. air pollution), ecosystems (e.g. food and water supply) or economies. The World Health Organization (WHO) estimated an additional 250,000 deaths annually worldwide for the impacts of climate change between 2030 and 2050 (Watts et al., 2015). However, to quantify the real health burden of climate change is challenging due to the difficulty to predict other risks with great impact, such as water and agriculture scarcity, the economic damage or large-scale migrations. It is worth mentioning that all these climate damages might be modified by social characteristics which can increase vulnerability among some groups of populations (see section *1.3. Vulnerabilities*).

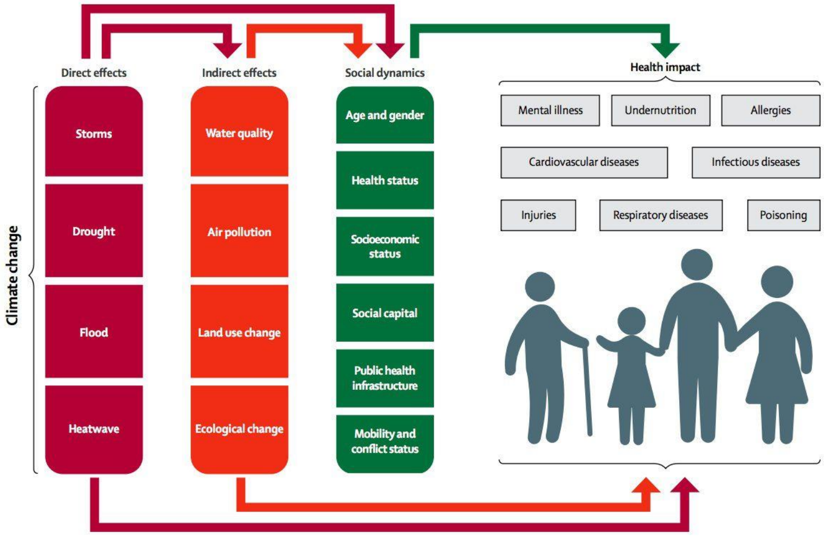


Figure 3: Direct and indirect mechanisms of climate change and their interaction with social characteristics

Source: Watts et al., 2015

One of the most direct effects of climate change is the impact of heat waves on health. As described in section *1.2.1.1. Mortality*, increase mortality due to heat and heat waves has been well-documented. Despite rising temperatures, cold events will continue to happen and, if the population is adapted to hotter temperatures, the effect of cold events may increase.

There are also indirect impacts of climate change on human health. Air pollution is described one of these indirect impacts, as rising temperatures may favour the creation of pollutants such as ozone, which have a harmful effect. Annually, around 7 million premature deaths worldwide are due to the effects of air pollution (World Health Organization, 2012) and about 150,000 premature deaths could be attributed to ambient ozone pollution (IPCC, 2014). In Europe, poor air quality was responsible of more than 422,000 premature deaths in 2015, about 28,000 deaths in Spain (Guerreiro et al., 2018).

Another indirect effect of climate change is the risk of forest fires, which is expected to increase in a warming climate. According to the IPCC, the number of harmful particles to human health can be doubled during a wildfire. A study conducted in Moscow in 2010 reported an excess of mortality of 11,000 people during a heat wave with a hundred of forest fires, which raised the levels of pollution (Shaposhnikov et al., 2014). Moreover, an increase in vector-borne diseases could be influenced by climate change. Mosquitoes, the vectors of these diseases, accelerate their development with warmer temperatures. With these conditions, there is also decrease mortality in winter and, therefore, an extension of the silent period of potential transmissions.

1.2.1. Extreme temperatures

Exposure to extreme ambient temperatures has an impact on the human body. It is known that core body temperature has to remain stable around 37 degrees. Although humans are able to tolerate a variation of about 4°C in internal body temperature without impairment of physical and mental performance (Nixdorf-Miller et al., 2006), this may not happen among those frail individuals or vulnerable groups of the population. When we are exposed to high or low ambient temperatures, the body suffers changes in order to keep dynamic balance, such as coetaneous vascular changes (vasodilator or vasoconstriction); increase blood viscosity, the number of platelets, red blood cells or cholesterol level in plasma; increase sweating to dissipate heat or shivering to produce heat; or an increase in blood pressure and also in heart rate, among other changes. However, all these mechanisms may not be sufficient and, therefore, body temperature may continue rising or dropping, causing hyperthermia or hypothermia. These two conditions, characterized by a core body temperature above 40°C and below 35°C, respectively, are extreme temperature-illnesses. Some of the aforementioned changes in body parameters, e.g. the increased heart rate, can put an extra stress on the body of frail individuals, which can then trigger acute health events that can lead to mortality or hospital admission. It is important to highlight that social and environmental factors like the lack of access to air conditioning, social isolation or living on the top floor, can exacerbate temperature-related risks.

The potential health impact of rising temperatures may depend on the degree of individual’s acclimatization. Acclimatization, defined as the physiological adaptation to climatic variations (IPCC, 2014), can happen through biological mechanisms or through other external factors, such as cultural practices (e.g. the improvement of household isolation or the use of air conditioning), urban and housing design, and people’s behaviour when clothing. Regarding to biological mechanisms, the human body is well adapted to its home climate. That means that, annually, within season, some changes occur in human body to adapt to heat (an increase in sweat rate dilute concentration of sweat, attenuated core and skin temperature, a decrease in basal metabolic rate and heart rate) and cold (elevated resting metabolism, a reduced fall in body temperature during acute cold stress, reduction in shivering, improvement in cold induced vasodilation and thermoregulatory efficiency and less of a rise in blood pressure and heart rate) (de Freitas and Grigorieva, 2015). Every year a short-term acclimatization is induced, which is achieved in between three and twelve days (Gasparrini et al., 2016). Some studies have found a reduction in heat-related mortality over the season, meaning that population is able to adapt to high temperatures in a relatively short time (Gasparrini et al., 2016). By contrast, long-term biological acclimation to a certain climate requires years and it also depends on structural, economic and behaviour changes, such as the use of air conditioning, better housing conditions and improvements in health system, among others.

1.2.1.1. Mortality

Exposure to extreme ambient temperatures has been described to increase mortality. Several studies have reported a U, V or J shaped relationship between mortality and temperature, indicating an increase in mortality with both cold and hot events (Basu, 2009) (Figure 4).

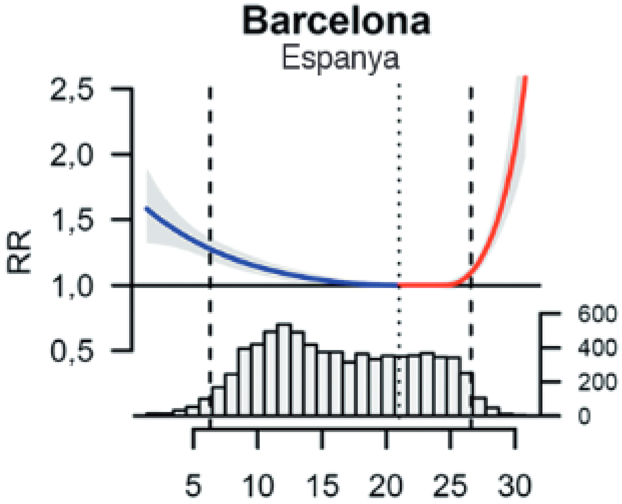


Figure 4: Relationship between daily mean temperature and mortality in Barcelona city. RR=relative risk. The temperature of minimum mortality and the 2.5 and 97.5 percentiles correspond to dotted lines and traces, respectively.

Source: Selected from Gasparrini et al, 2015.

Around 8% of mortality has been attributed to non-optimum temperatures, with cold accounting for more temperature-related deaths than heat (Gasparrini et al., 2015a). An important recent finding is that the majority of this mortality has been attributed to moderate temperatures, rather than extreme. This is due to the fact that, although extreme temperatures are associated with higher risks, extreme temperature days are less frequent than days with moderate heat or cold.

Another interesting finding is the fact that temperature-related mortality varies by country or region, mainly due to people's acclimatization. Thus, an international study concluded that the countries with higher percentage of cold attributable deaths were China, Japan and Italy. By contrast, the countries where cold had less impact on mortality were Brazil and Sweden. Differences were also seen for heat attributable mortality. The countries where heat had higher impact on mortality were Italy and Spain, whereas Sweden and UK were the ones with less heat attributable mortality (Gasparrini et al., 2015a). Figure 5 shows mortality risk due to temperatures in several cities. In general, the temperature of minimum mortality is different in each location. For example, in London the temperature of minimum mortality was found below 20ºC, while in New York or Spain it was higher. In addition, in New York the risk of death for cold temperatures was much smaller than in Madrid.

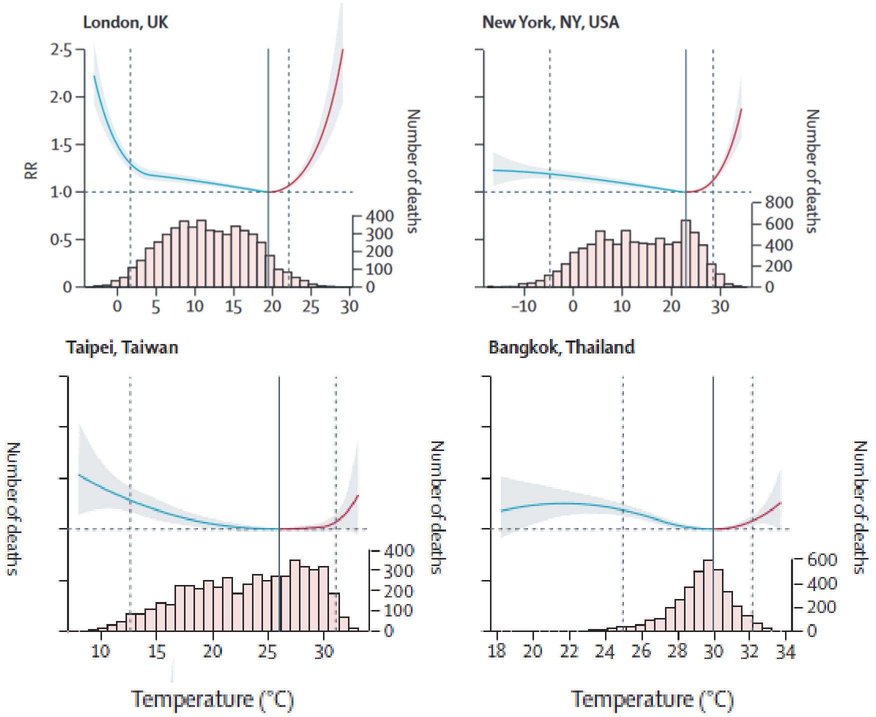


Figure 5: Relationship between temperature and mortality in different cities. Solid grey lines are minimum mortality temperatures and dashed grey lines are the 2.5th and 97.5th percentiles, respectively. RR=relative risk

Source: Selected from Gasparrini et al, 2015.

It is noteworthy, nevertheless, that there are differences also within a country. A study carried out in twelve different countries, including Spain, highlighted some variability in mortality-risk due to high and low temperatures (Guo et al., 2014). This was mainly due to the fact that population tends to adapt to their local climate. In this sense, epidemiological studies that combine data from different countries or regions tend to define cold or heat considering temperature percentiles rather than absolute values of temperature, because a specific temperature (e.g. 25°C) can be perceived as high in some places (e.g. UK) or low in some others (e.g. India).

Health effects of heat have been more widely analyzed than cold effects worldwide (Baccini et al., 2011; Basu, 2009). In Spain some studies have shown an increase in mortality risk at the highest temperatures, despite existing significant heterogeneity in the magnitude of effects and on thresholds temperatures by cities and geographical areas (Basagaña et al., 2011; Tobías et al., 2014). According to a multi-country study, about 6.5% of registered mortality in Spain can be attributed to extreme ambient temperatures, being cold more harmful (5.5% deaths for cold and 1.1% deaths for heat) (Gasparrini et al., 2015a). Similar findings were reported by (Carmona et al., 2016a), showing that, overall in Spain, cold was responsible of more daily mortality than heat (mean daily mortality in each provincial capital of 3.48 deaths and 3 deaths due to cold and heat, respectively). Geographical variability in the distribution of the estimates for the impact of high and also low temperatures on daily mortality was found in Spain (Carmona et al., 2016a; Tobías et al., 2014). In some cities, heat had more mortality impact than cold and vice versa. For example, in Barcelona there were 25 heat-related deaths and 11 cold-related deaths per day, while in Madrid more deaths due to cold were registered (11 heat-related deaths per day and 19 cold-related deaths per day) (Carmona et al., 2016a). These geographical differences were not attributed to climatic or socio-demographic variables, but it was more related to the difference between the 99th and 90th percentiles of maximum temperature, the way to represent the effect at high temperatures chose by the authors (Tobías et al., 2014).

The excess deaths attributable to heat and cold are mostly related to cardiovascular and respiratory diseases, although for heat there are also important increases in mortality for nervous system and mental health diseases, diabetes and kidney and urinary system diseases (Basagaña et al., 2011). In addition, there is huge evidence that temperature-related mortality is concentrated among the elderly (D’Ippoliti et al., 2010; Schifano et al., 2012). Some groups of population are more vulnerable to the effects of climate change, as described in section *1.3. Vulnerabilities*.

Of particular interest is the phenomenon described as urban heat island effect. It is characterized by the fact that urban areas are generally warmer than surrounding suburban and rural areas. Temperature in large cities can be 4°C higher than surrounding areas, and at night it can reach up to 10°C higher. The main causes of this difference are the land surface materials present in urban environments, which absorb energy from the sun during the day and release it as heat during night; the building geometry; and also the lack of vegetation (Heaviside et al., 2017). Considering the increasing urbanization and the ageing population, the urban heat island effect will exacerbate heat-related risks. Higher heat-related mortality has been reported in urban areas when comparing with rural areas in a few studies (Heaviside et al., 2017). Despite its importance, there are only few studies assessing the differences in heat-related mortality among rural and urban environments. There is also a lack of specific preventive interventions that take into account vulnerable populations living in large cities.

a) Indicators of heat waves and cold spells

It is difficult to establish a standard definition of heat wave or cold spell due to changes in susceptibility to extreme temperatures by region and, therefore, the threshold may vary depending on the local climate the population is acclimatized to. These meteorological events are characterized by an extended period of unusually high or low temperatures, which may have negative health consequences. Thus, heat waves and cold spells are commonly defined based on predictions of total mortality in the next few days, rather than other health metrics. Thresholds are established mainly by considering absolute values (physiological impact) and relative temperatures (sociological component) (Robinson, 2001). The following elements, in general, are used to define heat waves and cold spells: (1) temperature indicator (e.g., daily average, maximum, or minimum temperature), (2) temperature threshold (e.g., a relative threshold or an absolute threshold), and (3) duration. On the one hand, heat waves are commonly defined as temperatures above the 90th, 92.5th, 95th, and 97.5th percentiles of the temperature distribution and with a duration of more than 2, 3 or 4 consecutive days (Åström et al., 2013; Guo et al., 2017; Lee et al., 2018; Zhang et al., 2014). On the other hand, studies assessing the adverse health effects define cold spells considering a set of consecutive days (generally between ≥6 and ≥9 consecutive days and less frequent considering ≥2 or ≥3 days) in which temperatures are below a specific threshold. This threshold can be an absolute temperature or mainly different percentiles, such as the 1st, 2nd, 3rd or 5th (Ryti et al., 2016; Wang et al., 2016).

Apart from the most frequent weather metrics (mean, maximum, minimum temperature), some epidemiological studies have used apparent temperature to define exposure to ambient temperatures. Apparent temperature is an index of thermal discomfort that incorporates air temperature, relative humidity and wind speed (Stafoggia et al., 2006).

The vast majority of the studies reported an increased risk of death for any heat wave definition (Baccini et al., 2008; Gasparrini and Armstrong, 2011; Guo et al., 2017; Tong et al., 2012). In addition, the highest mortality effects were seen using higher temperature thresholds (≥ 95th temperature percentile) (Barnett et al., 2012; Guo et al., 2017). However, different conclusions have been reported regarding the duration of heat waves. Whereas some studies found more heat-related deaths for longer durations (3 or 4 consecutive days) (Gasparrini and Armstrong, 2011), others observed no effects considering heat wave duration (Guo et al., 2017). In the specific case of Spain, different studies have shown an increase in heat-mortality risk during heat waves (Basagaña et al., 2011). For instance, a study conducted in the Catalonia region considered heat wave those periods with temperatures exceeding the historical 95th temperature percentile and a duration of 3 consecutive days (Basagaña et al., 2011). In this case, authors found a 19% increase in mortality after 3 consecutive hot days. In several Spanish cities, such as Barcelona, Madrid and Seville, the temperature that rapidly raises mortality coincides with the 95th percentile of historical maximum temperature (Díaz et al., 2006; Tobías et al., 2010). Moreover, a study including all the 50 province capitals and comparing twelve definitions of heat wave, concluded that the highest heat-related mortality was when considering highest temperature percentile (97.5th) and longer durations (4 and more consecutive days) (Guo et al., 2017).

Regarding the effects of cold spells on health, a systematic review including 26 articles found an increase of 10% in total and nonaccidental mortality, 11% in mortality for cardiovascular diseases and 21% in mortality for respiratory diseases (Ryti et al., 2016). Moreover, in Spain a study that aimed to define the minimum temperature in which cold-related mortality significant increased, found huge geographical differences (Carmona et al., 2016b). This temperature threshold of minimum mortality ranged from -10°C in Ávila to 6°C in Almeria and Cadiz. Interestingly, these temperatures did not correspond to the same percentiles. Indeed, the highest percentile corresponded to the 19.5th (La Rioja) and the lowest to the 0.5th (Murcia and Toledo).

As previously highlighted, there are several different ways to define heat and cold waves. The reason behind the use of any definition of heat wave or cold spell based on a weather station-specific percentile consider the fact that population tend to adapt to their local climate and, therefore, health impacts should be observed especially for extreme episodes of heat or cold (Medina-Ramón and Schwartz, 2007). However, when exposure to temperature is described on a continuous scale, substantial effects on health (mainly mortality) have been reported for non-extreme temperatures (Medina-Ramón and Schwartz, 2007). On this basis, a large number of epidemiological studies have reported adverse health effects for single episodes of heat and cold (Basagaña et al., 2011; Gasparrini et al., 2015a). Of particular interest was a study conducted in the Catalonia region (Spain) that found that about 40% of attributable heat-mortality did not occur during periods classified as heat wave, but also to occasional days of extreme high temperatures (Basagaña et al., 2011).

A common approach to study the relationship between temperature and mortality is to model the curve, which is non-linear, in order to characterise the temperature-mortality association for all range of temperatures and not only the most extremes (Gasparrini et al., 2015b; Guo et al., 2014). Using this methodology, a temperature of minimum health risk is obtained. Some studies analysed the effects of temperatures on health for different regions using this approach, and usually a single combined estimation is given to represent the overall health effects of high (low) temperatures. In this case, it is interesting to report the effects in terms of temperature percentile rather than absolute temperatures, because regions can present huge variability in terms of weather conditions. As a result, some authors have reported the risk at the 1st and 99th temperature percentiles to represent the effects of heat and cold respectively (Guo et al., 2014), even though it could be given at any percentile.

Another important issue in the assessment of temperature-mortality relationship is to examine if, apart from the effect of single days of high temperature, heat waves have also added effects on mortality. This means that the effect of heat is due to the effect of the increase in daily temperature as well as to the duration, which persists several consecutive days. In one of the biggest studies analysing the impact of heat waves on mortality, including 13 countries, authors found no added effects on mortality for the majority of the regions (Guo et al., 2017). Although these results were in line with previous literature (Gasparrini and Armstrong, 2013), some others found that heat waves had added effects (Hajat et al., 2006; Rocklov et al., 2012).

b) Lagged effects of exposure to ambient temperatures

An important issue to consider in the analysis of health impacts of ambient temperatures is the concept of lagged effects. It represents the temporal change in risk after a specific exposure (extreme cold or heat) and it estimates the distribution of immediate and delayed effects that cumulate across the lag period. That is, it has been showed that temperature effects on mortality and morbidity may persist during several days after the exposure. There is controversy in the length of the lag period (delay) between exposure to temperature and its health effect, and this can vary depending on the outcome. For instance, a study conducted in Scotland found that cold weather was associated with increase mortality up to the following three and four weeks (Carder et al., 2005). It should be noted that in general, the health effects of heat are more immediate than for cold, which persists longer (Anderson and Bell, 2009). Usually epidemiological studies consider a lag period up to 21 days (i.e. three weeks) in order to capture the health effects of cold (Gasparrini et al., 2015a; Guo et al., 2014) and for heat, more variability is present, accounting for between two and ten days (Basagaña et al., 2011; Gasparrini et al., 2015b; Schifano et al., 2012; Tobías et al., 2014). The aforementioned multi-country study analyzing the impact of heat waves on mortality found that effects appears immediately and generally up to three or four days in all countries/regions, but not in Spain, where heat-mortality persists longer (Guo et al., 2017).

c) The harvesting effect

The harvesting phenomenon, or short-term mortality displacement, is another important aspect of the analysis of temperature-mortality and morbidity relationship. It corresponds to a short-term forward shift in an adverse health outcome; in other words, a strong health risk in the first lags appear when exposed to extreme ambient temperatures, and then it is followed by a protective association at longer lags (Hajat et al., 2005). This is explained by the fact that, among the very frail population (the elderly and those weakened by a chronic diseases (Hajat et al., 2005)), which is expected to die in the next days or weeks, the occurrence of an extreme temperature event may trigger their death, that is then advanced by a few days. Then, in the days following the episode, the pool of very frail population has been reduced and mortality counts may be lower than in normal days (Muggeo and Hajat, 2009). However, there is less evidence of this effect for morbidity studies (Ye et al., 2012). The understanding of the harvesting phenomenon is important as a public health policy point of view. If the adverse health effects of ambient temperatures occur only among those frail individuals with a short life-expectancy and not among the general population, the impact of temperatures has fewer consequences.

Different studies aimed to describe short-term mortality displacement. While some of them found no evidence of short-term harvesting effect (Tong et al., 2010), others observed that heat-related mortality is displaced by days or only a few weeks (Basu and Malig, 2011; Hajat et al., 2005; Qiao et al., 2015). In order to capture this short-term displacement, some studies have used the methodology distributed lag models which accounts for lags of several weeks (Gasparrini et al., 2015a). Indeed, the fact of include in the analysis lagged effects up to three weeks (21 days) and then calculate the effect of the temperature on accumulated mortality in this period, will allow including the long delay of the effects of both cold and heat as well as to exclude deaths that were advanced by only a few days (harvesting effect) (Armstrong et al., 2017).

1.2.1.2. Hospital admissions

Despite temperature-related mortality has been well-described, there is much less evidence about the effects of ambient temperatures on morbidity. Although several different outcomes regarding the use of health services have been examined to assess the impact of cold and heat, such as emergency department visits or general practice visits (Hajat et al., 2004; Lee et al., 2014), the most common is hospital admissions, with not conclusive results. In the case of cold, while some studies found an increased risk for cardiovascular and respiratory hospitalizations, others did not conclude this association (Bunker et al., 2016; Phung et al., 2016; Ye et al., 2012). Similar disputable findings were reported for heat exposure. For instance, a study in 12 European cities, found no increases in hospitalizations for cardiovascular and cerebrovascular causes during periods with high temperatures, while an increase for respiratory causes was observed, for all ages and for those patients older than 75 (Michelozzi et al., 2009). However, a systematic review highlighted a significant increase risk of cardiovascular hospitalizations in relation to heat waves periods, but authors did not conclude the same association for heat exposure (Phung et al., 2016).

Studies about ambient temperatures and their impact on hospital admissions in Spain are scarce. Only a few studies in some specific cities or regions of Spain assessed the temperature-hospitalizations relationship. This is the case of a study carried out in the region of Catalonia (Ponjoan et al., 2017). In this case, cold spells were associated with an increase in hospitalizations for cardiovascular diseases; however no effects of heat waves were seen for these cause-specific hospitalizations. Moreover, in the above-mentioned study, Michelozzi et al., 2009 included data from Barcelona. As previously highlighted, they found a positive association for respiratory causes (mainly in the oldest age group); while in the majority of cities they did not detect any association for cardiovascular and cerebrovascular admissions. Finally, in Madrid, a slight increase in hospital admissions for respiratory diseases at high temperatures was found, whilst for cardiovascular causes no association was detected (Linares and Diaz, 2008).

1.2.1.3. Occupational injuries

The IPCC, in its last assessment report, highlights the importance of occupational exposure to extreme temperatures, considering that they can cause physical problems and reduce the ability to perform mental and physical tasks (IPCC, 2014). It has been described that occupational exposure in both cold and hot environments may produce some changes in the human body (thermal discomfort, hypothermia or reduction in mobility caused by protective clothing in the case of cold, and dehydration, spasms or heat cramps for heat), leading to a decrease in workers’ performance and produce lack of concentration, increased distraction and fatigue, which may trigger occupational injuries (Mäkinen and Hassi, 2009; Rodahl, 2003; Schulte and Chun, 2009).

Some recent studies have quantified the economic burden of heat stress in terms of losses in labour productivity (Dunne et al., 2013; Hübler et al., 2008; Zander et al., 2015) or based on the increased number of subsidies paid to workers during high-temperature days (Zhao et al., 2016). The loss in Gross Domestic Product (GDP) in the studied countries was estimated to be between 0.1% and 0.5%, but none of those economic valuations included the costs associated with occupational injuries, except a study in Australia that focused only on 306 injury compensation claims that were explicitly classified as heat illnesses (Xiang et al., 2015).

Another interesting study in Australia has reported an increase in occupational injuries when temperature rises, although the number of injuries was reduced at extremely hot temperatures (Xiang et al., 2014a), probably due to the activation of preventive actions that restrict certain professional activities at very high temperatures. Additionally, authors found that young workers, those mainly performing outdoor activities and employees working in small and medium enterprises were the most vulnerable groups.

In Catalonia, (Basagaña et al., 2011) detected increases in mortality risk for external causes, including falls, injuries and traffic accidents during periods of extreme heat. Apart from this research and despite their potential importance, no studies in Spain have reported the proportion of occupational injuries due to ambient temperatures.

1.2.1.4. Gastroenteritis and diarrhea outbreaks

Gastroenteritis is one of the diseases that cause more morbidity and mortality in the world. According to the WHO, annually 400 million episodes of diarrhea occur globally (Jofre et al., 2010). In addition, it is considered the second leading cause of preventable illnesses among children under 5 years old (Fletcher et al., 2011). The majority of gastroenteritis cases worldwide are caused by rotavirus, although in some cases it is not possible to identify its etiology. Gastroenteritis is transmitted mainly by fecal-oral route through ingestion of pathogens that are found in unsafe drinking-water, contaminated food or unclean hands (Jofre et al., 2010; Prüss-Üstün et al., 2008).

In high-income countries there are several protective conditions, policies and regulations in place to prevent gastroenteritis outbreaks. However, meteorological factors may influence the risk of gastroenteritis. In temperate climates, there is high seasonality in the occurrence of gastroenteritis cases (Cook et al., 1990). Even though the biological mechanisms are poorly understood, it has been hypothesised that warm temperatures can promote bacterial growth through water or food, and this can lead to waterborne or foodborne diseases. Regarding the mechanisms of gastroenteritis for low temperatures, people staying more time indoors and an increase in person-to-person transmission could be possible explanations (IPCC, 2014).

Different studies have been conducted in high-income countries. While some authors have shown an association between higher ambient temperatures an increased gastroenteritis cases or waterborne diarrheal outbreaks, others did not find any relationship. For example, in countries like Canada or Australia increasing outbreaks and incidence of cryptosporidiosis, a disease transmitted by contaminated water and food, have been identified with rising temperatures (Hu et al., 2007; Thomas et al., 2006). By contrast, a protective effect of ambient temperature on cryptosporidiosis was found in New Zealand (Britton et al., 2010) and no temperature-related association with nurse advice calls due to gastrointestinal diseases in Sweden (Tornevi et al., 2013). A systematic review including 74 articles found evidence of a positive association between ambient temperature and diarrheal diseases (Levy et al., 2016). However, for a viral diarrheal pathogen (primarily rotavirus) there was a negative association between ambient temperature and diarrhea. In a Mediterranean study, that includes data from the

Spanish city of Valencia, authors found significant associations between summer temperature and gastrointestinal hospitalizations among children, but only when they consider specific temperature percentiles and for short lags (0-1 days) (Iñiguez et al., 2016).

Considering the diversity of the results and given that there are only a few studies in the Mediterranean region and none of them have focused in Spain as a whole country, more research is needed. One way to look at the effects of weather on gastroenteritis cases is through the metrics of hospital admissions. This allows having an accurate register of all cases register in a region, their main characteristics and with a reliable diagnosis. However, using hospital admissions as indicator only admits the consideration of the most severe cases, leading to underestimate the real impact of weather conditions on gastroenteritis cases.

1.2.2. Rainfall

In the context of climate change, apart from an increase in surface mean temperature, changes in global water cycle are also predicted. Indeed, increasing contrast in precipitation between wet and dry regions and between wet and dry seasons are likely to occur in the upcoming decades (IPCC, 2013). Moreover, in the last decades, higher atmospheric evaporative demand increased the severity of climatic droughts, and contributed to the decrease in surface water resources in the Iberian Peninsula (Vicente-Serrano et al., 2014).

This phenomenon was identified to compromise water supplies and cause political, social and economic tensions among regions in the near future (Vicente-Serrano et al., 2014). In Spain it is projected a reduction in precipitations but an increase in heavy precipitation events (Fundación Biodiversidad et al., 2013).

Heavy rainfall may affect health mainly through infectious diseases, e.g. diarrheal diseases (IPCC, 2014). Climate conditions such as heavy precipitations may act directly by influencing growth, survival, persistence, transmission, or virulence of pathogens (IPCC, 2014). Moreover, it has been reported that outbreaks of water-borne diseases could be affected by water scarcity or flooding, which at the same time could depend on several factors such as the level of water scarcity, the density of population, or the degree of economic development (Jofre et al., 2010).

Even though more gastroenteritis cases and outbreaks take place in low and middle-income countries, in high-income countries there is also an increasing concern due to heavy rainfall predictions in the context of climate change. Indeed, in Europe cases of gastroenteritis after heavy precipitations have been reported (Nichols et al., 2009). This was the case of Sweden and England and Wales, where it has been shown significant associations between episodes of gastroenteritis and previous heavy precipitation (Tornevi et al., 2013) but also low rainfall in the previous weeks (Nichols et al., 2009). However, others found no association between cumulative rainfall and norovirus incidence (Lopman et al., 2009). In France and Spain, using only data of two and one water sources, respectively, weather patterns, mainly dry periods followed by heavy rain, were significantly associated with acute gastroenteritis episodes (Setty et al., 2018). Furthermore, a systematic review concluded, after the analysis of 31 articles, that heavy rainfall events and also heavy rainfall following by dry periods were associated with elevated rates of diarrhea (Levy et al., 2016).

In the study of the association between precipitation and gastroenteritis is important to consider the delayed effects, given the disparity of results. Different gastrointestinal diseases outcomes have been associated with four-day lag after rainfall (Drayna et al., 2010), cumulative rainfall over five days (Thomas et al., 2006), previous heavy precipitation 5-6 days before (Tornevi et al., 2013), low rainfall (<20mm per week) in the three previous weeks or heavy rainfall (>40mm in a week) in the previous week of the gastroenteritis outcome (Nichols et al., 2009).

1.3. Vulnerabilities

According to the IPCC, vulnerability is the predisposition to be adversely affected (IPCC, 2014). It includes susceptibility to harm and also the lack of capacity to cope and adapt to climate change. There are several different individuals and groups of population more vulnerable to the adverse health effects of climate change. Generally, vulnerabilities are defined separately, but the greatest vulnerabilities happen with the combination of different factors and characteristics. Again, adaptation capacity varies from one region to another. Thus, while in Asia workers performing outdoors activities are more sensitive to the effects of increasing temperature, in the Pacific islands population will be more vulnerable to floods. Therefore, the most vulnerable populations in the European context are described below. Identifying the most vulnerable groups is essential for planning suitable public health interventions.

1.3.1. The elderly

The elderly, defined as those individuals older than 65 years, is one of the groups at higher risk of the impacts of climate change. It has been well-described that episodes of extreme heat and cold have higher impact among the elderly. This is due to the fact that usually they have pre-existing health conditions, a limited self-perception of heat, cold or thirst, slow or inefficient thermoregulatory mechanisms, and they usually take medications that can affect thermoregulation.

Several epidemiological studies have reported increases in temperature-mortality association in those individuals older than 65 years, being the oldest age groups the most vulnerable (Basu, 2009; Benmarhnia et al., 2015; Ryti et al., 2016). For instance, in Catalonia, during a heat wave mortality increased by 20% among those people between 60 and 70 years, while in the 80 to 90 age group this increase was greater than 40% (Basagaña et al., 2011). Stronger cold-related mortality has also been shown for people 65 years and older (Ryti et al., 2016). Analitis et al., 2008, after analysing weather-related mortality in 15 European countries, including two Spanish cities, Valencia and Barcelona, concluded that cold was associated with an increased mortality, with higher cold effects among the older age groups.

Similar findings have been addressed for morbidity outcomes, mainly regarding to hospital admissions and emergency department visits. There is evidence that the highest heat and cold-risk age groups are those older than 65 or 75 years of age (Ye et al., 2012).

1.3.2. Children

In the European context, higher health effects of climate change are also seen among children, especially due to the exposure to high ambient temperatures, as they have the physiological and metabolic system less developed, compared with adults, and they also do not have the chance to take care of themselves, and thus ensure a proper hydration or dressing. Children under 5 years old have higher risk of mortality and morbidity for both low and high ambient temperatures, although the estimated effects are in general lower than those reported among the elderly (Basu, 2009; Ye et al., 2012). A study conducted in Catalonia found an increase of 25% in infant mortality on those days with extreme heat (Basagaña et al., 2011).

Luckily, in high-income countries infant mortality is low. In addition, children under 5 years old are more likely to suffer gastroenteritis, a disease that can be affected by meteorological conditions (*see section 1.2.1.4. Gastroenteritis and diarrhea outbreaks*). Gastroenteritis has a huge impact among those children as it has been shown to be one of the leading causes of deaths, especially in low-income countries (Fletcher et al., 2011). Nonetheless, only a few cases have been reported in high-income countries like Spain. In Mallorca, a Spanish island, low temperatures have been associated with rotavirus infectious among children aged 0-5 years hospitalized for rotavirus gastroenteritis (Hervás et al., 2014).

1.3.3. Mental illness

As highlighted by the IPCC in its Fifth assessment report, people with mental health problems are at higher risk to suffer adverse effects of climate change. It includes people who suffer the effects of extreme meteorological events (e.g. droughts, floods, heat waves), but also those who already had an illness and the event aggravated their condition (IPCC, 2014). Results from a review observed higher risk of mortality and hospitalizations during heat waves in those people with previous psychiatric problems (Basu, 2009; Matthies, 2008). Several biological mechanisms may contribute to increase the adverse health among this population. Firstly, the use of psychotropic medications can increase body temperature and this can cause alteration and deterioration of thermoregulatory mechanisms, affecting sweating and increasing cardiac output and therefore reducing heat elimination, among others. These medications are used to treat diseases such as dementia, Alzheimer's disease, personality and anxiety disorders. Moreover, those affected by these kind of disorders are usually people with reduced or scarce capacity to take care of themselves, making them more vulnerable (Basagaña et al., 2011). In Catalonia, the risk of death during a heat wave increases by 30% among those with mental and nervous system problems (Basagaña et al., 2011).

1.3.4. Low socioeconomic status

It is well known that the poorest countries and regions are at higher risk to extreme meteorological events; however there is less evidence on the effects of other socioeconomic factors, like poverty or ethnicity. It has been hypothesised that the socioeconomic status could modify the temperature-mortality association. A review conducted by Basu, 2009, found that lower socioeconomic status (e.g. the less educated, persons living in lower income areas, poverty, lack of air conditioner) increased mortality risk for high ambient temperatures. Studies in United States and Asia have also reported an association between mortality and both cold and heat that is being modified by educational level (O’Neill et al., 2003). Only for heat-related mortality, Huang et al., 2015 observed that lower educational level increase the risk of death. However, this relationship was not clear in all studies. In the case of Barcelona metropolitan region, a study determined higher heat-related mortality in areas with the oldest buildings, with more manual workers and less perception of green spaces (Xu et al., 2013). By contrast, a study carries out in Barcelona found that men with more studies (as a proxy of educational level) were more vulnerable to moderate or extreme temperatures than those without studies. For women, despite all educational levels presented higher risks of heat-related mortality, those without studies were more vulnerable to cold temperatures (Marí-Dell’Olmo et al., 2018).

1.3.5. Workers

Recognized by the IPCC as one of the major occupational health hazards, exposure to extreme temperatures at workplace can have severe consequences for workers. The most vulnerable groups of workers are those mainly performing outdoor activities, especially if they carry out strong physical work, which is often done by young workers (Xiang et al., 2014b, 2015). As mentioned above, exposure to ambient temperatures may also increase the risk to suffer an occupational injury. In this sense, a study reported higher risk of injury for heat, although from a certain temperature threshold the number of occupational injuries decreased probably due to the activation of preventive plans (Xiang et al., 2014b). The majority of the studies did not include the burden associated with occupational injuries.

1.4. Adaptation strategies: Heat Health Prevention Plans

Adaptation, referred as the process of response to actual and future climate and its health effects, aims to reduce or avoid the adverse health effect of extreme weather events (IPCC, 2014). It can be explained by six levels of interventions, including individual, interpersonal, community, institutional, environmental, and public policy levels. All these interventions can change individual's behaviour and, therefore, reduce the impact of low and high temperatures (Guo et al., 2018).

One of the most widespread adaptation measures to prevent the burden of increased temperature on human health is heat health prevention plans (HHPPs). HHPPs are public policy instruments to prevent negative impacts of the thermal environment on health during heat-waves (Matthies, 2008). Generally, these prevention measures use weather forecast to predict heat waves and activate warnings and complementary measures, such as hospital or nursing homes emergency plans. Moreover, they also include general recommendations (e.g. reduce time spent outdoors, wearing proper clothing, healthy lifestyles), medical advice and improvements to health services, housing and urban planning. As the WHO recommends, HHPPs should focus on the identification of the most vulnerable groups but also on other factors that increase susceptibility and make populations more vulnerable.

1.4.1. The Spanish National plan for preventive actions against the effects of excess temperatures on health

In summer 2003 Western Europe suffered one of the worst heat waves. This historical heat wave was characterized by 1) extreme maximum temperatures, which in most of the European countries were around 30% higher than the summer average, and 2) the duration in terms of length of time, over 20 days (United Nations Environment Programme, 2004). Regarding the health impacts, the exceeded number of deaths caused by the 2003 European heat wave was quantified to be about 70,000 deaths, mostly in France (Robine et al., 2008). In Spain, there were 8% excess deaths, mainly among those aged 75 years and over (Simón et al., 2005).

After the devastating 2003 heat wave, the majority of the European countries implemented HHPPs. Indeed, Spain introduced in 2004 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 is 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 are defined depending on the number of forecasted days exceeding the threshold in the next five days (level 0: no exceedances; level 1: 1–2 days; level 2: 3–4 days; level 3: 5 days).

The thresholds were established based on temperatures registered in each capital of the province. In general, they correspond to the 95th percentiles of the historical series of summer maximum and minimum temperatures (Ministerio de Sanidad, Consumo y Bienestar Social, 2004).

The plan, activated from June 1st to September 15th, involves different institutions of the administration, such as social services and health professionals. Actions include dissemination of preventive information to the general population on how to protect themselves, and also take care of those at higher risk. General recommendations are issued through the media. There are specific interventions for high-risk groups as well as activation of a general hotline and emergency services. Actions are defined according to the aforementioned risk levels. 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.

As previously mentioned, the Spanish plan is designed only for high temperatures. Although some studies reflected the importance of cold in Spain in terms of increasing mortality and morbidity (e.g. 5.5% of mortality was attributed to cold whereas 1.1% to heat (Gasparrini et al., 2015a), there is no specific plan to prevent and avoid the health effects of cold temperatures.

1.5. Evaluation of public health policies

The evaluation of the effectiveness of a public health intervention is important for different reasons: 1) to guide practice and decision-making processes in public health, 2) to detect measures that do not work properly and to identify vulnerable populations, and 3) to better allocate the limited available resources (Matthies, 2008). Despite its importance, there is limited research in the evaluation of the effectiveness of HHPP (Boeckmann and Rohn, 2014; Toloo et al., 2013).

In Europe only few studies carried out the evaluation of the effectiveness of this kind of public health policies, showing different results (de’ Donato et al., 2015; Schifano et al., 2012). A reduction of the effect of high temperatures on mortality was observed in countries such as Italy (de’Donato et al., 2018), and in cities like Montreal (Benmarhnia et al., 2016), Rome or Paris (Schifano et al., 2012) after the implementation of prevention programs. However, a common characteristic of all these studies is the difficulty of evaluating if the reduction in weather-related mortality is due to the intervention programs or to other factors. In fact, evaluation is the most challenging aspect of HHPP. When an improvement of health risk associated with temperatures is observed, this may be caused by other several aspects, like methodological challenges, biological adaptation, improvements of the healthcare system, technological advancements, changes in the urban built environment or social progress, among other factors (Boeckmann and Rohn, 2014).

1.5.1. Different methods for evaluating public health policies

Public health interventions, as in the case of HHPPs, are complex and so is their evaluation, which should be done from multiple points of view and using different methodologies. Thus, our evaluation should be regarded as one item of a wider set of indicators needed to evaluate interventions.

The WHO has proposed some ways that can be used to evaluate heat-health action plans (Matthies, 2008). The different approaches, depending on the objective of the evaluation, are the following: 1) process evaluation, focused on assessing whether the plan has been implemented according to the expected standards; 2) outcome evaluation, characterized by analysing the impact of the intervention on a specific health outcome; 3) economic evaluation and 4) health impact assessment. To conduct a process evaluation, surveys and questionnaires to partner agencies are the most useful tool. In the case of HHPP, the idea would be to evaluate awareness of the heat wave plan. With regards to outcome evaluation, different methods have been proposed, although there is limited evidence related to heat-health action plans (Matthies, 2008). An approximation would be to compare a health outcome (e.g. number of deaths) on hot days with and without heat warnings. To apply this methodology, the HHPP should have a register with all the information regarding the activation of the plan. Furthermore, this information should be accessible under request. As an example, Weinberger et al., 2018, using the aforementioned approach, reported in Philadelphia a 4.4% lower mortality in days with heat alerts compared to comparable days with no alerts. Nonetheless, among other 19 US cities analysed, heat alerts were not associated with reductions in mortality. The evaluation conducted in this thesis, based on a before-after approach, also falls in the category of outcome evaluation.

Only a few studies have been conducted to evaluate cost-effectiveness of heat warnings systems (Toloo et al., 2013). For instance, Ebi et al., 2004, apart from quantifying the number of deaths that the Philadelphia HHPP saved after its implementation in 1995, estimated that $468 million would be attributed to the saved lives between 1995 and 1998. Considering that the Philadelphian plan cost around $210.000 in the same period, authors highlighted that the plan was highly cost effective. The health impact assessment (HIA) methodology, usually is done before the implementation of a public health policy, and has de aim to inform policy makers on the potential health impacts of a policy or program on a population. According to the WHO, HIA can help decision-makers to choose about programs to prevent disease and also to promote health. As far as we know, so far no studies have evaluated a HHPP using a HIA approach.

Another important aspect of the evaluation of a HHPP is the possibility to measure intermediate outcomes, such as changes in people's behaviour related to heat episodes, or the degree of knowledge of the plan by population (or target the most vulnerable). This could be done through community-based surveys, as previously reported (Kishonti et al., 2006; Sheridan, 2007). In this case, qualitative methods are the most appropriate to improve the plans and their contents. In a review analysing the effectiveness of HHPP, Toloo et al., 2013 highlighted that, even though the majority of participants were aware of the heat warnings, only those who consider themselves more vulnerable were more likely to take actions for protections. However, it has been reported that, in some cases, the elderly (the main group susceptible to heat) do not consider themselves as vulnerable. Therefore, public strategies should address people's perceptions in order to improve personal actions that can be taken to protect from heat.

As it will be widely discussed in the Discussion section (*5.1.1.4. Different designs to evaluate public health policies*), this thesis has been conducted following a before-after methodology, one of the most common approaches of the outcome evaluations.

2. RATIONALE

In the last recent years, climate change has gained more importance. The *2015 Paris Agreement* led to the inclusion of the effects of climate change on the political agendas in almost every country worldwide. Under this agreement within the *United Nations Framework Convention on Climate Change*, countries must determine actions to prevent and cope with climate change. There has been also growing interest of the impact of climate change on human’s health. Policy makers are interested in combatting the effects of climate change through adaptation and mitigation measures. One of the adaptation measures most widely implemented are prevention plans to prevent the health effects of high temperatures. Accordingly, several organisations such as the WHO and the European Regional Framework for Action (World Health Organization, 2017) have emphasized the importance of implementing this type of measure but also the need to evaluate it. Despite its importance and the hypothetical health benefits of these preventive measures, in practice they are usually not evaluated. Thus, only few studies have analysed the effectiveness of these public health interventions.

Likewise, although the effects of temperature on mortality are well established, the effects of temperature on other health outcomes has been less studied and more information is needed to characterize comprehensively the effects of temperature and of future climate change. This includes the effects of temperature on hospitalizations, on gastroenteritis, and especially on occupational injuries, which has received little attention. If more evidence is provided on these outcomes, HHPP can also incorporate actions specifically targeted to those groups.

Spain is one of the countries with a HHPP, implemented in 2004. Although the Spanish HHPP has been working for almost 15 years, its effectiveness has not yet been evaluated. Understanding how weather heat-related effects have changed over the years, by comparing periods with and without the implementation of these plans, will contribute to verify, improve and maintain the preventive actions.

3. OBJECTIVES

The aim of this thesis is to assess the relationship between ambient temperatures and human health, with a special emphasis on the evaluation of the effectiveness of the HHPP.

The specific objectives are:

1. To compare the temporal changes in the effects of cold, heat and heat waves on mortality in Spain (1993–2002 and 2004–2013) and to assess whether the effect of extreme heat changed considering the introduction of a HHPP in the second study-period. – Paper I
2. To compare the temporal changes in the effects of cold, heat and heat waves on hospital admissions for cardiovascular, cerebrovascular and respiratory diseases in Spain (1993–2002 and 2004–2013) and to assess whether the effect of extreme heat changed considering the introduction of a HHPP in the second study-period. – Paper II
3. To evaluate the association between meteorological variables and gastroenteritis hospitalizations in Spain for the period 1997-2013. – Paper III
4. To evaluate the association between ambient temperatures and occupational injuries in Spain for the period 1994-2013, its variation according to workers' characteristics and its associated economic costs. – Paper IV

4. RESULTS

4.1. Paper I

Martínez-Solanas È, Basagaña X. Temporal changes in temperature-related mortality in Spain and effect of implementation of a Heat Health Prevention. Environmental Research. 2019; 169:102-113.

DOI: 10.1016/j.envres.2018.11.006

4.2. Paper II

Martínez-Solanas È, Basagaña X. Temporal changes in the effects of ambient temperatures on hospital admissions in Spain. Shaman J, editor.

2019 Jun 13;14(6):e0218262. DOI: 10.1371/journal.pone.0218262

4.3. Paper III

Morral-Puigmal C, Martínez-Solanas È, Villanueva CM, Basagaña X. Weather and gastrointestinal disease in Spain: A retrospective time series regression study. Environmental International. 2018; 121(Pt 1): 649-657.

DOI: 10.1016/j.envint.2018.10.003

4.4. Paper IV

Martínez-Solanas È, López-Ruiz M, Wellenius GA, Gasparrini A, Sunyer J, Benavides FG, Basagaña X. Evaluation of the impact of ambient temperatures on occupational injuries in Spain. Environmental Health Perspectives. 2018; 126(6):067002.

DOI: 10.1289/EHP2590

5. DISCUSSION

The aim of this chapter is to provide a general and integrated interpretation of the results obtained in each article. It is therefore a section that complements the discussion addressed in each paper (section *4. Results*).

5.1. Main findings and contributions to current knowledge

Since the implementation of a number of HHPPs, several organizations such as the WHO encouraged governments to evaluate these public policies effectiveness. In spite of its importance, only a few regions have analysed the impact of these plans in terms of health benefits (Boeckmann and Rohn, 2014; Toloo et al., 2013).

In this thesis, we evaluated the Spanish plan by comparing the health effects of temperatures in two periods, the second one characterized by the introduction of this intervention. We structured the evaluation through the analysis of temporal trends in temperature-related mortality (Paper I), as the Spanish HHPP paid particular attention to this health impact, and also temperature-related hospitalizations (Paper II). The availability of hospitalization data provided us the opportunity to study hospitalizations for infectious gastroenteritis, a health outcome that has been related to climatic factors (temperature and precipitation), especially in low income countries but also in high-income countries (Paper III). The main aim in that analysis was to assess the associations in Spain using the full study period. In fact, the Spanish HHPP did not specify any detailed action for this health outcome. Still, the temporal variation was also explored as a secondary outcome. Finally, we included the analysis of the impact of ambient temperatures on occupational injuries (Paper IV) for two reasons. Firstly, occupational health has been recently considered an important climate change hazard (IPCC, 2014). Secondly, there is a lack of country-level studies quantifying the impact of ambient temperatures on workers' health. As in Paper III, the main aim of paper IV was the evaluation of this less studied health outcome in Spain using data from the full period. These were considered as two relatively novel health outcomes in the relationship with temperatures, not specifically targeted by the plan. Thus, instead of evaluating the effectiveness of the plan on those outcomes, the aim was that, if associations were confirmed, these health outcomes could be incorporated as targets in the plan in the future. Nonetheless, we also conducted some analyses comparing temperature-related injuries in the two evaluated periods (unpublished results), and they suggested that there were no differences.

The main findings of this doctoral thesis are presented in Table 1 and Figure 6.

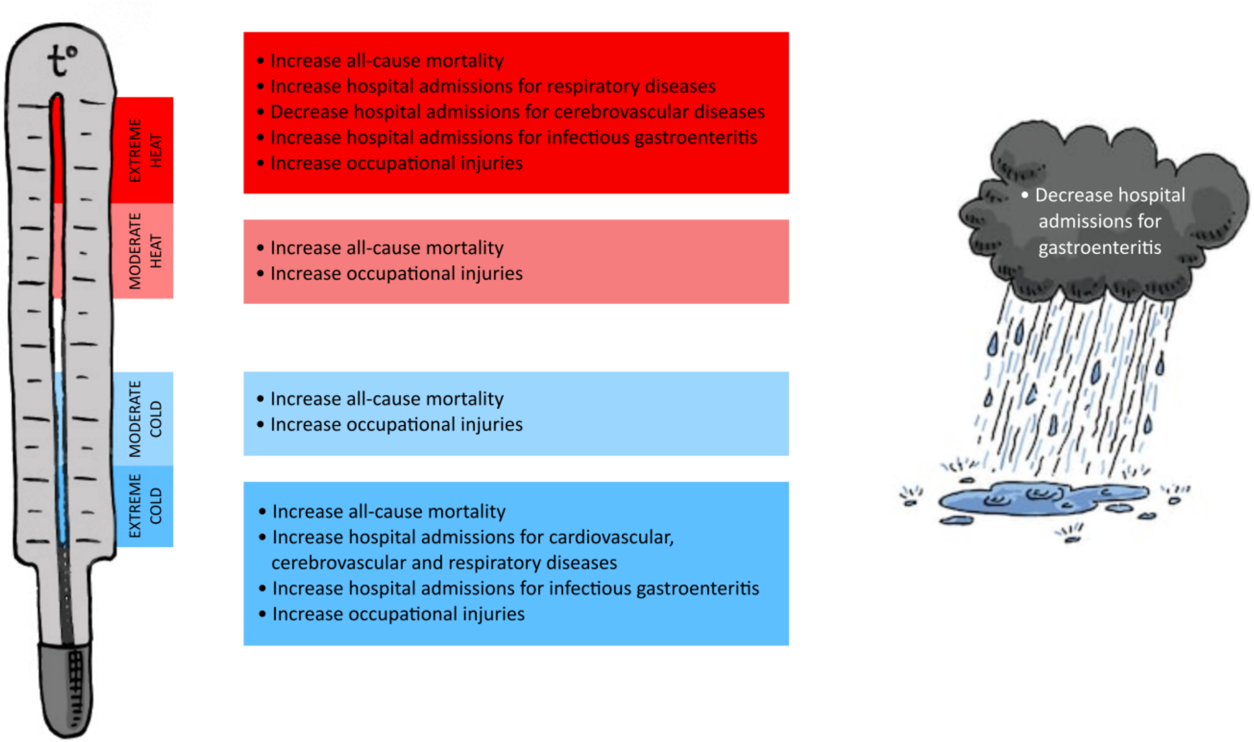
Table 1: Main findings of this doctoral thesis

Paper	What is known	What this study adds	Main conclusions
I. Temporal Changes Temperature and mortality	▪ Exposure to extreme temperatures has been widely found to increase mortality ▪ In 2004 Spain implemented HHPP ▪ Temporal changes in temperature-related mortality allows assessing the effects of public health policies	• We observed a decrease in mortality attributable to extreme heat but not to moderate heat • Mortality attributable to cold (extreme and moderate) was reduced • Provinces with more elements implemented in their plans had greatest reduction in mortality attributable to extreme heat	✓ The implementation of the Spanish HHPP could reduce extreme heat attributable mortality ✓ The number of preventive actions implemented may explain the highest reduction in extreme heat-related mortality ✓ Mortality attributable to moderate heat increased in the last years ✓ Unexpectedly, we detected higher mortality reduction for cold, despite the plan works only for heat
II. Temporal Changes Temperature and hospital admissions	▪ There is few evidence on the temperature effects on morbidity, with inconsistent results ▪ An increase of respiratory admissions for heat is the most consistent finding ▪ No clearer evidence for cold and heat effects on cardiovascular and cerebrovascular admissions have been reported	• Heat increased the risk of hospital admissions for respiratory causes, with a reduction in period 2 • No heat effects on cardiovascular and cerebrovascular admissions were detected • Cold increased hospitalizations for cardiovascular, cerebrovascular and respiratory causes. Only respiratory admissions reduced in period 2	✓ Heat increased hospitalizations for respiratory diseases ✓ The Spanish HHPP could help reducing respiratory admissions due to heat ✓ Cold temperatures led to increases in hospitalizations for cardiovascular, cerebrovascular and respiratory diseases

Paper	What is known	What this study adds	Main conclusions
III. Temperature, precipitation and gastrointestinal diseases	▪ Ambient temperatures can influence the risk of infectious gastroenteritis ▪ Heavy precipitation has also been suggested to increase gastroenteritis cases and outbreaks	• Extreme heat increased by 21% the risk of gastrointestinal hospitalization • The risk of hospitalizations for gastroenteritis increased by 7% for extreme cold • Heavy precipitation was associated with a reduction of risk of hospitalization of 26%	✓ Cold and hot temperatures might be associated with increased gastroenteritis hospitalizations ✓ Cold was associated with rotavirus gastroenteritis, while heat was more related to foodborne gastroenteritis ✓ Unexpectedly, our results suggested heavy rainfall may be a protective factor for gastroenteritis hospital admissions
IV. Temperature and occupational injuries	▪ Exposure to extreme heat has been considered an important occupational health hazard ▪ Few studies have suggested the link between extreme heat and the risk of an occupational injury ▪ Working at extreme temperatures may have an important economic impact, not only in terms of lost productivity	• Extreme cold and heat increased the risk of occupational injuries by 4% and 9%, respectively • 2.72% of all occupational injuries were attributed to non-optimal temperatures (the highest fraction for moderate heat) • The annual economic burden was estimated in €370 million, corresponding to 0.03% of Spain's GDP	✓ Both cold and hot temperatures increased the risk of occupational injury ✓ Moderate temperatures had higher impacts on occupational health than cold temperatures ✓ The identification of vulnerable workers may help reducing adverse health effects of climate change

HHPP: Heat Health Prevention Plan; GDP: Gross Domestic Product

Figure 6: Graphical overview of this doctoral thesis



- Increase all-cause mortality
- Increase hospital admissions for respiratory diseases
- Decrease hospital admissions for cerebrovascular diseases
- Increase hospital admissions for infectious gastroenteritis
- Increase occupational injuries

- Increase all-cause mortality
- Increase occupational injuries

- Increase all-cause mortality
- Increase occupational injuries

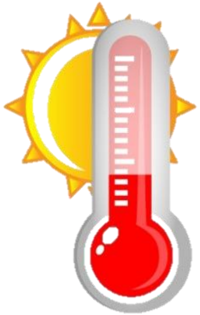
- Increase all-cause mortality
- Increase hospital admissions for cardiovascular, cerebrovascular and respiratory diseases
- Increase hospital admissions for infectious gastroenteritis
- Increase occupational injuries

- Decrease hospital admissions for gastroenteritis

5.1.1. Evaluation of the effectiveness of the Spanish HHPP

This section focuses on the evaluation of the HHPP implemented in Spain in 2004. We assessed temporal changes in the effects of temperature on mortality and hospitalizations. Results of this evaluation are reported in Figure 7. In the first paper, temperature-related mortality was compared for two 10-year periods (1993-2002 and 2004-2013) using more than 7 million deaths. We used mortality attributable fraction to evaluate the proportion of deaths caused by heat. In order to attribute the possible changes observed among the two periods only to changes in susceptibility to heat, we used a counterfactual scenario in which both periods had the same temperatures (those register in period 2) and same population. We found a slight decrease in mortality attributable to extreme heat in period 2 (period 1: 0.67%; period 2: 0.56%). However, mortality attributable to moderate heat increased in period 2 (period 1: 0.38%; period 2: 1.21%). In Paper II, we compared the impact of temperature on hospital admissions in two periods, 1997-2002 and 2004-2013 (the same second period used in Paper I). Around 10 million hospital admissions were included in the analysis, after selecting three causes: cardiovascular, cerebrovascular and respiratory diseases. In this case, results were reported as percent change in the risk of being admitted to hospital due to heat. Our main results for extreme heat indicated a reduction only in hospital admissions for respiratory diseases in period 2 (period 1: 9%; period 2: 6%).

Figure 7: Main findings after the implementation of the Spanish HHPP

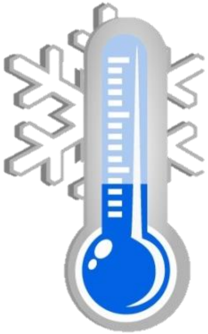


HEAT

↘ Extreme heat-related mortality

↘ Extreme heat-related hospitalizations for respiratory diseases

↗ Moderate heat-related mortality



COLD

↘ Extreme cold-related mortality

↘ Extreme cold- related hospitalizations for respiratory diseases

↗ Extreme cold- related hospitalizations for cardiovascular and cerebrovascular diseases

↘ Moderate cold-related mortality

Results of these two papers highlight a reduction in the health impacts of heat. Indeed, in Spain heat-related all-cause mortality and respiratory admissions have declined in the last years. These patterns agree with several international studies, where it has been reported a consistent decline in heat-related mortality (Arbuthnott et al., 2016; Vicedo-Cabrera et al., 2018). For instance, Vicedo-Cabrera et al., 2018 reported a reduction of 14% in heat-related mortality in Spain. In both cases, we computed heat as temperatures in the 99th percentile versus the temperature percentile of minimum mortality. The differences in the percentage of heat mortality reduction observed in the two studies could be explained by the different study period covered in Vicedo-Cabrera et al., 2018 (1990–2010), or our decision to exclude year 2003 due to the unusually high temperatures. Of particular interest is a recent study conducted in Spain, considering also the capital of the provinces as a unit of analysis, which was published during the journal review process of our Paper I (Achebak et al., 2018). This study found a progressive reduction in heat-related mortality for two causes, respiratory and circulatory diseases during a 36 year-period. However, in that case, authors reported higher respiratory-mortality attributable fractions than our estimates, both for moderate (15.9%) and extreme (1.37%) heat. Methodological issues might explain the differences observed with our Paper I, such as the study period covered (1980-2015), the inclusion of the year 2003 or the fact that authors only modelled summer. In Italy, Schifano et al., 2012 reported a 24% decrease in mortality for heat among people older than 65 years that authors attributed to variations in temperature distributions during summer and to the introduction of a national HHPP.

The comparison of two periods, the second characterized by the introduction of the HHPP, allows the evaluation of the effectiveness of this intervention. The results of this thesis, using a before-after comparison, suggest that the Spanish HHPP could help reducing the main adverse health effects of heat, even though such reductions are not large. Evaluating the effectiveness of such national public health policy is challenging because other temporal changes may occur concurrently to its implementation and therefore, changes in temperature effects might be really due to these other factors rather than the intervention. These other factors include demographic changes, biological adaptation, changes in healthcare systems, social progress or increased use of air conditioning (Boeckmann and Rohn, 2014). An example of this is the reduction in cold-related mortality in the second period, which occurred without the existence of a preventive plan. Thus, our results should be interpreted with caution.

Few studies have previously investigated the effectiveness of HHPP, by comparing periods before and after the intervention. This epidemiological evidence is mainly focused on investigating changes in heat-related mortality after the introduction of city-specific adaptation measures (Benmarhnia et al., 2016; Boeckmann and Rohn, 2014). Similar to our results, the vast majority of studies observed decreasing effects of extreme heat due to the introduction of adaptation measures in cities like Quebec, Rome or Paris (Benmarhnia et al., 2016; de' Donato et al., 2015). Nevertheless, others cities did not found a reduction in heat-related mortality after prevention plans (de' Donato et al., 2015). Apart from a study conducted in Italy (Schifano et al., 2012), our Paper I contributes to the understanding of the effects of a HHPP at a national level. As previously mentioned, so far studies evaluating public interventions have analyse the impact in terms of mortality. Therefore, to our knowledge, our Paper II is the first study assessing the effectiveness of a national public health policy focused on morbidity effects.

5.1.1.1. Results of different definitions of heat

As highlighted in the introduction of this thesis, there are several different ways to define heat exposure. Some studies have used isolated heat episodes, with an absolute threshold as a starting point where mortality starts rising (Stafoggia et al., 2006; Wellenius et al., 2017). This can be useful when heat effects are assessed in one region. However, if multiple cities, areas or regions are included in the study, then other metrics can better capture climatic variability among them. In this case, the majority of studies use temperature percentiles to combine heat-related effects in different places and report specific estimations (Gasparrini et al., 2015a; Guo et al., 2017). A recently common approach (as previously mentioned) is to define cold and heat as temperatures below and above the 1st and

99th percentiles, respectively, comparing with minimum mortality temperature (Guo et al., 2014).

Both Papers I and II included in this doctoral thesis analysed the full exposure-response relationship. This allows capturing specificities of different regions. The province-specific curves are also provided in Paper I as this information can be useful at the local level. Having the full exposure response curve allows assessing the effects of extreme heat using any threshold. For example, in paper I we used the estimated effects at the 99th percentile of temperature as representative of extreme heat effects, but other choices can lead to different results. When quantifying the attributable fractions across the entire temperature range, we defined extreme heat as those days with temperatures above the 97.5th percentile, to be consistent with some previous papers (Gasparrini et al., 2015a).

As explained above, the characterization of the full exposure-response curve allows the assessment of impact at any threshold. However, thresholds are important as the HHPP activated different phases of the plan based on thresholds. Thus, we wanted to assess the health effects for days that exceeded the plan. This led us to compare mortality and hospital admissions during the days of potential activation of the plan. It must be noted that the plan works considering forecasted temperatures and we used recorded (i.e. actual) temperatures which makes the comparison imperfect. This was done to use the same criteria in period 1 and period 2. Although in period 2 we could try to recover the periods of actual activation of the plan, which we did without success, the plan was not active in period 1 and forecasts were not available to apply exactly the same criteria.

We found more days exceeding the official thresholds in the second period, as it was hotter. Our results of Paper I pointed out a decrease in attributable mortality for those days of potential activation of the plan. This reduction was higher than if we considered extreme heat as temperatures above the 97.5th percentile, suggesting that the actions activated by the plan could have an effect. For hospital admissions (Paper II) this was not the case. When we took into account the official thresholds, a small reduction in respiratory admissions were detected comparing with the decline observed when extreme heat was defined as temperatures above the 99th percentile.

Our results showing a reduction in heat-related mortality and hospital admissions after the implementation of the HHPP were robust for different definitions of heat waves. Indeed, mortality attributable fraction decreased for temperatures greater than the 90th percentile, except for heat waves with a duration of 4 or more days, in which the effects were similar in the two periods. Results from Paper II demonstrated that the longest and more intense heat waves (4 or more consecutive days with temperatures above the 95th percentile) were associated with the strongest risk of respiratory hospital admissions. Greater health impacts have been suggested for the more intense and longer heat waves, as under these conditions the human cardiovascular system requires additional work to maintain normal temperature (Madaniyazi et al., 2016).

5.1.1.2. Impact of the HHPP on vulnerable populations

In this thesis we aimed to explore temporal changes of heat-related mortality and hospital admissions according to different socio-economic characteristics. Overall, Paper I showed evidence of some vulnerable populations to extreme heat in terms of mortality impacts. Women, the oldest age groups (mainly those 85 years and older), and people dying for mental, cardiovascular, respiratory and external diseases were the most vulnerable to extreme heat. These findings are in line with previous literature (Åström et al., 2013; Basu, 2009; Benmarhnia et al., 2016; Bunker et al., 2016; Song et al., 2017). We also included indicators at area level and we found that rural areas and those living in areas with high socioeconomic vulnerability were at higher heat-related mortality risk.

Comparing heat-related mortality before and after the plan, we detected that the older age groups, deaths for cardiovascular causes and towns with high socioeconomic vulnerability had the highest heat reduction mortality. When we looked at the extreme heat effects on hospital admissions (Paper II), as reported elsewhere (Åström et al., 2013; Song et al., 2017; Zhang et al., 2019), higher susceptibilities were seen among the elderly, mostly for patients with respiratory diseases. It was in the same oldest age groups where the most important reductions were detected after the plan. The Spanish HHPP targeted the elderly as one of the most vulnerable group to the effects of heat. For example, the regional plan of Catalonia included specific advices and recommendations for the elderly, a census of frail people (detected from health care centres), as well as an emergency plan for elderly homes, among others (Generalitat de Catalunya, 2004). All these specific measures could explain the higher reduction experienced among the older age groups, for both heat-related mortality and hospital admissions.

By contrast, we found that in the second period, heat-related mortality for mental diseases experienced an increment. Moreover, mental diseases had the highest heat-related mortality in both periods. In addition, patients with respiratory diseases were also at higher risk of dying for heat. Hence, the HHPP should establish specific actions targeted these vulnerable groups.

In conclusion, we found evidence supporting that the Spanish HHPP could reduce health effects among the most vulnerable populations, even though extreme heat remains an important risk factor for all these groups, especially the elderly and people with mental diseases.

5.1.1.3. Geographical pattern of the effects of the HHPP

We centered the evaluation of the plan on a before-after comparison. This kind of study provides stronger results if a control region can be included. Thus, including a control group allows comparing results obtained in the intervention group and those coming from a region without the specific intervention, and is a way to control for general temporal trends affecting both regions. Nevertheless, usually, for ethical reasons, public health interventions are implemented in a whole country, affecting all the population, and sometimes it is not possible to find a proper control group. In this case, interventions interact in a complex environment, where different other social, cultural, economic and administrative changes and conditions happen at the same time. This makes more difficult to attribute the health benefits to the intervention program.

The Spanish HHPP, a national public health policy, covers the full geographic extent of the country. The plan provides a national framework for the inclusion of preventive measures, but it also allows establishing specific actions in the different Autonomous Communities (regions). Therefore, we took advantage of the regional differences in the implementation of the plan (Table 3 of Paper I), and we included, in Paper I, the assessment of whether the reduction of mortality related to extreme heat changed according to the number of actions implemented in each region's preventive plan. To do so, we first considered the eight essential core elements identified by the WHO within the EuroHEAT project (Matthies,

2008) as the ones that should be included in HHPPs. Note that for some regions we were not able to find specific plans and consequently in these regions we considered that only the national program applied. As reported in Table 3 of Paper I, although in each Autonomous Community all plans included alert systems and cross-border collaboration, we observed some differences such as those related to the health information plan (dissemination of information and quality of advice), or to particular care of vulnerable groups. It is important to highlight that we were not able to detect measures about long-term urban planning. We then analysed the association between the difference in the fraction of deaths attributable to extreme heat in the two periods and the number of elements included in the HHPP in each province. This comparison is subject to some limitations. For example, we only counted the number of actions implemented, but could not investigate which of the individual actions seemed to be more effective because of the high correlation between actions implemented (e.g. all regions implementing health information plans also tended to have their health and social care systems better prepared, and also tended to have particular care for vulnerable groups).

We found that mortality attributable to extreme heat decreased more in those regions with more actions included in the HHPP. Provinces with higher number of measures were located in the south (Andalucia), center (Madrid) and north-east of Spain (Catalonia). As an example, Almeria, Huelva or Cordoba (in the south) had one of the highest reductions in extreme heat-related mortality. In these provinces a complete health information plan was included, they had particular care of the vulnerable groups, as well as they accounted for well-prepared health and social care systems to coping with heat. On the other hand, the provinces in the north of Spain presented poorest regional plans, with less measures implemented. They did not have a publicly available plan and hence we considered the national one, which is generic in terms of some core elements. These were also the provinces where an increase in mortality was observed after introduction of the plan. These results suggest that the inclusion of these extra actions in the plan can produce health benefits, although the nature of the data and of our analysis cannot confirm this causal link. In particular, there can be other ecological (i.e. province-level) or individual variables explaining the association.

To explore the role of other variables, we conducted additional analyses that found a correlation of other variables at provincial level with the reduction of heat mortality in the period where the plan was put in place. The strongest predictor of this decrease was average maximum temperature of the province. Hence, the hottest regions had higher reductions. These regions were also the ones that implemented more measures in the plan. Thus, the reductions in those areas could be due to the effectiveness of the extra actions, but could also be due to other reasons. For example, more people in those areas may have taken actions to reduce heat exposure, which could in part be induced by a greater perception of risks because of the dissemination of information of the HHPP, but could also be due to seeking more comfort. One potential explanation for the change is changes in air conditioning ownership. In this sense, we included in Paper I this variable, air conditioning ownership, and we found that the percentage of air conditioning was significantly associated with a heat-related mortality reduction in period 2. However, we were able to measure air conditioning only at a single point (2001) and not the trends in its use, which could be more useful and relevant.

5.1.1.4. Different designs to evaluate public health policies

We carried out an outcome evaluation, adopting a before-after approach, which has been widely used in the assessment of the effectiveness of public health interventions (Boeckmann and Rohn, 2014; Díaz et al., 2018; de' Donato et al., 2015; Linares et al., 2015; Schifano et al., 2012; Toloo et al., 2013). A before-after study allows comparing results observed after the implementation of the intervention with historical reference values, that is, results obtained before the intervention. It is mainly used for broad coverage programs, where it is difficult to find a proper control group, with similar population in terms of socio-economic characteristics and context but not affected by the intervention. Therefore, one of the main limitations of these studies is the difficulty to attribute the reduction of weather-related mortality and hospitalizations to the intervention rather than to other causes (Spiegelman, 2016). Thus, the findings we obtained could be as a consequence of a natural tendency (biological adaptation), improvements of healthcare system, technological advancements, changes in urban built environment or social progress (Boeckmann and Rohn, 2014). However, in order to control the differences in temperatures registered in the two study-periods, we evaluated only changes in the exposure-response function keeping temperature constants in the different periods.

As previously mentioned, no-experimental designs such as the before-after are the most commonly used approach. However, there are alternative evaluation designs that could be considered. Quasi-experimental designs, characterized by having a control group without randomization, could be a good alternative to evaluate a national public health policy. In this case, results from the intervention population could be compared with the following alternatives: 1) another control group with similar characteristics, 2) the ideal expected outcome, which in our case would be no effects of temperatures on mortality and hospital admissions (i.e. 0% increase risk), and 3) evidence-based theoretical values (López et al., 2011; Nebot et al., 2011). As it will be explained below, the first option could be applied in our case, but with some peculiarities. However, option 2) is highly unrealistic, as increases in temperature-related mortality are found in all parts of the world, and option 3) is not feasible as no such theoretical values exist.

Within the framework of exploring temporal-changes, other related methodologies have been used to assess the effect of heat action plans on health outcomes, mainly mortality. One of them is the difference-in-difference (DID) approach, which consists in comparing before and after changes in an intervention group with before and after changes in a comparison group (four groups in total). In this case, the comparison group allows providing the counterfactual scenario, that is, it helps to answer what would have happened in absence of the intervention. One of the advantages of this method is the possibility to control for both observed and unobserved characteristics that can vary in time similarly because they might simultaneously affect both state populations. In addition, the DID approach can be also applied when a proper control group is not available. It is possible to construct an “artificial” comparison group. For example, the intervention group can be constructed with eligible days, those days with temperatures up to the thresholds established for the activation of the plan, while the counterfactual scenario can be designed based on non-eligible days, days with temperatures below the thresholds that activate the plan. Then, each of these groups can be compare before and after the implementation of the HHPP. Using this DID approach, Benmarhnia et al., 2016 estimated the causal effect of the HHPP on mortality in Montreal. In this case, the authors calculated the difference between: a) the difference in the number of deaths on eligible days before and after the HHPP, and b) the difference in the number of deaths on ineligible days before and after implementation of the HHPP. Their main conclusion was that the heat action plan in Montreal reduced mortality on hot days by 2.52 deaths per day. One of the analyses that we conducted in this thesis is similar, as we also classified summer days according to the official thresholds used to activate the Spanish HHPP, but we calculated the attributable fractions in each period using the temperature percentile of minimum mortality as a reference.

Another way to deal with finding a control group in the evaluation of public health interventions is the Regression Discontinuity (RD) approach. This methodology can be applied when a control group is available (e.g. another region with similar characteristics but without the intervention), but also when there is no a control group with these characteristics and it has to be found within the same population with the intervention. The first case cannot be applied in this thesis, as the HHPP affected all the Spanish population. However, the RD approach allows constructing an artificial control group for the population affected for the intervention. It consists on comparing the population who minimally qualify for being affected by the intervention to those who minimally missed qualifying. In our case, the elderly (identified in the HHPP as a target population) could be compared with the middle age population, to whom the HHPP did not have specific actions. Then, changes in health outcomes (e.g. the number of deaths due to heat) before and after the implementation of the HHPP could be assessed within the two groups. Finally, in order to evaluate the effectiveness of the plan, we could compare temporal changes between the groups. Although it is a useful tool to assess public health interventions, so far, no studies assessing HHPPs have adopted this approach (Basu et al., 2017).

Given that the gold standard design, Randomized controlled trials (RCTs), are not possible for those programs at the population level, other methodologies have been proposed. Recently, interrupted time series analysis (ITS) has been considered a good strategy to evaluate the effectiveness of national public health interventions (Bernal et al., 2017). It establishes an underlying trend, which is ‘interrupted’ by the intervention at a specific point in time. Then, the counterfactual scenario is defined as the scenario in which the intervention had not been implemented and therefore the trend continues without changing. This scenario is considered the comparison group. Although not necessarily, an ideal ITS study should require a high number of points to analyse specifically the trend. Then, in this ITS approach researchers have to decide a priori how the intervention would impact on the outcome if it were effective. Indeed, they should be able to know whether the changes observed are a gradual change in the trend or it is consequence of the intervention. There are several methodological aspects to be considered, such as seasonality, confounders that vary over time or over-dispersion (Bernal et al., 2017). As far as we know, no HHPP have been evaluated using ITS. However, other public health policies, like smoking regulations (Barone-Adesi et al., 2011), new vaccines (Lau et al., 2015) or the impact of the economic crisis on suicides (Lopez Bernal et al., 2013), have applied the ITS approach.

This thesis could have evaluated the Spanish HHPP by applying the ITS approach. In order to estimate temporal trends in heat-related health outcomes (e.g. heat-related mortality), the study period

(1993-2013) could have been divided into four periods of 5 years, two before and two after the implementation of the plan. Accordingly, the possible estimated reduction in the trend could be used to predict changes in the two study-periods after the implementation. Thus, we could have assessed whether changes in the trend were due to a gradual change or due to the HHPP. However, note that there are some limitations when using this approach in our specific study. First, we would have a limited number of periods to compare the temporal trend. Second, the four study-periods would be very short. And third, if the trend was not lineal, we would not be able to attribute possible changes to the intervention. Nevertheless, the analysis we did in this thesis could be seen as an approximation of the ITS methodology, but instead of comparing temporal trends with several periods, we did include only two broader periods.

5.1.2. Effects of heat on gastroenteritis

Another objective of this thesis was to explore a wider range of health effects of heat exposure. For this purpose, we considered hospitalization data used in Paper II and we assessed the impact of heat on infectious gastroenteritis hospitalizations.

The effects of gastroenteritis cases and its relationship with weather variables have been less studied in high-income countries. Our results of Paper III supporting that heat increases gastroenteritis hospitalizations in Spain, mainly those that could be due to food-borne infections, are in line with those reported previously (Hu et al., 2007; Iñiguez et al., 2016; Thomas et al., 2006), although some authors did not find this association (Lopman et al., 2009; Tornevi et al., 2013). In particular, we reported a 21% higher increase risk of hospital admissions for gastroenteritis when temperatures are extremely high. Iñiguez et al., 2016 found increases over 60% of gastroenteritis hospitalizations for temperatures at different percentiles of the summer distribution compared to the 50th percentile of temperature in the whole year in Valencia, for short lags. This study was focused on children, what could embed differences. Our findings are difficult to compare with previous literature due to differences in the way of reporting the results. For example, Hu et al., 2007 concluded that 50 more cryptosporidiosis cases (a diarrheal disease) a year could be observed for an increase of 1°C maximum temperature in Brisbane.

In our study, we included different types of gastroenteritis hospitalizations. However, how meteorological factors influence on the risk of gastroenteritis may vary depending on the way of transmission. Indeed, temperature and precipitation can have an influence on the risk of gastroenteritis by promoting bacterial growth or through water contamination (Jofre et al., 2010; Prüss-Üstün et al., 2008). Taking into account the way of transmission, we classified gastroenteritis into four groups: waterborne, foodborne, other bacteria and viruses causing diarrhea, and idiopathic group.

Different temperature-gastroenteritis associations were found depending on the groups. Heat was associated only with foodborne infections and the idiopathic group. Related to foodborne infections, the hypothesis behind this relationship is that high temperatures can promote bacterial growth in food and therefore cause an increase in gastroenteritis admissions. For the idiopathic group, which includes gastroenteritis presumably infectious, it has been hypothesised that cases refer to heat exhaustion or dehydration could be included, leading to nausea, vomiting and diarrhea (Beltran, 2015). If so, the relationship heat-gastroenteritis hospitalizations could also reflect added effects of heat on dehydration.

In Paper III we stratified the analyses by period, considering two periods of 8 and 9 years, respectively (1997-2004 and 2005-2013). As the HHPP did not pay particular attention to gastroenteritis, we did not split the period as in Paper I and Paper II. Heat was associated with gastroenteritis hospitalizations only in the first period. Different changes have occurred in Spain during the study period that could explain the differences detected, such as coding practices for the diagnoses, the coverage of the system, an increase in temperatures in the second period or changes in people's behaviour (awareness of the risks of heat on food).

5.1.3. Effects of heat on occupational health

In Paper IV we found that heat increased the risk of occupational injuries in Spain. To our knowledge, our paper was the first assessing the relationship between ambient temperatures and occupational injuries at a country level. Extreme heat was associated with an increase of 9% occupational injuries. Our results showed an important impact of heat in occupational health. Lower effects were seen in Quebec, where authors found a 0.2% increase in daily compensation counts with an increase of 1°C in the daily maximum temperature (Adam-Poupart et al., 2015). For their part, (Xiang et al., 2014b) reported an increase of 6.2% in daily injury claims during heat waves in Adelaide. Apart from using different outcomes, the differences observed with our results could be to the fact that this last study analysed only outdoor industries, while we included workers in both indoor and outdoor sectors.

To better understand the impact of heat on occupational injuries we calculated the attributable measures. Thus, in our study 2.72% of occupational injuries occurred in Spain could be attributed to non-optimum temperatures, representing 60 injuries per day. Moderate heat accounted for higher injuries. Despite previous literature on occupational injuries did not look at different components of heat, our result was in line with some mortality-related studies reporting higher death rates for milder heat than extreme heat (Gasparrini et al., 2015a). This is due to the fact that there are more days with mild heat than extreme heat, as the risk of having an occupational injury is in fact higher on days of extreme heat. Unlike the case of mortality, though, most of the temperature effects are due to heat and not to cold.

Occupational injuries is a health outcome affecting the working population, and therefore to a young population. This is in contrast with mortality, where most of the effects of heat occur in the elderly. Apart from that, an interesting finding of Paper IV is that young workers and those performing mainly outdoor activities (agriculture, construction, and extractive industries) were found to be more susceptible to the effects of extreme heat. Thus, even within the working population, we observed higher impacts among young workers, who in principle tend to be healthier. Again, this is in contrast to what we saw for mortality (Paper I) and hospital admissions (Paper II), where we identify the elderly as the most susceptible to heat. This is an important contribution to the current knowledge, as the effects of climate change can also effect the working population, and this can result in high health and economic impacts. With the warming climate, it will become more dangerous to work outside during some parts of the year, especially in some countries such as Spain. As previously mentioned, our results for economic sectors are in agreement with previous articles (Adam-Poupart et al., 2015; Xiang et al., 2014b). Agriculture, construction and extractive industries, all with a high number of outdoor workers, were the sectors with higher risk of injury associated with heat. For these workers our study reflect their real conditions, however this is not the case of indoor workers, who are exposed to different temperatures.

Despite little is known so far about the biological mechanisms linking the exposure to extreme heat and the risk of occupational injuries, we performed several stratified analyses in order to provide an insight of these possible mechanisms. A potential explanation of the mechanisms arising from our findings of Paper IV is that exposure to heat may decrease concentration or impaired judgment and this compromise occupational safety. This hypothesis, previously suggested by Kjellstrom et al., 2016, is supported by the fact that the majority of the injuries included in Paper IV were bone fractures and superficial injuries. It is important to bear in mind the lag pattern observed, with remaining effects after an episode of extreme temperature and not limited to a specific day with high/low temperatures. Therefore, another possible explanation to this phenomenon is that fatigue and dehydration could have a role in the temperature-related injuries relationship.

In this paper, we also stratified the analysis in two time periods, 1994-2000 and 2001-2013. We used these two periods rather than the period before and after the implementation of the plan for two reasons. Firstly, the HHPP did not pay particular attention to occupational health. Second, in 2000 occupational injury prevention programs were implemented in Spain and, as a consequence, a reduction in occupational injury rates was reported after the implementation of these plans (Benavides et al., 2009). Our results by period were robust, indicating an increased risk of injuries for hot temperatures. Moreover, we also performed the analysis for the same periods than Paper I and Paper II (1994-2002 and 2004-2013), and we did not find differences in the heat effects on occupational injuries (data not published), indicating that the plan did not have any effect on reducing heat-related injuries.

5.1.4. Health effects of cold temperatures

In this thesis, we also explored adverse health effects of cold temperatures. Even though there is no a specific preventive plan in Spain covering cold temperatures, currently in Spain cold has more impact on mortality than heat. A previous paper already quantified that of all deaths, 5.5% could be attributed to cold, while heat accounted for 1.1% (Gasparrini et al., 2015a). Our study confirms these numbers, with estimations of 4.3% for cold (1% for heat) in Period 1 and 2.9% for cold (1.7% for heat) in Period 2. The other three papers included in the thesis further highlight that cold temperatures have an important impact on health, as all health outcomes analysed were associated with cold: mortality, hospital admissions for cardiovascular, cerebrovascular and respiratory diseases, hospitalizations due to infectious gastroenteritis and also occupational injuries.

Paper I concluded that extreme cold was associated with increased risk of mortality of 34% in period 1 and 15% in period 2. As we calculated mortality attributable fraction, we could see that in Spain the highest mortality attributable fraction was for cold temperatures, mainly moderate cold (period 1: 3.27%, period 2: 2.39%). Similar findings were reported by Gasparrini et al., 2015a. Moreover, Paper II showed an association between moderate and extreme cold and hospitalizations for cardiovascular, cerebrovascular and respiratory diseases. Respiratory admissions had the highest risk of being admitted to hospital when cold temperatures were registered. The most consistent result in the scientific literature is the effects of cold on respiratory admissions, even though in a meta-analysis Bunker et al., 2016 found lower effects (an increase of 2.70%). To better understand the differences of the effects of cold temperatures observed between mortality and hospitalization, it has been hypothesised that many deaths can occur rapidly in frail individuals before they receive medical treatment or are hospitalised (Mastrangelo et al., 2006) (see section *5.1.7. Differences in temperature-related mortality and hospitalizations*)

Stratification analyses in both Paper I and II showed evidence of the highest vulnerabilities to cold among the older age groups, especially for those 85 years and older. These results are in line with the vast majority of studies assessing cold effects on mortality and morbidity (Basu, 2009; Song et al., 2017). Furthermore, we also detected higher cold-related mortality for respiratory diseases, in rural areas and in those towns with higher socioeconomic vulnerability.

Another important finding of this doctoral thesis is the effects of cold on gastroenteritis hospitalizations. Results from paper III demonstrated the impact of cold temperatures in other diseases, which, although less studied, have an important impact on health. We found that extreme cold was associated with a 7% increase in hospitalizations for gastroenteritis, being children less than one year the most vulnerable to cold.

In Paper IV we also observed an association between cold exposure and the risk of suffering an occupational injury. In this case, in Spain extreme cold increased occupational injuries by 4%. Only a few studies in the literature can be used to compare with our results (Bonafede et al., 2016). For instance, in the Tuscany (an Italian region) 1°C decreased in temperature below the 10th centile increase outdoor occupational injuries by 2.3%. Thus, our results demonstrated higher impact of cold on occupational health.

For mortality and also for hospital admissions for cardiovascular, cerebrovascular and respiratory diseases, cold was proved to have a stronger effect than heat in Spain. In the case of occupational injuries, though, cold had a much lower effect than heat. Thus, occupational injuries are an important health indicator to monitor in the context of climate warming. Currently, we estimated that around 0.32% of total injuries in Spain could be attributed to cold, contrary to 2.40% attributed to heat. Thus, these results call for the application of policies and action to reduce this burden, with a special emphasis on hot temperatures.

There are several biological mechanisms of the exposure to cold temperatures derived from this thesis. It is suggested that exposure to cold could facilitate the occurrence of rotavirus gastroenteritis, which are more common in winter. Our stratification analysis in Paper III by way of transmission showed that only the ‘others’ group of gastroenteritis hospitalizations was associated with cold. The majority of gastroenteritis included in this group were infectious by rotavirus. This result, and the fact that children less than one year old were more vulnerable to cold, leads to hypothesise that during winter people spend more time indoors and this could facilitate the transmission (Patel et al., 2013).

On the other hand, the increase risk of occupational injuries with cold temperatures could be explained by the fact that low temperatures can reduce performance trough different sensations, such as unpleasant thermal sensations, numbness of hands or insufficient clothing, as it has been previously suggested (Mäkinen and Hassi, 2009; Rodahl, 2003).

5.1.4.1. Temporal changes of cold effects

Temporal changes in cold-related mortality and hospitalizations were also assessed in the first two papers. Overall, we found a reduction in mortality attributable to cold temperatures, much greater than the decrease observe for extreme heat. Both moderate and extreme cold attributable mortality experienced a decline in the period where the Spanish HHPP was implemented (moderate cold – period 1: 3.27%; period 2: 2.39%; extreme cold – period 1: 1.01%; period 2: 0.52%). On top of that, this cold reduction was much more noticeable than for extreme heat. These results are consistent with previous studies assessing temporal changes. A multi-country study that included data from 10 countries observed heterogeneous trends for the effects of cold. For Spain, a previous study also showed a decrease in cold-related mortality (Vicedo-Cabrera et al., 2018). However, in the Spanish city of Madrid, Díaz et al., 2015 found an increase in cold-related mortality in the last period of study.

Several factors could explain the decline in cold-related mortality. For example, a possible biological adaptation, the modification in people’s behaviour when they are exposed to extreme ambient temperatures, or changes such as improvements in healthcare system and the urban built environment, technological advancements or social progress.

The opposite pattern was observed in temporal trends of weather-related hospitalizations. Thus, in Paper II a slight increase in the risk of cardiovascular and cerebrovascular admissions were reported for cold (cardiovascular admissions – period 1: 31%; period 2: 40%; cerebrovascular admissions – period 1: 31%; period 2: 34%), while the risk of hospitalizations for respiratory diseases showed an important drop in the second period (period 1: 75%; period 2: 35%). As discussed in section *5.1.7. Differences in temperature-related mortality and hospitalizations*, mortality can be a competing event for hospitalizations, but it can also be the case that if there are measures that prevent cold-related mortality they can lead to an increase in cold-related hospitalizations. E.g. if there is a better surveillance of frail people, what could have become a death, can instead be a hospitalization by which the person can recover and not die. The comparison of our results with the scientific literature is difficult due to the lack of previous studies assessing temporal trends of cold-related hospitalizations. Therefore, we could only contrast our findings with patterns in cold-related mortality, with similar conclusions (Carmona et al., 2016b).

5.1.5. The impact of precipitation on gastroenteritis

We included in Paper III the analysis of the impact of another meteorological event, heavy precipitation, on hospital admissions for infectious gastroenteritis. Several studies have reported associations between heavy precipitation events and gastroenteritis cases and outbreaks, becoming one of the most studied climatic factor related to gastroenteritis (Nichols et al., 2009; Tornevi et al., 2013). The rationale for that is that especially heavy precipitation and flooding can lead to fecal microorganisms in surface water, through for example of sewer overflows and sewage discharges of untreated or ineffectively treated water from water treatment plants. Unexpectedly, we found that heavy precipitation (defined as daily precipitation above the 95th percentile) was protective for gastroenteritis hospitalizations in Spain. Specifically, precipitation was associated with a 26% reduction in risk of infectious gastroenteritis admissions. It is difficult to interpret these results, given that the majority of studies observe the opposite association. However, we believe that one hypothesis to understand our results could be related to people's behaviour. The fact of spending more time indoors those rainy days could protect us against to contaminated recreational waters.

Our data had some limitations that could explain this protective association. The most important is that Spain registers low amounts of rain, and this together with using data from only a single station of the capital of de province, could bias the association. Precipitation can be a much more localized event, in opposition with temperature that tends to maintain high correlations across large distances. Therefore, studies at municipal level, with data from more than one meteorological station, could better characterize the relationship between precipitation and gastroenteritis admissions. Consequently, more research is needed to better understand the role of precipitation on infectious gastroenteritis.

5.1.6. Geographical variability of the exposure to ambient temperatures

In this doctoral thesis we have assessed the effects of ambient temperatures and precipitation on health and we put especial attention to geographical differences within Spain. Paper I used data at municipal level, while in Papers II, III and IV the unit of analysis was the province. Spain is divided in 17 Autonomous Communities that at the same time are divided in provinces. In the 50 Spanish provinces climate presents a large variability between them. Even though the predominant climate of Spain is Mediterranean, with dry, hot summers and winters with balanced temperatures and low rainfall, there are other climates as well. There is the oceanic climate, in the north-western region, the arid and semi-arid, in the south-western regions, the subtropical in the Canary Islands, and the continental climate, in mountain ranges. Because of these differences, we included in three papers the geographical pattern of the temperature-related health association. These data can also be useful for local planning.

We found that cold had more impact in terms of mortality in the south and the Mediterranean provinces, while provinces in the northwest and center of Spain where the ones that cold presented the highest impact on occupational injuries. Otherwise, for extreme heat, we found that the south registered the highest effects in terms of both mortality and occupational injuries. The center was also seen to have a higher extreme heat-related mortality, while the east

Spain a higher impact on occupational injuries. These results are in line with those reporting that regions with mild climate tend to suffer higher impacts of cold, probably because people living in these warm areas are less prepared to low temperatures, in terms of fewer physical, social and behavioural adaptation (Lin et al., 2013). By contrast, areas with colder climate, in general, experience more impact of heat (Guo et al., 2014), since warm regions tend to be better prepared, for example without more rates of air conditioning ownership or personal behaviours to cope with high temperatures. However, and according to our results showing higher heat-related mortality in the warmest regions of Spain, although in hotter regions people are more acclimates to hotter temperatures, some studies have reported that they have also higher heat-related impacts and it is considered that will suffer the worst consequences of rising temperatures (Gasparrini et al., 2017; Keatinge et al., 2000).

We also analysed the temporal changes in temperature-related mortality by provinces (Paper I). As mentioned above, the changes were influenced by several province-level variables, such as average temperature or the number of actions included in the plan. Overall, the majority of the provinces experienced a decrease in both cold and extreme heat-related mortality, with some exceptions, such as Madrid where mortality for cold increased or Lleida (north-east) where extreme heat mortality rose.

In Paper III the analysis of the geographical pattern was different because we did not use the administrative aggregation (provinces) but we classified the Spanish provinces considering the average temperature and precipitation of each season. This was done because of the low number of cases at province level, and the need to aggregate to have more statistical power. This resulted in four different climatic regions: the northern regions characterized by low temperatures and the highest amount of precipitation; the south-eastern region, with the highest temperatures and the lowest precipitation; the center-north and center-eastern regions, with similar characteristics. We found that cold was only associated with gastroenteritis admissions in the northern region, while heat was only associated with gastroenteritis hospitalizations in the south-eastern regions. However, in the four climatic regions heavy precipitation was protective for hospitalizations due to gastroenteritis.

As a result of this thesis, some regions of Spain appear to be of a special interest due to the health impacts of ambient temperatures. In the southern regions, preventive measures should pay special interest in reducing cold-related mortality and also in reducing the impact of heat on mortality, occupational injuries and gastroenteritis. Regions located in the north Spain should focus on reducing the effects of cold temperatures, targeting mainly workers and infectious gastroenteritis. Moreover, areas of centre Spain have to protect workers mainly from cold temperatures and the general population from the effects of high temperatures, since in these regions we observed the highest heat-related mortality. Finally, in the Mediterranean area, efforts should be made to decrease the effects of hot temperatures on occupational injuries and on gastroenteritis, as well as to reduce cold-related mortality. To conclude, our findings highlight the need to incorporate specific measures to protect the most vulnerable, which result in some changes depending on the regions.

5.1.7. Differences in temperature-related mortality and hospitalizations

As previously mentioned in different section of this thesis, our results for mortality and hospitalizations lead to different conclusions. On the one hand, stratified analyses included in Paper I showed that heat increased the risk of mortality for all causes analysed, including cardiovascular and respiratory diseases. On the other hand, our Paper II highlighted that cardiovascular and cerebrovascular admissions were not associated with heat. Findings of this paper contradict what is found in the literature about heat-related mortality (Basu, 2009). Indeed, similar patterns of the effects of high temperatures would be expected for different health outcomes, i.e. if an increment of mortality is observed after an episode of heat, the same should be observed for morbidity, such as hospital admissions. However, different studies have previously reported similar findings when comparing the impacts of heat on hospital admissions and on mortality (Kovats et al., 2004; Linares and Diaz, 2008). In general, higher impacts of heat have been shown for mortality than hospitalizations, and even no heat effects on hospitalizations. In addition, results were similar using other health metrics of morbidity, such as emergency department visits (Kingsley et al., 2016).

In order to understand the differences between mortality and morbidity effects, some authors have hypothesised that, after an episode of high temperatures, many deaths can occur rapidly in frail and isolated people before they can go to the hospital and, therefore, receive medical treatment (Mastrangelo et al., 2006). This is a plausible explanation arising also from our findings. Nonetheless, more research is required to better interpret these differences, for example through the analysis of other health metrics, like general practitioners consultations.

We also observed in Paper II that the risk of hospital admission experienced a reduction for extreme low temperatures, below the 1st percentile (see Figure 2 of Paper II). This is also contradictory to mortality results of Paper I. One hypothesis behind results of hospital admissions could be changes in people’s behaviour when extremely low temperatures are registered, such as spending more time indoors and, therefore, protecting themselves for this hazard. However, more research is needed in order to understand the pattern observed.

5.1.8. Lagged pattern of the exposure to ambient temperatures

Different lagged structures have been used in this thesis depending on the health outcome. The lag period for the effects of temperature on mortality was extended up to 21 days, an approach commonly used to capture also possible short-term displacement (Gasparrini et al., 2015a; Guo et al., 2014). The same lagged structure (21 days) was considered as well for Paper II, which assess the effects of temperature on hospitalizations for cardiovascular, cerebrovascular and respiratory diseases. There is no a generalized strategy for the study of the temperature effects on morbidity. Previous studies have considered a variety of lag structures, such as 4 and 13 days, for the assessment of heat effects only (Kovats et al., 2004; Lin et al., 2009), or 7, 14, 21 or 30 days (Bai et al., 2016; Cheng et al., 2018; Lam et al., 2018; Royé et al., 2018), including both cold and heat effects. Our approach of including 21 days is reasonable because it tries to capture at the same time both cold and heat effects.

The lagged effects of temperature and infectious gastroenteritis hospitalizations (Paper III) were modelled considering 28 days in order to account for a delay in the appearance of symptoms (Hashizume et al., 2007), while 7 days were examined for the possible long delays in the effects of temperature on occupational injuries (Paper IV). A priori, we were expecting the effect on occupational injuries to be short, even restricted to the same day the temperature occurs. However, we examined the lag pattern and observed some effects in the most immediate days, up to lag 4. Only a few previous studies had considered lagged effects for this outcome, without showing a general consensus (Adam-Poupart et al., 2015; Morabito et al., 2014; Xiang et al., 2014a). Our results showing this lagged structure probably imply that other mechanisms can occur, other than the hypothesised one, i.e. that the temperature the worker is exposed to at the time of the injury or during the previous hours led to a decrease in performance that led to the accidents via, e.g. a distraction. One mechanism that could be compatible with a longer lag period includes the effect of heat on sleep. If hot temperatures preclude proper resting at night, this can lead to tiredness and to diminished performance and vigilance, which increase the likelihood of an accident. Another mechanism could be dehydration, which can be a process that can builds over several days. Dehydration has been linked to decreased attention.

Different lagged patterns were seen in this thesis for cold and heat effects, and within them. Cold effects lasted longer for its impact on gastroenteritis admissions, since we observed effects between 1 and 2 weeks after the cold episode. However, cold effects appeared immediately in the same and preceding day if we analyse the risk of occupational injuries. For heat the lagged pattern was shorter. Consequently, our findings were consistent with the general understanding that heat presents more immediate health effects than cold, where the effects persist longer (Anderson and Bell, 2009).

5.2. Strengths and limitations

In this thesis we conducted an extensive evaluation of the effects of temperature on several health outcomes using large nation-wide databases with long time series of individual data. With a focus on the HHPP, we assessed temporal changes on several outcomes, conducted analyses by region taking into account the preventive measures that were implemented, and provided new information on health outcomes that could also be the focus of adaptation policies.

One of the strengths of this thesis is that we have also provided results by provinces in three of the four papers. Understanding the geographical pattern of the impact of ambient temperatures on health is important for several reasons. Firstly, although Spain has a national HHPP covering the whole territory, there are differences within regions at climate level but also in terms of socio-economic characteristics, work activities and legislation. Therefore, reporting how temperatures impact on health in each region might help to implement specific interventions based on their detailed needs. Moreover, mapping the geographical health effects of temperatures can contribute to display the highest hazards and, consequently, share the most effective strategies to improve people’s health.

The stratification by rural and urban areas in the study of temporal trends of the temperature-mortality relationship is one of the strengths of Paper I. We observed higher mortality risks in rural areas, which was in principle unexpected, although only a few studies have included rural areas and the literature is not conclusive. It is difficult to evaluate rural areas because of their low population that leads to low statistical power. In that sense, nationwide studies with long time series are probably the only option to provide reliable results. However, as it will be widely explained in this section, our study is limited due to the fact that we only had data from the capital of the province, and thus could lead to misclassification.

The inclusion of the economic impact of working at extreme temperatures reported in Paper IV is another strength of this thesis. Recently, there has been an attempt to highlight the importance of climate change in terms of the economic impacts. In the USA for example, the *Fourth National Climate Assessment* affirms that there could be great annual losses by the end of this century in some economic sectors if no mitigation and adaptation strategies are put in place to cope with climate change (USGCRP, 2018). Specifically, it highlights how extreme weather events could reduce labor productivity in the USA. The 2018 report of the Lancet Countdown on health and climate change pointed out that in 2017 around 153 billion hours of labour were lost because of heat, representing an increase of more than 3,2 billion weeks of work since 2000 (Watts et al., 2018). The IPCC also put workers in the focus of interest, as it considers that working population is one of the most vulnerable groups to the effects of climate change (IPCC, 2014). All these evaluations did not include the costs of temperature-related occupational injuries, which we have shown to be sizable and should be added as additional potential costs of climate change.

In this thesis, we estimated that extreme temperatures in Spain had an annual economic burden of €370 million, which represents around 0.03% of the Spain's GDP (2015), and an annual loss of 42 workdays per 1,000 workers. The quantification of the economic burden of working at extreme temperatures is a novelty and it could be useful information for policy maker's point of view. Indeed, knowing the cost that this implies can help governments to implement adaptation measures for preventing occupational injuries, or it can help justifying the costs of existing preventive measures to protect worker's health.

The inclusion of attributable measures (fraction and number) in Papers I and IV is an important strength of this doctoral thesis. Usually, studies evaluating the effects of temperatures on health used other metrics to report the results, such as relative risks. In this thesis, apart from reporting relative risks, we have also calculated attributable measures. These measures, which can provide absolute numbers or put into perspective the results (e.g. by comparing them with the total number of deaths), are useful to help bring results of scientific papers to general population but also to policy makers.

Despite the difficulties of finding a proper control group, in this thesis we took advantage that the Spanish HHPP, apart from establishing measures at a national level, allows Autonomous

Communities to incorporate additional interventions. As a result, in Paper I we compared changes in temperature-related mortality in different regions with similar characteristics in terms of population and health services. This helped us to study if the number of actions implemented in each region could explain changes over time, in a way using some regions as controls for the others, based on the number of elements implemented in regional plans. Still, there was an important clustering in the specific elements implemented by the different regions. E.g. several actions were implemented by all regions, some were not implemented by any region, and the regions that implemented extra ones tended to implement the same ones. This lack of variability precluded the extraction of more useful information.

Another important limitation of the design used to evaluate the effectiveness of the HHPP is that we were not able to establish causality because the impossibility to assess other possible changes occurring during the study period. This is one of the most challenged aspects of the evaluation of public health policies, the unobserved confounders, that is, those factors unmeasured that can have an influence on the intervention and also on health outcomes.

A common limitation of all papers included in this thesis is that we only considered temperature registered at a single monitoring station in each province, located in the capital. This could lead to exposure misclassification. We performed a sub-analysis including data of between 14 and 21 monitoring stations located in four provinces. The within-province correlation between stations ranged from 0.87 to 1, indicating that the possible bias introduced could be small. This exposure misclassification resulted with a major concern in Paper I, where urban and rural areas were compared but using only temperatures from the capital. It is difficult to predict the potential bias in the overall estimates, as discussed in Paper I, which may depend on several factors, such as the differences in temperatures registered in the hottest days in rural and urban areas, that can be wider or smaller.

Moreover, we did not include data on air pollution in any of the papers, as this information was not available. It is important to note that it has been argued that air pollution should not be considered as confounder of the association between temperature and mortality (Buckley et al., 2014; Reid et al., 2012). Indeed, air pollution is affected by temperature and can also have an effect on mortality; therefore, air pollution is a casual pathway between exposure and the health outcome. By contrast, some authors have reported interactions between temperature and air pollution (Turner et al., 2012). That was the case of Stafoggia et al., 2008, who reported that temperature modifies the association between particulate matter less than 10 µm diameter (PM_{10}) and mortality. Another recent study also highlighted the interactive effects of heat-related mortality and ozone and PM_{10}. Consequently, future studies should assess the role of air pollution on temporal changes of temperature-related health effects. For example, if there is an interaction between temperature and air pollution, and the air pollution levels have changed over time, the before-after comparisons could be affected by this interaction, and some of the changes detected could be due to the air pollution changes.

In this thesis, we used maximum temperature as exposure measurement and we did not include any other meteorological metric. Some studies have used apparent temperature, an indicator for the perception of outdoor temperatures, which combines humidity and wind speed (Liu et al., 2018; Stafoggia et al., 2009). Even though this index can better measure thermal sensation, the lack of humidity data in our study did not allow us to include it in the analyses. Several studies have shown that apparent temperature is the best thermal predictor of the relationship between heat and mortality (Morabito et al., 2014; Zhang et al., 2014). However, Barnett et al., 2010 analysed different temperature indexes in the context of temperature-related mortality (mean, minimum and maximum temperature with and without humidity, as well as apparent temperature). They found a strong correlation between all these measures; therefore authors recommended the use of the most suitable index, e.g. the measure with less missing data. Moreover, Anderson et al., 2013, after investigating different heat index values (a combination of air temperature and moisture), concluded that results of epidemiological studies are comparable regardless of the heat index used. In our Paper IV, we performed sensitivity analyses where minimum and mean temperatures were tested. Results were robust and did not change too much depending on the outcome assessed.

5.3. Implications for public health and for policy making

As highlighted by the IPCC, climate change is unequivocal, and we are already suffering its effects (IPCC, 2014). Recently, it has been quantified that in 2017, there were 157 million more people exposed to heat waves, compared with 2000. This represents an additional 1.4 days of heat waves on average per person and year (Watts et al., 2018). All these facts indicate the importance of implementing adaptation measures to cope with climate change. These adaptation measures should be assessed to confirm they are effective in terms of reducing the health impacts and also they should be able to protect the most vulnerable populations.

Findings of this thesis indicate a reduction in extreme heat-related mortality after the introduction of the Spanish HHPP. We also observed that the risk of respiratory admissions decreased in the period where the HHPP was put in place, indicating that the plan could also have some beneficial effects on respiratory morbidity. This thesis suggests that the plan is effective for extreme heat episodes, although the observed reductions were small.

Several groups of population have been considered more vulnerable to the effects of heat, especially the elderly and those with pre-existing illnesses (Basu, 2009). Even though we found greater reductions in heat-related mortality and hospital admissions among the oldest age groups, they remain at higher risk to suffering the effects of extreme ambient temperatures. Consequently, the HHPP should maintain target measures and interventions focused on the elderly.

The mortality results presented in this thesis also highlight the importance of including many different measures at different levels. Indeed, the more actions implemented in the regional plans, the highest reduction in mortality for extreme heat. However, we could not differentiate which measures work and which do not work. Still, this thesis encourages regional governments to apply more ambitious plans, based on the WHO guidance “Heat-Health Action Plans”.

Based on the contribution of our findings, we identify several areas for potential improvement of the Spanish HHPP. First, the current HHPP implemented in Spain should cover not only extreme heat but also moderate heat, as no reduction in mortality for moderate heat was observed in the analysis of temporal trends. In addition, moderate heat has been also associated with an increase of occupational injuries, indicating the importance of the exposure of temperatures not classified as extreme heat, much more common and thus population is more frequently exposed.

Currently, the Spanish HHPP has a graded alert and actions for communication to the general population as well as specific target groups, but these actions arise only for extreme temperatures. Note that the purpose of the warnings included in a HHPP is to modify people’s behaviour during an episode of heat. However, with the aim of covering all range of high temperatures as well as raising the general awareness of the health risks of heat, some warnings should be included as a general community strategy, focused on the general population and specific groups. Even though establishing lower thresholds for the activation of the warnings could save more lives and also prevent more heat-related illnesses, it has to be noted that an excess advice may people to habituate to them and therefore, they may lose effectiveness (MacGregor and WMO, 2015). A possible strategy to draw people’s attention and awareness, and considering the fact that current advices were designed more than 10 years ago when there was less consciousness of the health hazards of heat, is to update both the content of the warnings as well as the strategy communication. The dissemination of the information should be done in the most effective and current way, depending on the group of population. For instance, a telephone system (as it is included in the regional plan of Catalonia) can be a good method of communication among the elderly, whilst for the youngest population, social media could better work.

The second improvement is connected by the fact that other health impacts should be included in the HHPP, such as the use of health services (hospitalizations) and infectious gastroenteritis. Therefore, the plan should include prevention measures targeting gastroenteritis outbreaks and reinforcing population with pre-existing respiratory diseases. For example, general advices should called in relation to the proper way to storage food and handling at the time of eating when high temperatures are registered, and also to provide information on the risks of the consumption of fresh meals and bacterial growth in food during high temperatures (European Centre for Disease Prevention and Control, 2012).

In this context, it is worth mentioning that the thresholds used to activate the Spanish plan (and also the majority of the HHPP) are based on temperatures in which mortality starts rising. However, as reported in this thesis, these public health prevention measures should revise these thresholds and define them according to a wider range of temperature-health impacts.

Regarding the third improvement area, the Spanish HHPP should incorporate specific preventive measures to protect workers from the effects of heat. Based on the identification of the most vulnerable workers, it would be necessary to protect specifically outdoors workers, those mainly working in the agriculture and construction sectors. Measures must be include actions such as drink plenty of water, alternate work and rest periods, take longer rest periods for days with intense heat, wear lightweight clothing and give training to workers related to first-aid to recognize and treat the first signs of heat stress (MacGregor and WMO, 2015).

Finally, based on our results of the lagged pattern, preventive measures included in the HHPP should be implemented not only the days immediately following the episode of cold or heat, but also actions should be extended in the following days to avoid greater effects on health.

Based on the geographical patterns of the health impacts of heat highlighted in this thesis, the Spanish HHPP should encourage the different regions to work together in the definition of strategies to cope with rising temperatures, and also to share experiences and therefore to improve population’s health. In addition, special emphasis should be placed on rural areas, where higher mortality effects were observed, as well as on reinforcing strategies in urban areas. As shown in our Paper I, the HHPP should also include long-term actions for reducing heat risks, such as include urban design and planning. Furthermore, as highlighted by the WHO and the World Meteorological Organization (WMO), HHPPs should be included in a long-terms adaptation measures, as the effects of heat is only one of the more impacts of climate change on health (MacGregor and WMO, 2015).

The reported results of this thesis can also help policy makers in implementing preventive measures for cold temperatures. Indeed, as low temperatures were associated with every outcome analysed in this thesis, the Spanish government should consider implementing a cold prevention plan. The prevention plan, which should cover a wide range of low temperatures, and not only the extreme ones, should consider the effects on mortality, but also in hospitalizations due to different causes (respiratory, cardiovascular and cerebrovascular, and others related to gastroenteritis), and should identify workers as an important vulnerable group for protecting.

Our results suggest that the current drinking water sanitation and treatment protocols are effective in terms of preventing infectious gastroenteritis outbreaks, as we even observed a protective effect of precipitation on these outcomes. Thus, our findings support that the government should maintain the current protocols and quality of water infrastructures as a public health measure.

In this thesis we derived estimates of the economic costs of working at extreme temperatures in terms of occupational injuries. This represents an extra piece that can be used in future cost-benefit analyses of HHPPs. Our calculations, that are restricted to occupational setting and do not cover losses in productivity, provided very high costs. Economic evaluations of the excess mortality or hospital admissions can further illustrate the costs associated to extreme temperatures, and especially illustrate the cost of not acting. Thus, although economic parameters should not be the main motivation for public health interventions, we believe that economic evaluations are actually a very useful tool to justify investments in preventive programs.

Considering the current health impacts showed in this doctoral thesis, public health policies should invest in structural measures that reduce exposure to extreme temperatures. These measures should be sustainable, to avoid worsening the rate of GHG emissions. It is well known that increasing the use of air conditioning, despite the short-term health benefits, increases energy consumption. Therefore, urban planning must encourage sustainable measures such as improving building insulation to reduce the need for air conditioning, switching to cool urban materials that absorbs less solar radiation or increasing urban vegetation to provide more shade and reduces radiant temperature.

5.4. Future research

At present, and after decades of research, enough scientific evidence is already available to understand that the exposure to extreme temperatures has an impact on health. The importance of adaptation strategies has been also previously established, as well as the health benefits of these measures. However, there are still gaps in the knowledge of how to implement the adaptation measures to bring the highest benefits to society, and also in understanding some mechanisms related to the relationship temperature and health. Hence, in this section we present some areas of knowledge in which more research is required.

In order to better assess the differences in temperature-related mortality in rural and urban areas, further research should improve the exposure assessment, and therefore, data from different meteorological stations (in both urban and rural settings) should be collected. In this sense, climate services like the *Pan-European*

Urban Climate Service, which aims to provide available scientific urban climate data to public and private users through complex climatic models, allow repeating the analyses with a better exposure variable, exploring the effects of other meteorological parameters (such as humidity), studying the heat island effect with a better approach, mapping with high resolution, as well as providing better estimates of the effects of temperatures in rural areas. This is an important aspect due to the fact that according to the United Nations, 68% of the world population is projected to live in urban areas by 2050. Therefore, disentangling the effects of temperatures (especially heat) in urban areas is crucial to protect people's health, considering the heat island effect, a well-described phenomenon happening in urban areas.

The role of other meteorological metrics, such as humidity or wind speed, in the relationship between temperatures and health should be assessed in order to investigate if the discomfort index may effect on temperature-related health relationship. The potential effect modifier or confounder of air pollution could be also assessed in future studies.

An area of future work can be analyses that jointly examine mortality and hospital admissions to account for competing risks. We and others have observed protective effects of extreme heat for cardiovascular hospitalizations, and these results could be partly explained by concurrent increases in heat-related mortality by cardiovascular causes. Such analyses probably require the development of new statistical models to account for competing risks in the context of time series analyses.

Although we used hospital admissions as a metric to assess temperature-related morbidity, other outcomes regarding the use of health services could be investigated. Some authors focused on emergency room visits or general practitioners consultations. Therefore, the comparison of our results with other morbidity outcomes could help to understand the differences observed when mortality is assessed.

Another area for future research involves the mechanisms behind the association between temperature and occupational injuries. Even though some mechanisms have been suggested, such as exposure to heat and cold directly having an influence on decreased performance, concentration and attention, and thus increasing distraction and fatigue, our results show also delayed effects, which are not consistent with an effect of present exposure. These could be due to effects on sleep or cumulative dehydration, for example. Panel studies of workers collecting individual data on personal exposure to temperature, worker’s behaviour, self-perception of risk, sleep, hydration, and assessment of attention, among other variables, can provide additional insights on this topic. Other interesting future studies include implementing preventive measures for workers and assessing their effectiveness. Another area of interest is to compare the effects of ambient temperatures among indoor versus outdoor workers. Even though some studies reported that indoor and outdoor temperatures correlate well at warmer temperatures (Nguyen et al., 2014), more research is needed to assess the differences among these workers. The geographical pattern observed in Paper IV drives to study more in depth the professional activities with higher risk of low and high temperatures

The protective role of precipitation we observed deserves attention in future studies. Restricted analyses in areas with local data on precipitation could be helpful, as well as trying to use other indicators of flooding that can be more specific for gastroenteritis risk.

6. CONCLUSIONS

The main conclusions of this doctoral thesis are:

1. A reduction of extreme heat-related mortality and respiratory hospitalizations was observed in the second period, which could be attributed to the implementation of the Spanish HHPP. The decrease in extreme heat mortality was more remarkable in those areas with more specific measures and actions included in their regional plans.

2. Mortality attributable to moderate heat showed an increase in the period after the implementation of the HHPP. This finding suggests that the Spanish HHPP should cover a broader range of high temperatures and not only the most extremes.

3. Although low temperatures still account for the highest proportion of deaths in Spain, mortality attributable to cold experienced a huge reduction in the second period. Moreover, extreme cold temperatures increased the risk of hospitalizations for cardiovascular, cerebrovascular and respiratory diseases. In the second period, only a reduction in respiratory hospitalizations was observed. Implementing a cold preventive plan should considered by Public Health authorities in Spain.

4. Both high and low temperatures increased the risk of gastrointestinal hospitalizations. Hot temperatures were associated with those hospitalizations classified as foodborne and idiopathic. By contrast, cold temperatures were associated with the group with more cases defined as rotavirus infections, being children less than one year the most vulnerable. Preventive strategies to cope with climate change should also focus on this disease to protect population.

5. The risk of gastrointestinal hospitalizations decreased after heavy precipitation events. More research is needed in order to disentangle the biological mechanisms underlying this protective association.

6. Cold and heat were associated with an increased risk of occupational injuries. Furthermore, an annual economic burden of €370 million (0.03% of Spain's GDP) was estimated to be associated with working at non-optimum temperatures. These results suggest that interventions to protect population from ambient temperatures should focus on other health impacts and not only mortality.

> "We are the first generation to be able to end poverty, and the last generation that can take steps to avoid the worst impacts of climate change. Future generations will judge us hasrshly if we fail to uphold our moral and historical responsabilities"
>
> Ban Ki-moon (secretary-General United Nations)

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8. ANNEXES

This section includes other activities that the PhD candidate has been doing during the thesis process.

8.1. Other papers co-authored

Agay-Shay K, Michael Y, Basagaña X, **Martínez-Solanas È**, Broday D, Lensky IM, Rudolf M, Rubin L, Kent R, Levy N, Haklai Z, Grotto I. *Mean and Variance of Greenness and Pregnancy Outcomes in Tel-Aviv during 2000-2014: Longitudinal and Cross-Sectional Approaches*. Int J Epidemiol. 2018 Dec 13. doi: doi.org/10.1093/ije/dyy249.

Vergara-Duarte M, Borrell C, Pérez G, Martín-Sánchez JC, Clèries R, Buxó M, **Martínez-Solanas È**, Yasui Y, Muntaner C, Benach J. *Sentinel Amenable Mortality: A New Way to Assess the Quality of Healthcare by Examining Causes of Premature Death for Which Highly Efficacious Medical Interventions Are Available*. Biomed Res Int. 2018 Sep 2;2018:5456074. doi: 10.1155/2018/5456074.

Ruiz, ME, Vives A, **Martínez-Solanas È**, Julià M, Benach J. *How does informal employment impact population health? Lessons from the Chilean employment conditions survey*. Safety Sci. 2017 Dec, doi: 10.1016/j.ssci.2017.02.009.

Martínez-Solanas È, Vergara-Duarte M, Ortega M, Martín-Sánchez JC, Buxó M, Rodríguez-Farré E, Benach J, Pérez G. *The Geography of the Alzheimer's Disease Mortality in Spain: Should We Focus on Industrial Pollutants Prevention?* Healthcare (Basel). 2017 Nov 25;5(4). pii: E89. doi: 10.3390/healthcare5040089.

de Keijzer C, Agis D, Ambrós A, Arévalo G, Baldasano JM, Bande S, Barrera-Gómez J, Benach J, Cirach M, Dadvand P, Ghigo S, **Martinez-Solanas È**, Nieuwenhuijsen M, Cadum E, Basagaña X; MED-HISS Study group. *The association of air pollution and greenness with mortality and life expectancy in Spain: A small-area study*. Environ Int. 2017 Feb; 99:170-176. doi: 10.1016/j.envint.2016.11.009.

Triguero-Mas M, **Martínez-Solanas È**, Barrera-Gómez J, Agis D, Pérez N, Reched C, Alastueyd A, Querol X, Pérez K, Basagaña X. *Public transport strikes and their relationship with air pollution, mortality and hospital admissions*. Submitted to American Journal of Epidemiology.

Triguero-Mas M, Saccor C, Chauque A, Hunguana A, Matsena T, Quintó L, **Martínez-Solanas È**, Bardají A, Menéndez C, Basagaña X. *Is temperature linked to mortality and hospitalizations in Africa settings?* In preparation.

8.2. Book chapter

The PhD candidate is a co-author of the Health chapter of the *Third Report on Climate Change in Catalonia*, commissioned by the Catalan government. This chapter describes the main impacts of climate change on health that are of interest in the Catalonia region.

Reference

Institut d'Estudis Catalans, 2016. *Tercer Informe sobre el Canvi Climàtic a Catalunya*. Barcelona, Spain.

Abstract

The objective of this chapter is to describe the main health impacts of climate change in Catalonia. The chapter is based on a review of recent scientific evidence focused in Catalonia and it also provides projections on the expected effects on health of the estimated climate conditions for the next few decades.

One of the most widely studied health effects are heat waves, causing increases in the number of deaths and hospitalizations by more than 20%, mostly among the elderly and in those with previous chronic pathologies. The results presented in this chapter show that the expected number of heat-related deaths in Catalonia can be multiplied by 8 in 2050, resulting in over 2,500 deaths per year during the summer months.

Air pollution is a problem that is aggravated in certain weather conditions, especially during periods of high temperatures, which cause numerous respiratory and cardiovascular problems among the

population. In Catalonia it is estimated that every year there are 3,500 premature deaths caused by the effects of air pollution.

Climate change can also have an impact on the incidence of vector-borne diseases. Changes in temperature and rainfall favor the development of mosquitoes, the main transmitter of this type of disease. In the case of Catalonia, the potential risk of diseases such as dengue, malaria or Chikungunya is estimated to increase.

But climate change may affect the health of the population by other means. The chapter describes the risks of cold waves and exposure to smoke from forest fires, which have been linked to increases in the number of hospitalizations and deaths, especially due to cardiopulmonary problems. It also briefly includes other factors that may mediate the relationship between climate change and health, but pose lesser risk for Catalonia (such as waterborne diseases) and presented several uncertainties about how can affect Catalonia in the future (as in the case of ultraviolet radiation).

Among the adaptation measures for global warming, the chapter discusses the plan of prevention of health effects of heat waves. In addition, we analyse two mitigation measures that have abundant health benefits: the presence of green spaces, especially in urban areas; and the promotion of active transportation.

In conclusion, health is a topic of great relevance to the effects of climate change. The chapter highlights, among others, the need to promote healthy lifestyles through policies that promote the use of active transportation, to maintain plans to prevent the effects of heat waves, to improve energy efficiency of buildings, and to implement policies to reduce social and economic inequalities.

The student has performed the analyses of the projections included in this chapter. These projections are the expected number of deaths due to heat in Catalonia for the years 2025 and 2050, considering two temperature scenarios based on the IPCC climate models of the Fifth Assessment Report (RCP 4.5 and RCP 8.5). This work was based on the projected average temperatures in the four provincial capitals of Catalonia (Barcelona, Girona, Lleida and Tarragona). In order to capture future changes in the Catalan population, we considered population projections of the Statistical Institute of Catalonia for the years 2025 and 2050, according to three growth scenarios (depending on migratory flow, mortality and fertility rates). Results obtained and included in the chapter are presented in the following table. In the reference period, 1971-2000, there was an annual average of 310 deaths attributable to heat in Catalonia. Considering the moderate emission scenario for the 21st century, and taking into account only rising temperatures, a doubling of cases (610) was estimated in 2025, and 718 deaths were projected for 2050. When we incorporated the predicted changes in the population and the changes in age structure (aging of population), the expected number of deaths attributable to heat increased up to 1,391 in 2025, and more than 2,500 deaths were expected in 2050, multiplying by 8 the number in the baseline period. Projections with the RCP8.5 scenario showed an increased in the expected number of deaths up to 200 in 2050. All figures consider situations in which no adaptation to warmer temperatures would occur.

Table 2: Estimation of mortality attributable to heat (and 95% confidence interval) in Catalonia for the years 2025 and 2050

	Model	**RCP 4.5 scenario**	**RCP 8.5 scenario**
Baseline	Period 1971-2000	310 (76, 668)	
2025			
	Increase in temperature	610 (291, 1.040)	639 (318, 1.058)
	Increase in temperature and population ageing	1.391 (670, 2.395)	1.459 (721, 2.435)
2050			
	Increase in temperature	718 (368, 1.218)	784 (408, 1.260)
	Increase in temperature and population ageing	2.504 (1.238, 4.394)	2.733 (1.352, 4.460)

Source: Institut d'Estudis Catalans, 2016. Tercer Informe sobre el Canvi Climàtic a Catalunya. Barcelona, Spain.

8.3. Presentations in scientific congresses

This section refers to the scientific presentations (talks and posters) related with the doctoral thesis that have been presented in national and international congresses.

- 14th International Conference on Urban Health (26th – 29th September 2017). Coimbra, Portugal. Oral presentation.

  Title: *Effect of ambient temperatures on hospital admissions in Spain*

- XXXV Reunión Científica de la Sociedad Española de Epidemiología (6th – 8th September 2017). Barcelona, Spain. Oral presentation.

  Title: *Impact of ambient temperatures on occupational injuries: differences among Spanish Provinces*

- XXXV Reunión Científica de la Sociedad Española de Epidemiología (6th – 8th September 2017). Barcelona, Spain. Poster.

  Title: *Effect of ambient temperatures on hospital admissions in Spain*

- 25th EPICOH - Epidemiology in Occupational Health Conference (5th – 7th September 2016). Barcelona, Spain. Oral presentation.

Title: *Evaluation of the impact of high ambient temperatures on work-related injuries in Spain (1994-2013)*

- 28th Annual Conference International Society for Environmental Epidemiology (1st – 3rd September 2016). Rome, Italy. Poster.

  Title: *High temperatures are associated with occupational injuries in Spain*

- 28th Annual Conference International Society for Environmental Epidemiology (1st – 3rd September 2016). Rome, Italy. Poster.

  Title: *Urban/rural differences in ecological studies linking mortality and air pollution (LIFE MEDHISS LIFE12 ENV/IT/000834)*

8.4. Outreach activities

- Institut Català de Seguretat i Salut Laboral (7th November 2018). Barcelona, Spain. Seminar.

  Title: *Avaluació de l'impacte de la temperatura ambient en lesions professionals a Espanya*

- 5th ISGlobal PhD Symposium (6th November 2018). Barcelona, Spain. Poster.

  Title*: Effect of ambient temperatures on hospital admissions in Spain*

- The Youth Mobile Festival (28th February 2018). Barcelona. Spain. Workshop BioJunior.

  Title: *El canvi climàtic a Catalunya: els efectes sobre la nostra salut*

- XXXIV Jornades Mèdiques i de la Salut de les Terres de l'Ebre (23rd February 2018). Tortosa, Spain. Participation in round table.

  Title: *Canvi climàtic a les Terres de l'Ebre i Salut*

- 4th ISGlobal PhD Symposium (28th November 2017). Barcelona, Spain. Poster.

  Title: *Changes on temperature-related mortality after the implementation of the Spanish Heat Health Prevention Plan*

- XXIII Jornades de Meteorologia Eduard Fontserè (26th November 2017). Barcelona, Spain. Oral presentation.

  Title: *Canvi climàtic i salut*

- Presentació del Tercer informe sobre canvi climàtic a Catalunya (9th November 2017). Sant Cugat del Vallès, Spain. Oral presentation.

  Title: *El canvi climàtic a Catalunya: els efectes sobre la nostra salut*

- Festa de la Ciència (27th May 2017). Barcelona, Spain. Oral presentation

  Title: *El canvi climàtic a Catalunya: els efectes sobre la nostra salut*

- Competition Rin4 (Research in 4 minutes), Universitat Pompeu Fabra (26th April 2017). Barcelona, Spain. Oral presentation.

  Title: *Els efectes del canvi climàtic en la salut: estem preparats?*

- Jornada d'Investigadors Predoctorals Interdisciplinària – JIPI (9th February 2017). Barcelona, Spain. Oral presentation. Received best communication award (Social Sciences Session)

  Title: *The effects of climate change on health: How prepared are we?*

- 3rd ISGlobal PhD Symposium (28th November 2016). Barcelona, Spain. Oral presentation.

  Title: *Evaluation of the impact of ambient temperatures on work-related injuries in Spain*

- Competition Rin4 (Research in 4 minutes), Universitat Pompeu Fabra (19th April 2016). Barcelona, Spain. Oral presentation.

  Title: *The effects of climate change on health: how prepared are we?*

- Seminar in the London School of Hygiene and Tropical Medicine (11th August 2016). London, United Kingdom.

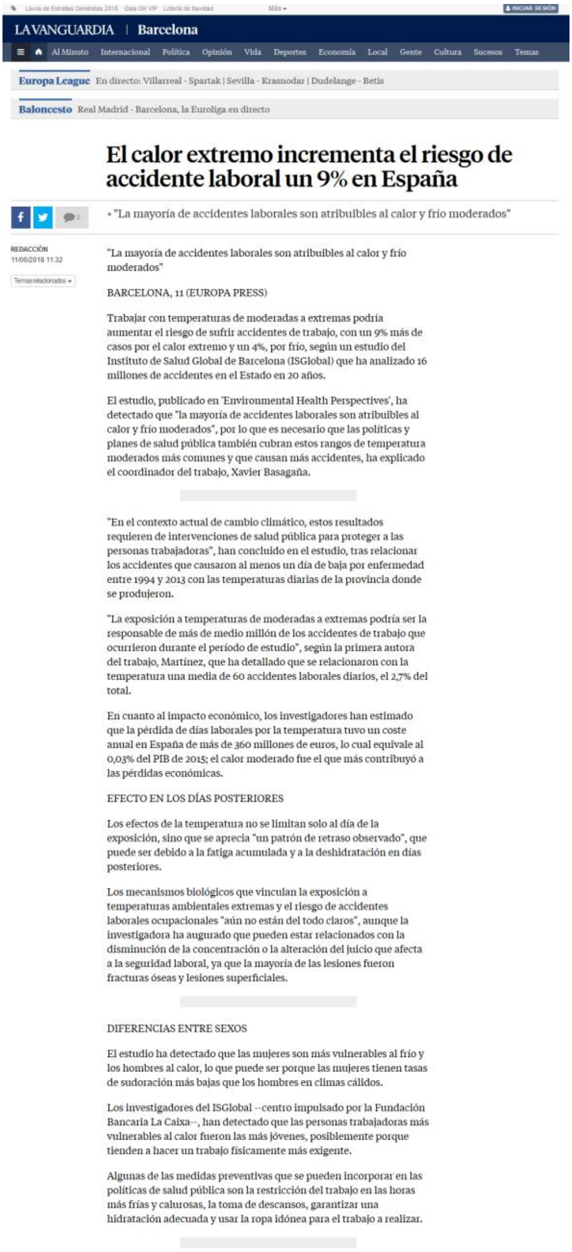
  Title: *Evaluation of the impact of ambient temperatures on work-related injuries in Spain*

8.5. News media impact

- TV program ‘Deuwatts’. Betevé TV channel (9th October 2018). Participiation in the documentary ‘*Malalties climàtiques*’.

- Radio program ‘El matí de Barcelona’. Betevé radio (24th October 2018). Participation in the debate ‘*Malalties climàtiques a Barcelona: causes i conseqüències*’.

- Article regarding the publication of Paper IV. This press release was published in June 2018 in several mass media, such as *La Vanguardia*, *Publico.es*, *Cadenaser.com*.



El calor extremo incrementa el riesgo de accidente laboral un 9% en España

- "La mayoría de accidentes laborales son atribuibles al calor y frío moderados"

REDACCIÓN
11/06/2018 11:32

"La mayoría de accidentes laborales son atribuibles al calor y frío moderados"

BARCELONA, 11 (EUROPA PRESS)

Trabajar con temperaturas de moderadas a extremas podría aumentar el riesgo de sufrir accidentes de trabajo, con un 9% más de casos por el calor extremo y un 4%, por frío, según un estudio del Instituto de Salud Global de Barcelona (ISGlobal) que ha analizado 16 millones de accidentes en el Estado en 20 años.

El estudio, publicado en 'Environmental Health Perspectives', ha detectado que "la mayoría de accidentes laborales son atribuibles al calor y frío moderados", por lo que es necesario que las políticas y planes de salud pública también cubran estos rangos de temperatura moderados más comunes y que causan más accidentes, ha explicado el coordinador del trabajo, Xavier Basagaña.

"En el contexto actual de cambio climático, estos resultados requieren de intervenciones de salud pública para proteger a las personas trabajadoras", han concluido en el estudio, tras relacionar los accidentes que causaron al menos un día de baja por enfermedad entre 1994 y 2013 con las temperaturas diarias de la provincia donde se produjeron.

"La exposición a temperaturas de moderadas a extremas podría ser la responsable de más de medio millón de los accidentes de trabajo que ocurrieron durante el periodo de estudio", según la primera autora del trabajo, Martínez, que ha detallado que se relacionaron con la temperatura una media de 60 accidentes laborales diarios, el 2,7% del total.

En cuanto al impacto económico, los investigadores han estimado que la pérdida de días laborales por la temperatura tuvo un coste anual en España de más de 360 millones de euros, lo cual equivale al 0,03% del PIB de 2015; el calor moderado fue el que más contribuyó a las pérdidas económicas.

EFECTO EN LOS DÍAS POSTERIORES

Los efectos de la temperatura no se limitan solo al día de la exposición, sino que se aprecia "un patrón de retraso observado", que puede ser debido a la fatiga acumulada y a la deshidratación en días posteriores.

Los mecanismos biológicos que vinculan la exposición a temperaturas ambientales extremas y el riesgo de accidentes laborales ocupacionales "aún no están del todo claros", aunque la investigadora ha augurado que pueden estar relacionados con la disminución de la concentración o la alteración del juicio que afecta a la seguridad laboral, ya que la mayoría de las lesiones fueron fracturas óseas y lesiones superficiales.

DIFERENCIAS ENTRE SEXOS

El estudio ha detectado que las mujeres son más vulnerables al frío y los hombres al calor, lo que puede ser porque las mujeres tienen tasas de sudoración más bajas que los hombres en climas cálidos.

Los investigadores del ISGlobal --centro impulsado por la Fundación Bancaria La Caixa--, han detectado que las personas trabajadoras más vulnerables al calor fueron las más jóvenes, posiblemente porque tienden a hacer un trabajo físicamente más exigente.

Algunas de las medidas preventivas que se pueden incorporar en las políticas de salud pública son la restricción del trabajo en las horas más frías y calurosas, la toma de descansos, garantizar una hidratación adecuada y usar la ropa idónea para el trabajo a realizar.

- Blog article in ISGlobal Blog Health. *How heatwaves affect our health*. 30th June 2017. https://www.isglobal.org/en/healthisglobal/-/custom-blog-portlet/-como-afectan-las-olas-de-calor-a-nuestra-salud-/5734329/0

- Blog article in ISGlobal Blog Health. *Climate change in Catalonia: how is it affecting our health?*. 28th February 2018. https://www.isglobal.org/en/healthisglobal/-/custom-blog-portlet/el-cambio-climatico-en-cataluna-como-nos-afecta-a-la-salud-/5083982/7901

- Participation in the monographic '5 Keys to Healthier Cities' (Temperature). April 2018. https://www.isglobal.org/en/ciudadesquequeremos #CitiesWeWant

8.6. Other activities

- Organization of the internal weekly ISGlobal seminars. January - December 2016. The PhD student was in charge of coordinate, propose and contact speakers invited at ISGlobal, as well as take care of all administrative and technical aspects related to the seminars.

Glossary

ACS	Acute coronary syndrome
Aemet	Agencia Estatal de Meteorología
CI	Confidence interval
CMBD	Conjunto Mínimo Básico de Datos
CO_2	Carbon dioxide
DID	Difference-in-difference
DLNM	Distributed lag non-linear model
GDP	Gross Domestic Product
GHG	Greenhouse gas
GP	General practitioner
HHPP	Heat health prevention plan
HIA	Health impact assessment
ICD	International Classification of Diseases
IPCC	Intergovernmental Panel on Climate Change
ITS	Interrupted time series
MHP	Temperature percentile of minimum hospitalizations
MI	Myocardial infarction
MMP	Temperature percentile of minimum mortality
PD	Percent difference
PM	Particulate matter
PM10	Particular matter less than 10µm
PMOI	Temperature percentile of minimum occupational injuries
RCP	Radiative Concentration Pathways
RCT	Randomized controll trial
RD	Regression discontinuity

RR	Relative risk
SD	Standard deviation
WHO	World Health Organization
WMO	World Meteorological Organization