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ORIGINAL PAPER

The effect of extreme cold temperatures on the risk of death in the two major Portuguese cities

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Abstract It is well known that meteorological conditions influence the comfort and human health. Southern European countries, including Portugal, show the highest mortality rates during winter, but the effects of extreme cold temperatures in Portugal have never been estimated. The objective of this study was the estimation of the effect of extreme cold temperatures on the risk of death in Lisbon and Oporto, aiming the production of scientific evidence for the development of a real-time health warning system. Poisson regression models combined with distributed lag non-linear models were applied to assess the exposure-response relation and lag patterns of the association between minimum temperature and all-causes mortality and between minimum temperature and circulatory and respiratory system diseases mortality from 1992 to 2012, stratified by age, for the period from November to March. The analysis was adjusted for over dispersion and population size, for the confounding effect of influenza epidemics and controlled for long-term trend, seasonality and day of the week. Results showed that the effect of cold temperatures in mortality was not immediate, presenting a 1–2-day delay, reaching maximum increased risk of death after 6–7 days and lasting up to 20–28 days. The overall effect was generally higher and more persistent in Lisbon than in Oporto, particularly for circulatory and respiratory mortality and for the elderly. Exposure to cold temperatures is an important public health problem for a relevant part of the Portuguese population, in particular in Lisbon.

Keywords Minimum temperature · Mortality · Cold effect · Distributed lag non-linear models · Relative risk

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Introduction

It has been described that meteorological conditions influence the human comfort and health. Results of several studies using long time series from the Northern Hemisphere revealed that the global temperature is increasing, both minimum and maximum temperatures (IPCC 2013); it has also been emphasized that the frequency of extreme temperature events, like cold or heat waves, is also increasing (IPCC 2007; Santos et al., 2002). The Global Framework for Climate Services, established in 2014 by the World Meteorological Organization (WMO), adopted Health as one of the priorities, recognizing the importance of further knowledge of the potential risk of death associated with adverse meteorological conditions. The variation of the mortality rate with time is known to be associated with meteorological conditions revealing a seasonal pattern, with a larger number of deaths in winter but also with occurrence of other events like influenza epidemics (Analitis et al. 2008; Mercer 2003; Nunes et al. 2011; The Eurowinter Group 1997). Although this is the general seasonal behaviour, studies in the Northern Hemisphere have shown that the winter to summer mortality rate amplitude varies across countries, with the largest amplitudes observed in milder winter climates (Analitis et al. 2008; Healy 2003; The Eurowinter Group 1997). This is the case of Portugal, characterized by a temperate climate and presenting the highest rate of excess winter mortality in Europe (Healy 2003). It has been also described that cardiovascular and respiratory disease-related deaths account for the majority of excess winter deaths, being the older age groups the most affected by cold temperatures (Analitis et al. 2008; Mercer 2003).

Taking into account the fact that excess winter deaths vary widely among European countries and this variation does not correlate negatively between temperature and mortality (Healy 2003), it is expectable that the Portuguese high excess death rates can decrease. The development of health watch warning systems for extreme temperatures have been shown to be effective in this field (Toloo et al. 2013), which increases the need of the development of tools for real-time monitoring the risk of excess deaths associated with extreme cold temperatures in the southern European countries. The objective of this study was to estimate the effect of extreme cold temperatures on all-causes and on circulatory and respiratory system diseases mortality in Portugal, aiming a framework of knowledge for the development and implementation of a real-time health watch warning system. The study is directed to Lisbon and Oporto, the most populated national cities, providing specific and accurate estimations in restricted geographical areas.

Material and methods

Data

Lisbon and Oporto are the two Portuguese cities with highest population density, being Lisbon the country's capital. In 2012, the population was of 2.2 and 1.8 million in Lisbon and Oporto, respectively. Both cities together comprehend 37 % of the national population. Oporto is located in the northern region of Portugal and Lisbon at the southern region. Mortality data was obtained from Statistics Portugal from 1 January 1992 to 31 December 2012, accounting for 20 winter seasons. All-causes mortality (ICD-10A00-Y98; ICD-9000-999) and circulatory (ICD-10 I00-I99; ICD-9390-459) plus respiratory (ICD-10J00-J99; ICD-9460-519) system diseases (C&R) mortality were the two outcomes analysed in the study, extracted from the 9th and 10th revision of International Classification of Diseases (ICD-9 and ICD-10). Circulatory and respiratory system diseases mortality were grouped due to small numbers of daily deaths from respiratory diseases and all mortality time series were stratified by age: 0 to 64 years old (0–64) and 65 years old or older (65+). The Instituto Português do mar e da Atmosfera provided meteorological data for the same period, namely the minimum and maximum air daily temperatures. The selection of the meteorological stations (Gago Coutinho in Lisbon and Pedras Rubras in Oporto) was based in their high quality data and their climatic representativeness location (Fig. 1). To control the analysis for the potential confounding bias associated with the influenza activity, when estimating the cold effect, data provided by the Instituto Nacional de Saúde Doutor Ricardo Jorge describing the influenza activity for the same period was used. Data consisted of the national weekly influenza-like illness (ILI) incidence rate per 10^5 inhabitants, available from the influenza surveillance system that is based in a General Practitioner's (GP) sentinel network. The analysis was preformed between the months from October to March.

Statistical modelling

To assess the exposure-lag-response relation between exposure variables and mortality, distributed lag non-linear models (DLNM) were applied. DLNM were developed to simultaneously estimate the non-linear and delayed effects of

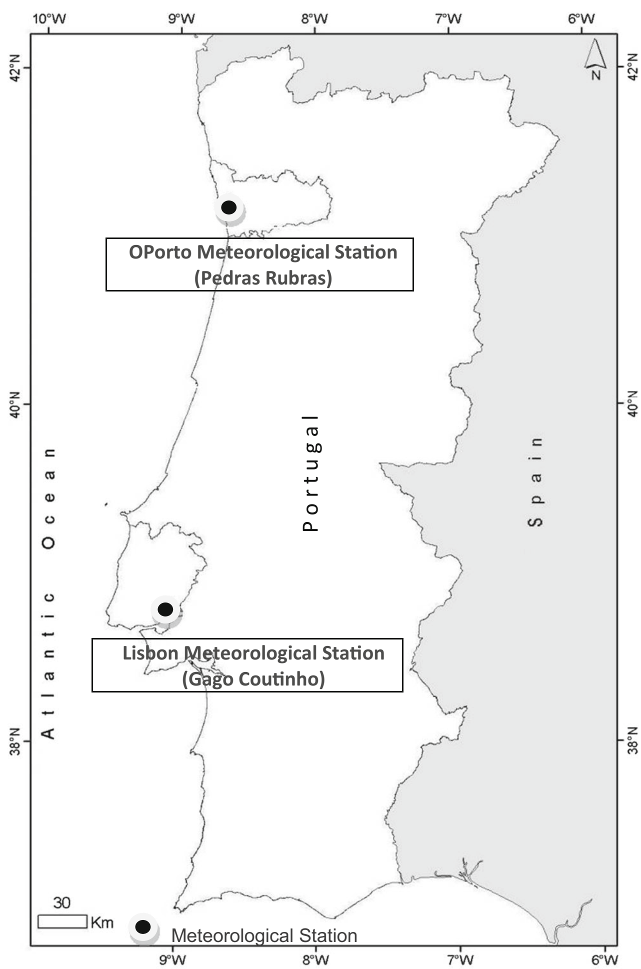

Fig. 1 Location of the meteorological stations where meteorological data was collected

temperature (or air pollution) on mortality (or morbidity) (Armstrong 2006; Gasparrini 2014; Gasparrini et al. 2010). These models were selected on the assumption that cold effects appear with delay, last for several days and to model potential non-linear effects between exposure variables and mortality (Analitis et al. 2008; Armstrong 2006; Carder et al. 2005; Guo et al. 2014; Mercer 2003). Models were adjusted for the confounding bias of the influenza activity, by including weekly ILI incidence rate as covariate and for over dispersion and population size, included as an offset of the log of the population size.

A linear exposure-response relation of minimum temperature and mortality was assumed since both graphical representations and previous studies results have shown that the relation is fairly linear (Carder et al. 2005; The Eurowinter Group 1997). To model the delay effect of the exposure variables, different assumptions were applied in order to find the best fitted model: lag structure described by a polynomial (3rd–4th order), a natural cubic B-spline function (3–5 degrees of freedom) or a simple moving average.

The ILI incidence rate and mortality exposure-response relation was modelled on daily ILI rates that were imputed from the weekly ILI rates by the use of a smoothing function, namely a natural cubic B-spline (3–5 degrees of freedom). Knots for the smoothing function were placed along the quantiles of lags. An alternative binary variable indicating an epidemic state was also tested, defined by ILI incidence rate higher than 50 per 10^5 inhabitants (Rebelo-de-Andrade 2001), considered as a simple approach to adjust the cold effect on mortality. Assumptions for the delay effects were based on both the analyses of the cross-correlation functions (Box et al. 2008; Cryer and Chang 2008) and the analysis of an unconstrained DLNM (Armstrong 2006; Bhaskaran et al. 2013).

Different functions for trend and seasonality were tested. A natural cubic B-spline with 4 degrees of freedom for trend, to capture smooth changes in time, and a natural cubic B-spline with 6 degrees of freedom (1 degree of freedom for each month in analysis) and a 2nd-order polynomial for seasonality. Day of the week of death was also included in the model as a categorical variable.

The general model had the form:

$$\begin{aligned}\log\ E[Y_t] &= a + \boldsymbol{\omega} S(\text{Trend}, \theta_1) + \boldsymbol{\eta} S(\text{Seasonality}, \theta_2) \\ &\quad + \tau\ DoW\ +\ \boldsymbol{\vartheta}\ \text{Influenza}_{t,l} + \boldsymbol{\beta} T\min_{t,l} \qquad (1) \\ &\quad + \text{offset}[\log(\text{population}_t)]\end{aligned}$$

where t is the day of the observation; Y_t is the number of deaths observed on day t; α is the intercept; $S(., \theta)$ represents a smoothing function (natural cubic B-spline or a polynomial with θ degrees of freedom); DoW is the day of the week as a categorical variable; Influenza$_{t,l}$ and Tmin$_{t,l}$ are matrices obtained by applying the DLNM to minimum temperature and ILI incidence rates, respectively; $\boldsymbol{\vartheta}$ and $\boldsymbol{\beta}$ are vectors of coefficients for Influenza$_{t,l}$ and Tmin$_{t,l}$; l is the lagged day; Population$_t$ is the population size.

The maximum lag was set as 31 days for both exposure variables in order to explore lag patterns and because there is evidence that these relations are persistent in time (Analitis et al. 2008; Armstrong 2006; Mercer 2003). The best fitted model for each group was chosen by Akaike's criterion for quasi-Poisson models (QAIC) (Gasparrini et al. 2010).

The overall relative risk (RR), estimated as the sum of the effect along lags, the percentage increased risk of death by a 1 °C decrease from the reference temperature and the RR of death at each minimum temperature lag were calculated using "DLMN" R package (Gasparrini 2011). Several studies suggested local adaptation of populations to their own climate, so the percentiles of temperatures were used as reference measure (Guo et al. 2014). The RR of death from extreme cold temperatures in the 1st percentile was compared with the 99th percentile of minimum temperatures for both cities.

All statistical analysis and modelling were performed in R version 3.1.1, using "DLNM" and "TSA" R packages (Chan and Ripley 2012; Gasparrini 2011; R core Team 2015).

Results

In the studied period, the mean minimum temperature was higher in Lisbon than in Oporto (Table 1). Minimum and maximum daily extremes of minimum temperatures observed for the same period were respectively −0.4 and 19.2 °C in Lisbon and −2.4 and 17.6 °C in Oporto (Table 1). Reference temperature was set to 16 ºC and 15 °C for Lisbon and Oporto, respectively, corresponding to the 99th percentile of minimum temperature. Extreme cold temperatures were set to 2.5 and −0.1 °C for Lisbon and Oporto, respectively, corresponding to the 1st percentile of the observed minimum temperature.

Results from cross-correlation function estimates revealed weaker correlations between minimum temperatures and mortality in the age group of 0–64 years old than those estimated on the older group and in the general population, and that minimum temperatures had a stronger relation with mortality than maximum temperatures. Since these two meteorological variables were highly correlated, only minimum temperature and mortality in the age group of 65+ were included in the modelling phase (Figs. A1, A2 and A3).

The best fitted model for each outcome (all-causes and C&R mortality) in each city, for the general population and the elderly, according to QAIC, described minimum temperature delayed effects by a 4th polynomial function, trend by a natural cubic B-spline with 4 degrees of freedom (*df*) and seasonality by a natural cubic B-spline with 6 *df* (Tables A1 and A2).

The exposure-lag-response surface for each outcome for the total population and in the age group 65+ is presented

Table 1 Descriptive statistics of mortality data (all-causes and circulatory and respiratory system diseases mortality for the general population and for the elderly) and meteorological data (minimum temperature) for Lisbon and Oporto

	Min	Max	Mean	Standard deviation	Percentiles						
					1	5	25	50	75	95	99
Lisbon (number of deaths)											
All-cause mortality	33	122	65	12	42	48	57	64	73	88	102
C&R mortality	10	86	34	9	17	21	28	33	39	50	61
All-cause mortality 65+	24	102	51	11	30	36	44	50	58	71	82
C&R mortality 65+	8	77	30	8	15	19	24	29	35	45	55
Min temperature (ºC)	−0.4	19.2	9.4	3.0	2.5	4.4	7.4	9.6	11.5	14.0	16.0
Oporto (number of deaths)											
All-cause mortality	18	82	44	9	26	31	38	43	50	60	70
C&R mortality	4	49	20	6	9	12	16	20	24	31	37
All-cause mortality 65+	12	71	34	8	18	22	28	33	39	48	56
C&R mortality 65+	4	46	18	5	8	10	14	17	21	28	34
Min temperature (ºC)	−2.4	17.6	7.7	3.5	−0.1	1.8	5.1	7.8	10.3	13.2	15.0

for both cities (Fig. 2). The same figure suggests that risk of death increases while minimum temperature decreases, being higher at the lowest minimum observed temperatures. However, the risk of death does not seem to be immediate but reveals persistence through time. In fact, results showed that the immediate effect of extreme cold temperatures (lag 0) was not statistically significant for both outcomes (all-causes and C&R mortality), in the total population and in the age group of 65+ for both cities. The significant increased risk of death started after 1–2 days and increased until 6–7 days where it reached its maximum effect. Percentage increase in risk of death from cold temperatures at lags 6–7 was generally higher in Lisbon than in Oporto, ranging between 4.34 and 6.08 % in Lisbon and 3.82 and 4.72 % in Oporto (Table 2).

The lag-specific effects analysis of the variation of the risk of death along lags at a specific minimum temperature (in this case at percentile 1 of the observed minimum temperature), can be found in Fig. 3.

Beyond lag days 6–7, the effect of extreme cold temperatures decreases but is still significant in Oporto until lag days 20–23. In Lisbon significant effects persist for longer, approximately 27–28 days, with exception for all-causes mortality in the total population, where extreme cold effect loses significance at lag 21. Between lag days 29 to 31, cold temperatures showed a protective effect in both outcomes, for the total population and the elderly, in both cities. This protective effect was only found to be significant at lag 31 in Lisbon, with exception for C&R mortality in the total population.

The overall effect or the cumulative effect of extreme cold temperatures over 31 days was also higher in Lisbon in comparison with Oporto (Table 2).

For all-causes mortality, the estimated overall RR for the general population was of 1.66 (95 % confidence interval (CI), 1.57–1.76) in Lisbon and 1.57 (95 % CI, 1.48–1.67) in Oporto. In the age group of 65+, this effect was of 1.81 (95 % CI, 1.70–1.94) in Lisbon and 1.71 (95 % CI, 1.60–1.84) in Oporto. For this outcome, the estimated effects were higher in Lisbon and for the elderly in comparison with the general population. However, the estimated effects of extreme cold between Lisbon and Oporto did not differ more than 10 %, leading to similar effects between both cities for all-causes mortality.

For C&R mortality, the cumulative effect of extreme cold temperatures for the general population was estimated in 1.96 (95 % CI, 1.81–2.13) for Lisbon and 1.76 (95 % CI, 1.61–1.93) for Oporto. For the elderly, this effect was estimated in 2.05 (95 % CI, 1.89–2.23) for Lisbon and 1.83 (95 % CI, 1.67–2.01) for Oporto.

As for all-causes mortality, the effect of extreme cold temperatures on C&R mortality was also higher in Lisbon and for the age group 65+. However, for this cause of death, the effect of cold was even higher in Lisbon. In fact, the highest risk of death from cold was estimated for C&R mortality in the elder population living in Lisbon.

Discussion

We have analysed the effect of extreme cold temperatures on the risk of death for the two major cities in Portugal that to our knowledge have never been examined before, using recent and consistent methods. Reported results showed a significant effect from cold temperatures on all-causes and C&R mortality for both Portuguese cities.

Reference temperatures set for each city were based on the 99th percentile, and the values found are in agreement with a

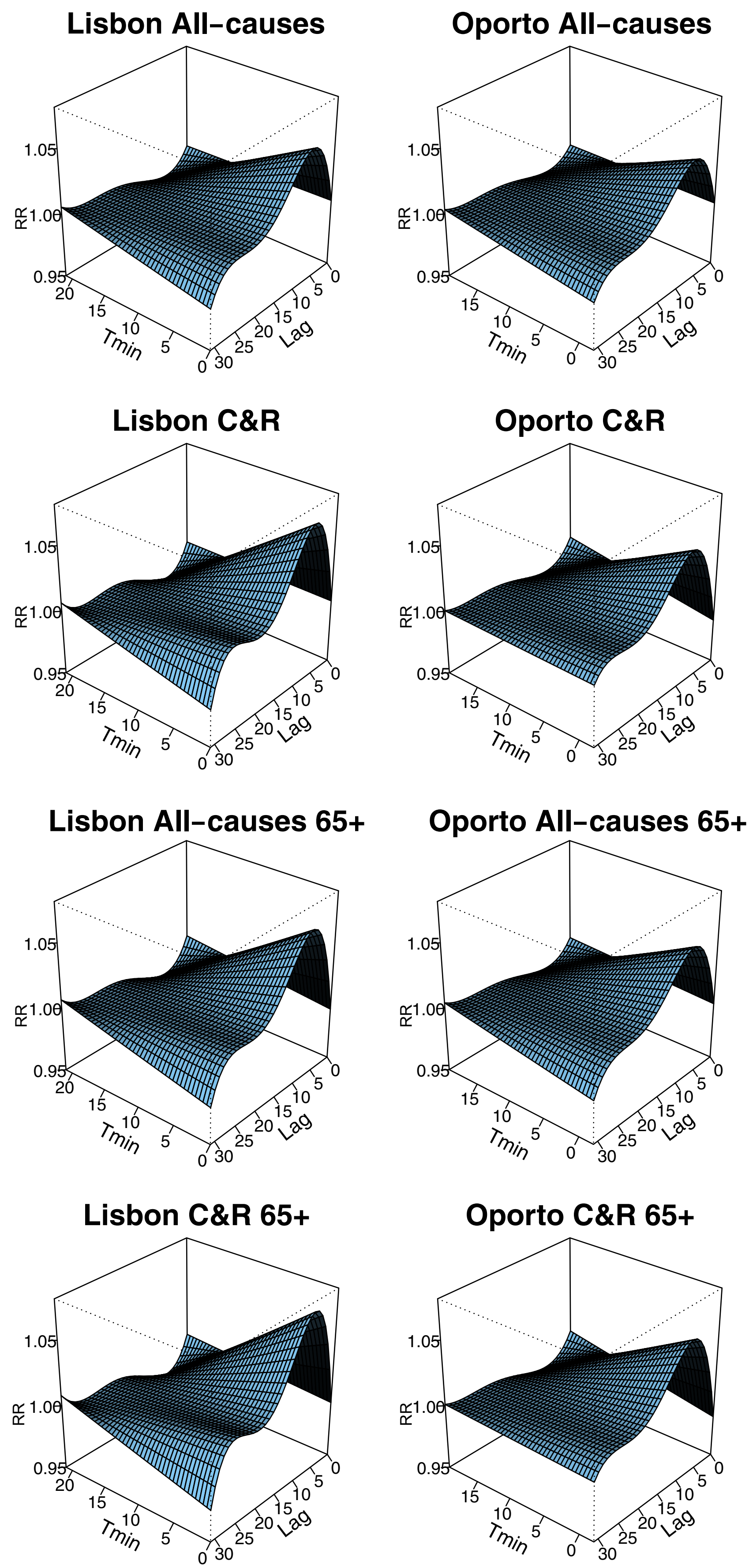

Fig. 2 Exposure-lag-response curves for each city and outcome (all-causes and circulatory and respiratory mortality) for the general population and for the age group of 65+ years

Table 2 Estimated relative risk from extreme cold (1st vs 99th percentile of minimum temperatures), percentage increase on the risk of death per 1 °C fall from reference temperature and maximum lag-specific increase on the risk of death for each outcome (all-causes and circulatory and respiratory mortality) and city (Lisbon and Oporto) for the total population and in the age group 65+ and their respective 95 % confidence intervals

	Extreme cold effects	Increase per 1 °C fall	Maximum lag-specific increase	
	RR (95 % CI)	% increase (95 % CI)	Lag	% increase (95 % CI)
Lisbon				
All-causes	1.66 (1.57–1.76)	3.84 (3.39–4.29)	6	4.34 (3.80–4.89)
C&R	1.96 (1.81–2.13)	5.12 (4.50–5.74)	6	5.64 (4.88–6.41)
All-causes 65+	1.81 (1.70–1.94)	4.51 (4.01–6.13)	6	5.17 (4.56–5.79)
C&R 65+	2.05 (1.89–2.23)	5.47 (4.81–6.13)	6	6.08 (5.27–6.89)
Oporto				
All-causes	1.57 (1.48–1.67)	3.06 (2.63–3.49)	6	3.82 (3.25–4.40)
C&R	1.76 (1.61–1.93)	3.85 (3.22–4.48)	7	4.37 (3.57–5.18)
All-causes 65+	1.71 (1.60–1.84)	3.66 (3.18–4.14)	6	4.31 (3.70–4.93)
C&R 65+	1.83 (1.67–2.01)	4.12 (3.46–4.78)	6	4.72 (3.88–5.57)

national study that estimated the comfort temperatures for Lisbon and Oporto (Marques et al. 2014). Extreme cold temperatures (1st percentile of minimum temperatures) were lower in Oporto than in Lisbon, indicating that lower temperatures are more frequent in Oporto. However, reference temperatures estimated for each city differ only for 1 °C, resulting in similar comfort temperatures.

Results reported in this study showed that the effect of extreme cold temperatures is not immediate, with significant increased risk effects starting with 1–2 days delay and reaching maximum increased risk of death with 6–7 days delay. These results are in agreement with similar studies that found significant increased risk of death associated with cold temperatures with delays of 1–2 days and maximum risk of death estimated with delays of 4–7 days (Analitis et al. 2008; Carder et al. 2005; Guo et al. 2014). Results also showed that cold temperatures effect persists through time, being in sum significant until lags 20–28 in Lisbon and Oporto. Reviewed studies reported similar results, estimating significant effects that last for 10–27 days (Analitis et al. 2008; Carder et al. 2005; Guo et al. 2014). However, it is also important to report that results found for each city suggest that the effect of cold was generally more persistent in Lisbon than in Oporto. A potential harvesting effect was estimated in Lisbon after 29 to 31 days, being significant only after 31 days. In Oporto, harvesting effect associated with cold temperatures was also estimated after 29 to 31 days but was not statistically significant. This could be explained by an insufficient number of lagged days included in the analysis considering the hypothesis that the harvesting effect by cold temperatures could occur latter in Oporto. Similarly, other studies that have included no more than 30 lag days, have not found harvesting effect from extreme cold events (Analitis et al. 2008; Carder et al. 2005; Guo et al. 2014).

Results also revealed that the highest estimated overall effect was for C&R mortality, particularly in the elder population living in Lisbon. Higher estimated effects for circulatory and respiratory causes of death than all-causes mortality has been reported in previous studies and can be explained by the lack of specificity of the latter, which takes into account deaths unrelated or with weak association with cold temperatures. In fact, low temperatures have been related with a large number of biological conditions considered risk factors for cardiovascular diseases including increases in heart rate, blood pressure, peripheral vasoconstriction, plasma fibrinogen concentrations, blood cholesterol levels and platelet viscosity (Carder et al. 2005; Mercer 2003; Mercer et al. 1999), and also with respiratory diseases from cross-infection from increased indoor crowding and from detrimental effect on the immune system's resistance to respiratory infection (Carder et al. 2005). European studies have also found the elderly to be the most affected by cold temperatures (Analitis et al. 2008; The Eurowinter Group 1997), and the higher prevalence of cardiovascular diseases in Portugal is estimated for the elderly (Instituto Nacional de Estatística and Instituto Nacional de Saúde Doutor Ricardo Jorge 2009).

Differences found between Lisbon and Oporto could eventually be explained by a more fragile population living in Lisbon than in Oporto, translated by a higher percentage of elderly individuals and higher prevalence of individuals with chronic diseases. The analysed data showed that the age distribution of the population with 65+ years during the period in study was identical between both cities (data not shown). Also, the prevalence of chronic diseases in the age group of 65+, reported in the national health survey in 2005 (Instituto Nacional de Estatística and Instituto Nacional de Saúde Doutor Ricardo Jorge 2009), such as asthma, high blood pressure and diabetes was similar between both cities. This means that the population age distribution and chronic disease prevalence, in both cities, probably does not explain the differences in the observed effects of the minimum temperature on mortality.

Also, differential housing conditions as well as individual measures taken to deal with cold could explain the differences between both cities. The Eurowinter group has found that

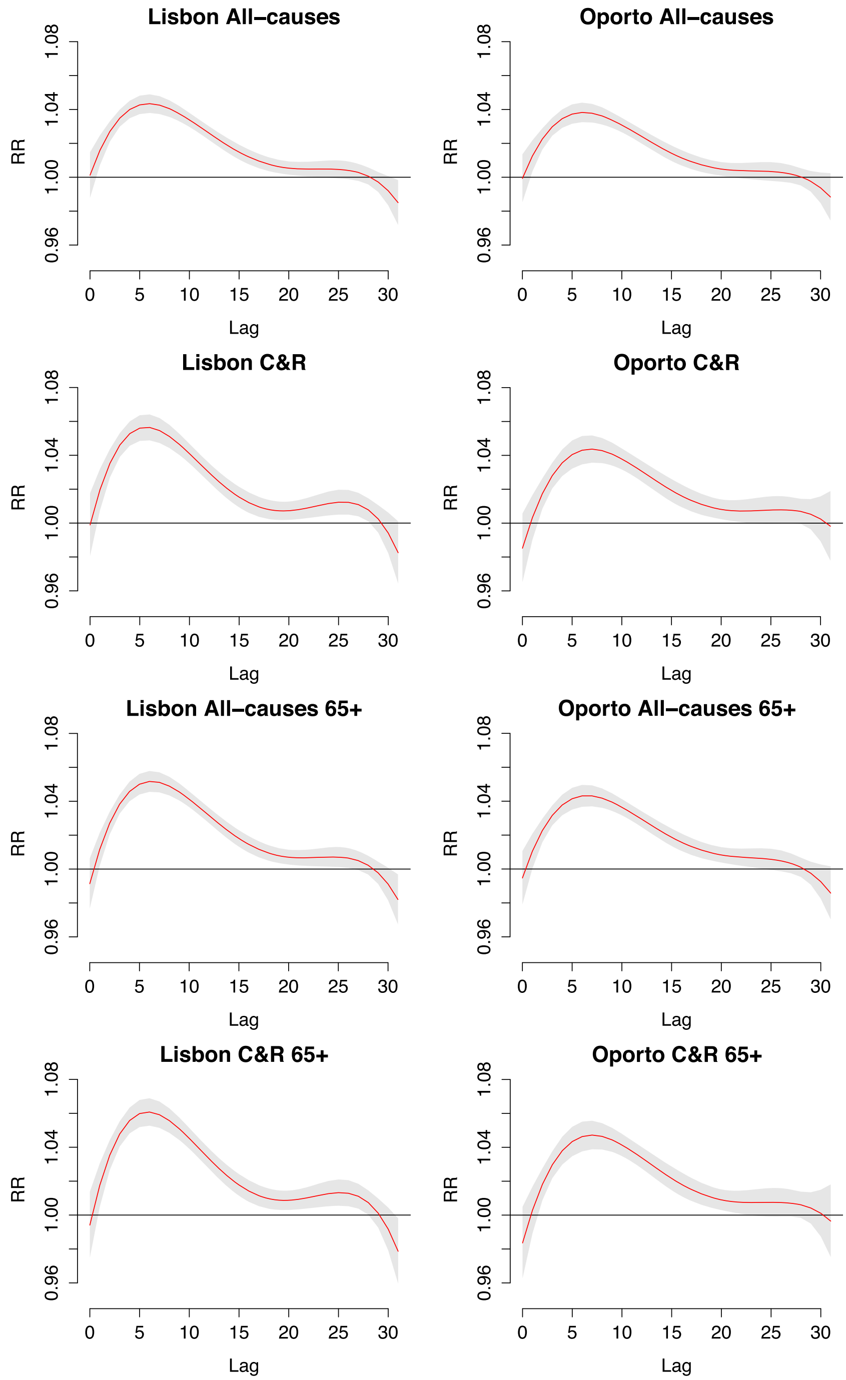

Fig. 3 Lag-response curves for extreme cold temperatures for each city and outcome (all-causes and circulatory and respiratory mortality) for the general population and for the age group of 65+ years

individuals living in countries with higher mean temperatures, in cooler homes, and who wore fewer clothes and were less active outdoor, were more susceptible to cold temperatures.

A less-prepared population for cold temperatures could also explain the results found for Lisbon. Oporto has lower mean and extreme (1st percentile of minimum temperatures) minimum temperatures than Lisbon and this can lead to a more alerted population to deal with cold temperatures, considering the similar comfort temperature in both cities.

However, research is needed to estimate individual factors on cold-related effect integrating area level as well as individual-level variables in Portugal but previous studies suggest that individual measures are associated with lower excess of winter mortality rates (The Eurowinter Group 1997), and measures can be taken to decrease high levels observed in Portugal.

In the absence of studies reporting the estimated relative risk from extreme cold temperatures on mortality in Portugal, comparisons are provided by Guo et al. (2014) study, although whole year's data was used and this could compromise comparisons with our results. Guo et al. (2014) study included estimated overall RR for Spain and Italy, two Southern

European countries with temperate climates. Regional significant cold effects in Spain varied between 1.19 in Santander to 1.72 in Pontevedra and in Italy varied between 1.32 in Bologna to 1.63 in Genova. The estimated effects for Lisbon and Oporto are similar to the effects found for Pontevedra, Ciudad Real and Cádiz, Spain and Genova, Italy. Similar climates can explain identical results also possibly leading to similar behavioural and housing conditions (Braga et al. 2002; Healy 2003; McKee 1989; The Eurowinter Group 1997).

Limitations

An assumed limitation of this study is related to the possible bias on the estimation of the cold effect by not being able to control to the potential confounding or modification effect of other meteorological variables. Meteorological variables such as wind speed, relative or absolute humidity and barometric pressure have been included in several temperature-mortality association studies, separately or by the use of apparent temperature indexes.

Yang et al. (2012) controlled for relative humidity but have not examined or reported its effects, Kunst et al. (1993) have found that wind speed and relative humidity modifies the effect of cold temperatures on mortality, and other authors found that the effect of cold temperatures did not change largely when controlling for the effect of humidity (Braga et al. 2002; Guo et al. 2014). Carder et al. (2005) found no evidence that wind chill, an apparent temperature index calculated using air temperature, wind speed and vapour pressure, is a better predictor than temperature and that relative humidity is not significantly associated with mortality. All these variables were not available at the time of the analysis but we believe that bias could be low.

In this study the effect of cold was not adjusted for the potential confounding effect of air pollution, however several studies have showed that bias would not be relevant (Buckley et al. 2014; Guo et al. 2014; Laaidi et al. 2013; O'Neill et al. 2005; von Klot et al. 2012).

Another important limitation is the nature of the ILI incidence rate used, given that it was measured weekly and at a national level and the outcome is a daily measure and at the city level. National ILI incidence rate can thus be a fragile representation of influenza activity at a regional level and can lead to a possible bias in the estimation of cold effect, resulting from imperfect confounding adjustment.

Other studies on this subject often analysed respiratory and circulatory system diseases separately and associations found are generally stronger for respiratory diseases (Analitis et al. 2008; Carder et al. 2005; Healy 2003). In this study, both causes were analysed together and that can also lead to an imprecise estimation of the cold effect for these outcomes since the effect of cold temperatures can be different between them.

It is important to emphasize that when interpreting coefficients from constrained distributed lag models (DLM) they reflect information from the constraint as well as the data (Armstrong 2006). However, estimated overall effects from constrained DLM do not differ significantly from overall effects estimated from unconstrained DLM (Armstrong 2006). Besides, constrained DLM allowed the reduction of collinearity in the model, caused by the correlation between the lag terms and the effects at individual lags, resulting in more precise estimates (Bhaskaran et al. 2013).

Conclusions

Different effects of cold temperatures in Lisbon and Oporto cities suggest that preventive measures can be taken to reduce the impact from cold, particularly in Lisbon. The first step should be predicting these events to allow mitigation of its impacts through a contingency plan. The Portuguese General Directorate of Health has already given the first steps issuing in 2015/2016 a Winter National Contingency Plan (Direção-Geral da Saúde 2015). We believe that this work will be a very relevant support for the social, governmental and policy awareness, on the need of reducing the impacts of extreme cold temperatures in Portugal and the basis for the development of an early warning system of cold snaps with severe impact on the elderly population to be integrated with the Winter National Contingency Plan. Also, given that it has been shown that extreme cold temperatures can have a severe health impact in south European countries, this line of research and development should probably be enlarged to other temperate climate countries.

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