

Anomalous temperature and seasonality of mortality in the United States

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Abstract

Measuring and identifying the correlates and drivers of mortality are key functions of public health research. Information on seasonal mortality, and its inter-annual variations, enables prioritising and evaluating interventions during particular times of the year. It also provides the basis to study the association of death rates with seasonal temperature. My thesis aimed to provide and apply a statistical framework to characterise seasonality of death rates by cause of death, month, sex and age group, and to understand the role of temperature ~~in the observed patterns as a predictor, and possibly determinant, of how seasonal mortality changes from year to year and geographically.~~ I generated death rates from geo-coded vital registration data on all 85.5 million deaths in the entire contiguous United States over a 37-year period (1980-2016). I grouped the underlying causes of death into mutually exclusive and collectively exhaustive broad causes (cardiorespiratory diseases, cancers, injuries, other) along with further sub-causes for cardiorespiratory diseases and injuries. I processed ERA-Interim reanalysis weather data to create population-weighted monthly temperature statistics. I applied wavelet, centre of gravity and circular statistics methods to analyse seasonal dynamics of mortality. I found that overall death rates for those 45 years and older were highest in the winter, mostly due to cardiorespiratory disease deaths. In contrast, death rates in adolescents and young adults peaked in the summer, mostly due to injury deaths. Seasonal differences in older age groups have changed little over time, whereas in young children they have largely disappeared. I then formulated a Bayesian spatio-temporal model to estimate how anomalous monthly temperature – defined as temperature deviation compared to long-term norm for each state and month – affects deaths from different causes. A 1°C anomalously warm year in the entire contiguous United States would be associated with an estimated 941 (95% credible interval (CrI) 831, 1,053) additional injury deaths (0.5% of total injury deaths in 2016), concentrated in adolescent to middle-aged males. There would be an estimated 4,369 (4,024, 4,706) fewer cardiorespiratory disease deaths (0.4% of total cardiorespiratory disease deaths in 2016), concentrated in those 55 years and older. There would be a decrease of cardiorespiratory disease deaths in all but summer months. I found no association between anomalous monthly temperature and cancer deaths. Continued efforts are necessary to address seasonal peaks in mortality, especially particularly in older age groups, across the United States, especially in a changing climate.

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List of abbreviations

3DVAR	Three-dimensional variational data assimilation
4DVAR	Four-dimensional variational data assimilation
ACME	Automated Classification of Medical Entities
BUGS	Bayesian inference Using Gibbs Sampling
CAR	Conditional autoregressive
CDC	Centers for Disease Control and Prevention
CKDu	Chronic kidney disease of unknown aetiology
COPD	Chronic obstructive pulmonary disease
CI	Confidence interval
CrI	Credible interval
DAG	Directed Acyclic Graph
DHS	Department of Homeland Security
DIC	Deviation information criterion
ECMWF	European Centre for Medium-Range Weather Forecasts
EPA	Environmental Protection Agency
ERA	ECMWF re-analysis
GMRF	Gaussian Markov random field
ICD	International Classification of Diseases
IHD	Ischaemic heart disease
INLA	Integrated nested Laplace approximation
IPCC	Intergovernmental Panel on Climate Change
JAGS	Just another Gibbs sampler
MCMC	Markov Chain Monte Carlo
NCAR	National Center for Atmospheric Research
NCEP	National Centers for Environmental Prediction
NCHS	National Center for Health Statistics
NOAA	National Oceanic and Atmospheric Administration
NUTS	No U-Turn Sampler
PM_{2.5}	Particulate matter with diameter less than 2.5 micrometres
PM₁₀	Particulate matter with diameter less than 10 micrometres
PRISM	Parameter-elevation Regression on Independent Slopes Model
SDG	Sustainable Development Goal

TMB	Template Model Builder
UN	United Nations
UNFCCC	United Nations Framework Convention on Climate Change
UNISDR	United Nations International Strategy for Disaster Reduction
VR	Vital registration
WHO	World Health Organization
WMO	World Meteorological Organization

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Declaration of originality

I hereby declare that the work in this thesis is my own original research and that I have appropriately cited any work that is not my own.

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1 Introduction

1.1 Rationale

~~Large~~Measuring seasonal mortality, and how it changes over time and geography, is a key input to public health function. For example, large-scale annual programmes in advanced temperate countries like the United States are concerned with minimising the peak in deaths observed every winter.¹ ~~Measuring trends in seasonal mortality is therefore a key input to public health research.~~ While mortality seasonality is well-established, there is limited information on how seasonality varies by cause of death, sex, age group, as well as over time and space. This information is needed to better identify and target at-risk groups during periods of elevated risk.

There are well-established links between daily temperature and mortality from several causes of death, particularly ~~deaths from~~ cardiorespiratory diseases.²⁻⁷ Further analysis is needed to understand the impact of ~~these~~ temperature shifts across a full range of causes of death, with a study design which will enable identification of particular vulnerable groups, such as by sex and age group.

Research ~~in this area~~on temperature and health is also motivated by global climate change, which will cause deviations from long-term norm temperatures and potentially have wide-ranging impacts on health.⁸ The Paris Agreement of 2015, within the framework of the United Nations Framework Convention on Climate Change (UNFCCC), mandated that ‘Parties should, when taking action to address climate change, respect, promote and consider their respective obligations on the right to health’.⁹ Further, the Lancet Commission on health and climate change, established in 2015, made a primary recommendation of more investment in climate change and public health research.¹⁰

1.2 Aims and objectives

The aim of my thesis is to provide and apply a statistical framework to estimate the geographical patterns and trends in seasonal mortality, and how shifts from long-term norm monthly temperatures may predict, and possibly impact, monthly mortality by cause of death, sex and age group in the United States. The research has two objectives that will help achieve this aim:

- 1) to identify and quantitatively describe seasonal dynamics of mortality; and
- 2) to develop a mathematical model to establish how monthly mortality is associated with deviations in temperature from long-term norms.

1.3 Structure of the thesis

In Chapter 2, I review the previous research related on temperature and mortality and methods related to spatial and temporal modelling. In Chapter 3, I summarise the temperature and mortality data for the United States and introduce the metric that I use to measure anomalous temperature-metrie. In Chapter 4, I present findings on the seasonal dynamics of mortality in the United States. In Chapter 5, I introduce the statistical model used to quantify the association of mortality with anomalous temperature. In Chapter 6, I present the findings of the association of injury mortality with anomalous temperature. In Chapter 7, I present the findings of the association of mortality from cardiopulmonary diseases and cancers with anomalous temperature. In Chapter 8, I-will conclude with a discussion on how my results compare with existing literature, the implications of the findings from a public health perspective and potential future directions.

2 Background

2.1 Trends in mortality in the United States

Accurate measurement of mortality is an essential public health function. Reliable mortality data can influence policy decisions and inform whether countries are on track to achieve targets such as the Sustainable Development Goals (SDGs)¹¹ as well as national and subnational goals. However, generating reliable mortality data requires considerable effort in accurately recording the number of deaths by cause and measuring the size of a population. In England and Wales, calculating mortality statistics goes back several centuries.¹² In the United States, records span over a century.¹³ However, in many other countries today, mortality data continue to be unreliable or unavailable.¹⁴

Over the 20th century, the burden of mortality in the United States has largely shifted from communicable towards non-communicable diseases, such as cardiorespiratory diseases and cancers.¹⁵ Mortality from most causes of death in the United States is on a long-term downwards trajectory,¹⁶ though recent trends show an increase in seven of the ten leading causes of death.¹⁷ Death rates stratified by sex and age group are often a particular focus in efforts to quantify mortality, which can then be processed to generate life expectancy by applying life table methods.¹⁸ Life expectancy in the United States, like other high-income countries,^{19,20} has steadily increased over the last few decades,¹⁶ though not all groups have shared this improvement,^{21–23} and life expectancy in the United States has recently slightly decreased.¹⁷ Improvements in income, nutrition, education, sanitation, health care and air quality have brought the United States to a life expectancy at birth of 76.1 years in men and 81.1 years in women in 2016.²⁴ Some predict that an overall long-term increase in life expectancy will continue, albeit at a slower pace,^{25,26} while others contend that a further decrease is imminent due to health risks as well as climate change.^{27–29}

2.2 Trends in temperature in the United States

In meteorological terms, recording weather (or short-term variation in meteorological conditions) is critical for understanding climate (or long-term meteorological conditions, usually an average of at least 30 years) in context.³⁰ The importance of recording and understanding weather is long-recognised. The ancient Sanskrit texts in the Upanishads from 3000 BC contain theories on how seasonal cycles in temperature may be caused by the Earth's movement around the sun.³¹ However, the invention of the liquid-in-glass thermometer and barometer in the 17th century provided the foundation for modern collection of temperature data.^{32,33} In some places, such as throughout the former British Empire, weather data have been collected from weather stations for over a century, with the British Isles' records dating back to the 1650s.³⁴ Temperature records in the United States go back to 1895 in some areas.³⁵ Land-based weather stations in the United States are now widespread.³⁶

The United States is a large temperate country possessing distinct climate regions,³⁷ with annual average temperatures within the climate time-scale of 1980 to 2009 ranging from 7.6°C in the West North Central region, to 18.4°C in the Southeast.³⁸ Annual average temperatures in the United States have increased by 0.7-1.0°C since records began in 1895.³⁹⁻⁴³ The greatest and most pervasive warming has occurred in winter months, with average increases of over 0.8°C.³⁵ Summer months experienced less consistent changes, with warming mainly along the western parts of the country, and some cooling in the South and Midwest.³⁵ Under future climate change, annual average temperature in the United States is projected to increase by 1.4°C by the middle of the 21st century (relative to the late 20th century reference period), with high confidence of up to a 6.6°C increase by 2100.⁴⁴ All regions of the United States are projected to experience significant warming, with the greatest warming expected in the northern half of the country.⁴⁴

Heat waves are multi-day extreme heat events which have no standard definition, but typically take place over consecutive days over a chosen temperature threshold.⁴⁵ However they are reasonably defined,⁴⁵ heat waves have increased in frequency and length over the past century throughout the United States.^{46,47} One study with a dataset covering the entire United States from 1961 to 2010 found that the number of heat waves annually in American cities has increased by 0.6 heat waves per decade; the length of heat waves has increased, and the length of the heat wave season has increased by six days per decade.⁴⁶ Exposure to extreme heat events in the United States is projected to increase four- to six-fold by the end of the 21st century compared to the end of the 20th century.⁴⁸ This increase in dangerous heat wave exposure is similarly projected worldwide.⁴⁹

2.3 Seasonal mortality

Death rates vary by season, and on monthly, weekly and daily scales.⁵⁰ Seasonal variation of death rates within a year has been studied since ancient times ~~in the West~~. The first record of this work was when the Greek physician Hippocrates wrote about the impact seasons have on deaths.⁵¹ A modern study has also shown that deaths were seasonal in ancient Rome.⁵²

2.3.1 Excess winter mortality

It has been conclusively established that in temperate countries, such as in Europe and the United States, death counts from all causes of death are higher overall in the winter than in the summer.⁵³⁻⁵⁵ This phenomenon is referred to as excess winter mortality or excess winter deaths. Excess winter mortality is defined either as the ratio or the absolute difference between the number of deaths in winter months (usually December to March) and those in the rest of the year. Excess winter mortality has become a common metric to quantify seasonal differences in mortality, exemplified by its use in annual statistical bulletins by the Office for National

Statistics in the United Kingdom to give a measure of the severity of a year's winter on mortality,⁵⁶ as well as in similar research in the United States.⁵⁴ Excess winter mortality for deaths from all causes in temperate high-income countries in Europe ranges from 5% to 30%.⁵³ In the United States, excess winter mortality is up to 40% in older age groups.³⁸ An assumption of excess winter mortality is that the number of deaths is highest in the winter. This assumption is invalid when examining seasonal dynamics of mortality in certain causes of death such as unintentional injuries and may also be inaccurate for certain sex, age group and location combinations within a cause of death.⁵⁷ The usefulness of excess winter mortality to measure the impact of cold weather has also been questioned, as the metric assumes that all cold-attributable deaths occur in the winter months.^{58,59}

2.3.2 Methods of analysing seasonal mortality

Alternative ways of assessing seasonal mortality exist. Studying the United States, some have employed algebraic techniques to examine seasonal mortality stratified by demographic group, cause of death and metropolitan areas.^{50,60–63} Others have used Fourier spectral analysis or cosinor functions to fit seasonal models to monthly death rates in several countries.^{64–68} One limitation of these analyses is the assumption that seasonal death rates have a fixed 12-month cycle. One study used a more flexible approach by including certain other pre-determined cycle lengths in an assessment of seasonality of mortality in Japan.⁶⁹ Another disadvantage of these types of analyses of seasonal mortality is that the difference between levels of maximum and minimum mortality in a year is assumed to be constant over the study period. However, over time, seasonal behaviour of seasonal mortality can change or disappear entirely. Lexis diagrams, which are two-dimensional plots of age against time used to show births and deaths that occur over time, have been adapted to analyse changes in seasonality of mortality over time.⁷⁰

2.3.3 Determinants of seasonal mortality

The existence of seasonal variation in mortality has stimulated research into why death rates vary over a year. Understanding the dynamics and drivers of seasonal mortality is required for planning interventions, which would aim to reduce the severity of peaks in death rates. Incidence of influenza, especially in the elderly, is considered an important determinant of winter mortality in temperate countries such as the United States.^{71,72} Influenza incidence in the United States is also a good predictor of cardiovascular disease mortality, which also peaks in winter months.^{73,74} However, targeting of the elderly with influenza vaccinations in high-income countries has shown limited ~~success~~impact on ~~influencing~~ seasonal mortality.^{75,76} This may be due to their underutilisation, with 37.1% of adults covered in the 2017-2018 season in the United States.¹ The vaccine effectiveness was 38% for this period.⁷⁷ Some have suggested that improvements in current vaccine production may yet further reduce influenza mortality in winter months.^{78,79} Some influenza vaccines are cultured using chicken eggs, which is posited as leading to mutations in the vaccine candidate and lower effectiveness as a vaccine in the general population.⁷⁸ An interaction between temperature and influenza in influencing seasonal increases in death rates in winter is also hypothesised.⁸⁰

Since temperature varies in a similar way to deaths from some causes throughout a year in temperate countries like the United States, some have investigated the link between them. If temperature were a primary driver of the seasonal mortality, places with larger average temperature ranges throughout a year may show larger excess winter mortality. This was not seen in a study of 36 cities in the United States.⁸¹ A similar study of European countries found that the difference between winter and summer mortality was lower in the colder Nordic countries than in warmer southern ones.⁵³ Others argue that weather is the main driver of winter deaths⁸² and that previous calculations using excess winter deaths ~~is confounded by~~are incorrect

as they do not ~~excluding~~exclude cold-attributable deaths outside the winter period or ~~accounting~~account for inter-annual variability of winter length.^{58,59} Beyond temperature variation and influenza severity, a further proposal is that additional drivers of seasonal mortality may be due to ~~a more advanced chain of causality. This would involve~~ social factors (such as housing conditions), biomedical reaction to climate (such as infections of respiratory systems) and demographic ~~reaction to biomedical changes~~factors (such as changed mortality risk in susceptible groups).⁵⁷

~~Beyond a seasonal cycle of mortality, inter-annual variation in mortality exists. For example, death rates in one or more months in a particular year may experience a deviation from the long-term smooth seasonal cycle. Temperature is well-established as a major source of variation in mortality and morbidity.~~³⁻⁷

Beyond a seasonal cycle of mortality, inter-annual variation in mortality, including in season-specific mortality, exists. For example, some monthly death rates in a particular year may deviate from the long-term seasonal cycle.

2.4 Temperature and mortality

2.4.1 Effects of temperature on humans

Humans, like other successful species on Earth, have ‘inherited or acquired the behavioural, morphological, and physiological attributes necessary to avoid, tolerate, and adapt to the stresses of life’.⁸² This process has included adapting to local climate along with its seasonal cycle. The Intergovernmental Panel on Climate Change (IPCC) defines climate adaptation as ‘the process of adjustment to actual or expected climate and its effects’.⁸³ Despite humans’ successful adaptation, the potential for unusual or extreme weather to disrupt society and health has been demonstrated and recognised throughout history. Exceptional temperature

events are known via numerous European town chronicles in the sixteenth century.⁸⁴

Measurements in Europe of the past 500 years also demonstrate further evidence of temperature anomalies.⁸⁵ More recent periods of extreme heat, such as the 1995 Chicago heat wave,^{86,87} or 2003 European heat wave,⁸⁸ claimed many victims.

The human body is in a state of normothermia, or comfortable resting temperature, between 36.5-37.5°C.⁸⁹ Heat stress, or the ‘perceived discomfort and physiological strain associated with exposure to a hot environment’, occurs at temperatures above this range.⁹⁰ Healthy adults have efficient corrective mechanisms to regulate high body temperature by vasodilation and perspiration.⁶ However, even a healthy human body has an upper limit to its endurance of excessively warm temperatures.⁸⁹

2.4.2 Extreme heat and cold

When heat stress becomes extreme, this can result in potentially deadly medical conditions such as heat stroke, heat exhaustion, heat syncope, heat rash and heat cramps.⁹¹ In the most acute cases, heat stress can lead to multiple organ failure and rapid death.⁶ The impact of periods of extreme heat on mortality is substantial. However, direct causes of death from extreme heat stress only make up a small proportion of deaths attributable to daily elevated temperatures.² Most temperature-related daily deaths are instead attributable to non-extreme deviations from acclimatised temperatures, which suggests other direct and indirect pathways to mortality from elevated temperatures.²⁻⁴

Though extreme heat was not included as a natural disaster under the United Nations (UN) Sendai Framework for Disaster Risk Reduction of 2015,⁹² there is a growing public awareness that prolonged periods of heat are dangerous and their worst effects need to be curbed.⁶ Projections of the future climate predict an ever-greater challenge of handling elevated heat

exposure worldwide.⁴⁹ In the United States, extreme heat is on average estimated to cause more deaths than any kind of weather-related hazard.^{93,94} This is true even of a year like 2018,⁹⁵ when flooding in Maryland, hurricanes Florence and Michael and the California wildfires occurred.⁹⁶ Records from the United States Environmental Protection Agency (EPA) claim that from 1979, over 9,000 deaths have been attributable to extreme heat.⁹⁷

There has been interest in establishing whether heat waves act as a modifier to the deadly effect of heat stress.^{98–101} Heat waves can be described in different ways. The minimum threshold temperature of a heat wave can be defined either relatively (e.g., certain number of days above 95th percentile of local long-run temperatures) or absolutely (e.g., number of days above 30°C).⁴⁵ The minimum number of consecutive days required above a heat wave threshold to qualify as a heat wave also varies, with studies using two days or more.⁴⁵ The heat stress metric can also vary, with apparent temperature or various heat indices previously used instead of temperature.⁴⁵ The temperature threshold can also be defined by daily mean, minimum, maximum temperature, or temperature at a particular time of day.⁴⁵ Some studies have found an added effect for consecutive extreme heat days beyond the contribution of individual days.^{98,100,102} Another study found that the total risk of consecutive days of elevated temperature can largely be explained by aggregating the independent effects of individual days' temperatures.⁹⁹ Others have found that estimates of the impact of a heat wave on mortality are sensitive to the definition of a heat wave itself.⁴⁵

Prolonged periods of cold weather, which along with extreme heat is not included in the UN Sendai Framework,⁹² are also a deadly risk to human health.¹⁰³ Below the range of normothermia, cold weather puts strain on the heart and respiratory system.⁸⁹ Extreme cold stress beyond the human body's ability to adapt leads to hypothermia and can quickly lead to complete organ failure and death.⁸⁹ Mild cold, however, leads to more cold-related deaths than

extreme levels of cold.² In the United States, there is evidence that the severity of winter storms have decreased in the South and lower Midwest but have increased in the Northeast and upper Midwest.¹⁰⁴ While cold weather is also known to have a large impact on mortality,^{2,103} global climate change will result in stronger and, on average, warmer deviations from long-term norm temperatures.¹⁰⁵

A study of cold waves in the United States, analogous to heat waves but for extreme cold, found no added effect beyond the contribution of individual days' risk.¹⁰²

2.4.3 Shape of temperature-Temperature-mortality relationship association

The shape of the temperature effect for daily mortality is non-linear and is variously described as a J-, U-, or V-shaped curve, with elevated risk both for warmer- and colder-than-average conditions.² Several designs of fitting temperature-mortality relationships exist with linear, polynomial and cubic spline curves.¹⁰⁶ With daily mortality, however, a death ~~attributable to temperature~~ on any given day may be due to the accumulation of ~~temperature~~ exposure ~~from over~~ a number of preceding days, ~~of which with~~ the heat effect ~~is generally~~ more immediate than the cold effect.² Distributed lag non-linear models were developed to account for the non-linear and delayed effects in temperature and daily time-series data.¹⁰⁷ The relationship between temperature and mortality on a monthly scale is less extensively studied. There are a few examples of studies using monthly temperatures and mortality using a linear or log-linear relationship.^{3,5,108–110}

2.4.4 Cause of death

Temperature variation has been associated with increased risk for all-cause mortality and mortality excluding injuries,^{2,3,5 7,87,88,98–101,103,109,111–119_{2,3,101,103,109,111–117,5,118,119,6,7,87,88,98–100}} as well as for cardiorespiratory diseases.^{3,5 7,87,88,115–117,120–127_{3,5,121–127,6,7,87,88,115–117,120}} In

particular, studies have found an association between temperature and deaths from cardiovascular diseases,^{7,87,115,117,1237,87,115,117,124} including ischaemic heart disease (IHD),^{103,117} myocardial infarction,^{117,128} cerebrovascular diseases^{7,103,117} and heart failure.¹¹⁷ Causality behind these associations has been detailed in previous work.^{103,129–131} In brief, higher-than-average temperature in warm months puts strain on the circulatory system by reduction of plasma volume from the release of platelets into the blood stream, as well as water and salt loss from sweating, which can cause artery blockages and sudden decreases in blood pressure.¹³¹ Previous studies have shown that warmer days in summer months increase cardiovascular deaths, while not increasing hospital admissions.¹³⁰ This suggests The study suggested that those who died in warmer weather may have already had pre-existing conditions, which made them more vulnerable and therefore caused rapid death before a patient could be admitted to hospital and receive medical treatment.¹³⁰

In colder conditions, warmer-than-average temperatures decrease cardiovascular deaths. This has been partially attributed to the inverse relationship between temperature and blood pressure.¹²⁹ Blood pressure increases during colder weather; higher blood pressure alters the ratio between supply and demand of oxygen delivered to the myocardium in the heart, which leads to greater stress in the ventricular wall and increases the work the heart needs to do.¹²⁹ Higher blood pressure also reduces mechanical efficiency of the heart and can impair blood flow in it, which may lead to myocardial ischaemia.¹²⁹ Vasoconstriction can also affect the ratio between systolic and diastolic blood pressure, producing vessel wall deformation and damage.¹²⁹ Other factors such as increased blood clotting and thrombosis may also have an influence on the increasing risk of cardiovascular disease death during colder weather.^{103,129}

Increases in deaths from respiratory diseases are also observed in warmer than comfortable temperatures,^{7,103,115,117,1237,103,115,117,124} including chronic obstructive pulmonary disease

(COPD),¹¹⁷ asthma¹¹⁷ and respiratory infections.^{7,117} These are believed to occur in warm weather due to airway inflammation, and with elderly patients with existing COPD unable to dissipate excess heat.¹³⁰ The association of cold temperatures with respiratory diseases may be accounted for by a suppression of immune responses by stress hormones during cold weather, which reduces the body's resistance to infection.¹⁰³

A few studies relating injuries to temperature exist.^{108,117,132,133} Removing injury deaths from a dataset has been a common part of data pre-processing for temperature mortality studies.^{2,3,5,98,99,101,114,116} High temperatures and increased work related injuries have previously been examined, with manual workers such as farmers, construction workers, firefighters, miners, soldiers and those in manufacturing roles highlighted as at increased risk.¹³⁴ A previous study of the United States has linked rising temperatures with feeling of despair, potentially leading to more suicides. Removing injury deaths has been a common part of data pre-processing for temperature-mortality studies.^{2,3,5,98,99,101,114,116} Nonetheless, a few studies relating injuries to temperature exist.^{108,117,132,133} Increased work-related injuries in high temperature have previously been examined, with manual workers such as farmers, construction workers, firefighters, miners, soldiers and those in manufacturing roles highlighted as at increased risk due to the outdoor and physical nature of their work.^{134,135}

Beyond injuries, a previous study of social media posts in the United States during periods of elevated temperatures found a positive association between higher temperatures and feelings of despair expressed in posts.¹⁰⁸

Some studies have related temperature to some other causes of death.^{7,108,116,117,126,128,135-139}

Some studies have related temperature to some other causes of death.^{7,108,140,116,117,127,128,136-139}

Deaths from endocrine diseases,¹¹⁷ diabetes,^{116,117} genitourinary diseases^{7,117} and some

psychiatric disorders^{108,116,117} have been identified as being sensitive to temperature. Deaths from cancers have been studied in association with temperature, ~~with~~ largely with no specific relationship observed.^{126,136,139,127,136,139} An older study which observed an association between cancer deaths and temperatures urged caution in interpretation of the results, as the study did not take into account local long-term temperature norm differences.^{126,136} Recent worldwide increases in chronic kidney disease of unknown origin (CKDu), which have been observed in agricultural communities in particular,^{140,141} have also been associated with rising temperature,^{135,140} along with other possible causes such as increasing use of pesticides.^{141,142} Others argue that there is not enough evidence to draw any firm conclusions about the origin of increases in CKDu incidence.^{140,141,142}

2.4.5 Demographic determinants

~~Men and women have different physiological responses to heat stress.¹⁴² Some studies have analysed separately by sex to establish if the temperature-mortality relationship is disintct.^{3,5-7,88,100,108,109,117,121,122,127,143-149} Women have been found to be more vulnerable than men from daily increases in temperature for all-cause mortality and cardiorespiratory disease deaths,^{3,5,88,100,116,122,127,143,147-149} whereas men were found to be more vulnerable for circulatory causes in one study.¹⁴⁵ Other work which explored differences between men and women's temperature-mortality relationship found no differences in vulnerability between men and women,^{108,109,121,144,146} though analysing deaths from all ages together. A recent review recommended further research by sex due to lack of existing evidence in differentials of the temperature-mortality relationship. Men and women may have different physiological responses to heat.¹⁴³ Some studies have analysed separately by sex to establish if the temperature-mortality relationship is disintct.^{3,5,122,123,144-150,6,7,88,100,108,109,117,120} Women have been found to be more vulnerable than men from daily increases in temperature for all-cause~~

mortality and cardiorespiratory disease deaths,^{3,5,150,88,100,116,120,123,144,148,149} whereas men were found to be more vulnerable for circulatory causes in one study.¹⁴⁶ Other work which explored differences between men and women's temperature-mortality relationship found no differences in vulnerability between men and women,^{108,109,122,145,147} though analysing deaths from all ages together. A recent review recommended further research by sex due to lack of existing evidence in differentials of the temperature-mortality relationship.⁷

The association between temperature and mortality also varies by age group. Where study design enabled comparison, greater vulnerability to rising temperatures was found for all cause and cardiorespiratory disease mortality in older age groups and the elderly compared with healthy adults.^{3,5,6,115,117,120–122,127,128,143,144,147,149–152} Children and adolescents were also shown to be at greater risk than healthy adults.^{3,5,121,145,153,154} Further work on differentials between age groups in temperature-mortality relationship is also recommended in a recent review. The association between temperature and mortality also varies by age group. Where study design enabled comparison, greater vulnerability to rising temperatures was found for all-cause and cardiorespiratory disease mortality in older age groups and the elderly compared with healthy adults.^{3,5,144,145,148,150–153,6,115,117,120–123,128} Children and adolescents were also shown to be at greater risk than healthy adults.^{3,5,122,146,154,155} Further work on differentials between age groups in temperature-mortality relationship is also recommended in a recent review.⁷

Urban-rural differences have been found in some studies, with those in urban areas more at risk of temperature increase.^{127,143} Other studies have also examined the differential impact of temperature by race and found that non-whites were at greater risk than whites in the United States,^{121,155} though some have not found any meaningful difference.^{109,123} Some socioeconomic factors were found to potentially elevate risk, such as living in a lower income

~~area, having a lower education, and increased poverty,^{3,156,157} though some studies found no association.^{123,143}~~

2.4.6 Other environmental determinants

~~Aside from air temperature, various other heat stress indices have been developed. These include apparent temperature, humidex, heat index, dew point temperature among others.¹⁵⁸ These metrics use meteorological variables besides temperature, such as humidity and wind. The main stimulus for suggesting these alternatives was that air temperature alone may not be the best predictor of a human's skin temperature, which plays a major role in a body's temperature regulation.¹⁵⁹ However, a study which attempted to systematically examine each of the proposed alternative heat stress metrics failed to find any that improved upon using the air temperature alone to predict mortality.¹⁵⁸~~

Urban-rural differences have been found in some studies, with those in urban areas more at risk of temperature increase.^{120,144} Other studies have also examined the differential impact of temperature by race and found that non-whites were at greater risk than whites in the United States,^{122,156} though some have not found any meaningful difference.^{109,124} Some socioeconomic factors were found to potentially elevate risk, such as living in a lower income area, having a lower education, and increased poverty,^{3,157,158} though some studies found no association.^{124,144}

2.4.6 Other environmental determinants

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the best predictor or a human's skin temperature, which plays a major role in a body's temperature regulation.¹⁶⁰ However, a study which attempted to systematically examine each of the proposed alternative heat stress metrics failed to find any that improved upon using the air temperature alone to predict mortality.¹⁵⁹

Other environmental measures that affect mortality, such as air pollution, including ozone, particulate matter (PM_{2.5}, PM₁₀), carbon dioxide, sulphur dioxide and nitrogen dioxide, have been includedinvestigated in some studies as covariates to establish whether they may act as confounders to the relationship between mortality and alongside temperature. A review of these studies found that no significant confounding or effect modification was evident on the inclusion of pollutants for the majority of the studies.³ It has also been argued that pollution should not be a confounder of temperature-mortality association, as adjusting for pollution excludes the interaction between temperature and pollution.¹⁶⁰

A review of these studies found that adjusting for pollutants did not significantly change the magnitude of the temperature-mortality relationship for the majority of the studies.³

2.4.7 Mortality displacement

When a spikerise in deaths occurs, but deaths in the spike are only brought forward by a short time, the number of deaths after the spike will be peak is lower than average., it implies that deaths are only brought forward by a short time. This phenomenon is known as mortality displacement.³ Some speculate that this occurs when increased mortality occurs during elevated temperatures. The implication is that the increase in deaths would not necessarily be of public health significance, since the deaths were only slightly brought forward in time. While some studies claim to have found mortality displacement in temperature studies,^{123,161,162} others claim to have found none.^{108,163} One publication¹⁶³ directly criticised another study's

~~methods.¹⁶² A study of suicides found no mortality displacement when associating mortality with temperature.¹⁰⁸~~

2.5 Modelling methodology and computation

In order to establish whether mortality displacement occurs after periods of elevated temperature, some have investigated the association between elevated temperature and mortality across time lags from a few days up to a month. This methodology enables insight into whether deaths would have happened shortly after the peak if the elevated temperature had not occurred. While there are personal and familial impacts from losing a loved one slightly earlier than expected or necessary complicated procedures caused by someone dying without a will, the deaths are displaced a matter of days or weeks, and typically claim the most susceptible in a population, such as infirm elderly or those of any age with a terminal illness at the end of their lives.¹⁶¹

While some studies have found mortality displacement in temperature studies,^{124,161,162} others have not.^{108,163}

2.5 Modelling methodologies and computational issues

When developing studies of the temperature-mortality relationship, the spatial and temporal variation of the exposure and outcome data are relevant to the design of a study. Both time series and cohort studies have been used to understand the impact of air pollution on mortality, as air pollution levels vary over both time and space. There are related but distinct considerations to incorporate into study design of the temperature-mortality relationship. I discuss these considerations here.

2.5.1 Treatment of time ~~in models~~

To establish a dataset for use in a study, often data across several years are collected. A large body of scientific work focuses on the association of daily mortality and morbidity with episodes of extreme heat lasting up to a few days.^{3–7} Various methods have been used for the time series data. The time series regression model uses techniques originally developed in pollution modelling to attribute mortality counts on a particular day to observed temperature and other time-varying factors, most commonly assuming an over-dispersed Poisson regression model.^{106,164,165} Other studies use case-crossover design, where temperatures on the day of death and those immediately preceding are compared to control days where death did not occur.¹⁶⁶ Case-crossover designs are commonly used for analysing effects of short-term exposures, such as temperature.¹⁶⁶

2.5.2 Accounting for month and season in models

Some studies have associated monthly or seasonal average temperatures with mortality.^{108,109} Other studies have accounted for seasonal impacts by stratifying daily data by month,⁸¹ ~~or further~~ allowing size of association with temperature to change throughout a season.¹¹⁴ Kinney highlighted how surprising it is that analysing by month or season to avoid potential seasonal confounding has to date ‘rarely been applied in temperature-mortality literature’.⁸¹ There is also evidence that the temperature-mortality relationship changes throughout a single season, indicating that monthly analysis of the temperature-mortality relationship is sensible.¹¹⁴

2.5.2 Geospatial modelling

2.5.3 Treatment of space

Mortality records are often geo-coded in addition to recording the time of death. Spatial studies have analysed the effects of countless factors on mortality along with disease incidence and

prevalence.¹⁶⁷ Much previous work with the temperature-mortality relationship do not account for the spatial nature of the mortality data available. In the United States, study areas have ranged from a single city or a few counties,^{86,87,121,138,168} to a region. In the United States, study areas have ranged from a single city or a few counties,^{86,87,122,138,168} to a region,^{109,169} to many sites across the country.^{81,101,114,118,120,123,126,137,144,146,155,161,170} A recent study used the entire United States dataset of suicide deaths^{81,101,156,162,170,114,118,121,124,127,137,145,147} to many sites across the country.^{81,101,156,162,170,114,118,121,124,127,137,145,147} A recent study used the entire United States dataset of suicide deaths.¹⁰⁸ Studies across different countries also compare temperature-mortality response using a consistent method.^{2,101,114} Studies which are spread across multiple sites have typically modelled each location, often cities, separately.^{81,101,114,119,120,123,137,144,146,155,161,170}

An alternative to analysing specific locations independently would be to account for the proximity or contiguity of the spatial units. A Bayesian formulation of a spatial model allows the ‘borrowing of strength’ across spatial and other units. This can be useful to create more stable estimates of risk where certain spatial units may have a relatively small amount of deaths and population levels but are next to a similar, but higher population, unit. Some recent work has used a Bayesian spatial framework to examine vulnerability to temperature.^{127,170,171} Other work with temperature and mortality has instead involved Bayesian random effect meta-analysis to pool relative risks from different locations.^{172,173}

2.5.3 Implementation of Bayesian models

Advances in computing over the past three decades have enabled Bayesian statistical inference to become more commonplace in medical and public health research. In the 1990s, Bayesian inference Using Gibbs Sampling (BUGS) and later WinBUGS employ a Gibbs sampling

~~algorithm to perform Markov Chain Monte Carlo (MCMC) iterations.¹⁷⁴ This was followed by Just Another Gibbs Sampler (JAGS).¹⁷⁵ Stan, an alternative program, uses the No U-Turn Sampler (NUTS) algorithm to improve speed and efficiency of inference.¹⁷⁶ Integrated nested Laplace approximation (INLA), using the R-INLA software, offers orders of magnitude of computational efficiency improvement in Bayesian inference compared to traditional MCMC for latent Gaussian models.¹⁷⁷ Template Model Builder (TMB) is another program which also uses Laplace approximation.¹⁷⁸~~

Much previous work with the temperature-mortality relationship do not account for the spatial nature of the mortality data. Studies which are spread across multiple sites have typically modelled each location, often cities, separately.^{81,101,162,170,114,119,121,124,137,145,147,156}

An alternative to analysing specific locations independently would be to account for the proximity or contiguity of the spatial units. In particular, a Bayesian formulation of a spatial model allows the ‘borrowing of strength’ across spatial and other units. This can be useful to create more stable estimates of risk where certain spatial units may have a relatively small amount of deaths and population levels but are next to a similar, but higher population, unit. A recent study used a Bayesian spatial framework to examine spatial variation in vulnerability to temperature.¹²⁰ Other work with temperature and mortality has instead involved Bayesian random-effect meta-analysis to pool relative risks from different locations.^{171,172}

2.5.4 Cohort studies

In studies of health effects of air pollution exposure in the United States, a common source of information is from prospective cohort studies.^{173–178} Time series studies have also been used to demonstrate short-term air pollution exposure effects, while evidence of the effect of long-term exposure to air pollution is obtained from cohort studies.¹⁷⁹ Whereas time series studies

of air pollution detect mortality which is triggered by recent air pollution (e.g., dying from complications of bronchitis during an elevated air pollution episode), cohort studies are also able to attribute mortality of the decedent due to a long-term cumulative exposure.¹⁷⁹

Though air pollution's deleterious cumulative effects are well-recognised,^{173–178} there is strong evidence that humans adapt to their local temperature, with minimal long-term impacts.² This would make it difficult for cohort studies to detect an effect for average absolute temperature. It may be possible to use a cohort study to detect the role of temperature variability, with metrics of variation used as exposure of interest. I am not aware of cohort studies that have done this. I discuss potential future work on cohort studies and the temperature-mortality relationship in Section 8.4.

2.5.5 Computational considerations

Advances in computing over the past three decades have enabled Bayesian statistical inference to become more commonplace in medical and public health research. In the 1990s, Bayesian inference Using Gibbs Sampling (BUGS) and later WinBUGS employ a Gibbs sampling algorithm to perform Markov Chain Monte Carlo (MCMC) iterations.¹⁸⁰ This was followed by Just Another Gibbs Sampler (JAGS), which enabled further speed with BUGS functionality.¹⁸¹ Stan, an alternative program, uses the No U-Turn Sampler (NUTS) algorithm to improve speed and efficiency of inference.¹⁸² Integrated nested Laplace approximation (INLA), using the R-INLA software, offers orders of magnitude of computational efficiency improvement in Bayesian inference compared to traditional MCMC for latent Gaussian models.¹⁸³ Template Model Builder (TMB) is another program which also uses Laplace approximation.¹⁸⁴ As a result of improvements in algorithms and programs performing Bayesian inference in the past few decades and vast increases in computing power, models can be run much faster than before.

Furthermore, running much more complicated hierarchical models is now possible, previously beyond available computational capabilities. These developments were essential in enabling me to build my Bayesian spatio-temporal model, described in Chapter 5.

2.6 Summary

Death rates in the United States vary by, sex, age group and across time and space. Temperatures in the United States have steadily increased, with marked changes since the 1970s. Death rates often vary seasonally. ~~A framework is necessary to understand how There are a number of frameworks for understanding seasonality has changed of mortality, and how it changes over time and space, and how temperature is associated with death rates by cause of death, sex and age group influences variations in seasonal mortality over time and space~~ in the United States. Previous work has established that temperature and mortality are associated, with most studies examining ~~different aspects of~~ the daily temperature-mortality relationship in the United States and elsewhere. Studies of the temperature-mortality relationship which have used data across multiple sites have mostly ~~treated each analysis independently from the others. analysed each location independently from the others. In Chapter 4 I use wavelets as an analytical framework for studying the seasonality of mortality in the United States, and in Chapter 5 I introduce a statistical approach for considering how anomalous temperature influences year to year variation in monthly mortality.~~

3 Data sources

3.1 Overview

I needed to identify and process appropriate data sources of mortality and temperature in the United States. This would enable me to carry out my analyses on the dynamics of seasonal mortality in Chapter 4 and the association of mortality with anomalous temperature in Chapters 6 and 7.

In this chapter, I give an overview of monthly mortality and temperature data sources, both large datasets which required considerable effort to process. I also present a generalisable algorithm for finding population-weighted monthly meteorological statistics, converting grid square temperature into state-level temperature values. The temperature output from this algorithm formed an essential data component of my thesis. My method is capable of turning commonly-found large datasets of gridded meteorological variables, such as ERA-Interim, into district-specific summaries anywhere in the world with an available shape file.

3.2 Cause-specific deaths and population

First, I describe how I processed vital registration death records; how I made choices in categorising death records by sex, age group, over time and space; and how I grouped categories into a mutually exclusive and collectively exhaustive combination of causes of death.

3.2.1 Objectives

My objectives in designing the cause of death classification included capturing significant causes of death within the country; collecting mutually exclusive and collectively exhaustive causes of death; grouping causes that possess comparable seasonal behaviour; generating monthly cause of death rates by state, sex, and age group; and avoiding small numbers issues.

3.2.2 Sources of mortality data

Sources of data on causes of death are available in various forms. These include vital registration (VR) systems, population censuses, mortality surveillance systems, verbal autopsy studies, hospital data, police records, mortuary records, and household surveys.^{179,185} These sources, however, are not consistently matched in terms of coverage (percentage of the population which is monitored), quality (accuracy of diagnosis in records) and completeness.^{179,185} VR systems are recognised as the highest quality mortality record data source,¹⁴ and VR systems with medically-certified causes of death are optimal.¹⁸⁰ ~~The United States possesses medically-certified VR records extending several decades.~~¹⁸⁶ The United States possesses medically-certified VR records extending several decades. This is in contrast to many other parts of the world, where an estimated 53% of deaths went unregistered in 2016.¹¹ The World Health Organization (WHO) currently recognises 68 countries that produce and share high-quality VR data.¹⁴

3.2.3 Population data

To create death rates, population data is also necessary, with the number of deaths in a particular spatial (e.g., country or state) and temporal (e.g., year or month) unit of analysis in the numerator and the respective population in the denominator (Equation 1):

$$\text{death rate} = \frac{\text{deaths}}{\text{population}}$$

Equation 1. Death rate calculation formula.

A census, whereby each member of a population is counted manually by registering members of a household, provides the most reliable way of obtaining population data. In the United

States, the census is every ten years, with the most recent in 2010.¹⁸¹ ~~The next United States census is due in 2020. Plans for the 2020 census, however, are controversial due to the proposed citizenship question potentially discouraging immigrants from contributing.~~¹⁸² Some analysts fear that this may lead to undercounting of over 5%.¹⁸³ While a census takes place only every ten years, methods have been developed which reliably interpolate population by county, sex and age group in intercensal years with census years as boundary conditions.¹⁸⁴ Population data in the United States is therefore publicly available by county, year, centred around July, from the National Center for Health Statistics (NCHS) bridged-race dataset for 1990 to 2016¹⁸⁵ and from the United States Census Bureau prior to 1990.¹⁸⁶¹⁸⁷ ~~The next United States census is due in 2020. Plans for the 2020 census, however, are controversial due to the proposed citizenship question potentially discouraging immigrants from contributing.~~¹⁸⁸ Some analysts fear that this may lead to undercounting of over 5%.¹⁸⁹ While a census takes place only every ten years, methods have been developed which reliably interpolate population by county, sex and age group in intercensal years with census years as boundary conditions.¹⁹⁰ Population data in the United States is therefore publicly available by county, year, centred around July, from the National Center for Health Statistics (NCHS) bridged-race dataset for 1990 to 2016¹⁹¹ and from the United States Census Bureau prior to 1990.¹⁹²

~~In a country like the United States, death rates in humans vary throughout the year.~~^{53,187,188} ~~Publicly available records of death from VR systems in the United States contain the month and day of week of death.~~ In a country like the United States, death rates in humans vary throughout the year.^{53,193,194} ~~Publicly-available records of death from VR systems in the United States contain the month and day of week of death.~~ It is therefore not possible to identify a death record by exact day and date. Nevertheless, a month timescale allows perceptible variations in sub-annual deaths.⁵⁷ When calculating monthly death rates, monthly population

data counts are required, which are not commonly available. Generating monthly population requires an algorithm to interpolate from yearly values.

For age-standardised death rate calculations in this Chapter as well as Chapters 3, 6 and 7, I used the WHO world standard population to create weighted averages of death rates from age-specific death rates.^{189,195}

3.2.4 Assigning causes of death

With VR data, each death is assigned a single underlying cause. This will typically take place shortly after a patient has died, after which a physician fills out the death certificate. In the United States, this will include filling out five or more lines listing the chain of events which led up to a death.¹⁹⁰ ~~Then the final underlying cause of death is processed using an algorithm, such as the Automated Classification of Medical Entities (ACME).~~^{191,192,196} Then the final underlying cause of death is processed using an algorithm, such as the Automated Classification of Medical Entities (ACME).^{197,198}

This underlying cause of death is coded using the international classification of diseases (ICD) convention. The ICD system is currently on its 11th revision (ICD-11), released by the WHO in 2018.^{193,199} However, each country decides when to adopt the latest ICD codes for recording underlying causes of death. The United States is currently still using its own variant of the ICD-10 coding,^{194,200} ICD-10 Clinical Modification (ICD-10-CM).^{195,201} ICD-10-CM was adopted in the United States in 1999, nine years after being endorsed by the Forty-third World Health Assembly.^{195,201} The ICD-10 revision of the ICD coding system contains thousands of five-digit codes to which a death can be assigned. The ICD-10 codes have a high level of detail. Using each code individually for an epidemiological study would quickly present issues regarding small absolute numbers of cases. Research in public health policy therefore often

requires that these causes of death are grouped into larger families. Though the ICD revisions provide a methodology to convert ICD codes into chapters,^{196,202} these groupings are too broad for specific public health interest.

~~The version of ICD coding used by physicians also varies every time a new coding system is updated, which can cause some issues of comparability across ICD revisions.^{197,198} When research spans multiple decades of mortality records in one country, there will almost certainly have been a change in ICD coding convention during that time. This can cause unusual changes in trajectory of death rates for certain causes of death.¹⁹⁹ This is complicated by the increase in number of ICD codes, which has expanded from 200 original codes to nearly 15,000.²⁰⁰ This requires creating a unifying list of causes that can be applied across ICD revisions using a bridge between ICD revisions.¹⁹⁷ Misclassification of cause of death within and across ICD coding revisions can also occur due to certification issues, with evidence that certain causes of death, such as HIV or diabetes, have been at times systematically underrepresented.^{191,201–203}~~

The version of ICD coding used by physicians also varies every time a new coding system is updated, which can cause some issues of comparability across ICD revisions.^{203,204} When research spans multiple decades of mortality records in one country, there will almost certainly have been a change in ICD coding convention during that time. This can cause unusual changes in trajectory of death rates for certain causes of death.²⁰⁵ This is complicated by the increase in number of ICD codes, which has expanded from 200 original codes to nearly 15,000.²⁰⁶ This requires creating a unifying list of causes that can be applied across ICD revisions using a bridge between ICD revisions.²⁰³ Misclassification of cause of death within and across ICD coding revisions can also occur due to certification issues, with evidence that certain causes of death, such as HIV or diabetes, have been at times systematically underrepresented.^{197,207–209}

I therefore needed to create a mutually exclusive and collectively exhaustive set of causes of death within an ICD revision, consistent cause of death mappings across ICD revisions, and coherent groupings of causes of death with similar seasonality.

3.2.5 Classifying causes of death

I used data on all 85,453,845 deaths in the contiguous United States (i.e., excluding Alaska, Hawaii and all other American off-shore insular areas) from 1980 to 2016. I chose this range because ICD codes changed in 1979 and 2016 was the last year of available data, as well as because the ERA-Interim dataset only begins in 1979. During this period, there were 400,331 deaths in Alaska and Hawaii, 0.5% of total deaths in the United States during this period. All data quoted on population and death from here on in will refer to the contiguous United States. I used data on deaths by sex, age, underlying cause of death and state of residence from 1980 to 2016 through the NCHS (https://www.cdc.gov/nchs/nvss/dvs_data_release.htm).https://www.cdc.gov/nchs/nvss/dvs_d ata_release.htm). I used data on population from the NCHS bridged-race dataset for 1990 to 2016,^{185₁₉₁} and from the United States Census Bureau prior to 1990.^{186₁₉₂}

I adapted the categories to those which would exhibit common monthly variation and with outcomes relevant to changes in temperature, as well as being relevant to the United States burden of disease. For example, while deaths from cancers are a significant burden of disease in the United States and globally, with an estimated 8.9 million deaths worldwide in 2016,²⁰⁴ death outcomes are not generally considered as sensitive to temperature changes, and so are all grouped as ‘cancers’ here. In comparison, cardiopulmonary diseases are also currently the leading cause of death in the United States, with cardiovascular diseases alone responsible for 900,000 deaths in 2016.²⁰⁴ Sub-causes of cardiopulmonary diseases also exhibit different seasonal properties by sex and age group,³⁸ and therefore deaths in these sub-causes may also have distinct associations with temperature. Injuries and injury sub-causes are of interest, as hitherto fewer studies have been made for these causes than others, even though death rates from injuries vary seasonally,^{38,57} and so there may be an association of their death rates with temperature change.

I show the tree structure in my mutually exclusive and collectively exhaustive cause of death hierarchy in Figure 1. The detailed causes of death can be aggregated to higher levels, such as grouping together all cardiovascular diseases or types of injuries. The causes of death can also be further aggregated up one additional level, such as grouping all cardiopulmonary diseases.

I used several competing models to generate monthly population estimates using yearly values, one of which modelled linear growth in months between years, with other more complex models such as exponential growth. The monthly population results were not sensitive to my choice. I calculated monthly population counts through linear interpolation, assigning each yearly count to July.

view of cause composition while avoiding small number concerns in modelling given the monthly and subnational nature of the data.

I adapted the categories to those which would exhibit common monthly variation and with outcomes relevant to changes in temperature, as well as being relevant to the United States burden of disease. For example, while deaths from cancers are a significant burden of disease in the United States and globally, with an estimated 8.9 million deaths worldwide in 2016,²¹⁰ death outcomes are not generally considered as sensitive to temperature changes, and so are all grouped as ‘cancers’ here. An exception may be terminally-ill cancer sufferers at the end of their lives, as described in Section 2.4.7, who are more frail and at higher risk of dying from non-optimal environmental conditions, such as elevated temperatures. The number of deaths for infectious diseases, such as HIV and diarrhoea, are large globally, but make up only a small share of deaths in the United States. In addition, beyond respiratory infections which in my analysis are included in respiratory diseases as part of cardiorespiratory diseases (Figure 1), the constituents of infectious diseases are heterogeneous across sex and age group. In comparison, cardiorespiratory diseases are also currently the leading cause of death in the United States, with cardiovascular diseases alone responsible for 900,000 deaths in 2016.²¹⁰ Sub-causes of cardiorespiratory diseases also exhibit different seasonal properties by sex and age group,³⁸ and therefore deaths in these sub-causes may also have distinct associations with temperature. Injuries and injury sub-causes are of interest, as hitherto fewer studies have been made for these causes than others, even though death rates from injuries vary seasonally,^{38,57} and so there may be an association of their death rates with temperature change.

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3.2.6 Age groups

I divided the data by sex and the following ten age groups: 0-4, 5-14, 15-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85+ years. I did this in part to avoid small numbers, as well as to minimise the impact of potential age misclassification.^{205²¹¹} I calculated monthly death rates for each sex and age group, both nationally and for the 48 contiguous mainland states and District of Columbia. Death rate calculations accounted for varying length of months, by multiplying each month's death count by a factor that would make it equivalent to a 31-day month. This factor multiplication process was reversed for any additional death estimation from anomalous temperature rise in Chapters 6 and 7.

3.2.7 Patterns and trend in mortality

In the period 1980-2016, 20,070,797 boys and men and 21,034,212 girls and women died from cardiorespiratory diseases in the contiguous United States, accounting for 46.3% and 49.9% of all male and female deaths respectively (Figure 2). Cardiorespiratory diseases accounted for 54.3% and 58.9% of total deaths in 1980, and 39.9% and 40.8% of total deaths in 2016, for males and females respectively. Seasonality is apparent for total cardiorespiratory disease

deaths, with a peak in the winter (Figure 3). I will further explore the presence of seasonality by sex and age group for various causes of death in Chapter 4.

Over time, cardiorespiratory disease death rates have decreased overall (Figure 4). Age-standardised death rates have decreased dramatically by over 50% during this period. This is replicated by most major sub-causes of death within cardiorespiratory disease deaths (Figure 49 in Chapter 7). Deaths from cardiovascular and respiratory diseases have previously been associated with variations in daily temperature from long-term norms.^{2-7,127,120}

10,428,202 boys and men and 9,434,558 girls and women died of a cancer in the contiguous United States, accounting for 24.0% and 22.4% of all male and female deaths respectively (Figure 2). Deaths from cancers accounted for 21.3% and 21.2% of total deaths in 1980, and 23.1% and 21.6% of total deaths in 2016, for males and females respectively, peaking in proportion of total deaths for males in the 1990s and 2000s then returning back to a lower value. There were slightly more deaths from cancers in the winter than in the summer (Figure 3). Over time, death rates from cancers have decreased overall (Figure 4).

4,006,454 boys and men and 1,757,862 girls and women died from an injury, accounting for 9.2% and 4.2% of all male and female deaths respectively (Figure 2). Deaths from injuries accounted for 10.7% and 4.7% of total deaths in 1980, and 9.6% and 4.9% of total deaths in 2016, for males and females respectively. Seasonality in total deaths was apparent for injury deaths, with a peak in the summer (Figure 3).

The remainder of the deaths were from other causes. These consisted of a heterogeneous group of causes of death, within which the cause that led to death varied by sex and age group. Causes of death in this group included infectious and parasitic diseases, endocrine diseases, nutritional

and metabolic diseases, immunity disorders, mental disorders, diseases of the nervous system, diseases of the digestive system, diseases of the genitourinary system, complications with pregnancy, skin diseases, diseases of the musculoskeletal system and connective tissue, and congenital anomalies.

Sub-national variation in death rates was also evident. This is illustrated by the state-level summaries of annual age-standardised death rates of cardiorespiratory disease deaths in Figure 5. Figure 5 also shows the variation in change of death rates over time, with death rates in different states changing more rapidly or slowly than other parts and with varying trajectories. This variation by time and space demonstrated that I needed to think about how a statistical model would incorporate sub-national variation, described in Chapter 5. Mortality characteristics of the states for the period of study (1980-2016) are summarised in Table 1.

		1980					2016				
		Sex	Min	25 th	50 th	75 th	Max	Min	25 th	50 th	75 th
Population	M	242,903	645,187	1,501,479	2,650,750	11,733,600	298,942	950,671	2,289,370	3,641,400	19,493,361
	F	231,478	663,921	1,608,566	2,825,623	1,2059,240	286,559	956,445	2,392,296	3,646,600	19,756,656
Deaths, all causes	M	1,870	5,389	14,481	25,063	99,751	2,514	9,378	21,640	33,661	135,238
	F	1,348	4,479	12,714	21,112	86,763	2,208	8,502	21,301	32,811	1,269,78
Deaths, cancers	M	313	1,118	3,129	5,411	21,301	518	1,852	5,142	8,041	31,547
	F	263	1,037	2,584	4,309	19,354	440	1,721	4,228	6,746	29,394
Cancer deaths as proportion of all deaths (%)	M	16.4	19.8	21.1	21.8	24.2	19.0	22.2	23.0	23.9	25.4
	F	18.1	19.7	21.0	22.2	24.3	17.1	20.5	21.1	22.6	23.6
Deaths, cardiorespiratory diseases	M	959	2,737	8,490	13,931	51,946	990	3,321	8,465	12,746	55,473
	F	754	2,665	7,687	12,141	51,843	862	3,226	8,431	12,802	54,008
Cardiorespiratory disease deaths as proportion of all deaths (%)	M	41.2	52.1	54.5	56.5	59.1	34.9	38.1	39.4	40.7	45.7
	F	47.1	56.6	58.5	59.9	63.2	33.9	38.4	40.1	41.5	45.5
Deaths, injuries	M	240	669	1,698	2,662	13,083	271	1,208	2,220	3,182	12,495
	F	108	288	627	949	4,864	121	623	1,131	1,635	5,241
Injury deaths as proportion of all deaths (%)	M	7.1	9.4	10.4	12.6	20.0	6.8	9.1	9.9	10.8	13.2
	F	3.1	4.1	4.8	5.7	12.1	3.5	4.7	5.2	5.8	7.9
Deaths, other causes	M	254	794	2,180	3,528	13,421	641	2,977	5,922	9,354	35,723
	F	221	708	2,006	3,474	12,311	698	2,887	7,120	11,053	38,335
Other cause deaths as proportion of all deaths (%)	M	11.3	12.8	13.4	14.5	21.4	22.6	25.8	27.6	29.0	33.4
	F	12.3	14.2	15.1	16.7	23.4	26.5	32.1	33.4	34.7	37.8

Table 1. Summary statistics by percentile for states used in the analysis.

3.3 Meteorological data

Here, I describe how I dealt with finding a reliable data source for meteorological records; how I developed an algorithm to process meteorological records for use as an input to my epidemiological model; how I tested results against another dataset; and how my methods are generalisable for use in other studies.

3.3.1 Objectives

My objectives in designing county- and state-level monthly temperature summaries involved taking gridded reanalysis weather data and converting it to United States county-level summaries; and creating population-weighted monthly means and anomalies by United States state.

3.3.2 Sources of meteorological data

Weather stations provide the apparatus to measure in-situ meteorological data. In industrialised nations, the density of weather stations has mostly remained high or increased. For example, in the United Kingdom, the average density of station networks measuring temperature over the past half century is one station per $21 \times 21 \text{ km}^2$, with little change throughout the period.²⁰⁶²¹² In the United States, this value is around one station per $40 \times 40 \text{ km}^2$.²⁰⁷²¹³ Particular challenges exist in the developing world, with coverage in Africa remaining generally below a required density to inform research and policy decisions.²⁰⁸²¹⁴

~~Additional measurement platforms such as ships, balloons, buoys, radiosondes, aircraft, scatterometers and satellites have supplemented weather stations to create a rich and live global dataset which are used in weather modelling and prediction.²⁰⁹ However, while crucial for~~

~~short term weather prediction, their use in climate research by themselves is limited due to frequent changes in systems of observation and data assimilation methods.~~^{210,211}

3.3.3 Weather reanalysis data

~~Creating reliable long-term global climate datasets has become a major national and international concern, partly to help understand the large-scale climate change occurring on Earth. Additional measurement platforms such as ships, balloons, buoys, radiosondes, aircraft, scatterometers and satellites have supplemented weather stations to create a rich and live global dataset which are used in weather modelling and prediction.~~²¹⁵ However, while crucial for short-term weather prediction, their use in climate research by themselves is limited due to frequent changes in systems of observation and data assimilation methods.

3.3.3 Weather reanalysis data

~~Creating reliable long-term global climate datasets has become a major national and international concern, partly to help understand the large-scale climate change occurring on earth.~~ The long-term data are therefore essential inputs into any historical climate record modelling.

Since the 1990s, retrospective analysis, or reanalysis, has provided an increasingly popular technique of assimilating millions of data points of meteorological data from disparate sources into a single model output. This process produces an estimate of the state of the atmosphere at a particular instant in time. Reanalysis of meteorological data consists broadly of three stages: a data quality control stage to ensure high data input standards, a data assimilation module to integrate historical data and an archiver to save the model output.^{212,213}

In the data assimilation stage, a physical model progresses through time in discrete steps while using data from weather measurements to correct and steer the model. The observational and model information is combined using a Bayesian statistical model in which probability distributions are associated with observations and model progress is dictated by physics. There are several basic strategies by which the data are assimilated. These strategies include sequential intermittent assimilation, or three-dimensional variational data assimilation (3DVAR), where a model run is only informed periodically by observations made in the time interval between assimilations. The state-of-the-art data assimilation methodology is four-dimensional variational data assimilation (4DVAR), where a model and the data analysis occur ‘live’, with observations included at the point in time at which they are made, which improves upon 3DVAR.²¹³²¹⁹ By assimilating data in this way, output from reanalysis have become ever more trustworthy where there is a good foundation of source data, such as in the United States in the past few decades.

~~There have been several notable reanalysis developments over time, starting with modelling a handful of atmospheric variables to more than 100. In the first generation, the NCEP/NCAR 40-year reanalysis project, released in the mid 1990s and using 3DVAR assimilation, provided the first global reanalysis at a resolution of around 210km worldwide.²¹² The second generation included ERA-40²¹⁴ (1957–2002), a reanalysis product developed by the European Centre for Medium Range Weather Forecasts (ECMWF), with successive improvements in data assimilation using 3DVAR and use of increased available computing power to provide higher resolution. ERA-Interim, released by the ECMWF in 2011 as an ‘interim’ update to ERA-40,²¹⁵ represents the third generation, with an improved atmospheric model and 4DVAR assimilation system. ERA-Interim has global coverage at a 4 times daily frequency across several decades, currently from 1979 to the present day at a resolution of 80km. The latest in line of ECMWF~~

~~reanalysis is ERA5, released by ECMWF in early 2019, which possesses a 31km spatial and hourly time resolution while also assimilating data using 4DVAR.²¹⁶~~

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3.3.4 Converting gridded meteorological data to area-weighted summaries

I developed an algorithm to convert gridded meteorological reanalysis datasets to population-weighted state summaries using open-source mapping shapefiles along with population data. I used this algorithm to prepare data for my thesis. It has further applicability outside of the bounds of my immediate focus; for example I used the same algorithm to prepare data in research in the impacts of air pollution on life expectancy in the United States.²¹⁷²²³

I summarised the 2-metre temperature estimates available on the ERA-Interim reanalysis. I downloaded each year in my period of study (1980-2016) in the netCDF file form from ERA-

Interim website (<https://apps.ecmwf.int/datasets/data/interim-full-daily/levtype=sfc/>). The file for each year contained data for 2-metre temperature in Kelvin in a global gridded dataset. The grid size, shape and position were consistent throughout the entire period of study. Each grid recorded temperature values at four times per day (00:00, 06:00, 12:00, 18:00) for the entire year. I calculated daily mean temperature for each grid by calculating the mean of the four values in each day. I also obtained the daily maximum and minimum temperatures for each grid by taking the maximum and minimum of the four values in each day. I converted the Kelvin values to Celsius.

A subset of grid squares from the files intersects the contiguous United States. Each of the 3,108 counties in the contiguous United States intersects at least one grid square. I calculated the proportion of each county's area intersecting with the grid squares incident upon it. Using these proportions, I calculated an area-weighted 2-metre temperature value based on grid values for each of the counties for each year's data. This process is illustrated in Figure 6.

3.3.5 Creating state-level summaries

The populations of the counties from 1980 to 2016 ranged from 32 (Loving County, Texas) to 10,043,000 (Los Angeles County, California). In small counties, some age groups had zero population in some years, which makes it impossible to calculate death rates. To avoid zero populations, I decided to summarise 2-metre temperature at a state level, which matched the unit of analysis for death rates. Summarising at state level also assures computational tractability for the Bayesian spatio-temporal model, described in Chapter 5.

The population within a state is usually distributed through its counties unevenly, mostly concentrated around urban areas. I needed to take this into consideration when creating state-level temperature summaries. I created a state-wide population-weighted average of 2-metre temperature for each sex and age group for the entire contiguous United States. This would ensure that at the scale of state, the temperature value assigned would reflect the experience of those within the state during that month. I then summarised for a particular month in my period of study in two ways. First, I calculated the county-level monthly averages and made a population-weighted average across the state. Second, I calculated the state population-weighted average by day and averaged across the month. The results were not sensitive to the choice of method. This was also true for generating anomalous temperature values, the concept of which I explain later in this chapter. I used values calculated from county-level averages with a population-weighted average made across the state. I then generated monthly temperature statistics. Figure 7 shows a map of the norm temperatures by state for each month across the contiguous United States during 1980-2016.

-As a sensitivity analysis, instead of building monthly temperature values based on daily mean temperatures, I used daily maxima and minima. These measures were strongly correlated to those generated from daily means (Table 2), and therefore I did not run models using these alternatives.

	Mean correlation coefficients between monthly anomaly summary values	
Month	Mean daily temperature with maximum daily temperature	Mean daily temperature with minimum daily temperature
January	0.98	0.98
February	0.98	0.98
March	0.97	0.97
April	0.97	0.96
May	0.96	0.94
June	0.95	0.92
July	0.97	0.94
August	0.96	0.93
September	0.93	0.91
October	0.91	0.93
November	0.96	0.97
December	0.98	0.92

Table 2. Correlation coefficients between monthly temperatures generated from mean daily and maximum or minimum daily temperatures. Each correlation coefficient was calculated in each state for each month for 1980-2016. The values shown are the means over all states for a particular month.

3.3.6 Anomalous temperature

To mimic the conditions that may arise with global climate change, I developed methodology to examine how deviations from long-term norm temperature may impact death rates. I defined a measure of anomalous temperature for each state and month compared to long-term norm temperature of the state in that month. To calculate the magnitude of temperature anomaly by state and month, I calculated 30-year (long-term) norm temperatures (from 1980-2009) for each month in each state. I calculated for 30 years because it is the duration used in climate assessments.³⁰ I subtracted these long-term norm temperatures from respective monthly temperature values to generate a temperature anomaly time series for each month and year in each state (Figure 8). The temperature anomaly metric measures the extent that temperature experienced in a specific month, year and state is warmer or cooler than the long-term norm to which the population of each state has acclimatised. These values can be different for neighbouring months in the same state, and neighbouring states in the same month.

In this approach, a state with higher, but more stable, temperature in a specific month has smaller anomalies than one with lower but more inter-annually variable temperature. The seasonal temperature variation across the country and year is internalised by the anomalous temperature metric, since the anomaly in a particular state and month is calculated relative to the long-term norm temperature. Average size of anomaly over the study period (1980-2016), a measure of how variable temperatures are around their central state-month long-term norm, ranged from 0.4°C for Florida in September, to 3.4°C for North Dakota in February (Figure 9). The size of anomaly had a median value of 1.2°C across all states and months, with 27% less than 1°C and 90% less than 2°C (Figure 9). Temperature anomalies were largest in January and December and smallest in August and September. They were larger in northern and central states than in southern and coastal ones.

3.3.7 Comparing county- with state-level anomalies

I also calculated county-level anomalies to compare how similar they would be to respective state-level ones. I followed the same process for county-level summaries as I did for states in Section 3.3.5. I then compared the county-level anomalies to the respective state-level anomalies over time and calculated the average difference between them (Figure 10). While there were some absolute differences within sets of counties, temperature anomalies in counties generally followed state-wide anomalies, as indicated by the proximity of most points on Figure 10 to the horizontal axes, with 94% an within an absolute deviation of 0.1°C , and 100% within 0.25°C . The largest deviations between county anomaly and state anomaly were typically for counties with lower proportion of population of the entire state. This minimised the impact of misclassification.

3.3.8 Comparison with PRISM dataset

Any new method of obtaining meteorological summaries should be compared with existing datasets. Other datasets include that from the Parameter-elevation Regressions on Independent Slopes Model (PRISM),²¹⁸ ~~which focuses on providing high resolution meteorological datasets for the contiguous United States.~~²²⁴ which focuses on providing high resolution meteorological datasets for the contiguous United States. In contrast, ERA-Interim provides global coverage, and is therefore a viable dataset if looking for consistent multi-national data sources. Even for the United States, ERA-Interim (and its successor ERA5) would provide additional coverage of non-contiguous states and other American off-shore insular areas, such as Hawaii, Alaska, Puerto Rico and Guam.

I compared the results of processing gridded ERA-Interim reanalysis data to those of the PRISM data. An example of the correlation between monthly temperature summaries for each grid square in the contiguous United States is demonstrated in Figure 11 (correlation coefficient 0.99). Other years and months in isolation were similarly correlated. The method of calculating temperature in PRISM was also different for the first year of my study, 1980, compared with 1981 onwards. This contrasted with ERA-Interim, which was consistent with the methodology and data assimilation across the entire period.

3.4 Summary

I selected a mutually exclusive and collectively exhaustive set of causes of death relevant for analysing the public health impacts of temperature in the United States. I created a consistent mapping across ICD-9 and ICD-10 codes. I extended previous work in producing national records of death in the United States by breaking the data down by month. My work here establishes a valuable dataset with which monthly and seasonal mortality can be analysed by several aggregated levels of causes of death, as I do in Chapter 4. It also provides the input mortality data for my analysis of anomalous temperature and mortality in Chapters 6 and 7.

I also developed an algorithm of converting gridded meteorological and environmental variables into area-weighted county-level data then state-level population-weighted data. The code I used to generate this algorithm is available via my ‘climate’ GitHub repository (<https://github.com/rmp15>). I also developed a temperature anomaly metric, which represents how a month’s temperature varies from what a population normally experiences: [in that month and state](#).

4 National and regional seasonal dynamics of cause-specific mortality

4.1 Overview

I used geo-coded all-cause and cause-specific mortality data, as described in Chapter 3, to comprehensively characterise the spatial and temporal patterns of all-cause and cause-specific mortality seasonality in the United States by sex and age group, through the application of wavelet analytical techniques. I used centre of gravity analysis and circular statistics methods to understand the timing of mortality minima and maxima. In addition, I identified how the percentage difference between death rates in maximum and minimum mortality months has changed over time. A total of 85.5 million deaths from all causes of death in the United States from 1980-2016 were used in this analysis.

In this chapter, I present the results of how the presence and seasonality of all-cause and cause-specific mortality has changed over time by sex and age group. I also present results on regional variation of seasonality of all-cause mortality and its relation to temperature.

4.2 Introduction

It is well-established that death rates vary throughout the year, and in temperate climates there tend to be more deaths in winter than in summer.^{53,187,188,219} ~~It has therefore been hypothesised that a warmer world may lower winter mortality in temperate climates.^{220,221} In a large country like the United States, which possesses distinct climate regions, the seasonality of mortality may vary geographically, due to localised weather patterns and regional differences in adaptation measures such as heating, air conditioning and healthcare.^{62,161,222,223} The presence and extent of seasonal variation in mortality may also itself change over time.²²⁴⁻²²⁷~~

The contents of this chapter have been published in a paper in *eLife*.³⁸

^{53,193,194,225} It has therefore been hypothesised that a warmer world may lower winter mortality in temperate climates.^{226,227} In a large country like the United States, which possesses distinct climate regions, the seasonality of mortality may vary geographically, due to localised weather patterns and regional differences in adaptation measures such as heating, air conditioning and healthcare.^{62,162,228,229} The presence and extent of seasonal variation in mortality may also itself change over time.^{230–233}

Climate region	Constituent states	Population (2016)	Mean annual temperature (1980-2016) (°C)
Central	Illinois, Indiana, Kentucky, Missouri, Ohio, Tennessee, West Virginia	50,191,326	11.6
East North Central	Iowa, Michigan, Minnesota, Wisconsin	24,418,738	8
Northeast	Connecticut, Delaware, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont	64,046,741	10.6
Northwest	Idaho, Oregon, Washington	13,069,916	8.2
South	Arkansas, Kansas, Louisiana, Mississippi, Oklahoma, Texas	45,388,414	18
Southeast	Alabama, Florida, Georgia, North Carolina, South Carolina, Virginia	59,356,072	18.4
Southwest	Arizona, Colorado, New Mexico, Utah	17,613,981	13.6
West	California, Nevada	42,280,017	16.6
West North Central	Montana, Nebraska, North Dakota, South Dakota, Wyoming	5,168,753	7.6

Table 3. Characteristics of climate regions of the United States.

4.3 Data

Full details of the data processing choices I made can be found in Chapter 3. I used VR data on all 85,453,845 deaths in the contiguous United States (i.e., excluding Alaska, Hawaii and all other American off-shore insular areas) from 1980 to 2016 along with population records to calculate monthly death rates for each age group, sex and state combination. In this analysis, I mapped each ICD-9 and ICD-10 code to four main disease categories (cancers, cardiorespiratory diseases, injuries, other). I obtained monthly population-weighted temperature from ERA-Interim.²⁴⁵²²¹

I also subdivided the national data geographically into nine climate regions used by the National Oceanic and Atmospheric Administration (Figure 12 and

~~Table 3~~ Table 3).³⁷ On average, the Southeast and South are the hottest climate regions with average annual temperatures of 18.4°C and 18°C respectively; the South also possesses the highest average maximum monthly temperature (27.9°C in July). The lowest variation in temperature throughout the year is that of the Southeast (an average range of 17.5°C). The three coldest climate regions are West North Central, East North Central and the Northwest (7.6°C, 8.0°C, 8.2°C respectively). The largest variation in temperature throughout the year is that of the coldest region, West North Central (an average range of 30.5°C), which also has the lowest average minimum monthly temperature (-6.5°C in January). The other climate regions, Northeast, Southwest, and Central, possess similar average temperatures (10 to 14°C) and variation within the year of (23°C to 26°C), with the Northeast being the most populous region in the United States.

4.4 Statistical methods

I used wavelet analysis to investigate seasonality for each age-sex group. Wavelet analysis uncovers the presence, and frequency, of repeated maxima and minima in each age-sex-specific death rate time series.^{228,229,234,235} Wavelets have been useful tools in studying the dynamics of seasonal signals in other fields of research, including weather phenomena^{230,236} and infectious disease modelling.^{231,237} Wavelet analysis is a more flexible tool than those used in previous studies to characterise seasonality, as described in Section 2.3. In brief, a Morlet wavelet, described in detail elsewhere,^{232,238} is equivalent to using a moving window on the death rate time series and analysing periodicity in each window using a short-form Fourier transform, hence generating a dynamic spectral analysis, which allows measuring dynamic seasonal patterns, in which the periodicity of death rates may disappear, emerge, or change over time. In addition to coefficients that measure the frequency of periodicity, wavelet analysis estimates the probability of whether the data are different from the null situation of random fluctuations that can be represented with white (an independent random process) or red (autoregressive of order 1 process) noise. For each age-sex group, I calculated the p-values of the presence of 12-month seasonality for the comparison of wavelet power spectra of the entire study period (1980-2016) with 1000 simulations against a white noise spectrum, which represents random fluctuations. I used the R package WaveletComp (version 1.0) for the wavelet analysis. Before analysis, I de-trended death rates using a polynomial regression, and rescaled each death rate time series so as to range between 1 and -1.

To identify the months of maximum and minimum death rates, I calculated the centre of gravity and the negative centre of gravity of monthly death rates. Centre of gravity was calculated as a weighted average of months of deaths, with each month weighted by its death rate; negative

centre of gravity was also calculated as a weighted average of months of deaths, but with each month weighted by the difference between its death rate and the year's maximum death rate. In taking the weighted average, I allowed December (month 12) to neighbour January (month 1), representing each month by an angle subtended from 12 equally-spaced points around a unit circle. Using a technique called circular statistics, a mean ($\bar{\theta}$) of the angles ($\theta_1, \theta_2, \theta_3 \dots, \theta_n$) representing the deaths (with n the total number of deaths in an age-sex group for a particular cause of death) is found using the relation below:

$$\bar{\theta} = \arg \left\{ \sum_{j=1}^n \exp(i\theta_j) \right\}.$$

Equation 2. Circular mean calculation.

In Equation 2, \arg denotes the complex number argument and θ_j denotes the month of death in angular form for a particular death j . The outcome of this calculation is then converted back into a month value.²³³ ~~Along with each circular mean, a 95% confidence interval (CI) was calculated by using 1000 bootstrap samples.~~²³⁹ Along with each circular mean, a 95% confidence interval (CI) was calculated by using 1000 bootstrap samples. The R package CircStats (version 0.2.4) was used for this analysis.

For each age-sex group and cause of death, and for each year, I calculated the percent difference in death rates between the maximum and minimum mortality months. I fitted a linear regression to the time series of seasonal differences from 1980 to 2016 and used the fitted trend line to estimate how much the percentage difference in death rates between the maximum and minimum mortality months had changed from 1980 to 2016. I weighted seasonal difference by

the inverse of the square of its standard error, which was calculated using a Poisson model to take population size of each age-sex group through time into account. This method gives a p-value for the change in seasonal difference per year, which I used to calculate the seasonal difference at the start (1980) and end (2016) of the period of study. My method of analysing seasonal differences avoids assuming that any specific month or group of months represent highest and lowest number of deaths for a particular cause of death, which is the approach taken by the traditional measure of excess winter mortality, described in Chapter 2. It also allows the maximum and minimum mortality months to vary by cause of death, sex and age group.

4.5 Results

4.5.1 Wavelet analysis

All-cause mortality in males had a 12-month seasonality in all age groups, except ages 35-44 years, for whom there was periodicity at 6 months (Figure 13). In females, there was 12-month seasonality in all groups except 5-14 and 25-34 years (p -values=0.21 and 0.25, respectively) (Figure 14). While seasonality persisted throughout the entire analysis period in older ages, it largely disappeared after late 1990s in children aged 0-4 years in both sexes and in women aged 15-24 years.

Deaths from all causes of death were seasonal in older adults (above 65 or 75 years depending on cause, p -values<0.06) (Figure 13 to Figure 22). Deaths from cardiorespiratory diseases exhibited seasonality throughout the life-course (p -values<0.06) except for males aged 5-24 years and females aged 15-24 years (p -values>0.11). In addition to older ages, injury deaths were seasonal from childhood through 44 years in women and through 64 years in men (p -

values <0.09). Consistent seasonality in cancer deaths (Figure 15 and Figure 16) only appeared after 55 years of age (p-values <0.05).

4.5.2 Centre of gravity analysis

Death rates in men aged 45 years and older and women aged 35 years and older peaked in December, January or February and were lowest in June to August, for all-cause mortality as well as for all non-injury causes of death (Figure 23). Deaths from cardiorespiratory diseases were also consistently highest in January and February and lowest in July and August across all ages. A similar temporal pattern was seen for all-cause and non-injury mortality in children younger than five years of age, whose all-cause death rate was highest in February and lowest in August. In contrast, among males aged 5-34 years, all-cause mortality peaked in June or July, as did deaths from injuries, which generally had a summer peak in males and females below 45 years of age. Where cancer deaths were found to be seasonal, in men and women 55 years and older, deaths were consistently highest in January. Peaks in cancer deaths for older age groups, along with similar results from all-cause and other cause-specific deaths, demonstrate that older age groups generally die more in the winter, a phenomenon that is largely independent of the cause of death.

The subnational centre of gravity analysis showed that all-cause mortality peaks and minima in different climate regions are consistent with the national ones (Figure 24 to Figure 27), indicating the seasonality is largely independent of geography. The relative homogeneity of the timing of maximum and minimum mortality contrasts with the large variation in seasonal temperatures among climate regions. For example, in men and women aged 65-74 years, all-cause mortality peaked in February in the Northeast and Southeast, even though the average temperatures for those regions were different by over 13°C in that month (9.3°C in the Southeast compared with -3.8°C in the Northeast). Furthermore, above 45 years of age, there was little inter-region variation in the percent seasonal difference in all-cause mortality, despite

the large variation in temperature difference between the peak and minimum months (Figure 28).

4.5.3 Change in percent difference in death rates

From 1980 to 2016, the proportional (percent) difference in all-cause death rates between peak and minimum months declined little for people older than 45 years of age (by less than eight percentage points with p-values for declining trend >0.1) ([Figure 29](#)). In contrast, the difference between peak (summer) and minimum (winter) death rates declined in younger ages, by over 25 percentage points in males aged 5-14 years and 15-24 years (p-values <0.01), largely driven in the declining difference between summer and winter injury deaths. Under five years of age, percent seasonal difference in all-cause death rates declined by 13 percentage points (p-value <0.01) for boys but only five percentage points (p-value=0.12) for girls. These declines in seasonality of child deaths were a net effect of declining winter-summer difference in cardiorespiratory disease deaths and increasing summer-winter difference in injury deaths.

4.6 Discussion

I used wavelet and centre of gravity analyses, which allowed systematic identification and characterization of seasonality of total and cause-specific mortality in the United States, and examination of how seasonality has changed over time. I identified distinct seasonal patterns in relation to sex and age group, including higher all-cause summer mortality in young men.^{61,70} Importantly, I also showed that all-cause and cause-specific mortality seasonality is largely similar in terms of both timing and magnitude across diverse climatic regions with substantially different summer and winter temperatures. Insights of this kind would not have been possible analysing data averaged over time or nationally or fixed to pre-specified frequencies.

Prior studies have noted seasonality of mortality for all-cause mortality and for specific causes of death in the United States.^{57,60–62,70,224,57,60–62,70,230} Few of these studies have done consistent national and subnational analyses, and none has done so over time, for a comprehensive set of age groups and causes of death, and in relation to regional temperature differences. My results on strong seasonality of cardiorespiratory diseases deaths and weak seasonality of cancer deaths, restricted to older ages, are broadly consistent with these studies,^{60,61,70,224,60,61,70,230} which had limited analysis on how seasonality changes over time and geography.^{60,61,70} Similarly, my results on seasonality of injury deaths are supported by a few prior studies.^{60,61,70} However, my analysis over three decades revealed variations in when injury deaths peaked and in how seasonal differences in these deaths have changed over time in relation to age group which had not been reported before.

A study of 36 cities in the United States, aggregated across age groups and over time, also found that excess mortality was not associated with seasonal temperature range.⁸¹ In contrast, a European study found that the difference between winter and summer mortality was lower in

the colder Nordic countries than in warmer southern European nations^{53,219} (the study's measure of temperature was mean annual temperature which differed from the temperature difference between maximum and minimum mortality used in my analysis although the two measures are correlated).^{53,225} (the study's measure of temperature was mean annual temperature which differed from the temperature difference between maximum and minimum mortality used in my analysis although the two measures are correlated). The absence of variation in the magnitude of mortality seasonality indicates that different regions in the United States are similarly adapted to temperature seasonality, whereas Nordic countries may have better environmental (e.g., housing insulation and heating) and health system measures to counter the effects of cold winters than those in southern Europe.

The cause-specific analysis showed that the substantial decline in seasonal mortality differences in adolescents and young adults was related to the diminishing seasonality of unintentional injuries, especially from road traffic crashes, which are more likely to occur in the summer months²³⁴ and are more common in men. The weakening of seasonality in boys under five years of age was related to two phenomena: first, the seasonality of death from cardiorespiratory diseases declined, and second, the proportion of deaths from perinatal conditions, which exhibit limited seasonality, increased.²³⁵

The cause-specific analysis showed that the substantial decline in seasonal mortality differences in adolescents and young adults was related to the diminishing seasonality of unintentional injuries, especially from road traffic crashes, which are more likely to occur in the summer months²⁴⁰ and are more common in men. The weakening of seasonality in boys under five years of age was related to two phenomena: first, the seasonality of death from cardiorespiratory diseases declined, and second, the proportion of deaths from perinatal conditions, which exhibit limited seasonality, increased.²⁴¹

In contrast to young and middle ages, mortality in older ages, where death rates are highest, maintained persistent seasonality over a period of three decades (I note that although the percent seasonal difference in mortality has remained largely unchanged in these ages, the absolute difference in death rates between the peak and minimum months has declined because total mortality has a declining long-term trend). This finding demonstrates the need for environmental and health service interventions targeted towards this group irrespective of geography and local climate. Examples of such interventions include enhancing the availability of both environmental and medical protective factors, such as better insulation of homes, winter heating provision and flu vaccinations, for the vulnerable older population.^{236,242} Social interventions, including regular visits to the isolated elderly during peak mortality periods to ensure that they are optimally prepared for adverse conditions, and responsive and high-quality emergency care, are also important to protect this vulnerable group.^{53,226,237,53,242,243} Emergent new technologies, such as always-connected hands-free communications devices with the outside world, in-house cameras, and personal sensors also provide an opportunity to enhance care for the older, more vulnerable groups in the population, especially in winter when the elderly have fewer social interactions.^{238,244} Such interventions are important today and will remain so as the population ages, and climate change increases the within- and between-season weather variability.

4.7 Summary

I used the mortality and weather data, described in Chapter 3, to analyse the dynamics of seasonal death rates in the United States from 1980 to 2016. Using a novel application of wavelets, centre of gravity analysis and circular statistics, I examined seasonality of death rates by climate region, cause of death sex and age group. While overall deaths in a year were highest in winter and lowest in summer, a greater number of young men died during summer – mainly

due to injuries – than during winter. Seasonal differences in deaths among young children have largely disappeared and seasonal differences in the deaths of older children and young adults have become smaller. Deaths among women and men aged 45 or older peaked between December and February – largely caused by respiratory and heart diseases, or injuries. Deaths in this older age group were lowest during the summer months. Death patterns in older people changed little over time. No regional differences were found in seasonal death patterns, despite large climate variation across the United States.

5 Statistical modelling of anomalous monthly temperature and monthly mortality

5.1 Overview

With few exceptions,^{108,109} current climate change risk assessments typically extrapolate from changes in mortality in relation to daily temperature, described in detail in Section 2.4.²⁻
~~4,119,239,2402-4,119,245,246~~ Climate change, however, will fundamentally modify weather, including seasonal weather patterns, compared to long-term norms, and hence can disrupt long-term adaptation. I have ~~built on adapted~~ previous work with Bayesian spatio-temporal modelling used to associate death rates with absolute pollution levels using annual data.²¹⁷ ~~When considering the association of temperature and mortality, an annual association approach can overlook the adaptation to the seasonal cycle throughout the year and therefore how monthly deviations from long term norm temperatures may impact health outcomes.~~²²³ ~~When considering the association of temperature and mortality, an annual association approach would overlook the adaptation to the seasonal cycle throughout the year. Further, while absolute pollution levels are appropriate for associating death rates with air pollution, associating absolute annual or monthly temperatures with death rates would overlook adaptation to local long-term norm temperatures. So rather than taking absolute temperatures, I consider deviation from monthly state-specific norm, as described in Chapter 3, and therefore how monthly deviations from long-term norm temperatures may impact health outcomes.~~

In this chapter, I describe how I ~~built upon adapted~~ previous work using Bayesian spatio-temporal models of health and environment to create a temperature-mortality association by cause of death, month, sex and age group. I summarise the model features. I then explain how I implemented the model.

5.2 Objectives

My aim was to quantify the association of monthly mortality with anomalous monthly temperature, and the potential change in numbers of deaths given an increase of anomalous temperature relative to a long-term norm temperature realistic under present weather dynamics, as described in Section 3.3.6, as well as future climate change.²⁴⁴²⁴⁷

5.3 Data

I fitted the model using United States VR data from 1980 to 2016, as well as anomalous temperature data for the same period from ERA-Interim reanalysis, described in Chapter 3. In brief, I divided up the data by cause of death, state, month, sex and age group for epidemiological reasons as well as computational tractability.

5.4 Model specification

I formulated a Bayesian spatio-temporal model. The outcome was deaths from various causes. I carried out all analyses separately by sex and age group, because death rates from various causes of death vary by sex and age group, as might their associations with temperature.

As is common in the field, I modelled the number of deaths in each year as following a Poisson distribution. For each state over time, I predicted the number of deaths, being the product of death rate ($death\ rate_{state-time}$) and population ($population_{state-time}$), evaluating against the observed number of deaths ($deaths_{state-time}$) as shown in Equation 3:

$$deaths_{state-time} \sim \text{Poisson}(death\ rate_{state-time} \cdot population_{state-time})$$

Equation 3. Temperature model Poisson distribution.

I modelled the log-transformed death rates as a sum of components that depend on location (*state*) of death, month of year (*month*), overall time (*time*) and temperature anomaly (*Anomaly*) as shown in Equation 4:

$$\begin{aligned}
\log(death\ rate_{state-time}) = & \\
& \alpha_0 + \beta_0 \cdot time + \\
& \alpha_{state} + \beta_{state} \cdot time + \\
& \alpha_{month} + \beta_{month} \cdot time + \\
& \alpha_{state-month} + \beta_{state-month} \cdot time + \\
& v_{time} + \\
& \gamma_{month} \cdot Anomaly_{state-time} + \\
& \varepsilon_{state-time}
\end{aligned}$$

Equation 4. Temperature model.

In summary, the α parameters are intercepts; β parameters are temporal slopes; the v parameter is a random walk over time; the γ parameter represents the logarithm of the rate ratio per 1°C increase in anomaly, with a term for each of the twelve months of the year; and the ε parameter is the overdispersion term. The model parameters and their priors from Equation 4 are included in Table 4 and Table 5 respectively for convenient reference.

Offset	
$population_{state-time}$	Population offset
Intercepts	
α_0	Global intercept
α_{state}	State intercept
α_{month}	Month intercept
$\alpha_{state-month}$	State-month interaction intercept
Time trends	
β_0	Global slope
β_{state}	State slope
β_{month}	Month slope
$\beta_{state-month}$	State-month interaction slope
Random walk	
v_{time}	Random walk over time
Temperature anomaly coefficient	
γ_{month}	Temperature slope
Overdispersion	
$\varepsilon_{state-time}$	Overdispersion

Table 4. Temperature model parameters.

Intercepts	
α_0	Uniform($-\infty, \infty$)
α_{state}	Multivariate Normal(0, $[\tau_{\alpha_{state}}(D - W)]^{-1}$)
$\log(\tau_{\alpha_{state}})$	logGamma(1,0.0001)
α_{month}	$\alpha_{month_m} \sim \text{Normal}(\alpha_{month_{m-1}}, \tau_{\alpha_{month}}^{-1})$
$\log(\tau_{\alpha_{month}})$	logGamma(1,0.0001)
$\alpha_{state-month}$	Multivariate Normal(0, $[\tau_{\alpha_{state-month}}(D - W)]^{-1}$)
$\log(\tau_{\alpha_{state-month}})$	logGamma(1,0.0001)
Time trends	
β_0	Normal(0, 1000)
β_{state}	Multivariate Normal(0, $[\tau_{\beta_{state}}(D - W)]^{-1}$)
$\log(\tau_{\beta_{state}})$	logGamma(1,0.0001)
β_{month}	$\beta_{month_m} \sim \text{Normal}(\beta_{month_{m-1}}, \tau_{\beta_{month}}^{-1})$
$\log(\tau_{\beta_{month}})$	logGamma(1,0.0001)
$\beta_{state-month}$	Multivariate Normal(0, $[\tau_{\beta_{state-month}}(D - W)]^{-1}$)
$\log(\tau_{\beta_{state-month}})$	logGamma(1,0.0001)
Random walk	
$v_{month-year}$	$v_{month-year_t} \sim \text{Normal}(v_{month-year_{t-1}}, \tau_{v_{month-year}}^{-1})$
$\log(\tau_{v_{month-year}})$	logGamma(1,0.0001)
Temperature anomaly coefficient	
γ_{month}	γ_{month}
$\log(\tau_{\gamma_{month}})$	$\log(\tau_{\gamma_{month}})$
Overdispersion	
$\epsilon_{state-time}$	Normal(0, τ_{ϵ}^{-1})
$\log(\tau_{\epsilon})$	logGamma(1,0.0001)

Table 5. Temperature model priors.

5.4.1 National terms

The model described in Equation 4 contains terms that represent the national level and trend in mortality, with α_0 as the common intercept for log-transformed death rates, and β_0 the common time slope. The national term α_0 represents the mean log death rate in the first year of the period of study (1980) across months and states conditioning on other terms in the model. β_0 captured the average change in log mortality over time across states and months. I gave both α_0 and β_0 non-informative uniform priors (Table 5).

5.4.2 Month terms

Death rates also vary by month, which may be partly related to temperature and partly due to other factors, and tend to do so smoothly across adjacent months.³⁸ ~~Therefore, I allowed each~~ Allowing for variation by month ~~of~~ here accounts for seasonal differences throughout a year, as, for example, a December will only be compared to another December, rather than to other points in the year. Therefore, I allowed each month of the year to have a different mortality level and trend, with α_{month} the month-specific intercept for log-transformed death rates and β_{month} the month-specific time slope. I used a first-order random walk for the month terms to smooth the coefficients, widely used to characterise smoothly varying associations.²⁴²²⁴⁸ The random walk between month terms had a cyclic structure, so that December was adjacent to January.

5.4.3 State terms

I also included state random intercepts and slopes for death rates, with α_{state} as the state-specific intercept for log-transformed death rates and β_{state} the state-specific time slope. These terms measure deviations of each state from national values and allow variation in level and trend in mortality by state.

In addition, death rates in neighbouring states may be more similar than in those further away. I specified the α_{state} and β_{state} parameters as multivariate normal (Table 5). The specification of the prior pertaining to α_{state} and β_{state} corresponds to a Conditional Autoregressive (CAR) spatial model.²⁴³²⁴⁹ This allows mortality levels and trends of states to be estimated based on their own data as well as using those of their neighbours via spatially-structured random effects. The extent to which information is shared between neighbouring states depends on the uncertainty of death rates in a state and the empirical similarity of death rates in neighbouring states. The spatial structure of the CAR prior is imposed via an adjacency matrix \mathbf{W} , where the off-diagonal elements of the matrix are specified as $w_{a,b}$, which is 1 if a and b are neighbours, and 0 otherwise. D represents the diagonal matrix of the number of neighbours for each point on the spatial region. The Gaussian Markov random field (GMRF) property in the formulation of the CAR model, specifically in the covariance matrix $[\tau_{\alpha_{state}}(D - \mathbf{W})]^{-1}$ for α_{state} gives rise to a sparse precision matrix (Table 5). This gives the model computational benefits for inference, with considerable gain in processing speeds.²⁴²²⁴⁸

5.4.4 Interaction terms

I also included state-month interactions for intercepts ($\alpha_{state-month}$) and slopes ($\beta_{state-month}$) to allow variation in mortality levels and trends in a particular state for different months and vice-versa. Each month for $\alpha_{state-month}$ and $\beta_{state-month}$ had a CAR specification with the spatially-structured random effect as described for α_{state} and β_{state} . This set of terms allowed each month to have a spatial pattern that differed from the mean month pattern and vice-versa.

5.4.5 Non-linear time trends

I captured non-linear change over time with a first order random walk, v_{time} .²⁴² An over-dispersion term ($\varepsilon_{state-time}$) captured the variation unaccounted for by other terms in the model, modelled as $Normal(0, \tau_\varepsilon^{-1})$.

The terms described in Sections 5.4.2-5.4.4 therefore implicitly adjusted any determinant of mortality that is state-, month-, or state-month-specific, as fixed effects (α_{month} , α_{state} , $\alpha_{state-month}$), as well as over time (β_{month} , β_{state} , $\beta_{state-month}$). Therefore, relevant to discussion of confounding factors in Section 1.1 below, the only factors with potentially confounding impact on my results that have not been adjusted for would be those that have the same state-month variability as anomalous temperature.

5.4.5 Non-linear time trends

I captured non-linear change over time with a first-order random walk, v_{time} .²⁴⁸ An over-dispersion term ($\varepsilon_{state-time}$) captured the variation unaccounted for by other terms in the model, modelled as $Normal(0, \tau_\varepsilon^{-1})$.

5.4.6 Temperature anomaly term

Finally, I included a term that relates log-transformed death rate to the state-month temperature anomaly, $\gamma_{month} \cdot Anomaly_{state-time}$. The coefficients of γ_{month} represent the logarithm of the rate ratio per 1°C increase in anomaly, akin to risk ratios in analyses of prospective cohorts. There was a separate coefficient for each month which means that an anomaly of the same magnitude could have different associations with mortality in different months. The design of this term, along with the terms described in Sections 5.4.2-5.4.4, also ensured that my model analysed the differences between the same month in different years, rather than between

months in the same year, which avoids issues regarding the confounding role of common holidays such as Christmas. As with the month-specific intercepts and trends, I used a cyclic random walk to smooth the coefficient of the temperature anomaly across months.

I also considered using apparent temperature described in Equation 5 below, as an alternative measure of temperature used in previous work on temperature and morbidity and mortality:²⁴⁴²⁵⁰

$$T_{app} = -2.563 + 0.944T_a + 0.0153(T_d)^2$$

Equation 5. Apparent temperature (T_{app}) calculation, where T_a is air temperature and T_d is dew-point temperature.

I plotted apparent temperature monthly anomalies derived from ERA-Interim against the equivalent 2-metre temperature values derived from my analysis in Chapter 3 by state (

Figure 30). Figure 30). The results were highly-correlated, with a correlation coefficient of 0.95 across all states and months during 1980-2016. I therefore decided to use 2-metre temperature-derived values for all further analyses.

5.4.7 Hyperparameters on precisions of random effects

As in previous work,²⁵ weakly informative hyper-priors were specified on the logarithm of the precisions of the random effects so that the parameters' estimates were data driven. Here, the **loglogs** of the hyper-priors were given a distribution of $\text{logGamma}(1, 0.0001)$.

Age group (years)	Percentage of total deaths 1980-2016	RW1 DIC	RW2 DIC	DIC difference	Minimum DIC	RW1 run time (mins)	RW2 run time (mins)	Minimum time
0-4	1.8	38136.7	38096.8	40.0	RW2	43.5	161.8	RW1
5-14	0.4	28354.6	28330.1	24.5	RW2	37.9	101.4	RW1
15-24	2.2	39053.2	39008.2	45.0	RW2	40.4	140.8	RW1
25-34	3.0	40502.7	40335.4	167.3	RW2	40.2	109.9	RW1
35-44	4.4	41266.8	41118.7	148.1	RW2	42.7	104.4	RW1
45-54	8.0	44345.3	44339.1	6.2	RW2	55.5	120.8	RW1
55-64	14.4	49154.6	49305.4	-150.8	RW1	40.1	94.4	RW1
65-74	22.1	52657.3	52999.1	-341.8	RW1	34.4	104.4	RW1
75-84	26.3	53059.1	53565.5	-506.4	RW1	39.9	97.8	RW1
85+	17.6	48906.7	49402.3	-495.6	RW1	41.4	111.6	RW1

Table 6. DIC values and run times from comparison of random walk terms. Orange colours indicate outcomes where the subnational RW model has performed better, with blue for the national RW model. The percentage of total deaths column is coloured by value, with darker values representing higher values.

5.4.8 Alternative random walk structure

In developing the temperature model, described in Equation 4, I also considered an alternative structure which included the extra non-linear time trend, $\nu_{state-time}$. This term contained independent first-order random walks for each state, added in Equation 6:

$$\begin{aligned} \log(death rate_{state-time}) = & \\ & \alpha_0 + \beta_0 \cdot time + \\ & \alpha_{state} + \beta_{state} \cdot time + \\ & \alpha_{month} + \beta_{month} \cdot time + \\ & \alpha_{state-month} + \beta_{state-month} \cdot time + \\ & \nu_{time} + \\ & \nu_{state-time} + \\ & \gamma_{month} \cdot Anomaly_{state-time} + \\ & \varepsilon_{state-time} \end{aligned}$$

Equation 6. Temperature model with alternative random walk structure.

I compared how these two models performed. I ran the models from the temperature model (Equation 4) and alternative model (Equation 6) for all-cause mortality for male age groups during a 10-year subset of the full set of years (1980-1989). This allowed me to test the model fit without the burden of the long run times using the full time series of data. I recorded the Deviation Information Criterion (DIC) values, as well as the run times (Table 6), where I called the original model ‘RW1’ (Equation 4) and the alternative ‘RW2’ (Equation 6). The DIC is commonly used to compare and evaluate the fit of models to the data in a Bayesian setting.²⁴⁵

~~It is a good candidate for evaluating hierarchical models as it takes into account parsimony as well as overall model fit.²⁵¹~~ It is a good candidate for evaluating hierarchical models as it takes into account parsimony as well as overall model fit. Differences in the DIC were small where values from the RW2 model were lower, and larger when values from the RW1 model were lower. Further, the RW1 model had a lower DIC for the highest four age groups (55-64, 65-74, 75-84, 85+ years), which contained the majority of the deaths in the data, at over 80% of deaths (Table 4). Run times for the subnational model were an order of magnitude longer

than the national model. This would have made the time required to run the model for all sub-causes of death unfeasible, especially considering that the models were tested repeatedly. Considering the run times in conjunction with DIC values, as well as where most of the deaths were by age group, I decided to perform the analysis with the original temperature model in Equation 4.

5.4.9 Inclusion of long-term norm temperature

In addition to the anomalous temperature term, γ_{month} , I also considered including the long-term norm values by state in the model. This was motivated by the idea that mortality may depend on mean monthly temperature in addition to anomalous temperature. I created the following model as a comparison to the original model (Equation 4), given below in Equation 7:

$$\begin{aligned} \log(death\ rate_{state-time}) = & \\ & \alpha_0 + \beta_0 \cdot time + \\ & \alpha_{state} + \beta_{state} \cdot time + \\ & \alpha_{month} + \beta_{month} \cdot time + \\ & \alpha_{state-month} + \beta_{state-month} \cdot time + \\ & \nu_{time} + \\ & \gamma_{month} \cdot Anomaly_{state-time} + \\ & \delta_{month} \cdot Norm\ temperature_{state-month} + \\ & \varepsilon_{state-time} \end{aligned}$$

Equation 7. Temperature model with long-term norm temperature term.

I performed sensitivity runs of models based on Equation 4 and Equation 7 with transport injuries, a subset of causes from unintentional injuries for the paper based on Chapter 6. Comparing γ_{month} parameters from model runs using Equation 4 and Equation 7, the values of γ_{month} were robust to the inclusion of δ_{month} terms (Figure 31). There was an overall correlation of 0.99 between the two sets of parameters. I did not include the term in my model.

5.4.10 Temperature anomaly coefficient structure

I also considered a temperature model with a piecewise linear structure for the temperature anomaly coefficients, as shown in Equation 8:

$$\begin{aligned} \log(death\ rate_{state-time}) = & \\ & \alpha_0 + \beta_0 \cdot time + \\ & \alpha_{state} + \beta_{state} \cdot time + \\ & \alpha_{month} + \beta_{month} \cdot time + \\ & \alpha_{state-month} + \beta_{state-month} \cdot time + \\ & v_{time} + \\ & (\gamma_{month+}) \cdot (\max(Anomaly_{state-time}, 0)) + \\ & (\gamma_{month-}) \cdot (\min(Anomaly_{state-time}, 0)) + \\ & \varepsilon_{state-time} \end{aligned}$$

Equation 8. Temperature model with piecewise temperature anomaly term.

This model gives two sets of monthly temperature coefficients; one set of twelve for negative anomalies (γ_{month-}), with another set of twelve for positive anomalies (γ_{month+}). The additional set of parameters would allow the potential for effects of anomalies below the long-term norm to be distinct from the effects of anomalies above the long-term norm. However, a disadvantage of this structure is that the amount of data available to infer each set of temperature coefficients would be reduced.

I compared models specified in Equation 4 and Equation 8 for all age groups and sexes for the four main causes of death groups for 1980-2016 and compared the DIC values. The results of this are summarised in Table 7. The DIC values indicate that 72/80 (90%) of the runs favoured the non-piecewise model overall (Equation 4). The case was the same for cardiorespiratory diseases, cancers, injuries, and other causes of death separately, with 20/20 (100%), 17/20 (85%) and 16/20 (80%) respectively of the comparisons favouring the non-piecewise model. The DIC preference for the non-piecewise model (Equation 4) is likely due to the fact that my temperature is centred around a long-term local norm temperature, which is a distinct approach

from considering the absolute local temperature as an input. Similar to a study of daily temperature and mortality,² where it was shown that the minimum mortality temperature was most often in the 80th to 90th percentile of the long-term temperature distribution for most cities, the absolute temperature which causes the lowest associated risk to mortality is unlikely to be the long-term norm. It is possible to choose a model for each age group-sex-cause of death combination separately, but I decided to select a consistent model to be parsimonious. Using a consistent model also means that equivalent parameters from model runs in various causes of death could be compared directly, as well as using the same amount of data points per inferred parameter of γ_{month} in the temperature model (Equation 4).

Cause	Males	Females	Both sexes together
Cardiorespiratory diseases	10/10	10/10	20/20
Cancers	9/10	10/10	19/20
Injuries	7/10	10/10	17/20
Other	8/10	8/10	16/20
All causes	34/40	38/40	72/80

Table 7. Number of model run comparisons which favoured the temperature model (Equation 4) over the temperature model with piecewise temperature anomaly term (Equation 8).

5.4.11 Additional extreme temperature measures

Together with a monthly temperature anomaly, I also tested including a second measure of anomaly in the model. The additional measures were related to extreme anomalous temperature:

- temperature anomaly based on 90th percentile (°C) of daily mean temperatures within a month, compared to 30-year (long-term) norm of 90th percentile for each state and month;
- number of days in a month above the long-term 90th percentile of norm temperature (adjusted for length of month); and
- number of 3+ day episodes above the long-term 90th percentile of norm temperature (adjusted for length of month).

The correlations among the variables and anomaly based on mean were between 0.60 and 0.89 (Table 8). The estimated rate ratios of temperature anomaly based on daily means (i.e., the anomaly measure used in the main analysis) were robust to the addition of alternative measures of anomaly, while the coefficients of the additional measures were generally not significant and with large credible intervals. Therefore, I did not include the alternative additional measures of extreme anomalous temperature in the main analysis.

Temperature variables	Anomaly of mean (main analysis)	Anomaly of 90 th percentile	Number of days above long-term 90 th percentile	Number of 3+ day episodes above long-term 90 th percentile
Anomaly of mean (main analysis)		0.79	0.75	0.6
Anomaly of 90 th percentile	0.79		0.89	0.77
Number of days above long-term 90 th percentile	0.75	0.89		0.86
Number of 3+ day episodes above long-term 90 th percentile	0.6	0.77	0.86	

Table 8. Correlation coefficients between anomaly of mean daily temperature and measures of extreme anomalous temperature. Each correlation coefficient was calculated in each state for each month for 1980-2016. The values shown are the means over all states and months.

5.4.12 State-specific temperature model specification

I also considered a temperature model which gave a separate coefficient for each state in each month. This means that an anomaly of the same magnitude could have different associations with mortality in different states for the same month, and vice-versa. The model is described below in Equation 9:

$$\begin{aligned} \log(death\ rate_{state-time}) = & \\ & \alpha_0 + \beta_0 \cdot time + \\ & \alpha_{state} + \beta_{state} \cdot time + \\ & \alpha_{month} + \beta_{month} \cdot time + \\ & \alpha_{state-month} + \beta_{state-month} \cdot time + \\ & v_{time} + \\ & \gamma_{state-month} \cdot Anomaly_{state-time} + \\ & \varepsilon_{state-time} \end{aligned}$$

Equation 9. Temperature model with state-specific anomaly coefficients.

However, the model in Equation 9 struggled to fit the extra temperature slopes and give plausible results when running tests on the causes of death with the smallest number of deaths. The fundamental problem of shrinkage of data emerges when trying to estimate slopes for each state. To avoid spurious results, I ran this model only using cardiorespiratory disease deaths aggregated together, as it is the cause of death group with the largest proportion of total deaths. The results of this analysis are found in Chapter 7.

To compare the results of my original temperature model based on Equation 4 and the alternative temperature model based on Equation 9, I summarised the total change in deaths predicted by each model for cardiorespiratory disease deaths for 1980-2016 in the entire contiguous United States, described fully in Chapter 7. The total reduction in cardiorespiratory disease deaths predicted by the original temperature model (Equation 4) is 4,369 (4,024, 4,705), whereas the alternative temperature model (Equation 9) predicted a total reduction of 5,369

(4,956, 5,793) (Figure 32). Of the difference between the model predictions, 69% were from differences in deaths from those 75 years and older across both sexes (Figure 32).

5.5 Model fitting

~~My temperature model, described by Equation 4, had a large number of parameters to estimate (over 5000). This high dimensionality and complex structure of correlation posed a great challenge to traditional MCMC samplers, such as Gibbs sampling in WinBUGS.~~¹⁷⁴

5.5 Confounders, effect modifiers and mediators

5.5.1 Confounders

A confounder is a variable that influences the exposure of interest (in my case anomalous monthly temperature) as well as the outcome variable (in my case monthly death rates).²⁵² Without adjusting for confounders in an analysis, the true causal effect of the original exposure could be over- or underestimated, depending on how the confounders are associated with the original exposure and outcome.

Figure 33 displays a Directed Acyclic Graph (DAG) relevant to considerations in my thesis. DAGs are commonly used in the epidemiological community to identify variables which must be measured and controlled for to obtain unconfounded effect estimates.²⁵³ In the DAG in Figure 33, both air pollution and temperature are exposures manifested by the physics of the atmosphere on earth, summarised in Figure 33 by the term ‘weather regimes’. Temperature itself can also affect levels of air pollution. Weather regimes are difficult to quantify, and are therefore difficult to adjust for. If appropriate adjustments cannot be made to account for the common influence of weather regimes, then the air pollution path is not fully blocked, and it should be adjusted for.

In my model, in particular in terms described in Sections 5.4.2-5.4.4, I implicitly adjusted for any (unmeasured) determinant of mortality that is state-, month-, or state-month specific.

Therefore, anything that affects mortality and changes linearly over time is adjusted for.
Beyond this, my choice of exposure, i.e., temperature anomaly, explains variation in mortality
in equivalent months beyond what is already accounted for. Only factors that have the same
anomaly as monthly temperature remain. Air pollution may be one such factor. While air
pollution levels may affect the temperature-mortality relationship, I have not included this in
my analysis, because the air pollution data I found only being annual data and not covering my
entire study period (1980-2016). A recent study I co-authored using air pollution data to
examine changes in life expectancy used data from 1999 onwards only.²²³ There would be
other potential meteorological exposure variables which may be relevant if the weather regimes
pathway is not fully blocked by the month stratification. These could include, for example,
relative humidity, amount of sunlight, and rainfall.

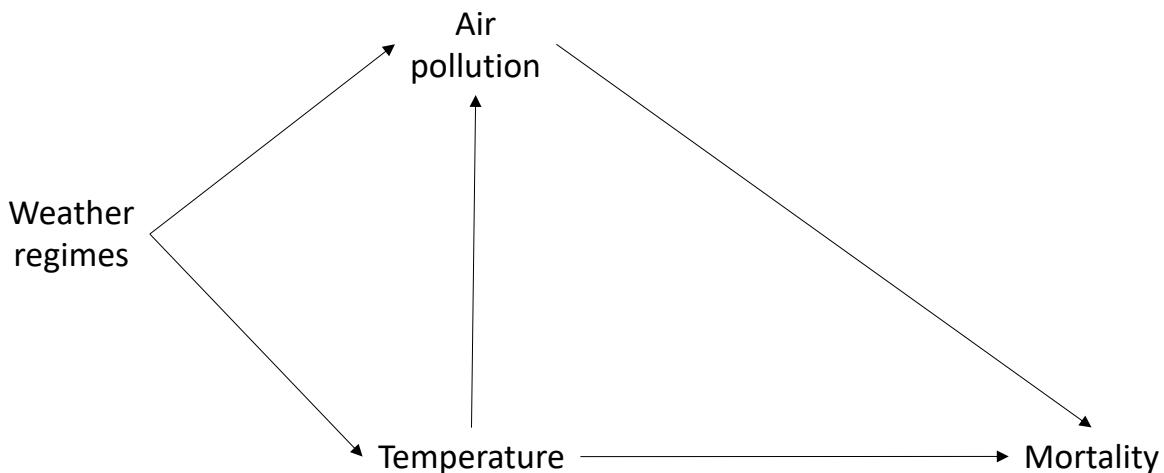


Figure 33. DAG describing the potential confounding of air pollution on a study of temperature and mortality.

5.5.2 Effect modifiers

Effect modification is where the magnitude of an exposure effect varies across levels of another variable.²⁵² In the model I used here for my thesis, I accounted for the potential effect modification by month, sex and age group (Equation 4 as used in Chapters 6 and 7) and by state (Equation 9 as used in Chapter 7), based on previous research explained in Chapter 2. In my thesis, I did not examine the effect modification by air pollution levels; rather, my results in Chapters 6 and 7 give the average effect across distributions of air pollution levels. This is analogous to summarising various age-modified risks by a single value to represent risk across all ages, common in epidemiological studies.

Depending on the cause of death, additional factors may be relevant to include in further analysis, which may also modify the association between anomalous temperature and death rates. For my study of injuries in Chapter 6, relevant effect modifiers could include coverage of rivers and lakes in a state, road density or availability of alcohol, and air conditioning usage, as some injury deaths may be more or less likely depending on the presence of these state characteristics. For my study of cardiorespiratory diseases and cancers in Chapter 7, relevant effect modifiers could include air conditioning use, obesity and smoking prevalence, as well as hospital access.

5.5.3 Mediators

A mediator is a variable along a causal pathway between the exposure and the outcome.²⁵² For example, warmer temperatures may result in people drinking more alcohol, and alcohol impairs a driver's ability to drive without getting into transport accidents. Both increases in temperature and increases in alcohol levels in a driver's blood increase the chances of dying, but increases in temperature may also increase the potential for the population to drink alcohol.

The fact that some potential mediators are not included in the model suggests that care is required when proposing mechanisms of causation between temperature and mortality for various causes of death. The causality mechanism may be direct, i.e., temperature directly affects mortality, or it may be indirect, i.e., temperature affects another exposure or variable, which in turn affects mortality. Whichever it may be, the predictive value of the work is not reduced. Rather, further exploration of the mechanisms behind the association would be valuable.

5.6 Model fitting

My temperature model, described by Equation 4, had a large number of parameters to estimate (over 5000). This high dimensionality and complex structure of correlation posed a great challenge to traditional MCMC samplers, such as Gibbs sampling in WinBUGS.¹⁸⁰

I fitted the models using INLA, via the R-INLA software (version 17.06.20) within the R software (version 3.5.2).²⁴⁶²⁵⁴ I ran my models on a computing cluster containing ten Intel Xeon E5-4650v2 processors, each of which have four cores clocked at 2.4 GHz. This resulted in 40 total cores for processing, with 512GB of RAM. The total time for the temperature model (Equation 4) runs was 40 days. The total time for temperature model with state-specific anomaly coefficients (Equation 9) runs for cardiorespiratory disease deaths was 21 days.

5.65.7 Model evaluation

To measure the performance of my temperature model, described in Equation 4, I calculated measures of performance based on the absolute difference between the raw death rates and the fitted death rates from my model output. This evaluation included the bias (sum of differences between the raw death rates and fitted death rates) and deviation (sum of the absolute value of these differences) as a non-directional measure of fit. I calculated all the bias and deviation

values for each cause of death, sex and age group across all states, months and years. Table 9 shows summary values for a representative age-sex group (males from 65-74 years) by cause of death from fitting for the entire period of study (1980-2016). An example of the fit for cardiorespiratory disease deaths is given in Figure 34. There is understandably smoothing of death rates in smaller states due to borrowing of information in the CAR model for intercepts and slopes from Equation 4.

Cause	Median bias	Median deviation
Average across causes	0.33	1.93
Ischaemic heart disease	0.29	4.16
Cerebrovascular diseases	0.33	2.00
Other cardiovascular diseases	0.26	2.85
Chronic obstructive pulmonary disease	0.31	2.32
Respiratory infections	0.30	1.25
Other respiratory diseases	0.32	1.27
Cancers	0.30	5.23
Transport	0.32	0.97
Falls	0.33	0.85
Drownings	0.34	0.38
Other unintentional injuries	0.45	0.62
Assault	0.40	0.50
Suicide	0.32	1.05
Causes other than cancers, cardiorespiratory diseases and injuries	0.32	3.53

Table 9. Predictive validity metrics of model fit for males aged 65 to 74 years for 1980-2016 using temperature model (Equation 4). All units are in deaths per 100,000.

5.75.8 Excess risk and uncertainty

I calculated the rate ratio per 1°C increase in temperature anomaly as the exponential of the coefficients of the temperature anomaly terms γ_{month} :

$$\text{Relative risk}_{month} = e^{(\gamma_{month})}$$

Equation 10. Relative risk calculation using anomalous temperature parameters from temperature model (Equation 4).

The excess relative risk is given by the relative risk minus 1. Excess relative risk here measures the proportional change in monthly death rate per 1°C increase in temperature anomaly.

In Chapters 6 and 7, I use excess risk values from my model to estimate the annual change in deaths predicted by a 1°C temperature anomaly in each month and state (Figure 46 in Chapter 6 and Figure 59 in Chapter 7). This is representative of an anomaly which is realistic in our lifetimes under current projections of global climate change,^{244²⁴⁷} as well as within the range of anomaly size experienced by many states (Figure 9 in Chapter 3). For this calculation, I multiplied the actual death counts for each state, month, sex and age group in 2016 by the corresponding excess relative risk.

The uncertainty in the annual change in deaths are obtained from 5000 draws from the posterior marginal of each month's excess relative risk, as in previous work in similar models of mortality.²⁵ The reported 95% credible intervals, quoted in brackets where appropriate, are the 2.5th to 97.5th percentiles of the sampled values.

5.85.9 Summary

I have developed a Bayesian spatio-temporal model (Equation 4) to quantify the association of anomalous temperature with causes of death in the United States at national and sub-national

levels. I fitted monthly death rates by sex and age group from a parsimonious but mutually exclusive and collectively exhaustive set of causes of death. Using these advances and the model output, I could generate estimates of the net change in deaths associated with increase in anomalous temperature, based on the model output, by cause of death, month, sex and age group in Chapters 6 and 7.

6 Anomalous monthly temperature and seasonality of monthly injury mortality

6.1 Overview

I applied the Bayesian spatio-temporal model, as described in Chapter 5, to injury mortality data in the United States, as described in Chapter 3. I estimated how anomalous temperatures, defined as in Chapter 3, affect deaths from different intentional (transport, falls and drownings) and unintentional (assault and suicide) injuries. A total of 5.8 million deaths from injury causes of death in the United States from 1980-2016 were used in this analysis. In this chapter, I present the results of how a 1°C anomalously warm year would change the total number of injury deaths in the United States, by type of injury, sex and age group.

6.2 Introduction

The potential health impacts of anthropogenic climate change are one of the key drivers for efforts to mitigate greenhouse gas emissions and for pursuing adaptation measures.²⁴⁷⁻²⁴⁹ ~~Current assessments of the health effects of climate change largely focus on parasitic and infectious diseases, and cardiorespiratory and other chronic diseases.~~^{10,119,239,240,247-249} Less research has been conducted on injuries,^{108,132,133,255-257} ~~Current assessments of the health effects of climate change largely focus on parasitic and infectious diseases, and cardiorespiratory and other chronic diseases.~~^{10,119,245,246,255-257} Less research has been conducted on injuries,^{108,132,133} especially in a consistent way across injury types and demographic subgroups of the population, even though death rates from injuries vary seasonally,^{38,57} which means that temperature may play a role in their pathogenesis.

My aim was to evaluate how deaths from various injuries may be affected by changes in temperature that could arise as a result of global climate change in the United States.

The contents of this chapter are in a paper which is currently under review in *The New England Journal of Nature Medicine*.

6.3 Data

Full details of the data processing choices I made can be found in Chapter 3. Here, I used VR data on all 5,764,316 injury deaths in the contiguous United States from 1980 to 2016 along with population records to calculate monthly death rates for each type of injury, state, sex and age group combination. In this analysis, I mapped each ICD-9 and ICD-10 code to three unintentional (transport, falls, drownings) and two intentional (assault, suicide) types of injury deaths (Table 10). The remainder were from a heterogeneous group of ‘other unintentional injuries’, within which the type of injury that led to death varied by sex and age group. I obtained monthly population-weighted temperature anomalies from ERA-Interim by a process described in Chapter 3.²¹⁵

²²¹

6.4 Statistical methods

I analysed the association of monthly injury death rates with anomalous temperature using a Bayesian spatio-temporal model, described in Chapter 5. ~~Analyses were done separately by injury type, sex and age group (0-4 years, 10-year age groups from 5 to 84 years, and 85+ years) because injury death rates vary by sex and age group,^{38,57,250} as might their associations with temperature.~~

. Analyses were done separately by injury type, sex and age group (0-4 years, 10-year age groups from 5 to 84 years, and 85+ years) because injury death rates vary by sex and age group,^{38,57,258} as might their associations with temperature.

Injury type	ICD-9	ICD-10
All injuries	E800-E999	V0-Y89
Unintentional injuries	E800-E949, E980-E989	V0-V99, W0-99, X0-X59, Y10-Y34, Y40-Y89
Transport	E800-E807, E810-E838, E840-E849	V0-V99
Falls	E880-E888	W0-W19
Drowning	E910-E910	W65-W74
Intentional injuries	E950-E979.9, E990-E999	X60-X99, Y0-Y9, Y35-Y39
Suicide	E950-E959	X60-X84
Assault	E960-E979, E990-E999	X85-X99, Y0-Y9, Y35-Y39

Table 10. Injury groups used in the analysis with ICD-9 and ICD-10 codes.

6.5 Results

6.5.1 Summary of injury deaths

From 1980 to 2016, 4,006,454 boys and men and 1,757,862 girls and women died from an injury, accounting for 9.2% and 4.2% of all male and female deaths respectively (Figure 35). 95.6% of male injury deaths and 93.9% of female injury deaths were in those aged 15 years and older, and over half (52.6%) of male injury deaths were in those aged 15-44 years (Figure 35). In contrast with males, there was less of an age gradient in females after 15 years of age.

Injuries from transport, falls, drownings, assault, and suicide accounted for 79.0% of injury deaths in males and 72.1% in females. Transport was the leading injury cause of death in women younger than 75 years and men younger than 35 years. Between 35 and 74 years of age, more men died of suicide than any other injury. Above 75 years of age, falls were the largest cause of death in both men and women.

Seasonality in total deaths in each type of injury is apparent in the period of study (Figure 36), except for assault in females. Where present, the seasonal cycle of each injury type peaks in the summer, with the exception of falls, which peaks in the winter. The peak in injury deaths in the summer for younger deaths from Figure 23 is further detailed in Figure 36, as the types of injury which are highest in the summer (transport, drownings, assault and suicide) are also those which occur mostly in younger ages. Deaths from falls peak in winter and occur mostly in older ages (Figure 36), which explains the peak in winter of injury deaths in older age groups (Figure 23).

6.5.2 Trends in injury mortality

There was a decline in age-standardised death rates of three out of five major injuries (transport, drownings and assault) from 1980 to 2016, although assault deaths have shown a recent increase since 2014 (Figure 37). In contrast, age-standardised death rates from falls increased over time while those from suicide initially decreased followed by an increase to surpass 1980 levels. The largest overall declines over time were for transport deaths in both sexes and for deaths from drownings in men, which declined by over 50% from 1980 to 2016. Age-standardised death rates for transport injuries and drownings peaked in summer months but deaths from other major injuries did not have clear seasonal patterns.

6.5.3 Excess risk of injury deaths associated with temperature anomaly

I used the resultant risk estimates (Figure 38-Figure 43) and the age-sex-specific death rates from each injury in 2016, to calculate additional deaths if each month in each state were +1°C above its long-term norm, realistic in our lifetimes under current projections of global climate change,^{244~~247~~} as well as within the range of anomaly size experienced by some states (Figure 9 in Chapter 3). I found no association between proportional change in deaths for the heterogeneous group of other unintentional injuries and anomalous temperature (Figure 43). I therefore did not include the results in further calculations.

6.5.4 Percentage change of injury deaths associated with anomalous temperature

Proportionally, deaths from drownings are predicted to increase more than those of other injury types, by as much 8.3% (7.3%, 9.3%) in men aged 15-24 years (Figure 44); the smallest proportional increase was that of assault and suicide (less than 2% in all age and sex groups). There was a larger percent increase in transport deaths for males than for females, especially in young and middle-ages (e.g., 1.253% (0.909%, 1.606%) for 25-34 year old men versus 0.232% (0.283%, 0.768%) for women of the same age) (Figure 44).

I also found some variation in association between proportional change in deaths for all ages combined and anomalous temperature across months for drownings, with excess risk from drownings exhibiting a distinct peak in summer months (Figure 45). In contrast, I found less variation in proportional change in deaths in the other four types of injuries, with transport, assault and suicide positively associated to a similar degree across all months, with falls consistently negatively associated apart from for females in late summer months (Figure 45).

6.5.5 Change in injury deaths associated with anomalous temperature

I estimated that there would be 941 (831, 1,053) excess injury deaths, equivalent to 0.5% of all injury deaths in 2016, in a year in which each month in each state were +1°C above its long-term norm (Figure 46). Deaths from drowning, transport, assault and suicide would be predicted to increase, partly offset by a decline in deaths from falls in middle and older ages and in winter months (Figure 46). Most excess deaths would be from transport injuries (448) followed by suicide (315). 87% of the excess deaths would occur in males and 13% in females. 80% of all male excess deaths would occur in those aged 15-64 years, who have higher rates of deaths from transport injuries. In those aged 85 years and older, there would be an estimated decline in injury deaths, because deaths from falls are expected to decline in a warmer year.

6.6 Discussion

While there are no previous studies of how temperature deviations from long-term norm in each month are associated with injury mortality, my results are broadly in agreement with those that have analysed associations with absolute temperature and for specific injury types. A study of suicide in US counties over 37 years (1968-2004) estimated that 1°C higher monthly temperature would lead to a 0.7% rise in suicides,¹⁰⁸ compared to my findings of 0.44-1% in males and 0.39-1.47% in females in different ages. In a study of six French heatwaves during 1971-2003, mortality from unintentional injuries rose by up to 4% during a heatwave period compared to a non-heatwave baseline.¹³³ A study of daily mortality from all injuries in Estonia found a 1.24% increase in mortality when daily maximum temperature went from the 75th to 99th percentile of long-term distribution.¹³²

That anomalously warm temperature influences deaths from drowning, although not previously quantified, is highly plausible because swimming is likely to be more common when monthly temperature is higher. The higher relative and absolute impacts on men compared with women may reflect differences in behaviour. For example, over half of swimming deaths for males occur in natural water, compared to about quarter for females (1999-2010),²⁵⁴ which may lead to a larger rise in the former in warmer weather:²⁵⁹ which may lead to a larger rise in the former in warmer weather. Similarly, the decline in deaths from falls, which are mostly in older ages, may be because falls in older people are more likely to be due to slipping on ice than in younger ages.^{252-254,260-262}

The pathways from anomalous temperature to transport injury are more varied. Firstly, driving performance deteriorates at higher temperatures.²⁵⁵⁻²⁵⁸ Further, alcohol consumption increases during warm temperature anomalies,²⁵⁹ potentially also explaining why teenagers, who are

~~more likely than other age groups to crash while intoxicated,²⁶⁰ experience a larger proportional rise in deaths from transport than older ages when temperatures are anomalously warm. Lastly, warmer temperatures generally increase road traffic in North America;^{261–264} With more people generally outdoors in warmer weather,²⁶⁵ this could lead to more fatal collisions.~~

~~Pathways linking anomalously high temperatures and deaths from assault and suicide are less established. One hypothesis is that, similar to transport, more time spent outdoors in anomalously warm temperatures leads to an increased number of face to face interactions, and hence arguments, confrontations, and ultimately assaults.^{266,267} These effects could be compounded by the greater anger levels linked to higher temperatures.^{268,269} Regarding suicide, higher temperature has been hypothesised as associated with higher levels of distress in younger people.²⁷⁰ Nonetheless, links between temperature and mental health requires further investigation,²⁷¹ including whether the relationship varies by sex and age group, as indicated by my results.~~

The pathways from anomalous temperature to transport injury are more varied. Firstly, driving performance deteriorates at higher temperatures.^{263–266} Further, alcohol consumption increases during warm temperature anomalies,²⁶⁷ potentially also explaining why teenagers, who are more likely than other age groups to crash while intoxicated,²⁶⁸ experience a larger proportional rise in deaths from transport than older ages when temperatures are anomalously warm. Lastly, warmer temperatures generally increase road traffic in North America;^{269–272} With more people generally outdoors in warmer weather,²⁷³ this could lead to more fatal collisions.

Pathways linking anomalously high temperatures and deaths from assault and suicide are less established. Pathways between temperature and assault or suicide are speculative at best, with a recent review into pathways between higher temperatures and conflict finding nothing

conclusive.²⁷⁴ One hypothesis is that, similar to transport, more time spent outdoors in anomalously warm temperatures leads to an increased number of face-to-face interactions, and hence arguments, confrontations, and ultimately assaults.^{275,276} These effects could be compounded by the greater anger levels linked to higher temperatures.^{277,278} Elevated temperatures in poorer areas are also associated with higher-than-average urban crime increases compared with richer areas in the United States and elsewhere, potentially due to lack of provision of indoor air conditioning, along with lower police street coverage and response rates.^{274,279} Regarding suicide, higher temperature has been hypothesised as associated with higher levels of distress in younger people due to their perceived lower coping capacity for negative events in life compared to older people.²⁸⁰ A emotion analysis of tweets from Twitter found that when temperatures rose in the United States, depressive language was more prevalent, which suggests that users were feeling more anxious and possibly more at risk of self-harm, including suicide.¹⁰⁸ Recent press reports have highlighted the potential for climate change to lead to a widespread mental health crisis, due to stress from seeing long-held societal and environmental norms under threat, such as reliability of obtaining food.^{281,282} Given my results and those from other recent studies, understanding links between temperature and mental health should be a high priority,^{108,283} including whether the relationship varies by sex and age group, as indicated by my results.

The major strength of my study is that I have comprehensively modelled the association of temperature anomaly with injury by type of injury, month, sex and age group. My measure of temperature anomaly internalises long-term historical experience of each state, and is closer to what climate change may bring about than solely examining daily episodes, or average temperature to which people have adapted. To utilise this metric, I integrated two large disparate national datasets on mortality (United States VR data) and meteorology (ERA-

Interim), described in Chapter 3, and developed a bespoke Bayesian spatio-temporal model, described in Chapter 5. A limitation of my study is that, like all observation studies, I cannot rule out confounding of results due to other factors, although it is unlikely that such factors will have the same anomalies as temperature, even if their average space and time patterns are the same.

My work highlights how deaths from injuries are not only currently susceptible to temperature anomalies but could also be modified by rising temperatures resulting from climate change, unless countered by social and health system interventions that mitigate these impacts. Though absolute impacts on mortality are modest, some groups, especially men in young to middle-ages, will experience larger impacts. Therefore, a combination of public health interventions that broadly target injuries in these groups – for example targeted messaging for younger males on the risks of transport injury and drowning – and those that trigger in relation to forecasted high temperature periods – for example more targeted blood alcohol level checks – should be a public health priority.

6.7 Summary

Using the mortality and temperature datasets I developed in Chapter 3 and the Bayesian spatio-temporal model I described in Chapter 5, I estimated how anomalous temperatures affect injury deaths in the United States. I calculated that a 1°C anomalously warm year would result in a net increase in injury deaths. The large majority of these additional injury deaths would occur in males of adolescent to middle ages. Four of the five injury groups (transport, drownings, assault and suicide) contribute to the increase in injury deaths under anomalously warm temperatures, with a decline in deaths from falls in older ages.

Anomalous temperature and seasonality of Little is currently known on the pathways between
anomalous temperature and injuries, and this area of research should be further investigated.

7 Anomalous monthly temperature and monthly cardiorespiratory disease and cancer mortality

7.1 Overview

I applied the Bayesian spatio-temporal model, as described in Chapter 5, to cardiorespiratory disease and cancer mortality data in the United States, as described in Chapter 3. I estimated how anomalous temperatures, defined in Chapter 3, affect deaths from different cardiovascular diseases (ischaemic heart disease (IHD), cerebrovascular disease, other cardiovascular diseases), respiratory diseases (chronic obstructive pulmonary disease (COPD), respiratory infections, other respiratory diseases) and cancers. A total of 61 million deaths from cardiorespiratory disease and cancer deaths in the United States from 1980-2016 were used in this analysis.

In this chapter, I present results of how a 1°C anomalously warm year would change the total number of cardiorespiratory disease and cancer deaths in the United States, by sex and age group. I then present additional results of how the percentage change of cardiorespiratory disease deaths would vary spatially for a 1°C anomalously warm year.

7.2 Introduction

The relationship between daily temperature and cardiorespiratory disease deaths is well-established.^{2-7,127} However, climate change is predicted to modify seasonal and monthly as well as daily patterns of temperature.^{2-7,120} This has the potential to disrupt long-term adaptation. This was one of the main motivations for building my Bayesian spatio-temporal model to associate monthly death rates with anomalous temperature, as detailed in Chapter 5. There is also limited analysis on how monthly deviations of temperature from long-

term norms will impact deaths in a consistent way across different types of cardiorespiratory disease and cancer deaths for demographic subgroups of the population.

My results from Chapter 6 predicted that there would be an increase in injury deaths, concentrated in younger males, with a 1°C anomalously warm year. In contrast, some previous studies predicted a decrease in cardiorespiratory disease deaths in a warmer climate.^{59,80,81,109} This would be the net effect of increases in cardiorespiratory disease deaths in the summer with larger decreases in the winter. Others argue that this may not be true due to a weakening association of excess winter mortality with temperature,^{272,273,284,285} though methods in these studies have been criticised as misinterpreting excess winter mortality.^{58,59} Cardiorespiratory diseases made up 40% of all deaths in the United States in 2016 and therefore remain significant to public health policy and planning. Deaths from cancers also make up a considerable proportion of deaths in the United States, with 23% of all deaths in 2016 being from cancers. Only a few studies have examined an association between temperature and deaths from cancers,^{126,136,139} though slight seasonality in cancer death rates exists for^{127,136,139} though cancer death rates exhibit seasonality in older age groups, shown in Chapter 4. My aim was to evaluate how deaths from cardiorespiratory diseases and cancers may be affected by changes in temperature that could arise as a result of global climate change in the United States.

7.3 Data

Full details of the data processing ~~choices I made can be found~~ are presented in Chapter 3. Here, I used VR data on all 60,967,769 cardiorespiratory disease and cancer deaths in the contiguous United States from 1980 to 2016 along with population records to calculate monthly death rates for each type of cardiorespiratory disease and cancer death, state, sex and age group combination. Of cardiorespiratory disease and cancer deaths, 41,105,009 (67.4%) were from cardiorespiratory diseases and 19,862,760 (35.6%) were from cancers. ~~For each death, I~~

mapped ~~each ICD-9 and ICD-10 coded deaths~~ to cardiorespiratory diseases and cancers using their ICD-9 and ICD-10 codes (Table 11). I separated ~~the~~ cardiorespiratory disease deaths into three cardiovascular (IHD, cerebrovascular disease, other cardiovascular diseases) and three respiratory (COPD, respiratory infections, other respiratory diseases) diseases. Other cardiovascular diseases included rheumatic, hypertensive and inflammatory heart diseases. Other respiratory diseases included asthma and bronchiectasis. I did not further subdivide cancer deaths as death outcomes are not generally considered as sensitive to temperature changes.^{[126,136,139](#)[127,136,139](#)} The remainder of deaths not included in analysis in Chapters 6 and 7 were from a heterogeneous group of causes other than cancers, cardiorespiratory diseases and injuries, described in more detail in Chapter 3. The causes of death that led to deaths in this group varied by sex and age group. Therefore, I did not include them in the analysis. I obtained monthly population-weighted temperature anomalies from ERA-Interim by a process described in Chapter 3.^{[215](#)[221](#)}

7.4 Statistical methods

I analysed the association of monthly death rates with anomalous temperature using a Bayesian spatio-temporal model, fully described in Chapter 5 and described in brief in Section 6.4.

Chronic disease	ICD-9	ICD-10
Cardiorespiratory diseases	381-382, 390-519	H65-H66, I00-J99
Cardiovascular diseases	390-459	I00-I99
Ischaemic heart disease (IHD)	410-414	I20-I25
Cerebrovascular disease	430-438	I60-I69
Other cardiovascular diseases	390-409, 415-429, 439-459	I00-I19, I26-I59, I70-I99
Respiratory diseases	381-382, 460-519	H65-H66, J00-J99
Chronic obstructive pulmonary disease (COPD)	490-492, 495-496	J40-J44
Respiratory infections	381-382, 460-466, 480-487	H65-H66, J00-J6, J9-J18, J20-J22
Other respiratory diseases	467-479, 488-489, 493-494, 497-519	J7-J8, J19, J23-J39, J45-J99
Cancers	140-239	C00-C99, D00-D48

Table 11. Cardiorespiratory disease and cancer groups used in the analysis with ICD-9 and ICD-10 codes.

7.5 Results

7.5.1 Summary of cardiorespiratory disease and cancer deaths

From 1980 to 2016, 20,070,797 boys and men and 21,034,212 girls and women died from cardiorespiratory diseases in the contiguous United States. These deaths accounted for 46.3% and 49.9% of all male and female deaths respectively (Figure 2 in Chapter 3). 77.1% of male cardiorespiratory disease deaths and 88.7% of female cardiorespiratory disease deaths were in those aged 65 years and older (Figure 47). For females, 42.7% of cardiorespiratory disease deaths were in those aged 85 years and older (Figure 47).

IHD accounted for 45.3% of cardiorespiratory disease deaths in males and 38.7% in females (Figure 47). Men 35 years and older and women 45 years and older died from IHD more than any other cardiorespiratory disease. Below 35 years of age for men and 45 years of age for women, other cardiovascular diseases were the largest single cause of cardiorespiratory disease death in both males and females (Figure 47). As I presented in Chapter 4, there has been a persistent seasonality of mortality in cardiorespiratory disease deaths over time for most age groups in both sexes (Figure 17 and Figure 18). For each of the six types of cardiorespiratory disease death, there were more deaths in the winter than in the summer (Figure 48).

There were 10,428,202 cancer deaths for boys and men and 9,434,558 for girls and women in the contiguous United States during 1980-2016 (Figure 2 in Chapter 3). There were slightly more deaths from cancers in winter than in summer (Figure 48) as I found for those 55 years and older in Chapter 4 (Figure 15 and Figure 16).

7.5.2 Trends in cardiorespiratory disease and cancer mortality

~~There was a decline in age~~Age-standardised death rates ~~of declined for~~ four out of six types of cardiorespiratory disease (IHD, cerebrovascular disease, other cardiovascular diseases and respiratory infections) for both men and women from 1980 to 2016. IHD death rate declined more than other cardiorespiratory diseases from 1980 to 2016, by over 50% for both men and women (Figure 49). COPD death rates increased in males from the 1980s until the late 1990s, and steadily decreased since then. In contrast, COPD death rates in females have increased since the 1980s (Figure 49). Age-standardised death rates from other respiratory diseases also increased over the time period (Figure 49). There is a discontinuity in age-standardised death rates in other cardiovascular diseases due to the change from the ICD-9 to ICD-10 coding in the United States in 1999, when some deaths in this group were assigned to IHD (Figure 49). Death rates from cancers have decreased over time (Figure 49).

7.5.3 Excess risk of cardiorespiratory disease and cancer deaths associated with temperature anomaly

I used the resultant risk estimates (Figure 50-Figure 56) to calculate additional deaths if each month in each state were +1°C above its long-term norm. I found no consistent association between deaths for cancers and anomalous temperature (Figure 56). I therefore did not include the results in further calculations.

7.5.4 Percentage change of cardiorespiratory disease deaths associated with anomalous temperature

Proportionally, deaths from IHD were ~~predicted~~projected to show the ~~most~~highest consistent ~~decrease~~inverse association in older age groups (Figure 57). Proportional reductions in deaths for those 55 years and older were greater than 0.5% in males and 0.2% in females in a year in which each month in each state were +1°C above its long-term norm (Figure 57). Younger age groups generally possess a large range of uncertainty in all types of cardiorespiratory disease death due to the small numbers of deaths (Figure 57). The largest single ~~age group~~ decrease was that of respiratory infections in males 85 and older (1.0% (0.7%, 1.3%)) (Figure 57). With few exceptions (~~e.g., those aged 15–24 years in deaths from other respiratory diseases~~) the scale and sign of the percent changes were similar in both males and females across ages and cardiorespiratory diseases (Figure 57).

There were variations in ~~association between~~ proportional ~~change in deaths~~changes of death rates for all ages combined across months (Figure 58). ~~The main exceptions were for COPD in females and other respiratory diseases in both sexes (Figure 57), though low absolute numbers of other respiratory disease deaths led to the large uncertainty in the estimated rate ratios (Figure 57)~~. The largest single monthly increase was for other cardiorespiratory diseases for females in July, 0.7% (0.4%, 1.0%), with the largest single decrease for IHD for males in December, 1.1% (0.9%, 1.2%) (~~Figure 57~~ Figure 58). ~~The main exceptions were for COPD in females and other respiratory diseases in both sexes (Figure 58), though low absolute numbers of deaths from this cause led to the large uncertainty in the estimated rate ratios (Figure 58)~~.

7.5.5 Change in cardiorespiratory disease deaths associated with anomalous temperature

I estimated that there would be 4,369 (4,024, 4,706) fewer cardiorespiratory disease deaths, equivalent to 0.4% of all cardiorespiratory disease deaths in 2016, in a year in which each month in each state were +1°C above its long-term norm (Figure 59). Deaths from all cardiovascular diseases (IHD, cerebrovascular disease and other cardiovascular diseases) and respiratory diseases (COPD, respiratory infections and other respiratory diseases) would be predicted to decrease (Figure 59). The biggest reduction of deaths would be from IHD, with 1,883 (1,706, 2,058) fewer deaths, followed by other cardiovascular diseases, with 1,039 (835, 1,243) fewer deaths. 81% of the total reduction in deaths would be from cardiovascular diseases, with the rest in respiratory diseases (Figure 59). 4,236 deaths (97%) of overall reduction would come from those aged 55 years and older. 55% of the reduction in deaths would occur in males and 45% in females (Figure 59). There would be decreases in all months across all cardiorespiratory diseases, with the exception of the summer months (June, July and August). The greatest single increase would be in July for other cardiovascular diseases for both males (76 (41, 112)) and females (103 (62, 144)). The biggest reductions would occur in the coldest months (November, December, January and February) (Figure 59).

7.5.6 Percentage change of sub-national cardiorespiratory disease deaths associated with anomalous temperature

I also ran a model where each state was given a separate temperature anomaly coefficient to examine spatial variation in ~~percentage change in deaths if each month in each state were +1°C above its long-term norm~~ the size of association between death rates and anomalous temperature, described by Equation 9 in Chapter 5. In this model, I used all cardiorespiratory diseases together, as models did not converge or give sensible results when breaking down deaths by type of cardiorespiratory disease in addition to state, sex and age group.

Percentage change in death rates in a year in which each month in each state were +1°C above its long-term norm varied by state and month in both males and females (Figure 60 and Figure 61), though in some months more than others. There were similar associations between males and females in the same state and month.). In January, an illustrative month for the impacts of anomalous temperature in winter months, there were decreases in percentage change in death rates across the entire contiguous United States for both males and females (Figure 60 and Figure 61). These decreases ranged from 1.5% (1.2%, 1.9%) (Louisiana) to 0.2% (0.1%, 0.4%) (New Mexico) in males (Figure 60), and 1.3% (1.0%, 1.7%) (Washington) to -0.1% (-0.35%, 0.53%) (Arizona) in females (Figure 61). In July, an illustrative month for the impact of anomalous temperature in summer months, there were increases in 47 out of the 49 spatial units for males (Figure 60) and all spatial units for females (Figure 61). The biggest increase in July for males was in New Mexico, at 1.1% (0.5%, 1.7%) (Figure 60) and in Utah, at 1.2% (0.6%, 1.7%) for females (Figure 61). In May and September, late spring and early autumn respectively, there were mixed positive and ~~negative~~inverse associations with anomalous temperature (Figure 60 and Figure 61). In these months, there were ~~negative~~inverse associations with anomalous temperature in coastal regions. In contrast, there were positive associations in the West North Central and Southwest regions of the United States, though it

should be noted that the ~~low population of estimates in these~~ states ~~in this region contributed to had~~ large uncertainties ~~in these estimates~~. There were similar associations in June and August across the United States in both males and females (Figure 60 and Figure 61). Overall, the Southeast region showed the greatest negative associations with anomalous temperature across all months for both sexes.

7.6 Discussion

My work here shows that there would be an expected net decrease from cardiorespiratory disease deaths in a year in which each month in each state were +1°C above its long-term norm (Figure 59). This reduction would be strongly concentrated in older ages, be shared almost evenly between males and females and occur in all but summer months (Figure 59).

Most previous studies have examined how deaths from all-causes^{2,3,5 7,87,88,98–101,103,109,111–118} and cardiorespiratory disease deaths^{3,5 7,87,88,115–117,120–127} are associated with daily, not monthly, temperature. Nevertheless, some limited comparisons can be made with other studies.^{103,117,121} It should be noted that for summer months one study examined effect of extreme high temperatures^{2,3,101,103,109,111–117,5,118,6,7,87,88,98–100} and cardiorespiratory disease deaths^{3,5,121–127,6,7,87,88,115–117,120} are associated with daily, not monthly, temperature. Nevertheless, some limited comparisons can be made with other studies.^{103,117,122} It should be noted that for summer months one study examined effect of extreme high temperatures¹¹⁷ and the other the effect of a 5°C increase in temperatures.¹²¹ A study of winter months looked at decreases below 18°C.¹⁰³ and the other the effect of a 5°C increase in temperatures.¹²² A study of winter months looked at decreases below 18°C.¹⁰³

Illustrative of summer months, there was an increase of IHD deaths in July of 0.4% (0.2%, 0.6%) for males and 0.5% (0.3%, 0.8%) in females for a 1°C anomalously warm year (Figure 58). Previous studies which studied association of IHD deaths in summer months with daily temperature found slightly higher (1.7% to 2.5%) increases of risk for all ~~deathsage groups~~ from both sexes.^{117,121,117,122} My cerebrovascular disease findings in July show a 0.1% (-0.3%, 0.4%) increase in males and 0.5% (0.2%, 0.8%) in females (Figure 58). Another study of daily temperature found higher risk (2.5%) than in my findings. For COPD, I found a negative association of percentage change across most months for both sexes (Figure 58). A previous

study found a large daily association for summer COPD deaths (4.3%), though this was for extreme high temperatures.¹¹⁷ This is in contrast to my study, which examined the association of mild deviations from long-term norm temperatures on mortality.

Representing winter months, my IHD findings in January show a 0.9% (0.8%, 1.1%) decrease in males and 0.6% (0.4%, 0.7%) in females for a 1°C anomalously warm year (Figure 58). This result is consistent with a previous study of cold months in Europe.¹⁰³

There are plausible explanations for my results. Cardiovascular deaths are higher in the winter than the summer (Figure 48). This is partially explained by blood pressure being inversely associated with temperature.¹²⁹ Cold temperature in the winter therefore results in generally higher blood pressure, placing strain on the heart and damaging vessel walls.¹²⁹ The lower norm temperatures in winter months can also lead to increased blood clotting and thrombosis.^{103,129} This increases the risk of IHD and cerebrovascular disease and ultimately death from these causes.¹⁰³ Warm temperatures in winter months would therefore reduce the risk of dying from these causes (Figure 59). That warmer temperatures in summer months increase the risk of death in cardiovascular diseases is thought to be due to the reduction of plasma volume by release of platelets and red blood cells into the blood stream and the loss of water and salt through sweating.¹³¹ This puts strain on the circulatory system by increasing sticking of platelets to artery walls which leads to blockages and sudden decrease in blood pressure and can lead to death.¹³¹ Further increases away from long-term norms increase strain on the circulatory system and risk of death from cardiovascular diseases. This explains why more deaths are expected from cardiovascular diseases in anomalously warm summer months (Figure 59).

Respiratory disease deaths are also higher in winter than at other times in the year in the United States (Figure 48). Colder temperatures are associated with suppression of the immune system,

which facilitates respiratory infections taking hold in humans.¹⁰³ Warmer anomalies in winter months can therefore reduce risks of respiratory infections, which explains the reduction in excess risk for older groups (Figure 54). Cold air can also cause airways to go into spasm and trigger coughing, wheezing, shortness of breath and tightness in the chest.^{274,286} Mould spores are more common in colder air, known to cause coughing and sneezing, which exacerbate existing respiratory conditions.²⁷⁵ ~~Warmer anomalies in winter would reduce these risk factors.~~²⁸⁷ Warmer anomalies in winter would reduce these risk factors. In contrast, warmer anomalous temperatures in summer months are associated with airway inflammation, which can lead to death from respiratory complications.¹³⁰ I note this though I found a non-significant increase for respiratory infections in summer months (Figure 58).

I found no consistent association between deaths from cancers and a year in which each month in each state were +1°C above its long-term norm (Figure 56). ~~This agrees with limited previous studies,^{126,139} with the exception of an old study which advised caution in its interpretation as it did not account for geographical differences.¹³⁶ Though I found that cancer deaths were weakly seasonal in males 55 years and in females 65 years and older ()~~. This agrees with limited previous studies,^{127,139} with the exception of an old study which advised caution in its interpretation as it did not account for geographical differences.¹³⁶ Though I found that cancer deaths were weakly seasonal in males 55 years and in females 65 years and older (Figure 15 and Figure 16 ~~in Chapter 1~~), this may be for reasons other than temperature variation. ~~I note this though I found a non-significant increase for respiratory infections in summer months and in no other respiratory disease (Figure 57).~~

in Chapter 4), my findings here show that cancer mortality is not sensitive to inter-annual variation in monthly temperature. This indicates that higher cancer death rates in winter is a general seasonal effect and not as such one associated with anomalous monthly temperature variation.

The major strength of my anomalous temperature study is that, when combined with work in Chapter 6, I comprehensively modelled the association of temperature anomaly with a comprehensive set of causes of death, by month, sex and age group. I did this using the two large datasets I processed in Chapter 3 and the Bayesian spatio-temporal model I developed in Chapter 5. The temperature anomaly metric I also described in Chapter 3 (Figure 8) factors in long-term local experience when examining temperature-mortality association. This has enabled me to make an estimate of the change in deaths with a 1°C anomaly increase, which is within the range of anomaly size experienced by many states (Figure 9 in Chapter 3). My study design has also enabled me to show that the reduction in deaths would be greatest in older groups in the winter months, and would be almost evenly shared between males and females (Figure 59). A limitation of my study is that I cannot rule out confounding of results due to other factors that may be correlated with temperature anomalies.

My work adds to the body of evidence that suggests that a warming world will reduce winter deaths.^{59,80,81,109} While increases in average temperatures would increase deaths in the summer, this would be outweighed by the reductions in winter (Figure 59). My work goes further than previous work by breaking down changes in deaths by cause of death, month, sex and age group (Figure 59). The predicted reduction of 0.4% of all cardiorespiratory disease deaths is slight and concentrated in older age groups. This demonstrates that the burden from cardiorespiratory disease deaths will remain large and a significant public health concern under climate change.

7.7 Summary

Using the mortality and temperature datasets I developed in Chapter 3 and the Bayesian spatio-temporal model I described in Chapter 5, I estimated how anomalous monthly temperatures affect cardiorespiratory disease and cancer deaths in the United States. I calculated that a 1°C

anomalously warm year would result in a net decrease in cardiorespiratory disease deaths. The large majority of this reduction would be concentrated in older age groups. The reduction would be across all cardiorespiratory diseases, with the largest in ischaemic heart disease. Reductions would be shared almost evenly between males and females. Reductions would occur across the year, apart from the summer months, when deaths would increase slightly. I found no association between anomalous temperature and cancer deaths.

8 Discussion

8.1 Comparison with published literature

8.1.1 Seasonal dynamics of mortality

Prior to my work, it had been established that total mortality from the entire population in the United States are higher in the winter than in the summer.^{57,60,70} This was known to be mainly due to higher winter death rates from influenza and cardiorespiratory diseases in older age groups.^{71–74} Previous studies in the United States have also identified seasonality for some causes of death.^{54,57,60–62,70,224} ~~No previous study made a consistent national and subnational analysis of seasonality in the United States by cause of death, sex, age group, over time and space, nor how it varies across climate regions.~~^{54,57,60–62,70,230} ~~No previous study made a consistent national and subnational analysis of seasonality in the United States by cause of death, sex, age group, over time and climate regions.~~ In Chapter 4 of this thesis, I used wavelet and centre of gravity analyses, which allowed me to identify seasonality of mortality and how it has changed over time. This work uncovered the distinct behaviours across causes of death, and by sex and age group.

Where studies were comparable, my results agreed with previous work. I demonstrated that the strong seasonality in older age groups of cardiorespiratory diseases and weak seasonality of cancer deaths, found in some previous studies,^{60,61,70,224}~~60,61,70,230~~ have endured over the last four decades. I also ~~extended~~made advances relative to previous work. For example, I showed that there have been variations in when injury deaths peaked and how the seasonal differences in injury deaths have changed over time in relation to sex and age group, not previously demonstrated. I also showed how changes in all-cause mortality seasonality by sex and age group can be explained by changes in particular causes of death, such as how substantial decline

in seasonal mortality differences in boys under five was due to the decreasing seasonality of death from cardiorespiratory diseases in that age group.

8.1.2 Anomalous monthly temperature and mortality

A large proportion of previous studies of the temperature-mortality relationship focused on single day or multi-day episodes and temperature.^{3–7} Other studies either associated monthly or seasonal average temperatures with mortality,^{108,109} or accounted for seasonal impacts by stratifying daily data by month.^{81,114} ~~Previous studies largely examined all-cause,^{2,3,5–7,87,88,98–101,103,109,111–117} or cardiorespiratory disease deaths.^{3,5–7,87,88,115–117,120–125,127} In the United States, studies ranged from a single spatial unit,^{86,87,109,121,138,168,169} to hundreds of independently-analysed units across the country.^{81,101,114,118,120,123,126,137,144,146,155,161,170} Some work used Bayesian methods to conduct meta-analyses of relative risks for temperature and mortality.^{172,173}~~

Previous studies largely examined all-cause,^{2,3,101,103,109,111–117,5–7,87,88,98–100} or cardiorespiratory disease deaths.^{3,5,121–126,6,7,87,88,115–117,120} In the United States, studies ranged from a single spatial unit,^{86,87,109,122,138,168,169} to hundreds of independently-analysed units across the country.^{81,101,156,162,170,114,118,121,124,127,137,145,147} Some work used Bayesian methods to meta-analytically pool relative risks for temperature and mortality.^{171,172}

To my knowledge, no previous study made an analysis of how temperature deviations from long-term norm in each month are associated with mortality by cause of death, sex and age group. In my work on anomalous temperature and mortality in Chapters 6 and 7, I examined deviations from long-term norms to analyse relationships using a Bayesian spatio-temporal model by cause of death, month, sex, age group and in the case of cardiorespiratory disease deaths (Chapter 7), by state.

Though previous studies did not examine anomalous temperature, some of my results can be compared with other studies of temperature. For example, my results for injury deaths, described in Chapter 6, align well with a previous study of the association between suicides and temperature in the entire contiguous United States and Mexico.¹⁰⁸ However, my work went further in demonstrating that while suicides are predicted to increase with rising anomalous temperature, the greatest absolute impact would be on younger men. With cardiorespiratory disease deaths, described in Chapter 7, I showed that there would be a net decrease expected with mild positive deviations from long-term norm temperatures. This would be concentrated in the oldest age groups and would be shared almost evenly between males and females. My results agreed with previous studies which predicted a decrease in absolute number of deaths for cardiorespiratory disease deaths.^{59,80,81,109} My study went further by showing that this would be concentrated in older age groups, and percentage change in cardiorespiratory disease deaths would be nearly homogeneous across space in the warmest and coldest months (Chapter 7). I also showed in Chapter 7 that there was no association with cancer and anomalous temperature across any month, sex and age group combination.

8.2 Strengths and limitations

In my thesis, I processed two large datasets on death rates from VR records and monthly anomalous temperature from ERA-Interim weather reanalysis, described in Chapter 3. My work here is the first comprehensive study of the United States to use a mutually exclusive and collectively exhaustive set of causes of death for both examining dynamics of seasonality of mortality, described in Chapter 4, as well as association between monthly anomalous temperature and mortality, described in Chapters 6 and 7.

The strengths of my dynamics of seasonality study, described in Chapter 4, were its innovative methods of characterizing seasonality of mortality dynamically over space and time, by cause

of death, sex and age group; using wavelet and centre of gravity analyses; and using ERA-Interim data to compare the association between seasonality of death rates and regional temperature.

I developed a Bayesian spatio-temporal model, described in Chapter 5, to borrow strength across spatial and temporal units. Using this model, I estimated excess risk of mortality from monthly anomalous temperature for injuries, described in Chapter 6, and cardiorespiratory disease and cancer deaths, described in Chapter 7. I was able to go further than previous studies by examining changes in deaths due to monthly anomalous temperature by cause of death, sex and age group.

A limitation of my results in Chapters 4 ,6 and 7 is that I did not investigate seasonality of mortality by socioeconomic characteristics which may help with understanding its determinants and planning responses. Whether temperature anomaly within a month is spread or concentrated, as described in Chapters 6 and 7, may also have different implications to health as single day or multi-day heat and cold events are known to be a threat to human lives. However, additional extreme temperature measures, which I described in Section 5.4.11, did not add any further insight to my analysis. Like all observation studies, confounding from other factors cannot be ruled out. However, it is unlikely that such factors will have the same anomalies as temperature, even if their average space and time patterns are the same. associations by socioeconomic characteristics, which may help with understanding the effect modifiers that can in turn influence planning responses. Socioeconomic characteristics could include levels of poverty, education, unemployment, urbanicity, as well as percentage of different races. A recent study of seasonal temperature and mortality in New England explored several potential effect modifiers, including sex, age group, urbanicity and race.¹⁰⁹ The study found no significant difference between urban and rural populations, and found inconsistent results based on race differences. Another study of Californian counties found elevated risk for

people of Black race, but no differences by gender or educational level.¹²² The overall picture is therefore mixed and warrants further investigation. Whether temperature anomaly within a month is spread or concentrated, as described in Chapters 6 and 7, may also have different implications to health as single-day or multi-day heat and cold events are known to be a threat to human lives. However, additional extreme temperature measures, which I described in Section 5.4.11, did not change the conclusions of my analysis based on anomalous mean monthly temperature. Future climate change may also produce different types and patterns of anomalies from the ones able to be studied historically.

Future climate change may also produce different types and patterns of anomalies from the ones able to be studied historically. Like all observation studies, impacts from other exposures and characteristics cannot be ruled out. Relevant to this, I have acknowledged in Section 1.1 of Chapter 5 that including air pollution in my model may have an impact on my results for cardiorespiratory diseases, if the air pollution pathway was not fully blocked in stratifying by month to account for weather regimes.

A further consideration may also be necessary if someone registered to one state dies in another state while visiting. One driver of this is seasonal internal migration. Seasonal internal migration occurs in mainly older ages in the United States. A ‘snow bird’ is a person who would seasonally move to Florida or another warm state in winter and move back in the spring. If snow birds happened to die on a winter visit, the deaths would be recorded in their home state. Therefore, the exposure and death would be registered in different places. Positively-correlated winter anomalies across the United States would minimise the impact of the registering a death in a wrong state, as anomalies in states would behave similarly in any given month. There is evidence that winter anomalies are positively-correlated throughout most of the United States.²⁸⁸ An exception to this is in the Northwest of the country, where winter anomalies have been negatively correlated with the rest of the country.²⁸⁸ This may contribute

to bias in my results, though I could not find any evidence that incorrect registration of state at time of death is a widespread phenomenon.

8.3 Public health and policy implications

Continued higher death counts in winter for cardiorespiratory diseases in older age groups, shown in Chapter 4, indicate that improving interventions during the winter months will remain a priority. These may include better insulation of homes, winter heat provision and influenza vaccinations. Social interventions will remain important in improving and maintaining health in older age, such as regular visits to older people or keeping them connected over the internet to other people with newer technologies. This effort is necessary irrespective of the geography and local climate in the United States, since I also showed in Chapter 4 that seasonality is present and similarly timed throughout the country. The relative difference in seasonality of mortality has decreased for children under five, which may help to demonstrate the effectiveness of efforts to reduce peaks of cardiorespiratory diseases in the winter. ~~The continued presence of cancer death seasonality in older groups may be due to co-morbidity in winter months, causing already frail sufferers to die.~~

~~There would be increases~~I projected an increase in deaths from injuries (transport, drownings, assault, suicides) in younger males, during periods of elevated anomalous temperature, as shown in Chapter 6. My analysis demonstrated that a 1°C anomalously warm year would result in 0.5% overall increase in injury deaths, concentrated in younger men. ~~This may have implications on interventions~~Interventions should therefore be targeted at younger age groups during periods of elevated temperature to minimise the impact of anomalous temperature on injuries. These could include targeted messaging for younger males on the dangers of driving and swimming triggered when higher-than-normal temperatures are forecast. The concentration of these deaths in younger age groups, particularly younger men, also means that

additional injury deaths from anomalous temperatures could result in loss to the economy through loss of otherwise healthy working years. The estimated reduction in cardiorespiratory disease deaths (0.4% overall decrease in a 1°C anomalously warm year), concentrated in older age groups, demonstrate that cardiorespiratory disease deaths would remain an ongoing concern under climate change, since climate change would not reduce cardiorespiratory disease deaths by a significant amount. Policy makers should continue to aim for further reductions in such chronic diseases which, along with cancers, remain the deadliest threat to most people in the United States.

8.4 Future work

My work in this thesis is translatable to other countries with reliable vital registration data. Though many countries are still lacking appropriate high quality mortality data,¹⁴ the analyses in Chapters 4, 6 and 7 could be replicated as data becomes available. The algorithm I developed for gridded weather data, described in Chapter 3, could be used anywhere in the world. Comparing differences between communities in different countries could serve as evidence to measure success of potential adaption measures enacted in one country but not another.

In the United States itself, other research on anomalous temperature and mortality could examine urban and rural differences. Similar work has been carried out in the United Kingdom.^{127,143} ~~Further work could examine how socioeconomic factors explain differences by state in excess risk per 1°C temperature anomaly by state, such as in my analysis of cardiorespiratory disease deaths in Chapter 120,144~~ Further work could examine how socioeconomic or environmental factors explain differences in the magnitude of association across states, seen in Chapter 7. By combining with climate model projections of future deviations of temperature from current long-term norms, my work here could be used to help further understand the implications of climate change on mortality by cause of death, sex and

age group. A recent study on all-cause mortality for several cities in the United States highlighted the differences in attributable heat mortality between meeting the Paris Agreement's temperature goals and current trajectory of about 3°C increase above preindustrial levels.¹¹⁹ Further work based on my thesis could expand this tranche of work on climate change and human mortality to multiple causes of death, by sex and age group and across the entire contiguous United States, using the benefits of Bayesian spatio-temporal modelling, such as the ‘borrowing of strength’ across different spatial and temporal subunits.

One longer-term aim may be to further explore mediators, mechanisms and effect modifiers of the temperature-mortality relationship for injuries, as this is an underdeveloped area of research.²⁷⁴ As previously discussed in my study of injuries in Section 6.6 of Chapter 6, the causal pathways between temperature and injury mortality are as of yet unclear, and so warrant further investigation via potential other exposures and variables. Another aim could be to compare any mismatch between attributable deaths from cohort studies of temperature to time series studies (Section 2.5.4).¹⁷⁹ For a cohort study of temperature, potential baseline exposure variables for a temperature study could include an absolute measurement of exposure (e.g., long-term (30-year) norm temperature) and/or a measurement of variability of temperature (e.g., standard deviation of temperature), though an absolute measure of exposure may not detect exposure effects due to local temperature adaption, as discussed in Section 2.5.4.

8.5 Conclusions

Seasonality of mortality persists for deaths in older age groups in the United States, though the timing and degree to which this occurs varies by cause of death, sex and age group. Seasonal differences in deaths among children and young adults have largely disappeared. There are impacts, though slight, in how injury and cardiopulmonary disease death rates would change under anomalous temperature. Injury deaths in young men, particularly for transport, drowning,

assault and suicide, are positively associated with anomalous warm temperature. In contrast, deaths from falls in older age groups were negatively associated with anomalous warm temperature. Anomalous warm temperature is also associated with decreases in cardiorespiratory disease deaths. This decrease would be concentrated in older age groups and shared almost equally between males and females. There is no association between cancer deaths and anomalous monthly temperatures although these deaths exhibit broad seasonality. My research shows that in the United States, continued efforts are required to further reduce peaks in mortality in older age groups through targeted interventions. Under climate change, while estimated modest increases in injury mortality in younger males is concerning, the burden of cardiorespiratory disease and cancer deaths will remain a high public health priority due to the small reduction in cardiorespiratory disease deaths. Further work should examine causal pathways between temperature and mortality for various causes of death (in particular injury deaths), as well as using cohort studies to further understand specific types of temperature-mortality relationship.

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