

# **HHS Public Access**

Author manuscript Environ Res Lett. Author manuscript; available in PMC 2016 June 01.

Published in final edited form as: *Environ Res Lett.* 2015 June ; 10(6): 064016–. doi:10.1088/1748-9326/10/6/064016.

# Winter Season Mortality: Will Climate Warming Bring Benefits?

Patrick L. Kinney<sup>1,\*</sup>, Joel Schwartz<sup>2</sup>, Mathilde Pascal<sup>3</sup>, Elisaveta Petkova<sup>4</sup>, Alain Le Tertre<sup>3</sup>, Sylvia Medina<sup>3</sup>, and Robert Vautard<sup>5</sup>

<sup>1</sup> Mailman School of Public Health, Columbia University, New York, NY 10032, USA

<sup>2</sup> Harvard School of Public Health, Boston, MA 02115, USA

<sup>3</sup> Institut de Veille Sanitaire, 94415 Saint-Maurice, France

<sup>4</sup> National Center for Disaster Preparedness, Earth Institute, Columbia University, New York, NY 10027, USA

<sup>5</sup> Laboratoire des Sciences du Climat et de l'Environment, 91191 Gif sur Yvette, France

# Abstract

Extreme heat events are associated with spikes in mortality, yet death rates are on average highest during the coldest months of the year. Under the assumption that most winter excess mortality is due to cold temperature, many previous studies have concluded that winter mortality will substantially decline in a warming climate. We analyzed whether and to what extent cold temperatures are associated with excess winter mortality across multiple cities and over multiple years within individual cities, using daily temperature and mortality data from 36 US cities (1985-2006) and 3 French cities (1971-2007). Comparing across cities, we found that excess winter mortality did not depend on seasonal temperature range, and was no lower in warmer vs. colder cities, suggesting that temperature is not a key driver of winter excess mortality. Using regression models within monthly strata, we found that variability in daily mortality within cities was not strongly influenced by winter temperature. Finally we found that inadequate control for seasonality in analyses of the effects of cold temperatures led to spuriously large assumed cold effects, and erroneous attribution of winter mortality to cold temperatures. Our findings suggest that reductions in cold-related mortality under warming climate may be much smaller than some have assumed. This should be of interest to researchers and policy makers concerned with projecting future health effects of climate change and developing relevant adaptation strategies.

# Introduction

While the importance of seasonal patterns for human health has been recognized since antiquity (Hippocrates, 400 BCE), understanding of the causal role of ambient temperature

Author Contribution

Competing Financial Interests

<sup>&</sup>lt;sup>\*</sup> corresponding author: plk3@columbia.edu.

P.K., J.S., M.P., and R.V. contributed to the research design, data analysis and paper writing. E.P. contributed data analysis. A.T. and S.M. provided input and edits on early drafts.

The authors declare no competing financial interests.

in these associations remains incomplete. It is well established that extreme heat can lead to increases in daily death counts in cities, with little doubt as to causality (Basu and Samet, 2002, Vandentorren et al., 2004, Semenza et al., 1996, Anderson and Bell, 2009). There is also evidence that extreme cold spells can lead to adverse cardiac events and death (Teng and Heyer, 1955, Huynen et al., 2001). What remains unclear, however, is whether cold temperature is a direct, proximal cause for the general elevation in death rates during the winter season in developed countries where heating is largely available. Clarifying whether temperature is a proximal cause of winter season excess mortality is key for understanding future impacts of climate change. If cold is responsible for a substantial fraction of winter mortality, then future warming would be expected to lead to substantial reductions in winter mortality. However, if seasonal factors other than temperature are mainly responsible for winter excess mortality, then climate warming might have little benefit.

There is a large and growing body of research literature and government reports which projects future temperature-related deaths under climate change scenarios, with a range of findings (Keatinge, 2002, Langford and Bentham, 1995, Martens, 1998, Martin et al., 2012, Hayashi et al., 2009, Huang et al., 2012, Donaldson et al., 2001, Li et al., 2013, Vardoulakis and Heaviside, 2012). Some analyses have predicted that increasing heat-related deaths will outweigh cold-related decreases, leading to increasing net mortality effects in future climates (Dear, 2011, Doyon et al., 2008, Li et al., 2013). Other studies report the opposite, i.e. that decreases in cold-related deaths will outweigh heat-related increases (Langford and Bentham, 1995, Martens, 1998, Martin et al., 2012, Hayashi et al., 2009, Vardoulakis and Heaviside, 2012).

A common approach to quantifying the effects of temperature on mortality is to analyze daily observations over time in a given city. A key challenge faced by these studies is separating temperature effects from seasonal effects, since temperature and season are very highly correlated across seasons. This latter challenge is crucial to studies that seek to fit exposure-response functions linking temperature with mortality, independent of seasonal effects. Such studies underlie much of our current understanding of the health effects of both hot and cold temperatures.

We suggest that underlying the wide range of findings regarding future climate impacts is a fundamental difference in implicit assumptions regarding the causal role of cold temperatures in winter season mortality, assumptions that derive in turn from subtle but critical differences in the statistical models used to estimate cold temperature effects in the presence of seasonal confounding. Studies that attribute large numbers of deaths to cold temperatures are based on statistical models that fit cold temperature effects using some form of multi-week moving average of lagged temperature (usually 21 days) (Anderson and Bell, 2009, Gasparrini et al., 2014). Studies that attribute small numbers of deaths to cold temperatures are based on statistical models that fit cold temperature effects using short lags (1-7 days) (Medina-Ramón and Schwartz, 2007, Li et al., 2013). Because long moving averages of temperature are highly correlated with seasonal patterns of mortality, estimating the mortality effects of long temperature lags can lead to multi-colinearity and residual confounding by season (Huang and Barnett, 2014, Woodward, 2014), even with seasonal variables included simultaneously in the model.

If cold temperatures were directly responsible for winter mortality, one might expect a more pronounced relative winter mortality excess in cities where winter to summer temperature differences are larger, or where winter temperatures are colder. We recently examined this issue by comparing Honolulu, HA and Detroit, MI and found a similar relative seasonal variation in mortality in Honolulu despite an order of magnitude smaller seasonal temperature difference (von Klot et al., 2012). This observation implies either that seasonal variation of mortality is not primarily driven by temperature variations or that residents of Honolulu are highly adapted to their climate and are at risk of death when temperatures dip below 20 °C. Indeed, the issue of adaptation to local climate is intimately connected to how one thinks about future mortality effects of changing temperatures.

Recent studies have questioned the potential future winter mortality benefits of warming temperatures (Staddon et al., 2014, Ebi and Mills, 2013). Using data from England and Wales spanning the period 1951 to 2011, Staddon and colleagues showed that cold temperature effects have largely disappeared in recent decades, and that there will not be future mortality benefits of climate warming. They suggest that improved housing and overall standards of living may have been responsible for the declining impact of cold. Based on a literature review, Ebi and Mills conclude that climate change is unlikely to result in a substantial reduction of winter mortality.

In the present paper we evaluate observational evidence for direct temperature effects on winter-season mortality by analyzing patterns over space and time of mortality and temperatures in a large set of cities in both the US and France. Our objective was to determine whether and to what extent cold temperatures are associated with excess winter mortality when examined across multiple cities and over multiple years within individual cities. Our focus here is only on direct effects of temperatures on mortality risk. We don't consider other pathways, such as storms, snowfall or ice, by which climate change could alter human health in winter.

# Methods

This study emerged from a collaboration between environmental health researchers in France and the US and thus focused on readily available data from cities in those two countries.

#### Data Sources

Total mortality for all age groups were obtained from the French National Institute for Statistics and Economics Studies (INSEE) for Paris, Lyon and Marseille for the period 1971-2007. Mortality data for 36 US cities (listed in supplemental Table 1) were obtained from the U.S. National Center for Health Statistics, and cover all non-accidental deaths (consistent with most previous studies).

For French cities, daily mean temperature data were obtained from Météo-France for a reference station (near city centre in Paris and Lyon, and at the airport in Marseilles) for the period 1971-2007. U.S. daily temperature data covering the years 1985-2006 were obtained from the National Climatic Data Center.

### **Data Analysis**

We computed winter and summer seasonal mean temperatures and deaths in 39 cities and examined whether there were associations between winter/summer mortality ratios and seasonal temperature differences using graphical displays and ordinary linear regression. We compared winter season excess deaths (the ratio of December, January and February deaths to June, July and August deaths) to the difference in mean temperature between these two seasons and to mean winter season temperature across the 39 cities. To examine the importance of controlling for season when testing for temperature effects on mortality over time, we fit a penalized spline function to the relation between same day temperature and mortality in four representative cities: two with substantial seasonal temperature swings (Paris and New York City), one with a hot, humid climate (Miami), and one with intermediate climate (Marseille).

To examine temporal associations between temperature and mortality with or without control for season, first we aggregated data into time series of daily deaths and daily weather for each of the four cities noted above. To compare the effects of average daily mean temperature ( $T_{mean}$ ) on mortality (Y) with different levels of control for season, we fit the Poisson regression model:

$$Log(E(Yt)) = b_0 + s(T_{mean}) + s(time, df = k^*years of study)$$

Where k was set to 0, 6, or 8 respectively. For the smooth function of time, natural splines with k\*(years of study) degrees of freedom were used. Yt is the time series of daily death counts for a city. Temperature was modelled using a 10 df spline function. The objective of these analyses was to explore the sensitivity of the fitted temperature function to differing amounts of seasonal adjustment (i.e., using different of freedom on the spline of time).

To further control of season, we used a similar Poisson regression model as above but stratified by month. The model took the form:

 $Log(E(Yt)) = b_0 + b_1^*$  month of year+s (T<sub>mean</sub>, by=month) +s (time, df=6^\* years of study).

Yt is again the time series of daily death counts, but now stratified within months. In the first set of analyses, we used  $T_{mean}$  on the day of death. In sensitivity analyses, we used  $T_{mean}$ =average temperature over the 5 days ending on the day of death.

All analyses were carried out in R. A similar modelling framework was described in a previous study (Lee et al., 2014).

### Results

If warmer climate leads to less winter mortality, we would expect to see less winter excess mortality in cities that have less extreme winter-summer temperature variations, or that have warmer winters. Figure 1 plots the winter to summer mortality ratio against the seasonal temperature difference across the 39 cities, with each data point representing one city.

Supplemental Figure 1 plots the same mortality ratio against mean winter season temperature. A similar level of winter excess mortality was observed for all cities (mean 1.16; IQR: 1.14-1.18), while seasonal temperature differences spanned a four-fold range, and winter mean temperatures ranging from -5 to over 20 °C. There was no statistical correlation between the magnitude of winter excess mortality and the seasonal range of temperature (R<sup>2</sup>=0.01, p=0.47).

In Figure 2 we plot penalized spline functions relating mortality with same day temperature in Paris, New York City, Miami, and Marseille. When season is left uncontrolled (black circles), cold effects appear much larger, and heat effects much smaller, than when season is controlled. (fitting splines of time with 6 and 8 degrees of freedom per year, as per (Peng et al., 2006)).

Penalized splines linking mortality with same-day temperature within calendar months for New York City, Paris, Miami and Marseille are shown in Figure 3. There was little relationship evident between mortality and cold temperatures, except in January in Paris and Marseilles. Moreover, the increased mortality with cold weather occurred on the relatively small number of days below 0°C in Paris, while more substantial increase in mortality for hot weather occurred on far more days when the mean temperature exceeded 20°C. In sensitivity analyses, we repeated the above analyses using the average of temperature over the five days preceding death. The results (Supplement Figure 3) showed a larger effect of cold temperature, but still smaller, and spread over fewer days, than the heat effects in the prior figure.

# Discussion

Our results suggest that most winter-excess mortality is not largely driven by cold temperature. Among 39 cities in the U.S. and France, there was no evidence that cities that have acclimatized to warm temperatures experience any less winter mortality than do cooler cities. These cities vary widely in demography, urban design, and socio-cultural background, all of which might influence exposure to outdoor temperature and related mortality risks. This is consistent with prior literature on winter excess mortality at the country level, which showed that warmer countries experience as much or more winter excess mortality as do colder countries (Healy, 2003, Laake and Sverre, 1996). Though cross-sectional in nature, this evidence is inconsistent with the notion that future warming would lead to diminished winter season mortality. The lack of correlation between seasonal temperature differences and winter season excess mortality suggests that winter excess mortality is driven mainly by seasonal factors other than temperature.

Our time series analyses of daily deaths in multiple cities demonstrated that exposureresponse findings for cold temperatures were sensitive to analytical methods to control for season, an issue well illustrated in the published literature, where studies that used little or no seasonal control reported large cold temperature effects (Martens, 1998, Gómez-Acebo et al., 2010, Martin et al., 2012), and those that used extensive seasonal control reported smaller cold temperature effects (Doyon et al., 2008, Medina-Ramón and Schwartz, 2007).

Lack of, or inadequate, control for season leads to spuriously large estimated cold effects due to confounding by season.

A standard epidemiologic approach to control of confounding is to analyze associations of interest within narrow strata of the confounder, in this case season. Surprisingly, this concept has rarely been applied in the temperature-mortality literature. There was relatively little relationship evident between mortality and cold temperatures after stratifying by month, except on a small number of very cold days. These analyses confirmed a pattern of modest to no increase in mortality on cold days, more substantial increases in mortality on warm days, and a larger range and number of days for which heat related mortality occurs. Because cold effects may be spread over multiple days (Braga et al., 2001), we repeated the above analyses using the average of temperature over the five days preceding death. The results (Supplement Figure 3) show a larger effect of cold temperature, but still smaller, and spread over fewer days, than the heat effects in the prior figure. While a 21 day distributed lag might show greater effects, that would obviously not be possible in an analysis stratified by month, which illustrates the difficulty of resolving such long lagged temperature effects from season.

In the more recent literature, the issue of confounding by season has re-emerged as a key challenge (Kinney et al., 2012, Huang and Barnett, 2014, Woodward, 2014). While most time series studies include splines of time to control for seasonality, the estimated effects of temperature in the cold season can still be confounded by season if long lags are assumed. A long moving average of temperature is highly co-linear with seasonal variations in mortality, and the slope on distributed lagged temperature may capture a part of that seasonality, even when a separate spline of time is included simultaneously in the model. This is a classic problem of multi-colinearity in regression. Studies that report large cold temperature effects invariably have fit long distributed lags, e.g., 21 days (Analitis et al., 2008, Anderson and Bell, 2009, Guo et al., 2012, McMichael et al., 2008).

There is a growing need for projections of future mortality impacts of temperature under scenarios of climate change, both for economic assessments and for adaptation planning. These analyses usually follow a health impact assessment methodology which first fits an exposure-response function (ERF) to observed data in a given locale (expressing the functional relationship between temperature and mortality in a baseline period) and then applies the ERF to future temperature scenarios for that locale to compute future deaths. As noted, some assessments of this kind have projected very large reductions in winter deaths (Hayashi et al., 2009, Langford and Bentham, 1995, Martin et al., 2012, Martens, 1998, Vardoulakis and Heaviside, 2012). We suggest that this is the case largely because the exposure-response functions for cold temperatures used in these studies were estimated using methodologies that did not adequately control for seasonal confounding. We argue that fitting time series regression models using long distributed lags of temperature leads to spuriously large associations with cold temperatures and that estimated cold effects diminish markedly when season is controlled for completely.

If cold temperature per se is not directly responsible for most winter excess mortality, what is? Influenza epidemics contribute substantially to winter mortality and also appear to

increase the risk of death due to cardiovascular events (von Klot et al., 2012, Bainton et al., 1978, Reichert et al., 2004, Steinvil et al., 2009). Notably, in an analysis of 40 years of mortality statistics in the U.S., Reichert and colleagues found a remarkable correspondence between temporal and age-specific patterns in influenza mortality and other death causes including ischemic heart disease (Reichert et al., 2004), a finding supported in more recent work (von Klot et al., 2012). These studies imply that influenza infections may underlie much of the winter excess in general mortality risk. One study hypothesized that observed winter season increases in plasma fibrinogen and other coagulation factors may be induced by respiratory infections via activation of the acute phase response (Woodhouse et al., 1994). Studies have shown elevations in a range of cardiac risk factors during winter, including vasoconstriction and blood pressure, platelet counts, blood cholesterol levels, heart rate, plasma fibrinogen concentrations, platelet viscosity and peripheral vasoconstriction (Hong et al., 2012, Mercer et al., 1999, Schauble et al., 2012, Donaldson and Keatinge, 1997, Halonen et al., 2010, Pell and Cobbe, 1999). The extent to which these findings reflect direct effects of exposure to cold temperatures vs. other pathways of risk remains unclear at present. Changes over time in seasonal patterns of cardiac mortality in the U.S. have been hypothesized to reflect increased prevalence of winter heating and summer air conditioning (Seretakis et al., 1997). Sorting out the role of temperature exposure in the range of factors influencing winter mortality risks is a major area for future research.

A range of seasonal factors other than cold, including overweight, lack of exercise, time spent indoors, school schedules, holiday gatherings, and air moisture content may lead to increased risks of respiratory infections during winter months (Pell and Cobbe, 1999, Phillips et al., 2004). Absolute humidity is one potential explanation for seasonality of mortality because it varies substantially by season, with much lower levels in winter than summer both indoors and outdoors (Nguyen et al., 2013). It has been shown that dry air increases the risk of influenza infection and probably other respiratory viruses (Shaman and Kohn, 2009). Dry air exposure has been associated with cardiac arrhythmias in an adult cohort (Nguyen et al., in press). Another recent study showed that indoor and outdoor absolute humidity was highly correlated in winter in Boston (Nguyen et al., 2013). In contrast, indoor and outdoor temperatures showed little correlation in winter. Since adults in developed countries spend more than 90 percent of their time indoors, and are largely protected in their daily lives from cold exposure via a range of infrastructure and personal adaptations, humidity may be a more plausible meteorological risk factor for winter season respiratory infections and related cardiovascular mortality. However, seasonal patterns of human exposure to dry air and respiratory viruses remain largely unexplored.

Several limitations should be kept in mind regarding our study. We did not disaggregate deaths into different causes, nor did we stratify by age, sex, ethnicity or economic status. Thus we were unable to assess the extent to which cold temperatures may differentially affect certain causes or population subgroups that may be more vulnerable. Also, temperatures were measured at only a single outdoor site in each city, which ignores spatial patterns of temperature exposure that might occur due to land surface characteristics including vegetation density.

Whatever the causal pathways that lead to winter excess mortality, in our view the evidence suggests that cold plays a limited direct role. Two recent studies have reached similar conclusions using different methods (Ebi and Mills, 2013, Staddon et al., 2014). The implications for assessing future health impacts of climate change are substantial. If winter-season excess mortality is not primarily caused by cold temperatures, future winter warming is likely to have far smaller health benefits than many previous studies have assumed.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgements

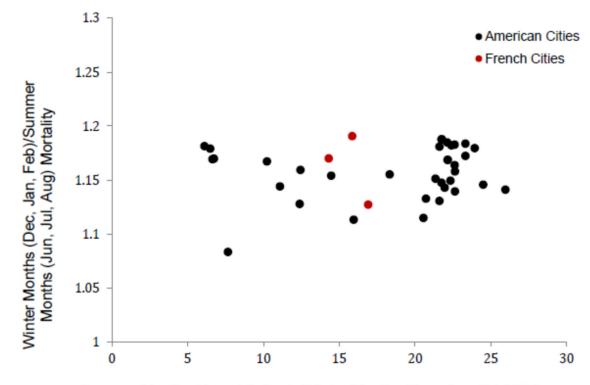
P.K. and E.P. were supported by grants #NA10OAR4310212 from the US National Oceanic and Atmospheric Administration and from grant #P30 ES09089 from the US National Institute of Environmental Health Sciences. Additional support was provided by the Earth Institute at Columbia University.

#### References

- ANALITIS A, KATSOUYANNI K, BIGGERI A, BACCINI M, FORSBERG B, BISANTI L, KIRCHMAYER U, BALLESTER F, CADUM E, GOODMAN PG, HOJS A, SUNYER J, TIITTANEN P, MICHELOZZI P. Effects of cold weather on mortality: results from 15 European cities within the PHEWE project. American journal of epidemiology. 2008; 168:1397–408. [PubMed: 18952849]
- ANDERSON BG, BELL ML. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. Epidemiology (Cambridge, Mass.). 2009; 20:205–13.
- BAINTON D, JONES GR, HOLE D. Influenza and Ischaemic Heart Disease-a Possible Trigger for Acute Myocardial Infarction? International Journal of Epidemiology. 1978; 7:231–239. [PubMed: 721358]
- BASU R, SAMET JM. Relation between Elevated Ambient Temperature and Mortality: A Review of the Epidemiologic Evidence. Epidemiologic Reviews. 2002; 24:190202.
- BRAGA ALF, ZANOBETTI A, SCHWARTZ J. The time course of weather-related deaths. Epidemiology (Cambridge, Mass.). 2001; 12:662–7.
- DEAR K. Deaths in Australia Attributable to Climate Change, Now and to 2100. Epidemiology. 2011; 22:S16.
- DONALDSON GC, KEATINGE WR. Early increases in ischaemic heart disease mortality dissociated from and later changes associated with respiratory mortality after cold weather in south east England. Journal of epidemiology and community health. 1997; 51:643–8. [PubMed: 9519127]
- DONALDSON GC, KOVATS RS, KEATINGE WR, MCMICHAEL A. Heat-and cold-related mortality and morbidity and climate change. 2001
- DOYON B, BÉLANGER D, GOSSELIN P. The potential impact of climate change on annual and seasonal mortality for three cities in Québec, Canada. International journal of health geographics. 2008; 7:23–23. [PubMed: 18498630]
- EBI KL, MILLS D. Winter mortality in a warming climate: a reassessment. WIREs Climate Change. 2013; 4:203–212.
- GASPARRINI A, GUO Y, HASHIZUME M, LAVIGNE E, ZANOBETTI A, SCHWARTZ J, TOBIAS A, TONG S, ROCKLÖV J, FORSBERG B, LEONE M, DE SARIO M, BELL ML, GUO Y-L, WU C-F, KAN H, YI S-M, DE SOUSA ZANOTTI M, COELHO S, SALDIVA PHN, HONDA Y, KIM H, ARMSTRONG B. Mortality risk attributable to high and low ambient temperature: a multi-country study. The Lancet. 2014
- GÓMEZ-ACEBO I, DIERSSEN-SOTOS T, LLORCA J. Effect of cold temperatures on mortality in Cantabria (Northern Spain): a case-crossover study. Public health. 2010; 124:398–403. [PubMed: 20541782]

- GUO Y, BARNETT AG, PAN X, YU W, TONG S. Brogan & Partners The Impact of Temperature on Mortality in Tianjin , China : A Case-Crossover Design with a Distributed Lag Nonlinear Model. Environmental Health Perspectives. 2012; 119:17191725.
- HALONEN JI, ZANOBETTI A, SPARROW D, VOKONAS PS, SCHWARTZ J. Associations between outdoor temperature and markers of inflammation: a cohort study. Environ Health. 2010; 9:42. [PubMed: 20653951]
- HAYASHI A, AKIMOTO K, SANO F, MORI S, TOMODA T. Evaluation of global warming impacts for different levels of stabilization as a step toward determination of the long-term stabilization target. Climatic Change. 2009; 98:87–112.
- HEALY JD. Excess winter mortality in Europe: a cross country analysis identifying key risk factors. J Epidemiol Community Health. 2003; 57:784–9. [PubMed: 14573581]
- HIPPOCRATES. [January 17 2013] 400 BCE.. On airs, waters, and places. [Online]. Available: http:// classics.mit.edu//Hippocrates/airwatpl.html
- HONG YC, KIM H, OH SY, LIM YH, KIM SY, YOON HJ, PARK M. Association of cold ambient temperature and cardiovascular markers. Sci Total Environ. 2012; 435-436:74–9. [PubMed: 22846766]
- HUANG C, BARNETT AG. Winter weather and health. Nature Climate Change. 2014; 4:173–174.
- HUANG C, BARNETT AG, WANG X, TONG S. The impact of temperature on years of life lost in Brisbane, Australia. Nature Climate Change. 2012; 2:265–270.
- HUYNEN MM, MARTENS P, SCHRAM D, WEIJENBERG MP, KUNST AE. The impact of heat waves and cold spells on mortality rates in the Dutch population. Environmental health perspectives. 2001; 109:463–70. [PubMed: 11401757]
- KEATINGE WR. Winter mortality and its causes. International journal of circumpolar health. 2002; 61:292–9. [PubMed: 12546188]
- KINNEY PL, PASCAL M, VAUTARD R, LAAIDI K. Winter mortality in a changing climate: will it go down? Bulletin épidémiologique hebdomadaire (BEH). 2012:148–151.
- LAAKE K, SVERRE JM. Winter excess mortality: a comparison between Norway and England plus Wales. Age and ageing. 1996; 25:343–8. [PubMed: 8921136]
- LANGFORD IH, BENTHAM G. The potential effects of climate change on winter mortality in England and Wales. International journal of biometeorology. 1995; 38:141–7. [PubMed: 7744529]
- LEE M, NORDIO F, ZANOBETTI A, KINNEY P, VAUTARD R, SCHWARTZ J. Acclimatization across space and time in the effects of temperature on mortality: a time-series analysis. Environmental Health. 2014:13. [PubMed: 24612632]
- LI T, HORTON RM, KINNEY PL. Projections of seasonal patterns in temperature-related deaths for Manhattan, New York. Nature Climate Change. 2013
- MARTENS WJ. Climate change, thermal stress and mortality changes. Social science & medicine. 1998; 46:331–44. [PubMed: 9460815]
- MARTIN SL, CAKMAK S, HEBBERN CA, AVRAMESCU M-L, TREMBLAY N. Climate change and future temperature-related mortality in 15 Canadian cities. International journal of biometeorology. 2012; 56:605–19. [PubMed: 21597936]
- MCMICHAEL AJ, WILKINSON P, KOVATS RS, PATTENDEN S, HAJAT S, ARMSTRONG B, VAJANAPOOM N, NICIU EM, MAHOMED H, KINGKEOW C, KOSNIK M, O'NEILL MS, ROMIEU I, RAMIREZ-AGUILAR M, BARRETO ML, GOUVEIA N, NIKIFOROV B. International study of temperature, heat and urban mortality: the 'ISOTHURM' project. International journal of epidemiology. 2008; 37:1121–31. [PubMed: 18522981]
- MEDINA-RAMÓN M, SCHWARTZ J. Temperature, Temperature Extremes, and Mortality: A Study of Acclimatization and Effect Modification in 50 United States Cities. Occupational and environmental medicine. 2007
- MERCER JB, OSTERUD B, TVEITA T. The effect of short-term cold exposure on risk factors for cardiovascular disease. Thromb Res. 1999; 95:93–104. [PubMed: 10418798]
- NGUYEN JL, LINK MS, LUTTMANN-GIBSON H, LADEN F, SCHWARTZ J, WESSLER BS, MITTLEMAN MA, GOLD DR, DOCKERY DW. Drier air and lower temperatures trigger paroxysmal atrial fibrilation. Epidemiology. in press.

- NGUYEN JL, SCHWARTZ J, DOCKERY DW. The relationship between indoor and outdoor temperature, apparent temperature, relative humidity, and absolute humidity. Indoro Air. 2013; 24:103–112.
- PELL JP, COBBE SM. Seasonal variations in coronary heart disease. Qjm-Monthly Journal of the Association of Physicians. 1999; 92:689–696. [PubMed: 10581331]
- PENG R, DOMINICI F, LOUIS T. Journal of the Royal Statistical Society Ser A. 2006; 169:198–203. Part 2.
- PHILLIPS DP, JARVINEN JR, ABRAMSON IS, PHILLIPS RR. Cardiac mortality is higher around Christmas and New Year's than at any other time - The holidays as a risk factor for death. Circulation. 2004; 110:3781–3788. [PubMed: 15596560]
- REICHERT TA, SIMONSEN L, SHARMA A, PARDO SA, FEDSON DS, MILLER MA. Influenza and the winter increase in mortality in the United States, 1959-1999. American journal of epidemiology. 2004; 160:492–502. [PubMed: 15321847]
- SCHAUBLE CL, HAMPEL R, BREITNER S, RUCKERL R, PHIPPS R, DIAZ-SANCHEZ D, DEVLIN RB, CARTER JD, SOUKUP J, SILBAJORIS R, DAILEY L, KOENIG W, CYRYS J, GERUSCHKAT U, BELCREDI P, KRAUS U, PETERS A, SCHNEIDER AE. Short-term effects of air temperature on blood markers of coagulation and inflammation in potentially susceptible individuals. Occup Environ Med. 2012; 69:670–8. [PubMed: 22833664]
- SEMENZA JC, RUBIN CH, FALTER KH, SELANIKIO JD, FLANDERS WD, HOWE HL, WILHELM JL. Heat-Related Deaths during the July 1995 Heat Wave in Chicago. New England Journal of Medicine. 1996:335. [PubMed: 8532046]
- SERETAKIS D, LAGIOU P, LIPWORTH L, SIGNORELLO LB, ROTHMAN KJ, TRICHOPOULOS D. Changing seasonality of mortality from coronary heart disease. JAMA : the journal of the American Medical Association. 1997; 278:1012–4. [PubMed: 9307350]
- SHAMAN J, KOHN M. Absolute humidity modulates influenza survival, transmission, and seasonality. Proceedings of the National Academy of Sciences of the United States of America. 2009; 106:3243–8. [PubMed: 19204283]
- STADDON PL, MONGOMERY HE, DEPLEDGE MH. Climate warming will not decrease winter mortality. Nature Climate Change. 2014; 4:190–194.
- STEINVIL A, BERLINER S, BROMBERG M, COHEN M, SHALEV V, SHAPIRA I, ROGOWSKI O. Micro-inflammatory changes in asymptomatic healthy adults during bouts of respiratory tract infections in the community: Potential triggers for atherothrombotic events. Atherosclerosis. 2009; 206:270–275. [PubMed: 19281986]
- TENG H, HEYER H. The relationship between sudden changes in weather and the occurence of acute myocardial infarction. American Heart Journal. 1955; 49:9–20. [PubMed: 13218000]
- VANDENTORREN S, SUZAN F, MEDINA S, PASCAL M, MAULPOIX A, COHEN J-C, LEDRANS M. Mortality in 13 French cities during the August 2003 heat wave. American journal of public health. 2004; 94:1518–20. [PubMed: 15333306]
- VARDOULAKIS, S.; HEAVISIDE, C. Health Effects of Climate Change in the UK 2012 Current evidence, recommendations and research gaps. UK Health Protection Agency; 2012.
- VON KLOT S, ZANOBETTI A, SCHWARTZ J. Influenza epidemics, seasonality, and the effects of cold weather on cardiac mortality. Environ Health. 2012; 11:74. [PubMed: 23025494]
- WOODHOUSE PR, KHAW KT, PLUMMER M, FOLEY A, MEADE TW. Seasonal variations of plasma fibrinogen and factor VII activity in the elderly: winter infections and death from cardiovascular disease. Lancet. 1994; 343:435–9. [PubMed: 7508540]
- WOODWARD A. Heat, cold and climate change. Journal of epidemiology and community health. 2014; 68:595–596. [PubMed: 24692630]

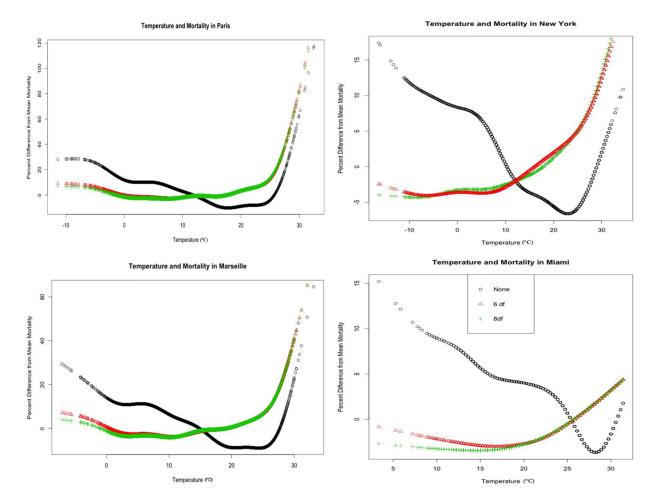




## Figure 1.

Scatter plot of winter excess mortality (the ratio of Dec, Jan, and Feb deaths to Jun, Jul, Aug deaths) vs. seasonal temperature difference for the same months over 22 years in 39 cities. See supplemental file, Table 1 for a list of cities and input data.

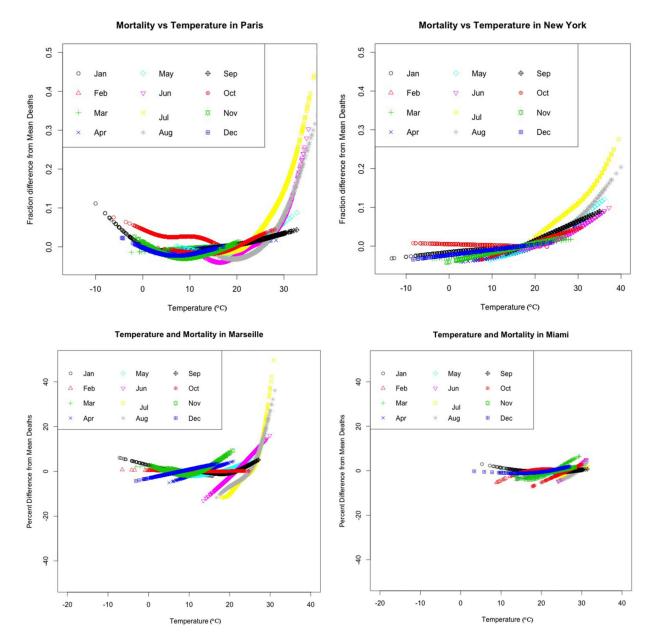
Kinney et al.



### Figure 2.

Penalized spline functions fit to the relation between temperature and mortality in Paris and New York City (top), and Marseille and Miami (bottom). The black circles show the relationship when season is left uncontrolled. The red triangles show the relationship when season is controlled using a natural spline with 6 degrees of freedom per year, and the green crosses show the relation with 8 degrees of freedom per year of seasonal control. The French data are for 1971 to 2007 and the US data are for 1985 to 2006.

Kinney et al.



#### Figure 3.

Penalized spline functions relating mortality with temperature on the day of death by calendar month in Paris and New York City (top) and Marseille and Miami (bottom). The Paris and Marseille data are for 1971 to 2007 and the NYC and Miami data are for 1985 to 2006.