EFFECTS OF DIURNAL VARIATIONS IN TEMPERATURE ON MORTALITY AMONG THE ELDERLY

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Abstract

The association between short-term changes in ambient temperature and daily mortality has been described widely in the literature. A few recent papers support the hypothesis that diurnal variations in temperature may also have an impact on mortality, independent of the effect of daily mean temperature. The objective of the thesis was to determine whether variations in diurnal temperature increased daily non-accidental mortality among the elderly population of Montreal, Quebec, during the 1984-2007 study period. We used distributed lag non-linear models constrained over a 30 day lag period, and adjusted for temporal trends, mean daily temperature, and mean daily concentrations of nitrogen dioxide and ozone. We found over the 30 day lag period a cumulative increase of 5.12% (95% confidence interval (CI): 0.02 to 10.49) in daily mortality for an increase of the diurnal temperature range from 6 °C to 11 °C and a 11.27% (95% CI: 2.08 to 21.29) increase in mortality associated with an increase of the diurnal temperature range from 11 to 16 °C. The results were relatively robust to adjustment for mean temperature. In conclusion, we found that in Montreal daily diurnal variations in temperature are associated with a small increase in mortality among the elderly population. More studies are needed in different geographical locations to confirm these effects.

Résumé

L'association entre les variations à court terme de la température ambiante et la mortalité quotidienne a été largement décrite dans la littérature. Quelques articles récents supportent l'hypothèse que les variations diurnes de la température peuvent également avoir un impact notable sur la mortalité, indépendamment de l'effet de la température moyenne. L'objectif de la thèse était de déterminer si les variations de température diurne provoquent une augmentation de la mortalité quotidienne non accidentelle chez les personnes âgées de Montréal, Québec, durant la période d'étude couvrant les années 1984 à 2007. Nous avons utilisé les modèles distribués non linéairs restraints à une période de latence de 30 jours, et ajustés pour les tendances temporelles, la température moyenne quotidienne, le dioxyde d'azote et l'ozone. Nous avons trouvé une augmentation cumulative de 5,12% (intervalle de confiance (IC) 95%: 0,02 à 10.49) de la mortalité pour une augmentation de la température diurne de 6 à 11 °C et une augmentation de 11,27% (IC 95%: 2,08 à 21,29) de la mortalité associée à une augmentation des températures diurnes de 11 à 16 °C. Les résultats sont relativement robustes à l'ajustement pour la température moyenne. Nous avons constaté que les variations quotidiennes des températures à Montréal sont associées à une faible augmentation de la mortalité chez la population âgée. Plus d'études sont nécessaires dans différents lieux géographiques pour confirmer un tel effet.

Preface

Contribution of authors

The principal author of this manuscript-based thesis is Maria Vutcovici, with feedback provided by Dr. Mark S. Goldberg. Data management and statistical analysis were done by Maria Vutcovici with the assistance of biostatistician Marie-France Valois and under the supervision of Dr. Goldberg.

Organization of thesis

The objective of the thesis was to assess the impact of diurnal temperature variations on non-accidental mortality among the elderly population of Montreal during the period 1984 to 2007. This manuscript-based thesis has a unified theme, as required by McGill University. A separate introduction, literature review and conclusion have been included as chapters, and as such, some repetition is unavoidable. The manuscript has not yet been submitted for publication.

Chapter 1 provides an introduction to current issues related to climate change and projected increases in global temperature. It also details the impact of extremes of temperature on human health, highlighting the factors that make elderly adults a subgroup of the population particularly vulnerable to ambient temperature changes.

Chapter 2 includes a literature review of the temperature-mortality association with a section specifically addressing the impact of diurnal temperature variations on human health.

Chapter 3 provides the rationale and objective of the thesis.

Chapter 4 consists of the manuscript entitled "Effects of diurnal variations in temperature on non-accidental mortality among the elderly population of Montreal, Quebec, 1984-2007."

Chapter 5 provides a summary of the findings, a discussion, and the conclusions of the thesis.

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Chapter 1: Introduction

> "Warming of the climate system is unequivocal, as is now evident from observations of increases in global average air and ocean temperatures, widespread melting of snow and ice and rising global average sea level. The temperature increase is widespread over the globe and is greater at higher northern latitudes." (IPCC Core Writing Team 2008)

In order to understand the importance that warming of the global climate system has for humans and other species, certain terms such as climate change and global warming have to be defined clearly. Climate change refers to any changes in climate due to natural factors, human activity or both that occur over time (Lemmen et al. 2008). Global warming represents an increase in the average temperatures near the Earth's surface and in the lowest layer of the atmosphere (troposphere). Global warming, along with other changes, such as changes in precipitation and increases in sea level, can be considered as part of climate change (US Environmental Protection Agency 2009).

The magnitude of the changes already occurring has been estimated by the Intergovernmental Panel on Climate Change, which, in its Fourth Assessment Report issued in 2007, concluded that during the second half of the 20th century the average temperatures in the Northern Hemisphere were very likely higher than during any other 50-year period in the last 500 years (Parry et al. 2007). As of this writing, the Fifth Assessment is in preparation. There is clear evidence that mean surface temperatures have increased and more days with higher temperatures are being recorded, with the extent of change varying by region (Schar and Jendritzky 2004). While an increase in the number of heat waves in the mid-latitudes over Europe and the USA (Rosenzweig et al. 2007) and cold-waves in northern latitudes (Confalonieri et al. 2007) has also been observed, there is yet no consensus whether these are due to global warming. As well, there is no formal definition for either heat- or cold-waves. In some studies, definitions based on the duration of the extreme weather event and the absolute value of temperature reached were used (Huynen et al. 2001;Tan et al. 2007), while other authors preferred a combination of duration of the event and the temperature (Beniston and Diaz 2004;Gosling et al. 2007;Hajat et al. 2002).

While the Third Assessment Report issued by the Intergovernmental Panel on Climate Change in 2001 projected for North America less extreme winter cold for the northern cities and more extreme heat in other cities across the continent (Cohen et al. 2001), the Fourth Assessment Report further emphasized that cities which currently experience heat waves are expected to be confronted with an increased number, intensity and duration of such extreme events during the course of this century (IPCC Core Writing Team 2008). In North America, the annual mean warming seems likely to exceed the global mean warming in most areas, with the most pronounced warming occurring in the northern latitudes during the winter season (Christensen et al. 2007). Most of the combinations of global circulation models for North America project a warming in the range of 1 to 3 ºC during the 2010 to 2039 time period (Christensen et al. 2007;Field et al. 2007) as compared to the baseline period of 1961-1990 (Ruosteenoja et al. 2003), but this depends strongly on the actual amount of emissions of greenhouse gases, especially carbon dioxide (CO_2). Beyond 2040 and toward the end of the century, the projected annual warming is approximately 2 to 3 °C for the western, southern, and eastern continental edges, and more than 5 ºC at high latitudes. For the southwest United States the warming will be greatest in the summer season, whereas for the northern latitudes the largest changes will be recorded during the winter season (Christensen et al. 2007).

Many of Earth's environmental systems may suffer an abrupt, non-linear transition from one state to another when approaching threshold levels of certain key variables (Rockstrom et al. 2009). A recent report on planetary boundaries, based mostly on an analysis of the paleo-climatic records, suggests that the threshold for irreversible climate change may be in the order of 350 parts per million (ppm) CO_2 (Rockstrom et al. 2009); a value of 380 ppm of CO_2 was already reached in 2005 and the annual rate of increase is about 1 ppm (Solomon et al. 2007).

Given the present changes in climate and the projections for the next decades, the evaluation of the impact on human health, and especially for the projected changes in climate, are of obvious importance for adopting appropriate public health plans to minimize adverse health effects at population level.

1.1 Physiological changes due to extreme temperatures

Effects from depressed temperatures

Before one can address the effects of temperature at population level, it is important to describe the changes at an individual level that occur in the human body exposed to extreme temperatures.

The skin and the subcutaneous layer of fat act as a natural insulator that protects the body from the ambient temperature. But as the temperature of the skin rises and falls with ambient temperature, the core body temperature also changes, and complex thermoregulatory processes immediately intervene to bring it back within the optimum levels of 36.8 – 37.4 °C. These processes are coordinated by the body's thermoregulatory center located in the hypothalamic area of the brain (Guyton and Hall 2005;Miller 2009).

When the temperature of the skin decreases, colder blood reaches the brain and stimulates both the cortex and the hypothalamic thermoregulatory center. The cortex of the brain initiates behavioural responses, such as seeking shelter, adding additional layers of clothing, or drinking warm fluids (Guyton and Hall 2005). The thermoregulatory center in turn initiates responses to reduce heat loss and increase heat generation (Beers et al. 2004). The functioning of this center is greatly impaired when the core body temperature drops to 34 °C and is completely lost at approximately 30 °C.

Heat loss is mainly prevented by reducing the blood flow to the skin, thus increasing the flow toward the vital internal organs. When this mechanism fails to maintain the core body temperature within optimum levels, the increased excretion of water and electrolytes that follows leaves a high proportion of blood cells and fibrinogen in circulation that promote clotting (Keatinge and Donaldson 2004). The generation of additional heat is the effect of a combined neuro-endocrine stimulation of the activity of peripheral muscles and heat-generating internal organs, such as the liver, heart and brain, by increasing their metabolic rate (Guyton and Hall 2005).

The symptoms of exposure to cold, in order of appearance, are: the rising of skin hairs; shivering (usually starts when skin temperature approaches 20 °C); a change in the coloration of the skin from pink to pale to blue; sleepiness; and coma (Guyton and Hall 2005;Simon 1993). The clinical outcomes of exposure to cold range from localized frostbite lesions to the more severe and life-threatening conditions such as cardiac fibrillation and cardiac or cerebral stroke (Guyton and Hall 2005;Havenith 2005).

There are certain changes in the thermoregulatory mechanisms that develop with age, making elderly adults a susceptible population to the effects of both cold and heat (Beers et al. 2004;Miller 2009). The changes that interfere with thermoregulation in cold environments include the thinning of the subcutaneous layer of fat that provides insulation, delayed and diminished shivering reflex, decreased muscle mass to provide additional heat, reduced peripheral circulation (giving the sensation of cold in the extremities), an inefficient reduction of blood flow to the skin resulting in increased heat loss and a decreased cardiac output to cope with the increased flow of blood directed toward the internal organs (Beers et al. 2004;Miller 2009;Worfolk 2000).

Even though such changes appear usually in the fifth decade of life, their impacts are not fully felt until the seventh or eighth decade, when the overall dulled perception of cold environments prevents the elderly adults from taking protective action when needed (Miller 2009). Furthermore, the proportion of people with illnesses and disabilities increases with age (Havenith 2005). Certain medical conditions may interfere with the normal response of the body to cold. Hypothyroidism, cancer and malnutrition limit the heat generation process; diabetes reduces the body's ability to retain heat; diseases or traumatic injuries such as arthritis or stroke, limit the ability of the body to move, interfere with muscle contraction and thus with heat generation (Beers et al. 2004). Usage of therapeutic drugs also increases with age. Among the drugs that interfere with thermoregulation in cold environments by suppressing shivering or inducing vasodilatation are cyclic antidepressants, barbiturates, benzodiazepines and phenothiazines. Alcohol has vasodilatation effects, but it also interferes with the perception of cold environments and the initiation of protective behavioural responses (Beers et al. 2004;Miller 2009;Yoda et al. 2008).

Effects from elevated temperatures

When the human body is exposed to high temperatures, the thermoregulatory system is responsible for cooling it by increasing the blood flow toward the skin, vasodilatation (heat loss through conduction), sweating (heat loss through evaporation) and decreasing heat production by inhibiting chemical reactions which generate heat (Guyton and Hall 2005;Simon 1993). Sweating increases abruptly when the core body temperature exceeds 37 °C**,** each additional 1 °C above this critical level causing a ten-fold increase in the rate of evaporation (Guyton and Hall 2005).

The symptoms of exposure to heat range from mild weakness, dizziness, fatigue to syncope, exhaustion, and even coma and death. The clinical outcomes of heat exposure include heat induced oedema, cramps, syncope, exhaustion and heat stroke (Barrow and Clark 1998).

Heat oedema is the mildest form of heat-related illness, characterized by swelling of the extremities due to heat-induced peripheral vasodilatation and orthostatic pooling of blood (Lugo-Amador et al. 2004). Heat cramps usually occur in the arms, legs or abdomen during or after exertion in the heat. They are caused by the electrolyte imbalance resulting from loss of body fluids and minerals through sweating, corrected by the intake of water without minerals (Beers et al. 2004). Heat syncope occurs mostly in elderly or poorly acclimatized individuals, and it results from either an inadequate cardiac output or from postural hypotension due to volume depletion, peripheral vasodilatation, and a decreased tone of the blood vessels (Barrow and Clark 1998;Lugo-Amador et al. 2004).

Heat exhaustion, the most common heat-related illness (Knochel 1974), occurs when a person experiences excess sweating in a hot humid environment, resulting in loss of water and electrolytes (Barrow and Clark 1998). The symptoms include fatigue, weakness, dizziness, headache, nausea, vomiting, and muscle cramps. The patient shows clinical signs of dehydration and is sweating profusely (Lugo-Amador et al. 2004). Orthostatic syncope, visual disturbances and flushing of the skin may also be present. The body temperature is usually between 38.0 °C (100.4°F) and 40.5 °C (104.9 °F) (Barrow and Clark 1998).

Heat stroke is a true medical emergency. The diagnosis is made when a markedly elevated body temperature (above 40.5 °C) and changes in mental status follow heat exposure (Barrow and Clark 1998). Progression to death can be very rapid (within hours), through multiple organ failure (Kovats and Hajat 2008). Survivors of an acute event have an increased risk of early mortality (Wallace et al. 2007).

Certain changes that develop with age interfere with the thermoregulatory capacity of elderly adults in warm environments. As the body ages, the number of sweat glands decreases, the threshold for the onset of sweating is higher and the response reduced compared to younger adults, resulting in a diminished cooling effect from perspiration (Miller 2009;Worfolk 2000). There is also a decreased vasodilatation response, which the diminished cardiac output cannot counterbalance. The thirst response is delayed, and access to replenishing liquids may be impeded in people with reduced mobility (Barrow and Clark 1998). The neuro-sensory reflexes in older adults are delayed and decreased, dulling their awareness of changes in temperature (Miller 2009). Furthermore, a variety of medical conditions (such as cardiovascular diseases, kidney diseases, diabetes, thyroid diseases, disorders of the nervous system, psychiatric disorders, eating disorders), physiological conditions (e.g., fever, dehydration, prolonged exertion), medications (e.g., antihistamines, diuretics, laxatives, antidepressants) and abuse of substances (e.g., alcohol, cocaine, heroin, LSD, amphetamines) can increase the risk of developing these heat-related illnesses (Barrow and Clark 1998;Miller 2009;Worfolk 2000).

The combined effect of naturally occurring changes and pathological changes caused by the illnesses associated with older age, along with an increase in the use of medication, makes the elderly population more at risk for developing heat stroke, cardiovascular events (such as heart failure) or cerebral stroke during hot days as compared to the younger adult population (Havenith 2005).

1.2 Epidemiology of Ambient Temperature on Health

Numerous studies have been conducted to investigate the short-term effects of changes in ambient temperature on mortality, and various study designs have been used to characterize or quantify the relationships, including time series (Curriero et al. 2002;Goldberg et al. 2011;Hajat et al. 2005;Hajat et al. 2002;Huynen et al. 2001;LeTertre et al. 2006;Saez et al. 2000) and related case-crossover designs (Bell et al. 2008;Chen et al. 2007;Stafoggia et al. 2008;Stafoggia et al. 2006). The objectives of these studies were related to answering questions regarding triggering mechanisms, such as “Do the number of adverse health events increase when temperature increases or decreases?”

Time series studies

Time-series studies are used to assess short-term changes in health outcomes for exposure variables that have considerable short-term variability. Good quality exposure measurements over a considerable time period are needed; therefore, data from routinely monitoring or surveillance networks are often used because of their coverage of large populations (Katsouyanni and Touloumi 2008).

Time series studies have been used to assess the effects of heat- and cold-waves on human mortality in single or multiple locations (Braga et al. 2001;Curriero et al. 2002;Hajat et al. 2002;LeTertre et al. 2006;Saez et al. 1995). More often than not, grouped population data on a health outcome, such as non-accidental mortality, are obtained in a specific geographical region over a specific period of time. The day is used as the unit of observation and the number of daily events is tabulated (the outcome time series). Next, estimates of daily parameters of weather are obtained and these represent the exposure time series. Statistical models (Poisson regression) are used to estimate the association between daily numbers of events and daily changes in, say, mean temperature, after removing longer-term temporal fluctuations in the daily counts that should not affect short-term effects (e.g., those occurring on the same day or the next day). As well, other time series, such as representing mean daily concentrations of air pollutants or influenza epidemics are added to the model as covariates. There are specific issues with developing the statistical models, including eliminating the usual strong serial autocorrelation in the outcome time series, that can render the model invalid, and extra-Poisson variability (or overdispersion) that is usually modeled through quasi-likelihood techniques. The modern statistical methods allow for a large number of tuneable parameters and because it is difficult to select the "best" model, sensitivity analyses are often carried out (Goldberg et al. 2003).

The time series design has several advantages, including covering large segments of the general population and being less expensive than other designs, such as panel studies, because administrative data are often used. A disadvantage is that the exposure data from monitoring and surveillance networks does not accurately reflect individual exposure and the choice of outcome measures is restricted to available data, such as daily mortality or the number of admissions to hospitals. Although it is difficult to know whether a specific statistical model is appropriate the large number of events allows small effects to be identified. At the same time, however, the considerable random noise in the time series makes it often difficult to distinguish which subgroups of the population may be at higher risk.

Another advantage is that time series studies cannot be confounded by individual or behavioural characteristics that do not change over short time periods, but seasonal or other periodic pattern in both exposure and outcome measures, such as influenza epidemics, may have a strong confounding effect (Katsouyanni and Touloumi 2008).

Case-crossover studies

The case-crossover design was introduced in 1991 by Malcolm Maclure to investigate the transient effect of brief exposure on the risk of an acute event or disease (Maclure 1991). It is closely related to the time series study. The characteristic of this design is that the individuals serve as their own control, with two or more periods being defined for each subject: a "case period" representing when the outcome occurred (e.g., myocardial infarction), with exposures occurring just prior to the outcome of interest, and one or more control periods experienced before and/or after the occurrence of the event (Basu and Samet 2002;Maclure 1991).

The case-crossover design has been used mostly in epidemiological studies of the effects of air pollution on human health and in studies of acute events such as myocardial infarction, but there are also studies of the effects of temperature on human health using either the case-crossover design alone (Bell et al. 2008;Stafoggia et al. 2008;Stafoggia et al. 2006) or both the time-series and case-crossover designs (Chen et al. 2007;Medina-Ramon and Schwartz 2007).

As with time series studies, confounding resulting from measured or unmeasured differences between individuals that do not vary in time (such as genetic and physiologic configuration, health behaviours, socio-economic differences) is also minimized (Basu and Samet 2002). A disadvantage is that the reference periods are fixed and “matched” to the case period, whereas the time series study has the advantage of being able to compare different statistical models for adjusting for temporal trends and other distorting effects (such as those caused by influenza epidemics).

1.3 Effects of short-term variations in temperature

It has been hypothesized that, in addition to daily changes in temperature, there may be additional effects from short-term variations of temperature within the day (Cao et al. 2009;Kan et al. 2007;Liang et al. 2009;Song et al. 2008;Tam et al. 2009). One such measure of within-day variability is the diurnal temperature range, which is defined by the US National Weather Service (NOAA National Weather Service 2009) as the temperature difference between the minimum at night and the maximum during the day. This meteorological indicator has been shown to be decreasing over time in some parts of the world such as in the United States but increasing in others such as India (Easterling et al. 1997) and parts of Europe (Makowski et al. 2008).

The Montreal, Quebec, area is in the north temperate zone and consequently daily mean temperatures and the diurnal temperature range vary considerably: from approximately -27 °C to 29 °C for mean daily temperature and from 1 °C to 28 °C for the diurnal temperature range (1984 - 2007). With the percentage of the population over 65 years of age increasing (0.7% increase between 2001 and 2006, from 12.9 to 13.6%; Statistics Canada 2001 and 2006 Census), a thorough investigation of the association between diurnal variations in temperature (as measured by the diurnal temperature range) and non-accidental mortality among the elderly adult population of Montreal is warranted, and this is the subject of my thesis.

Chapter 2: Review of the literature

2.1 The temperature-mortality relationship

The association between changes in daily temperature and daily mortality was described as early as the mid-18th century. Among the first articles to mention this association were Dr. Thomas Short's "On the Weather and Meteors" (1750) and Dr. William Heberden's "Observations on the Increase and Decrease of Different Diseases and Particularly of the Plague" (1801). In the mid-19th century, Dr. Scoresby-Jackson published "On the Influence of Weather upon Disease and Mortality" (1863) in *Transactions of the Royal Society of Edinburgh* and William Guy wrote "On Temperature and its Relation to Mortality" (1881) in the *Journal of the Royal Statistical Society*. In this latter article, Guy summarizes his findings by concluding that "the number of deaths [per day] varies inversely as the temperature" and he found this to be true "not only in this country [England] for all ages, but also among insured lives in Germany".

The relationship between ambient temperature and daily mortality continues to be a subject of interest for scientists, as well as the public, with many researchers quantifying the association or making comparisons between different regions or years. Within the current context of global warming, the importance of the effects of temperature on human health has been underscored by extreme events, such as the 2003 summer heat wave in Europe (Conti et al. 2007;Garssen et al. 2005;LeTertre et al. 2006;Schar and Jendritzky 2004;Simon et al. 2005;Vandentorren et al. 2004) or the 1995 Chicago heat-wave (Cervantes 1996;Jones 1996;Kaiser et al. 2007;Semenza et al. 1996;Whitman et al. 1997). In the wake of such extreme events, international projects such as the ISOTHURM

(McMichael et al. 2008) and EUROWINTER (Eurowinter Group 1997) have been designed to describe, quantify and contrast the response of diverse populations to changes in temperature. But it is not just the heat waves that confer higher risks; there is substantial data from around the world implicating increased daily temperatures, usually above a location-specific "threshold", with increased counts of mortality and hospitalizations (Basu and Samet 2002;Doyon et al. 2008;Gosling et al. 2009;Gouveia et al. 2003;Kovats et al. 1998;Martens 1998;McMichael et al. 2006). These "thresholds" are about 17-18°C in Northern and Central Europe, 22-23°C in Southern Europe, 25°C on the Eastern Coast of the United States, and 26-29°C in Australia and South-East Asia. The adverse effects of increased temperatures can be prolonged for many days (so-called lagged effects) (Braga and Zanobetti 2002;Conti et al. 2005;Curriero et al. 2002;Davis et al. 2003a;Davis et al. 2003b;Dessai 2002;Donaldson et al. 2001;Donaldson et al. 2003;Gosling et al. 2007;Gouveia et al. 2003;Hajat et al. 2005;Huynen et al. 2001;Keatinge et al. 2000;Michelozzi et al. 2005;O'Neill et al. 2003;Paldy et al. 2005;Pattenden et al. 2003;Sartor et al. 1995;Vandentorren et al. 2004). In addition, there is evidence suggesting that colder than normal temperatures can increase mortality (Carson et al. 2001;Doyon et al. 2008;Goodwin 2007;Gouveia et al. 2003;Kovats et al. 1998;Martens 1998;McMichael et al. 2006), although these effects appear to be delayed for as many as two weeks into the future (Braga and Zanobetti 2002;Gouveia et al. 2003;Huynen et al. 2001;Pattenden et al. 2003).

In the past decade, research has focused mainly on the effects of elevated temperatures on human mortality (Basu and Samet 2002;Gosling et al. 2009) and on the effects of cold temperatures (Goodwin 2007), some of the authors addressing simultaneously both effects from heat and cold (Doyon et al. 2008;Kovats and Haines 2005;McMichael et al. 2006).

2.2 Review of the literature

To meet the objective of my thesis, which is related to the association between daily mortality and diurnal variations in temperature, I searched the literature for scientific papers related to the short-term effects of temperature on mortality. However, to provide a context for this objective and to summarize the findings of the associations between daily metrics of temperature (such as mean temperature) and daily mortality, I will refer only to the most recent comprehensive review published in 2009 by Gosling et al. "Associations between elevated atmospheric temperature and human mortality: a critical review of the literature" (Gosling et al. 2009). I will then describe in depth the few papers that addressed associations with diurnal variations in temperature.

Summary of the association between daily mortality and ambient temperature

Among the 40 papers included in the review of Gosling et al., I selected the ones that respected the following criteria: published in peer-reviewed journals; used ambient temperature as the exposure variable (papers using indexes derived from different combinations of variables, such as the humidex or wind-chill, as exposure metrics were excluded); made use of a study design best fit to capture the effect of interest (either time series or case-crossover); and provided quantitative results regarding the change in mortality by change in temperature (which facilitates the comparison of results). A total of 12 papers fulfilled these criteria, of which nine provided quantitative results (Ballester et al. 1997;Braga and Zanobetti 2002;Curriero et al. 2002;Gemmell et al. 2000;Hajat et al.

2005;Hajat et al. 2002;Huynen et al. 2001;Pattenden et al. 2003;Saez et al. 2000) and three more addressed the same relationship but in the context of a heat wave (LeTertre et al. 2006;Rooney et al. 1998;Sartor et al. 1995). All of the selected studies used the time series design.

Table 1, ordered by date of publication, presents the general characteristics of these selected time series studies. All of these studies investigated the acute effects of weather on health, and were developed to determine whether changes in temperature were associated with increased counts of mortality. Because of relatively small effects of concurrent day (or previous days) temperature, the target populations were selected from large urban centers (Ballester et al. 1997;Braga and Zanobetti 2002;Curriero et al. 2002;Hajat et al. 2005;Hajat et al. 2002;LeTertre et al. 2006;Pattenden et al. 2003;Saez et al. 2000) or sometimes from even larger areas (Gemmell et al. 2000;Huynen et al. 2001;Rooney et al. 1998;Sartor et al. 1995), where measures of ambient temperature were available from meteorological stations, usually located at airports.

The typical statistical analysis is to treat the outcome as an overdispersed Poisson variable and to regress the natural logarithm of the daily counts on daily measures of temperature, after accounting for long-term and seasonal trends in the data. This leads to an estimate in the change in daily mortality per change in daily temperature. Often, the association is non-linear (on the natural logarithm scale), and simple measures of change cannot be used.

For the studies quantifying the impact of specific heat waves on mortality, the outcome measure used was excess mortality. This was calculated as the percent difference in mortality counts from the baseline mortality, defined as the expected counts of death occurring in the comparison period.

Table 1. General characteristics of selected time series studies assessing the effects of ambient temperature on human mortality. Adapted from Gosling et al., 2009.

A. Studies quantifying the temperature-mortality association in a general context

Author/ Year	**Study population**	**Location**	**Age group**	**Time period**	**Temporal smoother**	**Statistical method**
Ballester/ 1997	750,000	Valencia, Spain	all; 70+	1991-1993	Loess smoother	autoregressive Poisson regression; SPSS
Gemmell/ 2000	not presented	Scotland, United Kingdom	0-9; 10-59; 60-69; 70-79; 80+	1981-1993	used expected mortality counts as offset term in regression	GAMs using Poisson regression/ Splus
Saez/ 2000	not presented	Barcelona, Spain	45+	1986-1991	linear splines for each lag of each of the response covariate	piecewise linear regression using semi-parametric transfer function model in RATS
Braga/ 2001	~19 million	12 cities, United States	all	1986-1993	smooth function for time	GAMs using Poisson regression; distributed lag models
Huynen/ 2001	not presented	Netherlands	0-64; 65+	1979-1997 for all cause mortality; 1988-1997 for cause-specific mortality	not presented	Poisson log-linear regression; SAS
Curriero/ 2002	30,806,200	11 metropolitan areas, United States	<65; 65-75; >75	1973-1994	spline function of time	GAMs with splines for time, average daily temperature and average daily dew point at several lags
Hajat/ 2002	7,000,000	London, United Kingdom	all	1976-1996	loess smoother with 183 day span for season	GAMs in Splus
Pattenden/ 2003	not presented	London, United Kingdom; Sofia, Bulgaria	all	1993-1996 London; 1996-1999 Sofia	7 df/year smoother for season	GAMs with overdispersion factor estimated from Poisson model in Stata 6.0
Hajat/ 2005	9,900,000 Delhi; 9,700,000 Sao Paolo; 7,400,000 London	Delhi, India; Sao Paolo, Brazil; London, United Kingdom	0-14; 15-64; 65+	1991-1994	7 df/year smoothing splines for season	Poisson generalized linear models allowing for over-dispersion

Table 1. (continued)

B. Studies quantifying the temperature-mortality association within a heat wave context					
Author/ Year	**Study population**	**Location**	**Age group**	**Heat wave period/ Comparison period**	**Statistical method**
Sartor/ 1995	10,000,000	Belgium	0-64; 65+	Jun 27-Aug 7 1994/May 15-June26; Aug 8-Sep 15 1994	multiple regression analysis based on Gaussian distribution of mortality counts; SAS
Rooney/ 1998	51,820,200	England, Wales, greater London area, United Kingdom	all	Jul 30-Aug 3 1995/1995 average; 1993-1994 average	comparison of daily mortality with baseline calculated as a 31 day moving average
LeTertre/ 2006	11,300,000	9 cities, France	all	Jul 22-Sep 2 2003/1996-2003	time series Poisson regression models using penalized regression splines allowing for overdispersion

Note: GAM = generalized additive model; spline = smoothing function; df = degrees of freedom; SPSS, SAS, Splus, RATS = computer software.

Table 2 presents the main characteristics of the same time series studies, ordered by the magnitude of the effect of heat on mortality. Six out of the nine studies in Table 2 part A used mean daily temperature as the main exposure measure. The most common covariates included in the analyses were relative humidity and various metrics of criteria air pollutants, such as mean daily concentrations of fine particles or nitrogen dioxide.

With just one exception (Saez et al. 2000), all of the studies incorporated analyses of the lagged effects of temperature on mortality, ranging from 0 to as much as 30 days. These lagged effects are often estimated within the context of a distributed lag model (Zanobetti et al. 2000). Whereas most of the authors reported only estimates cumulated across lags, Hajat et al. showed that the heat effects decreased in London from 3.34% in the concurrent day, to 2.3 and 1.4% for lag 1 day and lag 2 days, respectively (Hajat et al. 2002). In a subsequent study, the same author reported that the heat estimates increased in Delhi from 2.2% on the concurrent day to 3.2% when summed across 7 days. For the cities of Sao Paolo and London, however, the cumulative estimates for up to one week were slightly lower than those for the concurrent day (Hajat et al. 2005). Ballester et al. (1997) showed that the estimates for increases in temperature increased from 2.4% in the concurrent day to 3.7% when three to six days of lag were considered. The effects for cold, however, were practically unchanged for the first six lag days, 1.6% change in mortality for a 1 ˚C drop in temperature below 15 ˚C, and significantly increased to 3.1% when effects over 7 to 14 days of lag were considered (Ballester et al. 1997).

Among the studies that used selected age groups to isolate the effects of temperature on the elderly, Curriero et al. found that the percentage of population over 65 years was associated with the steepness of the cold slope, with or without adjustment for the latitude of the city in question (Curriero et al. 2002). Hajat and coworkers showed that the estimates for those 65 years of age and older were higher than those for the rest of the age groups in all of the cities, and also that these estimates increased when effects were cumulated across 7 days of lag for each of the cities, with the exception of London (Hajat et al. 2005). The results of Ballester et al. also showed that for the age group 70 years and older the estimates were higher than for all ages considered together, and also that the effects of both heat and cold in this age group increase with lag, showing a maximum of 4.2% increase in mortality for heat and a 3.7% increase for cold (Ballester et al. 1997).

The results of the three studies quantifying the temperature-mortality association in the context of a heat wave included in Table 2 part B showed an increase in mortality in the range of 8.9% (Rooney et al. 1998) up to 400% (LeTertre et al. 2006). However, the use of different statistical approaches prevents comparisons between the studies.

Three of the studies reported separate estimates for cause-specific mortality. For the cold season, Gemmell et al. estimated a 0.9% increase in deaths from ischemic heart disease in the first week after a 1°C decrease in temperature below the mean value of the previous week, and a 1.04% increase after 1 lag week (Gemmell et al. 2000). Ballester and colleagues found a 4.6% increase in respiratory mortality 1 to 2 lag days after a 1 °C drop in temperature below 15 °C, and a 2.1 to 4.3% increase in cardiovascular mortality after 7 to 14 lag days (Ballester et al. 1997). Huynen et al. reported a 5.15% increase in respiratory mortality and a 1.69% increase in cardiovascular mortality for a 1 °C decrease in temperature below 16.5 °C (Huynen et al. 2001). For the hot season, Ballester et al. reported a 9.8% increase in respiratory mortality for the concurrent day (Ballester et al. 1997), while Huynen et al. estimated a 12.82% increase in respiratory mortality and a 1.86% increase in cardiovascular mortality.

Humidity does not appear to have an important effect on the association between diurnal temperature range and mortality. Just one of the six studies that included relative humidity as a covariate in the analysis found a considerable change in the estimates of effect (Saez et al. 2000).

Table 2. Main features of selected time series studies assessing ambient temperature effects on human mortality.

A. Studies quantifying the temperature-mortality association in a general context

Author/ Year	Exposure measure	Environmental covariates	Other covariates	Outcome	Lag	Results for heat %change (95% CI)	Results for cold %change (95% CI)	Other findings
Gemmell/ 2000	mean weekly temperature		socio-economic status	weekly number of deaths from ischemic heart disease (IHD), cardiovascular and respiratory diseases	1 week		0.9% (0.66-1.13%)[a] lag 0 week for IHD; 1.04% (0.78-1.29%) lag 1 week for IHD	no clear evidence of a relationship between socio-economic status and seasonal mortality
Pattenden /2003	mean daily temperature	relative humidity, black smoke in London, total suspended particulates (TSP) in Sofia	public holidays	mean daily mortality	0 to 3 days for heat; 0-22 days for cold	1.3%(0.99-1.62%)[b] in London, and 2.2%(1.55-2.87%) in Sofia	1.43%(1.28-1.58%) in London, 0.7%(0.51-0.88%) in Sofia	0.06%(0.03-0.1%) for TSP; 0.08%(-0.67-0.84%) for black smoke[c]; excluding air pollution from model changed the estimates just slightly
Curriero/ 2002	mean daily temperature, dew point temperature		education, poverty level, use of air conditioning, heating type, proportion of >65years adults with disability	daily mortality counts from all causes, cardiovascular and respiratory diseases	0 to 3 days	1.43 to 6.28%[d], different for each city (CI not presented)	2.25 to 7.12% different for each city (CI not presented)	a 10% increase in proportion of population over 65 years increased risk on mortality by 4% for a 10 ˚F decrease in temperature; a 10% increase in poverty increased risk of mortality by 4.3% for a 10 ˚F increase in temperature
Hajat/ 2005	mean daily temperature	PM_{10}, TSP		daily non-accidental mortality	0	2.2%(1.3-3.2%)[e] Delhi 1.6%(1.2-2%) Sao Paolo 1.4%(0.8-2%) London		2.5%(0-5%) for 65+ age group Delhi; 1.9%(1.3-2.4%) for 65+ age group Sao Paolo; 1.7%(1-2.3%) for 65+ age group London
					0-1 week	3.2%(1.8-4.5%) Delhi 1.4%(0.8-2%) Sao Paolo 0.9%(-0.2-2%) London		4%(0.5-7.6%) for 65+ age group Delhi; 2%(1.1-2.8%) for 65+ age group Sao Paolo; 0.9%(-0.3-2.1%) for 65+ age group London

Table 2. (continued)

Author/ Year	Exposure measure	Environmental covariates	Other covariates	Outcome	Lag	Results heat %change (95% CI)	Results cold %change (95% CI)	Other findings
Ballester/ 1997	mean daily temperature	relative humidity, black smoke	influenza incidence, holidays	all causes, non-accidental, cardiovascular, respiratory and neoplasm mortality counts	0 1-2 days 3-6 days 7-14 days	2.4%(0.2-4.6%)[f] all ages 3.8%(1.1-6.6%) 70+ age group 3.4%(1-5.9%) all ages 5%(2.1-8%) 70+ age group 3.7%(1-6.5%) all ages 4.2%(0.8-7.6%) 70+ age group	1.6%(0.6-2.6%) all ages[g] 1.6%(0.5-2.8%) 70+ age group 1.6%(0.6-2.7%) all ages 2.4%(1.1-3.7%) 70+ age group 1.7%(0.5-2.9%) all ages 2.3%(0.9-3.7%) 70+ age group 3.1%(1.7-4.5%) all ages 3.7%(2.1-5.4%) 70+ age group	2.1-4.3% change in cardiovascular mortality in cold season, percent highest after 7-14 lag days; 4.6%(1.3-8%) increase in respiratory mortality in cold season after 1-2 lag days; 9.8%(2.4-17.9%) increase in respiratory mortality in hot season at lag 0.
Huynen/ 2001	mean daily temperature			all causes, cardiovascular, respiratory and neoplasm mortality counts		2.72%(CI not presented)[h]	1.37%(CI not presented)	1.86% and 12.82% increase in cardiovascular and respiratory mortality for heat; 1.69% and 5.15% increase in cardiovascular and respiratory mortality for cold;
Hajat/ 2002	mean daily temperature	relative humidity	influenza incidence, public holidays	non-accidental, cardiovascular and respiratory mortality counts	0 1 day 2 days	3.34% (2.47-4.23%)[i] 2.3%(1.6-3.3%) 1.4%(0.6-2.3%)		3.18%(2.14-4.24%) for lag 0 after adjusting for SO_2, O_3 and PM
Braga/ 2001	mean daily temperature	relative humidity, barometric pressure		non-accidental mortality	0-3 weeks	4% (CI not presented)[j]	3% (CI not presented)	no evidence that relative humidity or barometric pressure have effects on mortality
Saez/ 2000	weekly mean temperature	relative humidity, black smoke, SO_2, NO_2, O_3	influenza epidemics, social class, area-based deprivation groups	daily mortality counts from ischemic heart disease	-	4.1% (3.7-4.5%)[k]	2.4% (0.1-4.85)[l]	4.4% increase in mortality per unit drop in temperature (below 6.5 ˚C) and humidity 9below 70%); 9.6% increase in mortality per unit rise in temperature (above 23 ˚C) and humidity (above 85%)

Table 2. (continued)

B. Studies quantifying the temperature-mortality association within a heat wave context							
Author/ Year	**Exposure measure**	**Environmental covariates**	**Other covariates**	**Outcome**	**Lag**	**Results heat wave %change (95% CI) from baseline daily death counts**	**Other findings**
Rooney/ 1998	mean daily central England temperature	PM_{10}, NO_2, O_3		excess mortality	-	8.9%(6.4-11%)	62% of the increase attributed to air pollution
Sartor/ 1995	mean daily temperature	relative humidity, suspended particulates, SO_2, NO_x, O_3		excess mortality	0-2 days	9.4% (CI not presented) for the 0-64 age group; 13.2%(CI not presented) in the elderly	in both age groups, temperature and O_3 were found to interact in their effects on mortality
LeTertre/ 2006	not clearly stated	current day minimum temperature, previous day maximum temperature, average of current and previous day O_3 8-hour levels	influenza epidemics, holidays	excess mortality	-	from 16%(-7-44%) to 400%(362-440%), different for each of the 9 cities	1-30% short-term harvesting effect

Note1. Particulate matter (PM) represents a complex mixture of extremely small particles and liquid droplets of different chemical components, including acids (such as nitrates and sulphates), organic chemicals, metals, and soil or dust particles (US Environmental Protection Agency 2009). Note2. Harvesting effect: The majority of deaths in the first days of a heat wave occur among terminal patients who would have died anyhow within the next few days or weeks (Kunst et al. 1993). Abbreviations: CI = confidence interval; lag period shown represents the lag period during which the strongest effect was found; IHD = ischemic heart disease; TSP = total suspended particulates; SO_2 = sulphate dioxide; NO_2 = nitrate dioxide; NO_x = nitric oxides; O_3 = ozone.

a.Percent change in mortality by 1°C decrease in temperature below the weekly mean average temperature of previous week.

b.Percent change in mortality by 1°C change in temperature above or below 18°C (cut-off point for the assumed V-shape relationship between temperature and mortality).

c.Percent change in mortality by 1 unit increase in total suspended particulates (Sofia) or black smoke (London).

d.Percent change in mortality by 10°F change in mean daily temperature above or below the minimum mortality temperature.

e.Percent change in mortality by 1°C increase in temperature above 20°C, summed across lags;

f.Percent change in mortality by 1°C increase in temperature above 24°C.

g.Percent change in mortality by 1°C decrease in temperature below 15°C.

h.Percent change in mortality by 1°C change in temperature from 16.5°C, aggregated across 30 lag days.

i.Percent change in mortality by 1°C increase in temperature above the 99th percentile value (21.5°C) of temperature average over the 21 years under study.

j.Overall effect across the 12 cities.

k.Percent change in mortality by 1°C increase in temperature above 25°C.

l.Percent change in mortality by 1°C decrease in temperature below 4.7°C.

Among the four studies reporting effects on mortality from air pollution, one found evidence of an interaction between daily mean temperature and concentrations of ozone (Sartor et al. 1995), and another estimated that about 62% of the increase in mortality during a heat wave was attributed to air pollution (Rooney et al. 1998). The results of the two other studies show only a slight effect of adjusting to air pollution on the overall estimates (Hajat et al. 2002;Pattenden et al. 2003).

Effects of diurnal temperature variations on daily mortality

Less known than the effects of ambient temperature on human health are the effects of variations in diurnal temperature. An analysis of temporal trends in daily temperature shows that the diurnal temperature range, the metric used for diurnal temperature variations, is decreasing over time in some parts of the world, such as the United States, and increasing in others, such as India (Easterling et al. 1997).

I searched for relevant papers in the Medline databases of indexed articles from 1950 to 2009 and the In-process & Non-indexed articles using the keywords "diurnal temperature range", "DTR", "daily temperature range", "daily temperature varia$", "diurnal temperature varia$", "diurnal temperature change", "daily temperature change", "daily temperature fluctuation", "diurnal temperature fluctuation", "diurnal temperature difference" and "daily temperature difference". Figure 1 presents a flowchart of the results.

I retrieved 236 papers, 218 of them relating to plants or animals and 18 related to human health. Ten of the 18 papers referred to the association between diurnal temperature variations and human mortality, the other eight using different metrics for temperature, such as body temperature. Of the 10 studies using diurnal temperature range, three were written in languages other than English (one in Chinese and two in Japanese, which are not included in this review). After thorough examination of the full-text version of the remaining seven papers, two more were excluded from further analysis: one letter to the editor that did not provide details about methods and the statistical methods (Chen et al. 2007), and one more paper due to its descriptive design and statistical approach (Heunis et al. 1995) that rendered the results not informative for the purpose of the thesis.

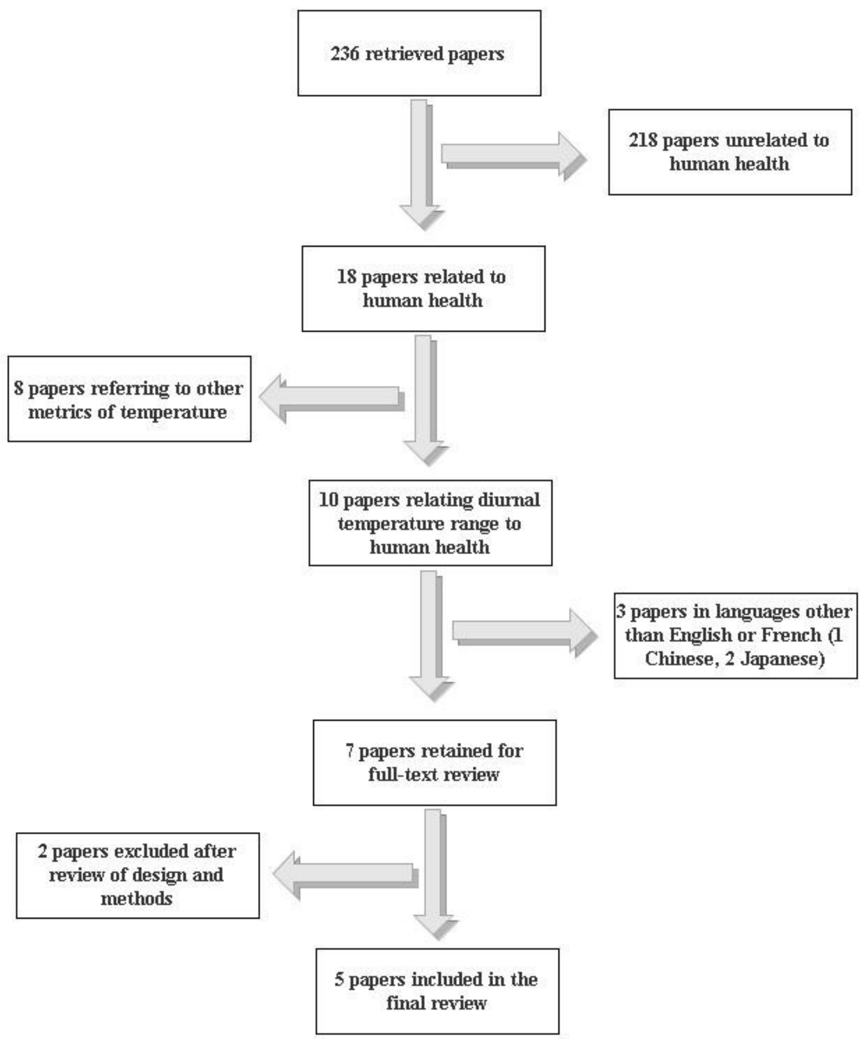


Figure 1. Flowchart showing the results of the search of electronic bibliographic databases for papers related to the effects on human health from fluctuations in diurnal temperature.

Table 3 shows selected characteristics of the time series studies that quantify the effects of diurnal variations in temperature on human health, ordered by date of publication. All papers present results of the time series analysis using generalized distributed models assuming a Poisson distribution of the outcome variable. Aside from the time series analysis, one paper also made use of a case-crossover analysis, using unidirectional and bidirectional methods for selecting control periods (Cao et al. 2009). The long-term and seasonal trends in mortality were removed using spline functions (smoothing functions of time) in all studies presented. In two of the five papers moving averages of diurnal temperature range were used to model the effects on the outcome of interest.

The results of these studies, shown in Table 4, are roughly in the same range, 1.37% to 2.63% change in mortality per 1˚C increase in diurnal temperature range, even if the cause of death was different: non-accidental, cardiovascular or respiratory mortality (Kan et al. 2007;Tam et al. 2009), chronic obstructive pulmonary disease (COPD) (Song et al. 2008), coronary heart disease (CHD) (Cao et al. 2009). Of interest is the large 13.9% (95%CI: 0.8 to 28.8%) percentage increase in emergency room admissions for COPD that Liang et al. found to be associated to a 1˚C increase in diurnal temperature range above the 9.6 ˚C cut-off point in Taiwan (Liang et al. 2009), an effect six orders of magnitude larger than the effect on daily mortality counts. These findings suggest that estimations of impact on mortality should take into account delayed effects that may result from exacerbations of chronic illnesses that lag beyond 2 to 7 days.

None of the authors reported confounding effects from the air pollution variables included in the analyses.

In conclusion, the association between ambient temperature and human health has been studied extensively. Recently, new scientific evidence is emerging regarding the independent contribution of daily variations in temperature, using diurnal temperature range as exposure metric, to the increase of the relative risk of mortality and other health outcomes, such as daily admissions to emergency units. The few papers addressing this issue are based on relatively short time series, four to six years, and come from the same geographical area, south-east Asia. The results indicate a 1.37 to 2.46% increase in mortality for each 1 °C increase in diurnal temperature range. To date, such results have not been reproduced in areas where daily variations in temperature may be greater.

Table 3. General characteristics of the five time series studies assessing effects of diurnal temperature range on human health.

Author/ Year	Study population	Location	Age group	Time period	Statistical method
Kan/ 2007	6,300,000	Shanghai, China	0-4;5-44; 45-64;>65	2001-2004	GAMs based on Poisson distribution in S-plus 6.2
Song/ 2008	not presented	Shanghai, China	all	2001-2004	GAMs in S-plus 6.2 and penalized and natural splines in R
Cao/ 2009	6,300,000	Shanghai, China	all	2001-2004	GAMs in S-plus 7.0; logistic regression in Stata
Liang/ 2009	not presented	Taichung, Taiwan	all	2001-2002	Poisson multivariate regression models allowing for overdispersion in SAS
Tam/ 2009	not presented	Hong Kong, China	65+	1997-2002	GAMs based on Poisson distribution allowing for overdispersion in S-plus 4.0

Abbreviations: GAM = generalized additive models; S-plus, R, Stata, SAS = statistical software.

Table 4. Main features of the five time series studies assessing effects of diurnal temperature range on human health.

Author/ Year	Exposure measure	Environmental covariates	Outcome	Lag	Results %change (95% CI)	Other findings
Kan/ 2007	3-day moving average of diurnal temperature range	relative humidity, temperature, PM_{10}, SO_2, NO_2, O_3	daily non-accidental, cardiovascular and respiratory mortality	0-2 days	1.37% (1.0-1.65%)[a]	1.86% (1.4-2.3%) for cardiovascular mortality 1.29% (0.4-2.0%) for respiratory mortality
Song/ 2008	4-day moving average of diurnal temperature range	relative humidity, temperature, PM_{10}, SO_2, NO_2, O_3	daily mortality from COPD	-	1.57% (0.5-2.6%)[b] 0.51% (0.04-0.9%)[c]	
Cao/ 2009	diurnal temperature range	relative humidity, PM_{10}, SO_2, NO_2, O_3	daily coronary heart disease (CHD) mortality	0-3 days	2.46%(1.76-3.16%)[d]	2.13%(1.04-3.22%)[d] using bi-directional case-crossover analysis
Liang/ 2009	mean daily temperature, diurnal temperature range	PM_{10}, SO_2, CO, NO, NO_2, O_3	emergency room admissions for COPD	-	13.9%(0.8-28.8%)[e]	
Tam/ 2009	diurnal temperature range	relative humidity, PM_{10}, SO_2, NO_2, O_3	daily cardiovascular disease mortality	0-7 days	1.7%(0.3-3.1%)[f]	

Abbreviations: PM = particulate matter; SO_2 = sulphate dioxide; NO_2 = nitrate dioxide; O_3 = ozone; COPD = chronic obstructive pulmonary disease; CO = carbon monoxide; NO = nitrate monoxide.

aPercent change in non-accidental mortality by 1 °C change in the 3-day moving average of diurnal temperature range.

bPercent change in COPD mortality by 1 °C change in the 4-day moving average of diurnal temperature range above 22 °C.

cPercent change in COPD mortality by 1 °C change in the 4-day moving average of diurnal temperature range below 22 °C.

dPercent change in CHD mortality by 1 °C change in diurnal temperature range using 3-day lagged models.

ePercent change in COPD emergency room admissions by 1 °C change in diurnal temperature range above 9.6 °C.

fPercent change in cardiovascular mortality cumulated over the first 3 days of lag.

Chapter 3: Rationale and objective

Rationale

Within the overarching context of climate change, global temperature increases play a key role. Both current and projected changes in temperature have important public health implications and, due to the fact that the impact on health is not limited only to short-term effects, statistical approaches that attempt to capture delayed effects are constantly being perfected. While an abundance of literature is currently available in this field, only a handful of papers focus on the effect daily variations in temperature may have on health.

Elderly adults represent a growing subgroup of the population in developed countries such as Canada, and some of the particularities characterising this age group makes them more susceptible to the effects of both heat and cold.

Objective

To determine whether variations in diurnal temperature increased daily non-accidental mortality among the elderly population of Montreal, Quebec, during the 1984-2007 period.

Chapter 4: Manuscript

4.1 Title

Effects of diurnal variations in temperature on non-accidental mortality among the elderly population of Montreal, Quebec, 1984-2007.

4.2 Authors

Maria Vutcovici, Mark S. Goldberg, Marie-France Valois.

4.3 Abstract

Background: The association between ambient temperature and mortality has been studied extensively. Recently, evidence is emerging regarding the independent role of diurnal temperature variations in increasing daily mortality.

Objective: To determine whether variations in diurnal temperature increased daily non-accidental mortality among residents of Montreal, Quebec, who were 65 years of age and over during the 1984-2007 period.

Methods: We used distributed lag non-linear Poisson models constrained over a 30 day lag period, and adjusted for temporal trends, mean daily temperature, and mean daily concentrations of nitrogen dioxide and ozone.

Results: We found, over the 30 day lag period, a cumulative increase of 5.12% (95%CI: 0.02 to 10.49) in daily mortality for a change from 6°C to 11°C (25^{th} to 75^{th} percentiles) in diurnal temperature, and a 11.27% (95%CI: 2.08 to 21.29) increase in mortality associated with an increase of the diurnal temperature range from 11 to 16 °C

(75th to 99th percentiles). The results were relatively robust to adjustment for daily mean temperature.

Conclusion: We found that in Montreal daily diurnal variations in temperature are associated with a small increase in mortality among the elderly population. More studies are needed in different geographical locations to confirm such an effect.

Keywords: diurnal temperature range, mortality, time series, distributed lag non-linear models, air pollution

4.4 Introduction

The effects of increasing temperatures on human health are underscored by extremely hot episodes that have occurred recently, such as during the summer of 2003 in Europe (Conti et al. 2007;Garssen et al. 2005;LeTertre et al. 2006;Schar and Jendritzky 2004;Simon et al. 2005;Vandentorren et al. 2004) and during the summer of 1995 in Chicago (Kaiser et al. 2007;Semenza et al. 1996;Whitman et al. 1997).

There are also indications that the elderly may be more susceptible to daily changes in temperature. Biology suggests that these effects occur because of the combined effect of physiological and pathological changes that come with age, increased use of medication, and lack of social support (Gemmell et al. 2000;Havenith 2005). Socio-economic factors most commonly associated with mortality in the elderly during extreme heat or cold events are poverty, social isolation (Worfolk 2000) and the level of dependency (Belmin et al. 2007). Belmin and collaborators found an association between the level of dependency and daily mortality among the elderly population in France during the August 2003 heat wave, explained most likely by a direct impact on the selfprotective behaviour against heat through impaired cognitive functioning and mobility (Belmin et al. 2007).

Substantial data from around the world has implicated increased daily temperatures, usually above a location-specific “threshold”, with increased counts of mortality and hospitalizations (Basu and Samet 2002;Doyon et al. 2008;Gosling et al. 2009;Gouveia et al. 2003;Kovats et al. 1998;Martens 1998;McMichael et al. 2006). These “thresholds” are about 17-18°C in Northern and Central Europe, 22-23°C in Southern Europe, 25°C on the Eastern Coast of the United States, and 26-29°C in Australia and South-East Asia. The adverse effects of increased temperatures can be prolonged for many days (so-called lagged effects) (Braga and Zanobetti 2002;Conti et al. 2005;Curriero et al. 2002;Davis et al. 2003a;Davis et al. 2003b;Dessai 2002;Donaldson et al. 2001;Donaldson et al. 2003;Goldberg et al. 2011;Gosling et al. 2007;Gouveia et al. 2003;Hajat et al. 2005;Huynen et al. 2001;Keatinge et al. 2000;Michelozzi et al. 2005;O'Neill et al. 2003;Paldy et al. 2005;Pattenden et al. 2003;Sartor et al. 1995;Vandentorren et al. 2004). In addition, there is some evidence suggesting that colder than normal temperatures can increase risk (Carson et al. 2001;Doyon et al. 2008;Goodwin 2007;Gouveia et al. 2003;Kovats et al. 1998;Martens 1998;McMichael et al. 2006), and these effects can be delayed for as many as two weeks into the future (Braga and Zanobetti 2002;Goldberg et al. 2011;Gouveia et al. 2003;Huynen et al. 2001;Pattenden et al. 2003).

Despite the burgeoning literature addressing the effects of temperature on human health, there are only a handful of papers in which the short-term effects on health of diurnal variations in temperature have been investigated (Cao et al. 2009;Kan et al. 2007;Liang et al. 2009;Song et al. 2008;Tam et al. 2009).

Diurnal temperature range is defined by the US National Weather Service (NOAA National Weather Service 2009) as the temperature difference between the minimum at night and the maximum during the day. This meteorological indicator has been shown to be decreasing over time in some parts of the world such as in the United States but increasing in others such as India (Easterling et al. 1997) and parts of Europe (Makowski et al. 2008).

The Montreal, Quebec, area is in the north temperate zone, and consequently, daily mean temperatures as well as the diurnal temperature range vary considerably. With the possibility of sufficient variability in diurnal temperatures, we decided to investigate whether changes in the diurnal temperature range were associated with non-accidental mortality among the elderly population of Montreal.

4.5 Material and methods

The study population

The study population comprised residents of the Montreal metropolitan area who were 65 years of age and older, and who died between 1984 and 2007 in Montreal from any non-accidental cause. Deceased subjects, and their cause of death and age at death, were identified from the Quebec computerized provincial database of death certificates (coded according to the Ninth and Tenth Revisions of the International Classification of Diseases; ICD 9: 1-799 and ICD 10: A00-R99). Approval to have access to the denominalized mortality data was granted by the provincial agency responsible for allowing access (Commission de l’accès à l’information du Québec) and ethical approval was granted by the Institutional Review Board of the Faculty of Medicine, McGill University.

Weather and air pollution data

Hourly records of temperature, relative humidity, barometric pressure and other weather parameters measured at Montreal's Pierre-Elliot-Trudeau International Airport were obtained from the Environment Canada website (Environment Canada - National Climate Data and Information Archive 2010). We calculated the diurnal temperature range as the difference between the maximum and minimum daily temperature.

The air pollution data comprised hourly measurements of a number of criteria gaseous pollutants (sulphur dioxide, carbon monoxide, nitrogen dioxide (NO_2), ozone (O_3)) at 12 fixed-site monitoring stations in Montreal. We chose to include two of these as covariates in the substantive analysis: NO_2 was measured at eight stations and O_3 was measured at nine stations using chemiluminescence (Thermo electron 14V). Mean daily concentrations of NO_2 and O_3 were derived by taking a simple daily average for each monitor and then averaging these across monitors to obtain a final daily mean value. Respirable and fine particles were measured using high-volume samplers approximately every six days during 1984-2004 period, and in 1996 these were replaced by tapered element oscillating microbalances. Because of the large number of missing days in the early part of the study period and the difficulty of combining high-volume samples with tapered element oscillating microbalances, we excluded fine particles from the analyses.

Statistical methods

We used a generalized non-linear Poisson regression model to assess the association between the diurnal temperature range and the daily counts of non-accidental mortality. The generalization of the distributed lag models (Moshammer 2006, Zanobetti 2000) referred to as the distributed lag non-linear models (dlnm) was developed by

Armstrong and Gasparrini (Armstrong 2006, Gasparrini 2010). These models allow for simultaneous estimation of multiple non-linear function terms across lags of covariates with delayed dependencies in the association. Under the assumption that the total variance was proportional to the counts of mortality, we used quasi-likelihood Poisson models to account for extra Poisson variation.

As a first step in the analysis we applied a temporal smoother to remove the long-term, seasonal and sub-seasonal trends from the mortality time series; we used a natural cubic spline function on day of study, and we included a categorical term for day of the week. We selected 7 degrees of freedom (df) per year for the temporal smoother based on the analyses of the National Morbidity, Mortality and Air Pollution Study (Samet 2000) and our analysis of temperature in Montreal (Goldberg et al. 2011). We also carried out sensitivity analyses using temporal smoothers with 5, 9 and 13 degrees of freedom per year.

We estimated the lagged non-linear effect of the range of diurnal temperature on mortality using the dlnm models, as implemented in the R statistical package (version 2.11.1, http://www.r-project.org/). This method allows the definition of a cross-basis function that is a combination of basis functions for the two dimensions considered (range of diurnal temperature and lag). We constrained the dlnm models up to lag 30 days. We used cubic b-splines to model all functions of temperature (diurnal, mean) with knots chosen from the quantiles of the specific temperature range distribution. From these models, we also estimated the effects on mortality between selected cut-points of the temperature range distribution: 1^{st}, 25^{th}, 75^{th} and 99^{th} percentiles.

We adjusted for the potential confounding effect of the two air pollutants with a linear distributed lag function from 0 to 2 days. This three-day lag was based on previous analyses which showed that the effects of air pollution did not persist past lag 2 days and the response functions were consistent with linearity (Brook et al. 2007;Goldberg 2003;Goldberg 2006;Goldberg et al. 2011).

We conducted a sensitivity analysis that made use of the same covariates and functional forms, but used for the diurnal temperature range the interval 7am to 22 pm, instead of the 24 hour data, to better reflect individual exposure to changes in temperature. Another sensitivity analysis was based on dlnm models constrained to a 15 day lag period, instead of the 30 day lag.

4.6 Results

Table 5 shows the distributions across all days of the study, 1984-2007, of daily non-accidental mortality and selected metrics of temperature and air pollution. The mean number of daily non-accidental deaths for the population age 65 years and older was 30.3, varying from 6 to 79 deaths per day (standard deviation of 6.9). The average diurnal temperature range in Montreal was 8.6˚C, varying from 0.7 to 28.1˚C (interquartile range of 5.2˚C). The mean temperature during the study period was 7.1˚C, ranging from -27.6˚C to 29.2˚C. Mean daily concentrations of NO_2 and O_3 were 38 μg/m^3 and 33 μg/m^3, respectively.

As illustrated in

Table 6, modest Spearman correlation coefficients (r) were found between diurnal temperature range, mean temperature (r=0.24), O_3 (r=0.25), and NO_2 (r=0.13).

Our primary model comprised a natural cubic spline smoother for day of study using 7 df per year and a categorical term for day of the week. We modeled the response function of the diurnal temperature range using a cubic B-spline with 3 df and a natural cubic spline for the lag space of 3 df. This base model had a serial autocorrelation coefficient that approached zero at lag 5 days and an over-dispersion parameter of 1.09. The base model was expanded to include non-linear terms for mean temperature using a B-spline with 3 df, as well as terms for the two air pollutants, NO_2 and O_3, in which the response functions and the lag space were modeled as linear functions using a constrained distributed lag model over three days. In addition, we conducted a detailed series of sensitivity analyses using a variety of temporal smoothers (see Annex).

The results of our primary models are shown in Figure 2, where we plot the cumulative effects of the diurnal temperature range accumulated over the concurrent day up to 30 days of lag. This figure has three panels that represent, from left to right, the base model, the model adjusted for mean temperature, and the model adjusted for mean temperature and the two air pollutants. The ordinate represents the relative increase in daily mortality (RR), the smooth line represents the best fit, and the shaded areas represent the area contained between the upper and lower 95% confidence intervals (CI). An increase in cumulative mortality of the diurnal temperature range was observed starting about 10°C and increasing monotonically, although after about 17°C the number of days with extreme values was very small and thus the confidence intervals were broad. The models presented in the middle and right panels show that this association was relatively robust to adjustment for mean temperature and mean concentration of the two air pollutants, although the response functions were attenuated.

Table 5. Distribution of mortality, selected metrics of temperature and air pollution, Montreal, 1984-2007.

		Units	Number of days measured	Mean	Standard deviation	Minimum	Percentiles			Maximum	IQR
							25th	50th	75th		
Mortality for age group 65+	All		8766	30.3	6.9	6	26	30	35	79	9
	Women		8766	16.5	4.8	1	13	16	20	48	7
	Men		8766	13.8	4.1	2	11	14	16	33	5
Diurnal temperature range		°C	8766	8.6	3.6	0.7	5.9	8.5	11.1	28.1	5.2
Maximum temperature		°C	8766	11.2	12.3	-24.1	1.6	12	22.1	35.4	20.5
Mean temperature		°C	8766	7.1	11.8	-27.6	-1.7	7.9	17.5	29.2	19.1
Minimum temperature		°C	8766	2.6	11.6	-31.2	-5.4	3.4	12.4	25.8	17.8
NO_2		$\mu g/m^3$	8764	37.9	14.9	7	27	36	46	166	19
O_3		$\mu g/m^3$	8764	32.8	18.0	2	20	30	43	164	23

Abbreviations: IQR = interquartile range.

Table 6. Spearman correlation coefficients between selected temperature and air pollution variables, Montreal, 1984-2007.

	Diurnal temperature range	Maximum temperature	Mean temperature	Minimum temperature	NO_2	O_3
Diurnal temperature range (°C)	1	0.36	0.24	0.09	0.13	0.25
Maximum temperature (°C)		1	0.99	0.96	-0.22	0.41
Mean temperature (°C)			1	0.98	-0.25	0.39
Minimum temperature (°C)				1	-0.28	0.35
NO_2 ($\mu g/m^3$)					1	-0.24
O_3 (µg/m3)						1

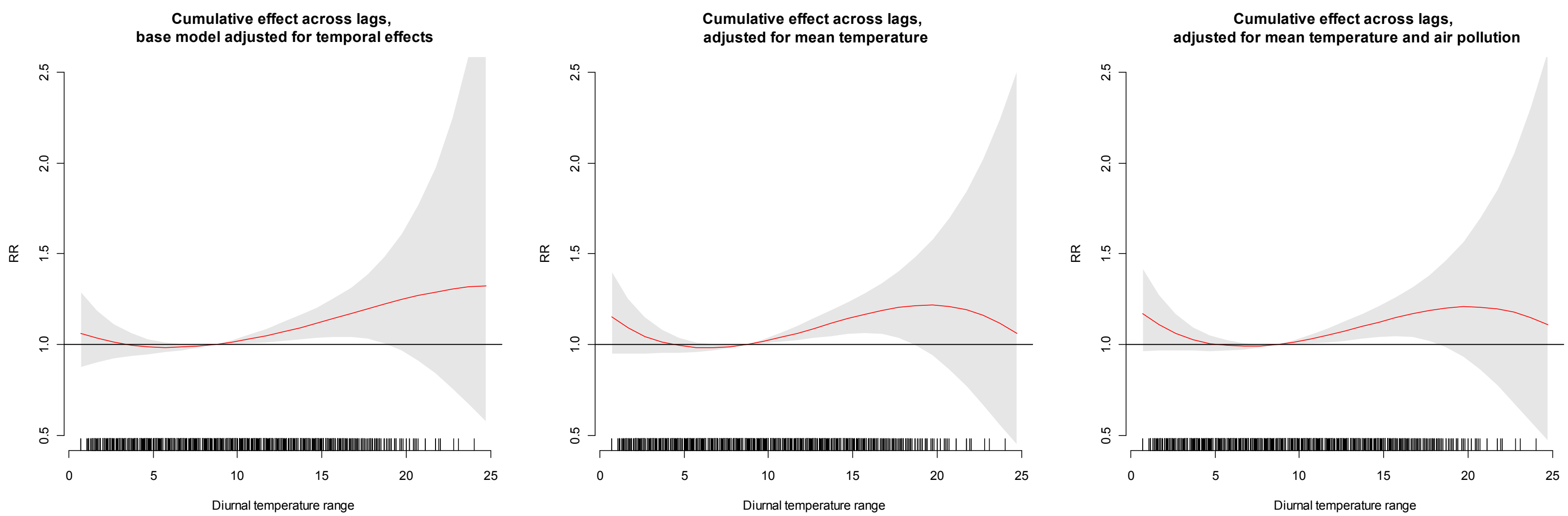


Figure 2. Cumulative effect of diurnal temperature variations on mortality among persons 65 years of age and over from distributed lag non-linear models, Montreal, 1984-2007.

All models comprised a temporal smoother of 7 df per annum, a cubic b-spline with 3 df for diurnal temperature range and 3 df for the lag space. Adjusted models also included: a natural cubic spline with 3 df for mean daily temperature (middle panel) and linear terms for nitrogen dioxide and ozone (right panel). The y-axis represents the relative increase in daily counts of mortality with respect to the mean diurnal temperature range value (5.9˚C), the maximum likelihood estimate is shown as a smooth line and the shaded area represents the 95% confidence interval.

Figure 3 shows the response function evaluated at lag 0 and lag 4 days, as derived from the models described above. The three panels show the results from the base model (left), the model adjusted for mean daily temperature (middle), and the model adjusted for mean temperature and air pollution (right). Adjusting for both mean temperature and air pollution reduced the effect of diurnal temperature variations on mortality.

Table 7 shows the cumulative and lagged percent changes in daily non-accidental mortality from the base model that was adjusted only for temporal effects. The columns summarize the percent change in daily mortality comparing the 25th percentile (5.9˚C) to the 1st percentile (1.8˚C) of the diurnal temperature range distribution, the 75th percentile (11.1˚C) to the 25th percentile, and the 99th percentile (17.5˚C) to the 75th percentile, respectively. We found a cumulative mean percent change in mortality of 5.12% (95% CI: 0.02-10.49) when the diurnal temperature range increased from 6˚C to 11˚C. The effects were strongest on the concurrent day, but persisted through lag 9 days. A more pronounced cumulative effect was observed as the diurnal temperature variation increased, as shown in the third column, but the small number of days with diurnal temperature range values higher than the 75th percentile (216 days in the 24 year study period) increased the uncertainty of these estimates.

Table 8 shows the cumulative and lagged percent changes in daily non-accidental mortality from the base model (also shown in Table 7) and from models including the two air pollutants and mean daily temperature. We only show comparisons in the percent change in daily mortality between the 75th percentile (11.1˚C) and the 25th percentile (5.9˚C). Adjusting for daily mean temperature slightly increased the cumulative effect to 6.28% (95% CI: 1.04-11.78) but adjustment for daily air pollution attenuated the effect to 4.46% (95%CI: -0.71-9.91).

Table 7. Mean percent change in daily non-accidental mortality and 95% confidence intervals (CI) associated with changes in diurnal temperature range between selected cut-points in the distribution, base model adjusted for temporal effects, Montreal, 1984-2007.[a]

Lagged effect (days)	25th percentile[b] relative to the 1st percentile[b]		75th percentile[b] relative to the 25th percentile		99th percentile[b] relative to the 75th percentile	
	% change	95% CI	% change	95% CI	% change	95% CI
Cumulative	-6.57	-20.93-10.39	5.12	0.02-10.49	11.27	2.08-21.29
0 days	0.11	-1.12-1.36	0.69	0.31-1.08	0.44	-0.16-1.04
1	0.11	-0.96-1.20	0.63	0.30-0.96	0.43	-0.09-0.96
2	0.11	-0.83-1.05	0.56	0.27-0.85	0.42	-0.04-0.88
3	0.10	-0.72-0.93	0.50	0.24-0.75	0.41	0.001-0.82
4	0.10	-0.64-0.84	0.44	0.21-0.66	0.41	0.03-0.77
5	0.09	-0.60-0.78	0.38	0.17-0.59	0.40	0.05-0.75
6	0.07	-0.59-0.74	0.33	0.13-0.53	0.39	0.05-0.73
7	0.06	-0.60-0.72	0.29	0.09-0.48	0.38	0.05-0.72
8	0.04	-0.62-0.70	0.24	0.05-0.44	0.38	0.04-0.71
9	0.02	-0.65-0.69	0.21	0.01-0.40	0.37	0.03-0.71
10	0.01	-0.69-0.68	0.17	-0.03-0.37	0.36	0.01-0.71
11	-0.03	-0.72-0.67	0.14	-0.06-0.34	0.36	0.01-0.71
12	-0.06	-0.76-0.65	0.12	-0.09-0.32	0.35	0.00-0.71
13	-0.09	-0.79-0.62	0.09	-0.11-0.30	0.35	-0.01-0.70
14	-0.12	-0.82-0.59	0.07	-0.13-0.27	0.34	-0.01-0.70

a. The model included a cubic b-spline (3 df) for the diurnal temperature range effect on mortality, natural cubic splines for lag (3 df) and temporal smoother (7 df), and a linear term for the day of the week.

b. 1st percentile = 1.8˚C, 25th percentile = 5.9˚C, 75th percentile = 11.1˚C, 99th percentile = 17.5˚C

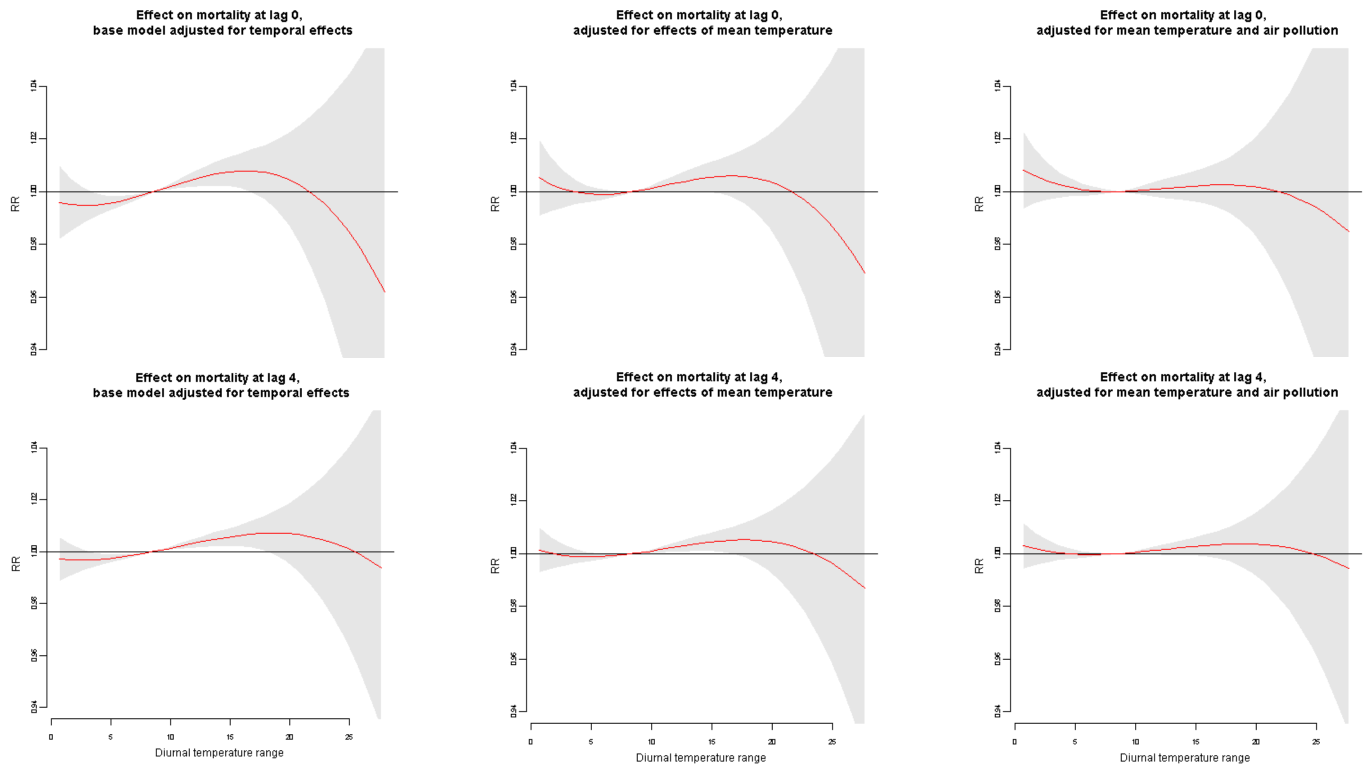


Figure 3. Effects of diurnal temperature range on daily non-accidental mortality among persons 65 years of age and over evaluated at 0 and 4 lag days from distributed lag models, Montreal, 1984-2007.

All models comprised a temporal smoother of 7 df per annum, a cubic b-spline for diurnal temperature range and 3df for the lag space. The adjusted models also included a cubic b-spline with 3 df for mean temperature and linear terms for nitrogen dioxide and ozone. The y-axis represents the relative increase in daily counts of mortality with respect to the mean diurnal temperature range value (5.9°C). The maximum likelihood estimate is shown as a smooth line and shaded areas represent the 95% confidence interval.

Table 8. Mean percent change in daily non-accidental mortality and 95% confidence intervals (CI) associated with changes in diurnal temperature range between selected cut-points in the distribution, base model and models adjusted for mean daily temperature and air pollution, Montreal, 1984-2007.

Lagged effect (days)	75th percentile relative to the 25th percentile, base model adjusted only for temporal effects [a]		75th percentile relative to the 25th percentile, adjusted also for daily mean temperature [b]		75th percentile relative to the 25th percentile, adjusted also for daily mean temperature and air pollution [c]	
	% change	95% CI	% change	95% CI	% change	95% CI
Cumulative	5.12	0.02-10.49	6.28	1.04-11.78	4.46	-0.71-9.91
0 days	0.69	0.31-1.08	0.33	-0.05-0.72	0.00	-0.39-0.4
1	0.63	0.30-0.96	0.32	-0.01-0.66	0.04	-0.31-0.38
2	0.56	0.27-0.85	0.31	0.02-0.60	0.07	-0.23-0.37
3	0.50	0.24-0.75	0.30	0.05-0.55	0.10	-0.16-0.36
4	0.44	0.21-0.66	0.29	0.06-0.52	0.13	-0.11-0.36
5	0.38	0.17-0.59	0.28	0.07-0.49	0.15	-0.06-0.36
6	0.33	0.13-0.53	0.27	0.07-0.47	0.17	-0.03-0.37
7	0.29	0.09-0.48	0.26	0.06-0.46	0.19	-0.01-0.39
8	0.24	0.05-0.44	0.25	0.05-0.45	0.20	0.00-0.40
9	0.21	0.01-0.40	0.24	0.04-0.44	0.21	0.01-0.41
10	0.17	-0.03-0.37	0.23	0.03-0.44	0.22	0.02-0.42
11	0.14	-0.06-0.34	0.22	0.02-0.43	0.23	0.02-0.43
12	0.12	-0.09-0.32	0.22	0.01-0.42	0.23	0.02-0.44
13	0.09	-0.11-0.30	0.21	0.00-0.42	0.23	0.02-0.44
14	0.07	-0.13-0.27	0.20	-0.01-0.41	0.23	0.02-0.43

a. The main model included a cubic b-spline (3 df) for the diurnal temperature range effect on mortality, natural cubic splines for lag (3 df) and temporal smoother (7 df), and a linear term for the day of the week; 25th percentile = 5.9˚C, 75th percentile = 11.1˚C.
b. Model included a natural cubic spline (3 df) for the 3 day lagged effects of mean daily temperature on mortality in addition to the main model.
c. Model included linear terms for the 3 day lagged effects of NO2 and O3 in addition to the mean temperature adjusted model

Sensitivity analysis

We conducted sensitivity analyses using temporal smoothers with varying degrees of freedom (Annex Table 1 and Annex Figure 1). We found that the effects of diurnal temperature range on mortality were fairly similar when using temporal smoothers with 5 or 7 df per year. However, temporal smoothers with 9 or 13 df per year seemed to be over-fitting the data as the autocorrelation coefficients within 15 day lags were mostly negative. (Annex Table 1). We also carried out analyses of models in which the number of degrees of freedom for both the variable space and lag space were varied, while using the temporal smoothers with 5 df per year (Annex Figure 3), 7 df per year (Annex Figure 2) and 9 df per year (Annex Figure 4) per year did not lead to important differences in the response functions. When a subset of data using only the 7 am – 22 pm time interval was used to better reflect exposure to diurnal temperature variations of the study population (Annex Figure 5), the effects on mortality were slightly reduced but still present for the cumulative effect.

We carried out a separate analysis using models constrained to 15 lag days instead of the 30 we used for the base model. The results obtained were very similar (Annex Figure 6).

4.7 Discussion

The association between short-term changes in ambient temperature and daily mortality has been described widely in the literature. A few recent papers support the hypothesis that diurnal variations in temperature may also have a notable impact on mortality, independent of the effect of the mean temperature (Cao et al. 2009;Kan et al. 2007;Song et al. 2008;Tam et al. 2009) and robust to adjustment for air pollution (Cao et al. 2009;Kan et al. 2007;Song et al. 2008). In Shanghai, a time-series analysis showed a 1.37% (95% CI 1.08–1.65%) increase in total non-accidental mortality, 1.86% (95% CI 1.40–2.32%) increase in cardiovascular mortality, and a 1.29% (95% CI 0.49–2.09%) increase in respiratory mortality for a 1°C increase in the 3-day moving average for diurnal temperature range (Kan et al. 2007). Subsequent studies showed a 1.25% (95% confidence interval: 0.35–2.15) increase in deaths from chronic obstructive pulmonary disease for a 1°C increase in the 4-day moving average of diurnal temperature range (Song et al. 2008) and a 2.46% (95% CI, 1.76% to 3.16%) increase in coronary heart disease mortality for a 1°C increase in the 2-day lagged diurnal temperature range (Cao et al. 2009). In a bidirectional case-crossover analysis, Cao et al. (Cao et al. 2009) reported a 2.13% (95% CI, 1.04% to 3.22%) increase per 1°C increase in the 2-day lagged diurnal temperature range. In Hong Kong, Tam et al. (Tam et al. 2009) reported a 1.7% increase in cardiovascular mortality among the elderly per 1°C increase in diurnal temperature range at lag days 0–3, while Liang et al. (Liang et al. 2009) found in Shanghai a 14% (95% CI, 0.8% to 28.8%) increase in the number of hospital admissions for chronic obstructive pulmonary disease with each 1°C increase in the diurnal temperature range above 9.6°C.

In our analysis of the impact of variations of diurnal temperature on daily mortality of residents of Montreal age 65 years and older during the period 1984 to 2007, we found a 5.12% (95%CI: 0.02 to 10.49) increase in the cumulative effects on mortality for an increase of the diurnal temperature range from 6°C to 11°C. When diurnal temperature increased from 11°C to 16°C we found a 11.27% (95%CI: 2.08 to 21.29) increase in mortality, but the small number of days when such values were recorded (216 days in the 24 year study period) increased the uncertainty of the estimates. The effect was the strongest on the concurrent day, persisted through lag 9 days, and was relatively robust to adjustment to mean temperature. However, when air pollution (NO_2, O_3) was also added to the model, the effects on mortality were attenuated.

Our findings are somewhat in contradiction to those reported in the literature, where air pollution was not found to have a confounding effect on the association between mortality and diurnal temperature range (Cao et al. 2009;Kan et al. 2007;Song et al. 2008;Tam et al. 2009). The difference in findings may be explained by our use of improved statistical models (the dlnm package), constraining the models to a 30-day lag period, while 3-day (Kan et al. 2007), 5-day (Cao et al. 2009) or 8-day (Tam et al. 2009) lag periods were preferred in other studies, and using a 24 year long time series while the results reported in the literature were drawn from 4 or 6 year long series (Cao et al. 2009;Kan et al. 2007;Song et al. 2008;Tam et al. 2009). We acknowledge the uncertainty regarding the appropriateness of adjusting for air pollution variables in the statistical model, as the effect of air pollution on mortality was shown to be influenced by temperature (Ren et al. 2008;Ren and Tong 2006;Roberts 2004). It is thus possible that air pollution may be on a causal pathway between diurnal variations in temperature and mortality.

One important limitation of the present and other studies was the use of ambient temperature measured at fixed stations (usually airport weather stations) to compute the exposure measure, diurnal temperature range, as it is known that there are spatial variations in temperature especially in urban areas that may influence individual exposure (Smargiassi et al. 2009).

In assessing the confounding effect of air pollution, we did not account for the effect of concentrations of fine particles as daily measurements were not available. It is unlikely that this affected the findings greatly, as the two air pollutants included in our analysis account for variations in pollution in the cold and warm periods of the year. We also could not account for the effect of infectious disease epidemics since such data are not available through administrative databases. The temporal smoothers would likely account for most of these effects, should they exist.

In conclusion, we found that in Montreal daily diurnal variations in temperature are associated with a small increase in mortality among the elderly population. More studies are needed in different geographical locations to confirm such an effect.

4.8 Annex

CONTENTS

Annex Table 1. Selected dispersion, autocorrelation and other parameters for different temporal smoothers.

Error! Reference source not found. Comparison of cumulative effects of diurnal temperature range on mortality among the 65 years and older age group, using different temporal smoothers; Montreal 1984-2007. All models used a cubic b-spline function with 3 df for diurnal temperature range effects, a natural spline with 3 df for the lag effects and a categorical term for the day of the week. For the model in the left panel we used 5 df for the temporal smoother, the model in the middle panel is the base model using 7 df for the temporal smoother, and for the model in the right panel we used 9 df.

Error! Reference source not found. Comparison of cumulative effects of diurnal temperature range on mortality among the 65 years and older age group, using a 7 df temporal smoother; Montreal 1984-2007. The model in the left panel is the base model using a cubic b-spline with 3 df for the diurnal temperature range effects and a natural cubic spline function with 3 df for lagged effects. The model in the middle panel used 5 df for the cubic b-spline and 4 df for the lagged effects while the model in the right panel used 6 df for the cubic b-spline and 5 df for the lagged effects.

Error! Reference source not found. Comparison of cumulative effects of diurnal temperature range on mortality among the 65 years and older age group, using a 5 df temporal smoother; Montreal 1984-2007. The model in the left panel is the base model using a cubic b-spline with 3 df for the diurnal temperature range effects and a natural cubic spline function with 3 df for lagged effects. The model in the middle panel used 5 df for the cubic b-spline and 4 df for the lagged effects while the model in the right panel used 6 df for the cubic b-spline and 5 df for the lagged effects.

Error! Reference source not found. Comparison of cumulative effects of diurnal temperature range on mortality among the 65 years and older age group, using a 9 df temporal smoother; Montreal 1984-2007. The model in the left panel is the base model using a cubic b-spline with 3 df for the diurnal temperature range effects and a natural cubic spline function with 3 df for lagged effects. The model in the middle panel used 5 df for the cubic b-spline and 4 df for the lagged effects while the model in the right panel used 6 df for the cubic b-spline and 5 df for the lagged effects.

Error! Reference source not found. Comparison of cumulative effects of diurnal temperature range among persons 65 years of age and over, using in the left-hand panel the diurnal temperature range for the entire day and in the right hand panel the diurnal temperature range for the entire day from 7AM to 22PM, Montreal, 1984-2007. Both models comprised a temporal smoother of 7 df per annum, a cubic b-spline for diurnal temperature range and 3df for the lag space.

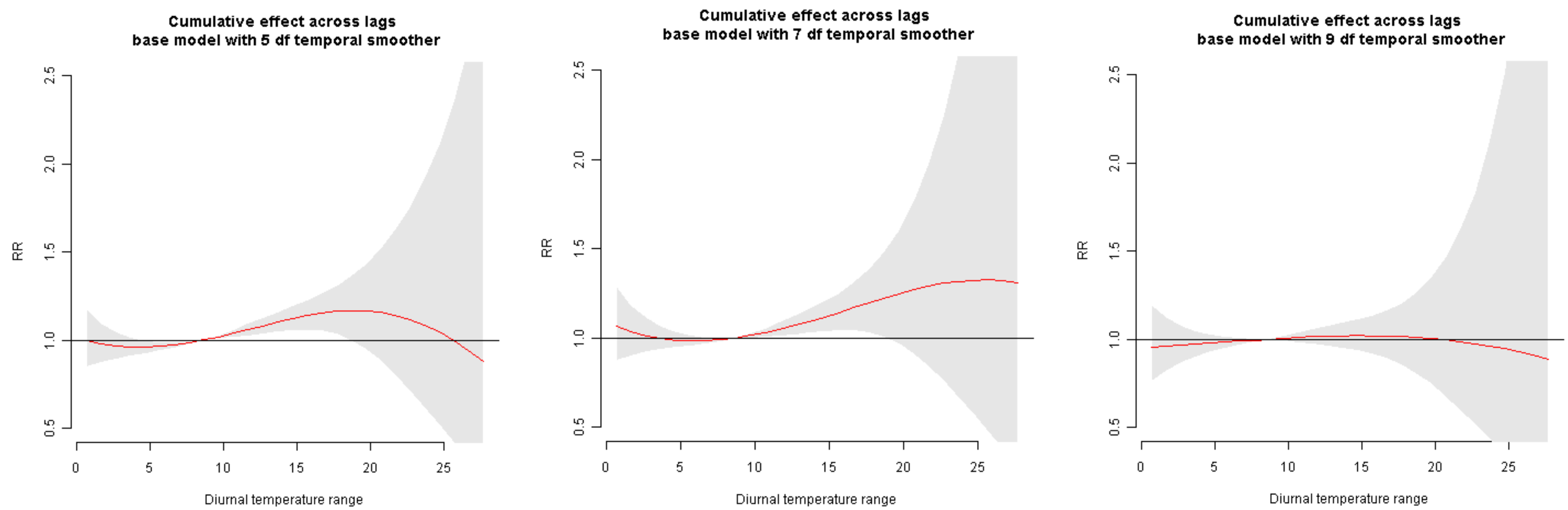
Annex Figure 6. Comparison of cumulative effects of diurnal temperature range on mortality among the 65 years and older age group, distributed lag models constrained over different lag intervals; Montreal 1984-2007.

Both models comprised a temporal smoother of 7 df per annum, a cubic b-spline for diurnal temperature range and a natural spline with 3df for the lag space. The y-axis represents the relative increase in daily counts of mortality with respect to the mean diurnal temperature range value (5.9˚C), the maximum likelihood estimate is shown as a smooth line and the shaded area represents the 95% confidence interval.

Annex Table 1 Over-dispersion coefficients, AIC and ACF parameters for the different temporal smoother models[a]

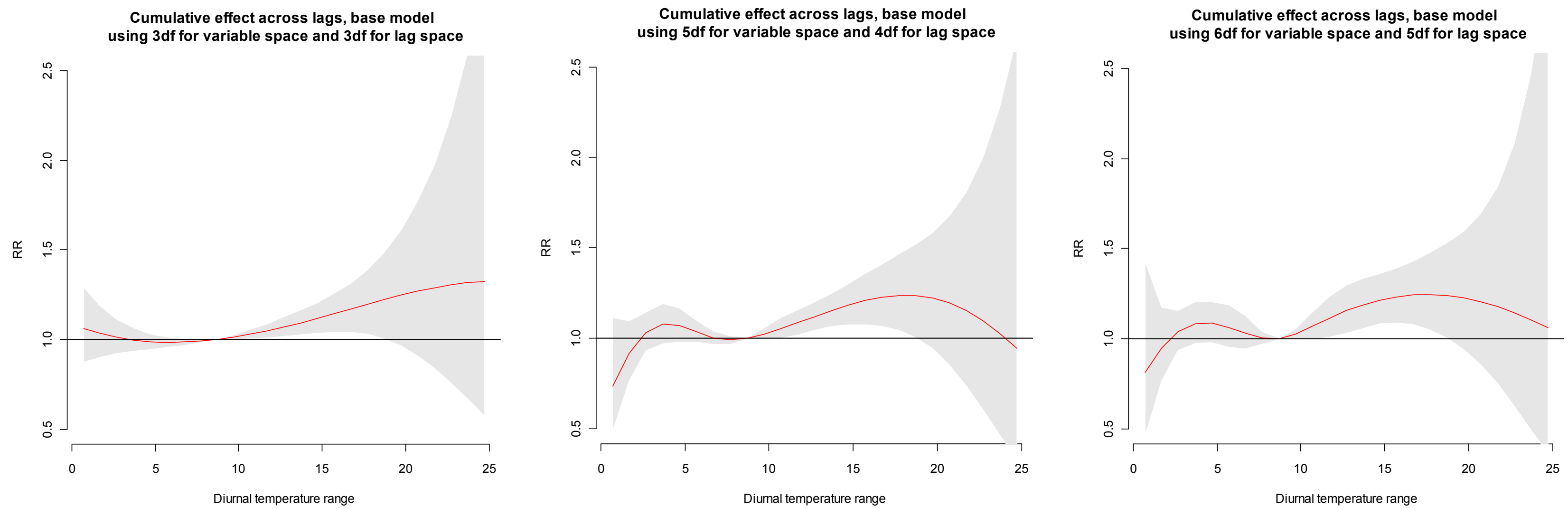
Temporal smoother model	AIC[b]	BIC[c]	Over-dispersion	Autocorrelation function															
				0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
4 df	10089.1	10789.9	1.14	1.00	0.09	0.08	0.07	0.06	0.04	0.05	0.03	0.03	0.03	0.04	0.03	0.03	0.03	0.02	0.01
5 df	10015.9	10883.0	1.13	1.00	0.08	0.07	0.06	0.05	0.03	0.04	0.02	0.02	0.02	0.02	0.01	0.02	0.02	0.01	0.00
6 df	9901.6	10937.8	1.11	1.00	0.06	0.06	0.04	0.03	0.01	0.02	0.00	0.01	0.01	0.01	0.00	0.00	0.00	-0.01	-0.01
7 df	9843.8	11047.7	1.09	1.00	0.05	0.05	0.03	0.02	0.00	0.01	-0.01	-0.01	0.00	0.00	-0.01	-0.01	-0.01	-0.01	-0.02
8 df	9788.8	11161.4	1.09	1.00	0.04	0.03	0.02	0.01	-0.01	0.00	-0.02	-0.02	-0.01	-0.01	-0.02	-0.02	-0.01	-0.02	-0.02
9 df	9756.7	11297.8	1.08	1.00	0.03	0.03	0.01	0.01	-0.02	-0.01	-0.03	-0.02	-0.02	-0.02	-0.03	-0.02	-0.02	-0.03	-0.03
10 df	9761.2	11469.3	1.08	1.00	0.03	0.02	0.01	0.00	-0.02	-0.01	-0.03	-0.03	-0.02	-0.02	-0.03	-0.02	-0.02	-0.03	-0.03
11 df	9766.1	11642.0	1.07	1.00	0.02	0.02	0.00	0.00	-0.03	-0.02	-0.03	-0.03	-0.03	-0.02	-0.03	-0.03	-0.02	-0.03	-0.03
12 df	9756.8	11800.7	1.07	1.00	0.02	0.01	0.00	-0.01	-0.03	-0.02	-0.04	-0.04	-0.03	-0.03	-0.03	-0.03	-0.02	-0.03	-0.03
13 df	9753.9	11966.7	1.07	1.00	0.01	0.00	-0.01	-0.02	-0.04	-0.03	-0.04	-0.04	-0.03	-0.03	-0.04	-0.03	-0.03	-0.03	-0.03
14 df	9779.4	12158.4	1.07	1.00	0.01	0.00	-0.01	-0.02	-0.04	-0.03	-0.05	-0.04	-0.04	-0.03	-0.04	-0.03	-0.03	-0.03	-0.03
15 df	9758.2	12307.9	1.06	1.00	0.00	-0.01	-0.02	-0.03	-0.05	-0.03	-0.05	-0.05	-0.04	-0.03	-0.04	-0.03	-0.03	-0.03	-0.03

a. Models included a natural cubic spline with different degrees of freedom for the temporal smoother component and a categorical term for the day of the week.
b. AIC – Akaike Information Criteria
c. BIC – Bayesian Information criteria



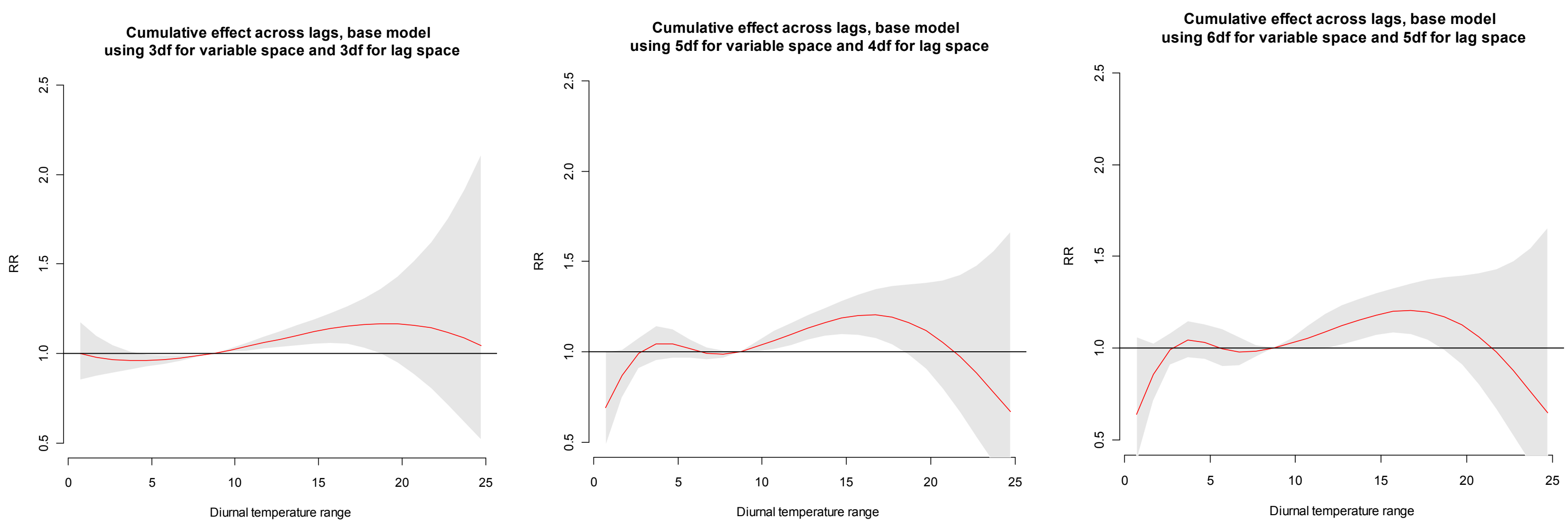
Annex Figure 1. Comparison of cumulative effects of diurnal temperature range on mortality among the 65 years and older age group, using different temporal smoothers; Montreal 1984-2007.

All models used a cubic b-spline function with 3 df for diurnal temperature range effects, a natural spline with 3 df for the lag effects and a categorical term for the day of the week. For the model in the left panel we used 5 df for the temporal smoother, the model in the middle panel is the base model using 7 df for the temporal smoother, and for the model in the right panel we used 9 df. The y-axis represents the relative increase in daily counts of mortality with respect to the mean diurnal temperature range value (5.9˚C), the maximum likelihood estimate is shown as a smooth line and the shaded area represents the 95% confidence interval.

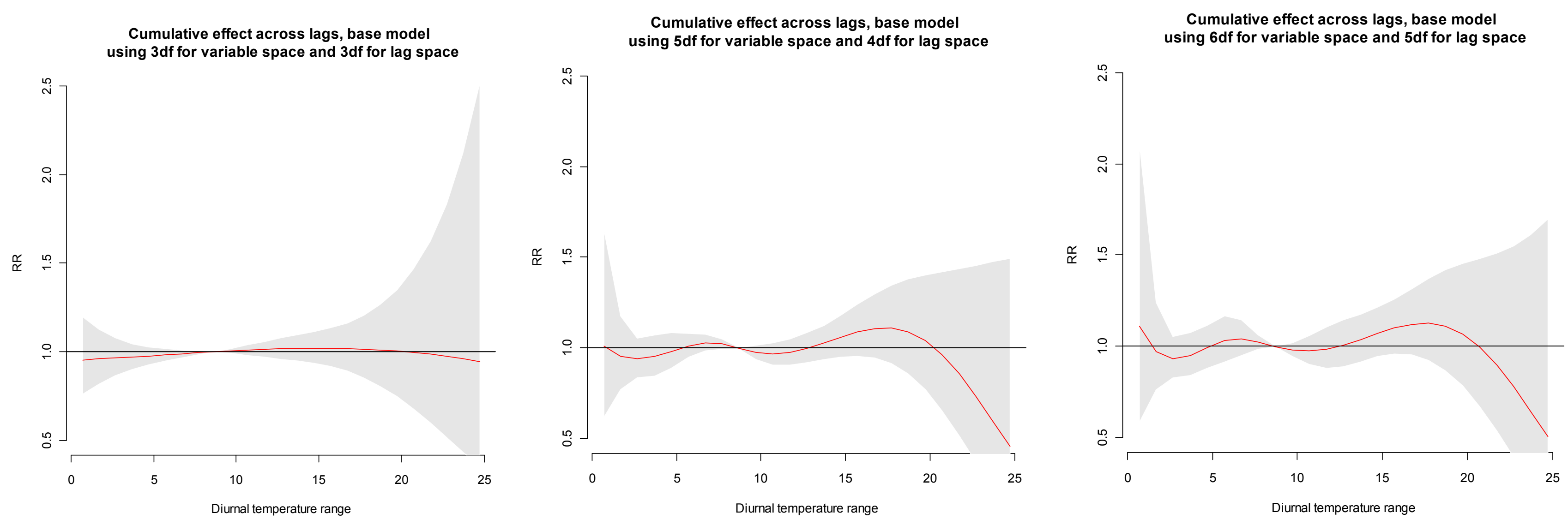


Annex Figure 2. Comparison of cumulative effects of diurnal temperature range on mortality among the 65 years and older age group, using a 7 df temporal smoother; Montreal 1984-2007.

The model in the left panel is the base model using a cubic b-spline with 3 df for the diurnal temperature range effects and a natural cubic spline function with 3 df for lagged effects. The model in the middle panel used 5 df for the cubic b-spline and 4 df for the lagged effects while the model in the right panel used 6 df for the cubic b-spline and 5 df for the lagged effects. The y-axis represents the relative increase in daily counts of mortality with respect to the mean diurnal temperature range value (5.9˚C), the maximum likelihood estimate is shown as a smooth line and the shaded area represents the 95% confidence interval.

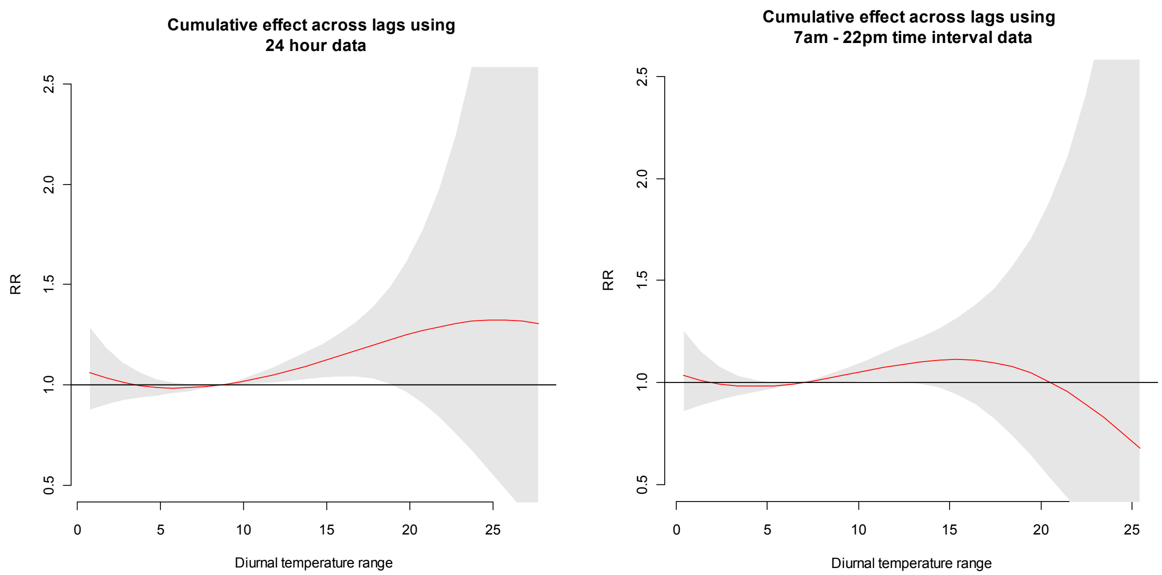


Annex Figure 3. Comparison of cumulative effects of diurnal temperature range on mortality among the 65 years and older age group, using a 5 df temporal smoother; Montreal 1984-2007.
The model in the left panel is the base model using a cubic b-spline with 3 df for the diurnal temperature range effects and a natural cubic spline function with 3 df for lagged effects. The model in the middle panel used 5 df for the cubic b-spline and 4 df for the lagged effects while the model in the right panel used 6 df for the cubic b-spline and 5 df for the lagged effects. The y-axis represents the relative increase in daily counts of mortality with respect to the mean diurnal temperature range value (5.9˚C), the maximum likelihood estimate is shown as a smooth line and the shaded area represents the 95% confidence interval.



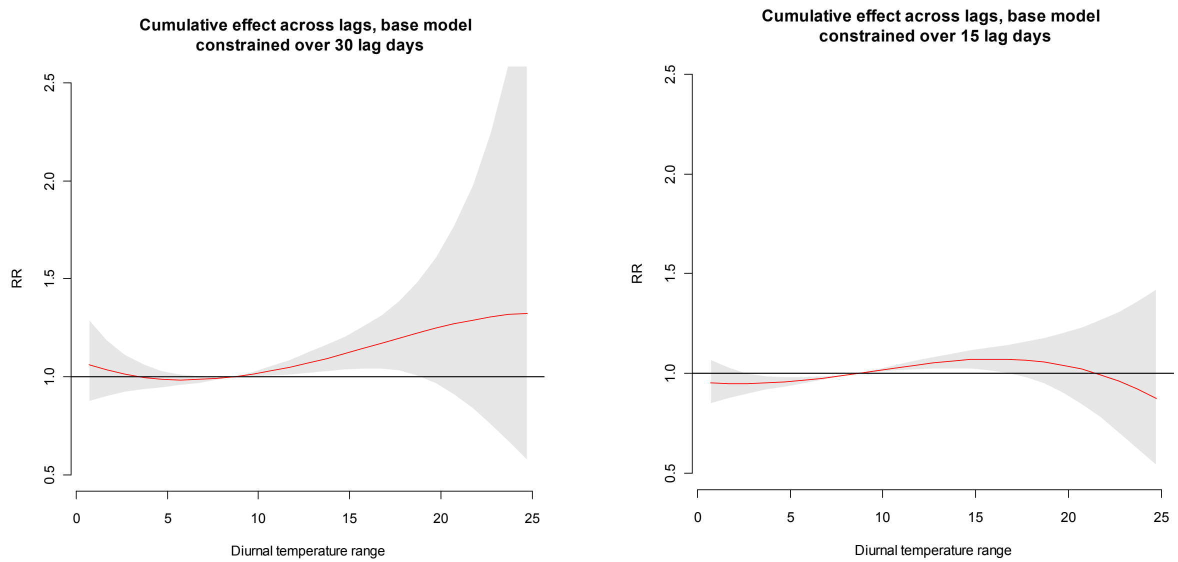
Annex Figure 4. Comparison of cumulative effects of diurnal temperature range on mortality among the 65 years and older age group, using a 9 df temporal smoother; Montreal 1984-2007.

The model in the left panel is the base model using a cubic b-spline with 3 df for the diurnal temperature range effects and a natural cubic spline function with 3 df for lagged effects. The model in the middle panel used 5 df for the cubic b-spline and 4 df for the lagged effects while the model in the right panel used 6 df for the cubic b-spline and 5 df for the lagged effects. The y-axis represents the relative increase in daily counts of mortality with respect to the mean diurnal temperature range value (5.9˚C), the maximum likelihood estimate is shown as a smooth line and the shaded area represents the 95% confidence interval.



Annex Figure 5. Comparison of cumulative effects of diurnal temperature range on mortality among the 65 years and older age group, using different time intervals; Montreal 1984-2007.

Both models comprised a temporal smoother of 7 df per annum, a cubic b-spline for diurnal temperature range and a natural spline with 3df for the lag space. The y-axis represents the relative increase in daily counts of mortality with respect to the mean diurnal temperature range value (5.9˚C), the maximum likelihood estimate is shown as a smooth line and the shaded area represents the 95% confidence interval.



Annex Figure 6. Comparison of cumulative effects of diurnal temperature range on mortality among the 65 years and older age group, distributed lag models constrained over different lag intervals; Montreal 1984-2007.
Both models comprised a temporal smoother of 7 df per annum, a cubic b-spline for diurnal temperature range and a natural spline with 3df for the lag space. The y-axis represents the relative increase in daily counts of mortality with respect to the mean diurnal temperature range value (5.9˚C), the maximum likelihood estimate is shown as a smooth line and the shaded area represents the 95% confidence interval.

Chapter 5: Discussion and Conclusions

The Fourth Assessment Report of the Intergovernmental Panel on Climate Change highlights the unprecedented increase in mean surface temperatures around the globe (Parry et al. 2007). Extreme weather events with severe impact on human mortality, such as the summer 2003 heat wave in Europe or the 1995 Chicago heat wave, prompted a more detailed analysis of the factors influencing the temperature-mortality association. New research points to a possible independent contribution of daily variations in temperature to the increase of the relative risk of mortality and other health outcomes, such as daily admissions to emergency units. However, the few papers addressing this issue are based on relatively short time series, four to six years, and come from the same geographical area, south-east Asia (Cao et al. 2009;Kan et al. 2007;Song et al. 2008;Tam et al. 2009). The estimated results indicate a 1.37 to 2.46% increase in mortality for 1 °C increase in diurnal temperature range after adjusting for the potential confounding effects of mean temperature and air pollution. To date, such results have not been reproduced in other geographical areas where daily variations in temperature may be greater.

This study took advantage of available weather and mortality records in Montreal for the 1984 – 2007 period so as to determine the association between diurnal temperature variations and daily counts of non-accidental mortality among Montreal residents 65 years of age and older. This subgroup of the population may be more susceptible to daily changes in temperature due to the combined effect of natural changes that occur with age and pathological changes caused by the illnesses associated with older age, as well as an increase in the use of medication and possible lack of social support.

The statistical approach we used was the distributed lag non-linear models developed recently by Armstrong and Gasparrini (Armstrong 2006;Gasparrini et al. 2010) which, in contrast to the generalized additive models used in four out of the five papers from south-east Asia (Cao et al. 2009;Kan et al. 2007;Song et al. 2008;Tam et al. 2009), allow for simultaneous estimation of multiple non-linear function terms across lags of covariates with delayed dependencies in the association.

Our findings show a modest increase in non-accidental mortality among Montreal residents 65 years and older when diurnal temperature range rises from 6 to 11 °C. A stronger effect on mortality was found for diurnal variations in the range of 11 to 16 °C, but the small number of days when such variations were recorded increased the uncertainty of the estimates. The effect on mortality was the strongest on the concurrent day, persisted through lag 9 days and was relatively robust to adjustment for mean temperature.

We found attenuated but similar effects on mortality when the analysis was repeated with a subset of the data using temperature records restricted to the 7 am – 22 pm time interval, to better reflect the population's exposure to diurnal variations in temperature.

In contrast to previous studies, we found that adjusting for air pollution resulted in a reduced effect on mortality that was delayed with more than 7 days, with inconclusive cumulative effects. The appropriateness of such an adjustment is still under debate, since the effect of air pollution on mortality was shown to be influenced by temperature (Ren et al. 2008;Ren and Tong 2006;Roberts 2004).

An important limitation of the present and other studies was the use of ambient temperature measured at fixed stations (usually airport weather stations) to compute the exposure measure, diurnal temperature range, as it is known that there are spatial variations in temperature especially in urban areas, the “heat islands”, that may influence individual exposure (Smargiassi et al. 2009).

In assessing the confounding effect of air pollution, we did not account for the effect of concentrations of fine particles as daily measurements were not available. It is unlikely that this affected the findings greatly, as the two air pollutants accounted for variations in pollution in the cold (NO_2) and warm (O_3) periods of the year. We also could not account for the effect of infectious disease epidemics since such data are not available through administrative databases. The temporal smoothers would likely account for most of these effects, should they exist

This study is the only one that we are aware of to assess the impact of diurnal temperature variations on mortality in North America, using a 24 year long time series that reduces the probability that the results reflect the effect of unmeasured confounding factors with short-term impact on mortality. Further research in different geographical locations is needed to confirm these results. Focusing on cause-specific mortality, such as derived from chronic cardiovascular or respiratory conditions, may also be of importance since these illnesses are especially common in the elderly.

If effects such as those reported in this thesis and the Asian studies are confirmed by future work, the contribution of diurnal temperature variations needs to be taken into account, along with the effects of ambient temperature, for projections of the impact of extreme weather events on human health.

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