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Temperature related effects on mortality and years of life lost in the UK for current and future climates

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LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE

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Abstract

Background: In the context of a warming climate, understanding current and potential future temperature risks to health is vital to allow effective prioritisation of resources and protect public health. However, important gaps in knowledge remain around current temperature-related risks and premature mortality, population adaptation to temperature effects, the best use of temperature thresholds in epidemiological models and local climate health impacts under conditions of the 2015 Paris Agreement, which aims to limit increases in global average temperature to well below 2 °C (preferably below 1.5°C) compared to pre-industrial levels.

Methods: In this thesis, I used a number of methods to assess current and future impacts of temperature on health, including: a systematic review to assess temporal changes in temperature-related health risks; epidemiological time series regression analysis of UK mortality data from Greater London, Greater Manchester and the West Midlands to estimate effects of ambient temperature on mortality and years of life lost (YLL) and evidence for temporal changes in temperature-related risk; a case study approach to examine cold definition and threshold use within studies; and quantitative health impact assessment methods to estimate changes in heat related mortality (HRM) under the Paris agreement in the 3 largest UK conurbations.

Results: In Greater London, estimated risk and attributable burdens are sensitive to cold threshold choice (below which effects are quantified). Integrating evidence from multiple disciplines allowed causality across the range of ‘cold’ temperatures used and the implications of threshold placement for policy and research to be better understood.

Evaluating temperature effects on (premature) mortality, I found an increased risk of YLL and mortality for each 1°C above or below the heat and cold thresholds, e.g. heat-effects were greatest in London, where for each 1 °C above the heat-threshold the risk of mortality increased by 3.9% (95% CI 3.5%, 4.3%) and YLL increased by 3.0 % (95% CI 2.5%, 3.5%).

The systematic review found evidence of decreasing temporal susceptibility to heat in certain populations but little evidence for changes in cold related risks. Analysing UK data, however, I found no evidence of decreasing vulnerability to risk of heat or cold related mortality or YLL between 1996-2013.

Lastly, I found that under conditions of the Paris agreement in the 3 largest English conurbations, HRM is projected to increase by 60-68% if the climate stabilises at 1.5°C compared to an increase of 100-110% under 2°C scenarios, depending on location.

Conclusions: This PhD has demonstrated an increased risk of heat and cold related mortality and YLL in the 3 largest UK conurbations. Alongside the lack of evidence for attenuation in this risk and projections of future HRM, this has direct implications for UK public health planning and adaptation needs. Quantifying avoidable deaths under 1.5 degrees compared to 2 degrees of global warming provides timely motivation for increased climate mitigation ambition.

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List of Abbreviations

CCRA	Climate Change Risk Assessment
CET	Central England Temperature
COP26	26th session of the Conference of the Parties of the UNFCCC
CVD	Cardiovascular Disease
CVA	Cerebrovascular Accident
CI	Confidence Interval: unless stated otherwise, 95% CI are given
CWP	Cold Weather Plan
DALY	Disability Adjusted Life Year
GCM	Global Circulation Model
HES	Hospital Episode Statistics
HIC	High Income Country (World Bank classification)
HMIC	High- and Middle-Income Countries (World Bank Classification)
HRM	Heat Related Mortality
HWP	Heatwave Plan

IHD	Ischaemic Heart Disease
IPCC	Intergovernmental Panel on Climate Change
MI	Myocardial Infarction
MMT	Minimum Mortality Temperature
NAP	National Adaptation Programme
NICE	The National Institute for Health and Care Excellence
NO_2	Nitrogen Dioxide
O_3	Ozone
OR	Odds Ratio
PHE	Public Health England
PM	Particulate Matter
$PM_{2.5}$	Particulate matter with less than 2.5 µm in aerodynamic diameter
PM_{10}	Particulate matter with less than 10µm in aerodynamic diameter
RCM	Regional Circulation Model
RCP	Representative Concentration Pathway (IPCC fifth assessment report - AR5)

RR	Relative Risk
SRES	Special Report on Emissions Scenarios
SSPs	Shared Socio-Economic Pathways
UK	United Kingdom
US	United States of America
UN	United Nations
UNFCCC	United Nations Framework Convention on Climate Change
WHO	World Health Organisation
YLL	Years of Life Lost
°C	Degrees Celsius
°F	Degrees Fahrenheit

PART I: BACKGROUND TO THE THESIS

1. INTRODUCTION

1.1 Context: Ambient temperature and health in the context of climate change

Heat and cold related mortality present an important public health problem within the UK, with a well-established link between short-term ambient temperature (both heat and cold) and adverse health outcomes. This has been demonstrated not only for the United Kingdom (UK), but also across a range of settings globally (Basu, 2009, Gasparrini et al., 2015, Green et al., 2019, Hajat, 2017, Hajat et al., 2006, Hajat and Kosatky, 2010). In the UK, this relationship is best defined for mortality, compared to other health outcomes – for example, indicators of morbidity, such as acute hospital admissions, GP visits or specific outcomes such as myocardial infarction (Arbuthnott and Hajat, 2017, Bhaskaran et al., 2010, Kovats et al., 2004). Typically, studies have demonstrated a 'U', 'V' or 'J' shaped relationship between the daily risk of mortality and daily ambient temperature, with mortality increasing above or below given heat and cold thresholds or minimum mortality temperatures (MMTs). Extreme temperature events are also associated with increased mortality – during the 2003 heatwave there were over 14,000 excess deaths in France alone (Fouillet et al., 2006, Robine et al., 2008) and 2,000 excess deaths in England and Wales (Johnson et al., 2005). In the UK, older age groups are known to be at increased risk of temperature related mortality. In England, the risk of heat related mortality is greater in London and the South East (Hajat et al., 2007), and risk of cold related mortality greater in London, the North East and North West (Hajat et al., 2016). However, less is known about the impacts of ambient temperature at a conurbation or city level, compared to regional levels. This is important, for a number of reasons. The majority of the UK population live within urban areas (Office for National Statistics) and much public health and climate change planning and policy making takes place at this level (Birmingham City Council, Council, Mayor of London, 2018, Lee and Koski, 2014). Residents in built up areas are also thought to be more vulnerable to the effects of heat due to the Urban Heat Island (UHI), which describes the occurrence of higher temperatures within cities and towns compared to rural areas, potentially due to a variety of factors such as urban surfaces and building materials, lack of vegetation and tree cover and anthropogenic heating (Heaviside et al., 2017).

The importance of the relationship between temperature and health has received increasing attention in the context of climate change. According to their 2014 report, the International Panel on Climate Change (IPCC) estimate that combined land and ocean surface temperatures have warmed by 0.85 °C (0.65°C -1.06°C) between 1880-2012 and are confident that the cause of this recent climate warming is anthropogenic (Pachauri et al., 2014). Attribution analysis indicates that increases in anthropogenic Greenhouse Gases (GHGs) such as carbon dioxide, methane and nitrous oxide, combined with other anthropogenic drivers of radiative forcing, such as land use change, are very likely to be responsible for over half of the observed warming from 1951-2010 (Pachauri et al., 2014). By the end of the century, the most recent climate projections for the UK (UKCP18) estimate that under a high emissions scenario, temperatures over the UK will rise by between 0.9 °C to 5.4 °C in summer, and 0.7 °C to 4.2 °C in winter (50% probability level) relative to a 1961-1990 baseline. In addition to this, the frequency of extreme events, such as heat waves, is likely to increase (Christidis et al., 2015, Meehl and Tebaldi, 2004).

In order to be able to carry out effective public health practice, for example minimizing avoidable deaths and protecting the health of vulnerable populations now and in the future, quantifying past and current burdens of temperature related mortality and also potential future burdens of temperature related death under different climate scenarios is necessary. This enables decisions about mitigation and adaptive actions for current and future health risks to be taken, and can help provide traction for policy implementation. Knowledge of whether populations within the UK have become more or less vulnerable to the effects of heat and cold (or have 'adapted' to different temperatures) could also inform whether adaptation should be factored into future UK climate change impact assessments and helps highlight priority areas for action. Understanding the causal pathways between ambient temperature and health effects can further identify places for public health intervention and aid interpretation of epidemiological and health impact studies.

There are a number of national and international frameworks and structures aimed at mitigating and adapting to climate change, and situating research on the health effects of climate change within this policy context is important.

In 1992, the United Nations Framework Convention on Climate Change (UNFCCC) was opened for signature at the Rio Earth Summit, four years after the IPCC was established in 1988. Its main purpose is to prevent greenhouse gas (GHG) emissions reaching a level that would dangerously interfere with the climate system. Since this time, there have been a number of negotiations and climate change agreements, undertaken by parties to the UNFCCC. Most recently, in 2015 parties of the UNFCCC announced the Paris Agreement (United Nations / Framework Convention on Climate Change., 2015). The agreement came into force in November 2016, after ratification by at least 55 of the Parties responsible for at least an estimated 55% of current total GHG emissions. The central aim of the agreement, the long-term temperature goal (LTTG), as stated in article 2.1 (a) is

"Holding the increase in the global average temperature to well below 2 °C above pre-industrial levels and pursuing efforts to limit the temperature increase to 1.5 °C above pre-

industrial levels, recognizing that this would significantly reduce the risks and impacts of climate change."

The agreement allows Parties to determine their "nationally determined contribution(s)" (NDC) to the long-term mitigation goals, under a common and binding framework and the NDCs are designed to become increasingly ambitious.

In addition to ratifying the Paris agreement, the UK's 2008 Climate Change Act established a national framework for action on climate change (HM Government., 2008). This includes the setting of targets for reduction of GHG emissions to 2050 and recently the UK has committed to net zero emissions by 2050 (HM Government., 2019a). Under the 2008 Climate Change Act, there is a requirement for the Government to evaluate the risk that climate change poses to the UK every five years and to develop an adaptation programme. The most recent Climate Change Risk Assessment (CCRA), including information on health impact assessment, was completed in 2017 (Kovats and Osborn, 2016). Previously, the health effects of climate change were assessed by the UK's Health Protection Agency (now Public Health England(PHE)) (Vardoulakis and Heaviside, 2012) and PHE is now required to update the formal assessment of the health effects of climate change to health. The National Adaptation Programme (NAP), established under the Climate Change Act, focuses on preparing for and adaptation to climate risks, including risks to health and the development of indicators for health adaptation (HM Government., 2019b).

Understanding how the national and international policy context, with associated climate change adaptation and mitigation options, acts to modify risk to public health is critical, to inform risk assessments of climate change and to inform policies targeted at minimising the impact of weather related harm to public health, for example the Heat Wave and Cold Weather Plans for England (Public Health England., 2019, Public Health England., 2015).

1.2 Scope of the thesis

This thesis examines the relationship between ambient temperature and health outcomes in the context of climate change and international policy agreements – namely the Paris agreement. It seeks to deepen our understanding of a number of important issues within this area, contributing to methodology (e.g. by examining how 'cold' is defined within epidemiological studies and whether this reflects true causality) and to novel policy-relevant knowledge (e.g. by quantifying potential years of life lost (YLL) associated with heat and cold within the UK and providing an impact assessment of heat related mortality under conditions of the Paris agreement in the three largest UK conurbations). Given this thesis addresses issues pertinent to public health concerns around the direct effects of temperature on health, it is not as such bounded by one specific disciplinary focus. It draws on methods and integrates knowledge from many different of disciplines – for example, epidemiology, physiology and quantitative risk assessment – to answer questions relevant to environmental public health.

This thesis assesses the direct impact of health temperature effects only in terms of mortality and YLL (and does not include wider impacts such as economic impacts or effects on health service provision, for example). Specifically, the thesis does not address the numerous indirect effects of temperature on health outcomes (e.g. effects of temperature on vector borne or diarrheal disease, wider effects of temperature on environmental determinants of health such as diet, food prices etc.).

This is a research paper-style thesis. It comprises four published and one soon to be submitted journal papers, linked by supporting material. Where possible, duplication of material has been kept to a minimum, although with this style of thesis it is inevitable that there will be some repetition of ideas and supporting literature, as each chapter or paper is intended to be read also as a stand-alone piece of work. Where the published results papers need updating (e.g. there is a significant gap between publication date and thesis submission), updates have been added in the chapter's supporting material.

1.3 Thesis outline

The thesis is divided into three main parts: part one gives the background to the thesis (chapters 1-3); part two, the research component ('results' chapters 4-7) and part three, the discussion (chapter 8) which brings the findings of the thesis together in the overall context of climate change and the policy environment.

- Part I: The next part of the background section provides a brief overview of the aims and objectives of the thesis (the methods used to address each of the aims and objectives are detailed within the relevant research chapters). It is followed by the background literature review which consists of two parts – a published review on the effects of heat on health outcomes within the UK, which includes information on published health impact assessments of heat related mortality under climate change (Chapter 3, Parts 1 and 2) and a brief summary of cold effects on health is also included (Chapter 3, Part 3). Given that the effects of low temperatures on health have been extensively reviewed elsewhere (Hajat, 2017) and also in the introduction to chapter 4 - the first research paper (Arbuthnott et al., 2018), they are not included in full again in this section.
- Part II: Chapters 4-7 comprise the main results of the thesis. Chapter 4 is a research paper, which examines the effect of cold threshold placement on cold-related attributable mortality and questions around causality. Chapter 5 is a systematic literature review, which examines whether there have been changes to temperature-related mortality risks over time. Chapter 6 comprises an empirical research paper addressing two pertinent issues – the relationship between YLL, mortality and temperature in the three major UK conurbations and whether this

has changed in recent years. Lastly chapter 7 is an empirical research paper which details results of an impact assessment of the direct effects of temperature on mortality within UK conurbations under the Paris agreement using projections of future climate change.

- Part III: The third part of the thesis (Chapter 8) is the main discussion chapter. It brings together the main findings from each of the results chapters, discusses the strengths and limitations of this body of research as a whole and assesses the contribution of the thesis to knowledge. It also outlines the policy and research implications of the thesis and areas for further work.

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2 Aims and Objectives of the thesis

The overall aim of this PhD is to examine current and potential future effects of temperature on health (mortality and YLL) in the UK.

Whilst much is known about current effects of temperature on mortality within England, and specifically at a regional level, there remain many important gaps in knowledge. These gaps affect both our understanding of current and future impacts of temperature on population health and are important for public health policy. Through the background literature review (chapter 3) and work for early chapters, five specific knowledge gaps were identified as being significant, relevant to public health and policy, and possible to address within the scope of this PhD. These informed the research questions and objectives for this PhD. Where possible these objectives build upon each other, to allow a better understanding of temperature related effects within the UK within the context of climate change.

Additionally, one over-arching gap in knowledge is the geographical level at which heat risks are understood: less is known in England about the impacts of ambient temperature at a conurbation or city level, compared to regional levels (see section 1.1 for more details). Therefore, the primary research undertaken for this PhD has been at conurbation level. Specifically, the three largest English conurbations were selected: Greater London, Greater Manchester and the West Midlands (including Birmingham). These allowed for more precise epidemiological estimates (compared to locations with smaller populations), whilst also including cities from different geographical/climatic regions (the South East, the Midlands and the North West) with their own climate change action plans (Birmingham City Council, Manchester City Council., Mayor of London, 2018).

2.1 Objective One

There is no consensus on how 'cold' is defined – i.e. the 'cold' thresholds, below which temperature effects are modelled are highly variable within the UK – ranging from the 5th percentile to the 85th percentile of the mean temperature distribution. This is likely to affect not only the quantified impact of temperature-related mortality but also how 'policy' thresholds for action (e.g. in cold weather plans) are set, and how we think of future cold related burdens. There is also little discussion in the epidemiological literature on whether the effects of cold on mortality are causal across the broad spectrum of threshold temperatures used. Given that the cold and heat threshold need to be set in any epidemiological model before quantifying temperature risk and also that impact assessment requires a temperature threshold to be set, this issue needed to be understood before going on to model the current and potential future effects of heat and cold.

Research question:

How does the definition of cold used within epidemiological studies relate to causality and affect quantified burdens of cold-related mortality?

Objective(s):

Assess the implications of cold threshold placement on quantified cold related burdens and the evidence on causal pathways linking low ambient temperature, mortality and morbidity.

Specific objectives:

- Determine the range of cold thresholds used in previous UK studies and use London as a case study to model the sensitivity of relative risk (RR) and attributable burdens to cold threshold placement.

- Determine an appropriate framework and method of integrating knowledge from different disciplines to inform whether the relationship between temperature and mortality over the range of temperatures in UK studies can be deemed causal

- Discuss whether the above can inform appropriate temperature threshold placement and interpretation of health impact assessment results, and to examine the policy and research implications of this

2.2 Objective Two

The term 'adaptation' is used widely within epidemiological and health impact literature, and assumptions about adaptation to heat are often made within impact assessments of future heat-health effects. However, this has been often been undertaken without reflection upon whether past adaptation has occurred in a given location. At the time of undertaking the research, there had been no systematic review of changes in temperature-related health risk across given locations, and the methods used to assess this. Knowledge and understanding of the empirical evidence for population changes in susceptibility over time could inform projected temperature related mortality impacts under climate change.

Research question:

Is there evidence for decreasing susceptibility to heat and cold over time in high/middle income countries and what methods are used to address this?

Objective(s):

Systematically review the epidemiological literature to assess evidence for changes in susceptibility to health-related temperature effects over time and specifically:

Review evidence for past 'adaptation' (reduction in susceptibility to temperature related morbidity or mortality) in the epidemiological literature by:

  - examining the quantified risk of health-related events with changing ambient temperature in one location over a given time period (not limited); or
  - comparing outcomes between two different discrete extreme temperature events (>1 day, for example, usually defined by the context specific definition of a heatwave or cold spell) in one location

- Summarise the methods used in studies to assess changes in susceptibility to temperature related morbidity or mortality, to inform future PhD chapters.

2.3 Objective three:

In UK studies, health outcomes have been limited to mortality (all-cause and cause-specific) and certain morbidity outcomes/indicators (e.g. hospital and GP attendances (Arbuthnott and Hajat, 2017)). There are health outcomes which could be used to inform health policy, which have not been examined. Potential years of life lost (YLL) take into account population life expectancy and age at which mortality occurs, but have not been used in the UK as an outcome-metric in studies of temperature-related mortality (with the exception of one study using London data which used indirect methods and to derive estimates of temperature-attributable YLL and therefore has some methodological limitations (Baccini et al., 2013)).

Understanding the relationship between ambient temperature and YLL could inform resource prioritisation and is important in the context of climate change and an ageing UK population.

Research question:

What is the risk to mortality and potential Years of Life Lost at temperatures above and below a given threshold in the largest three English conurbations?

Objective(s):

Undertake an ecological time series analysis, to quantify the epidemiological relationship between temperature, mortality and YLL in the three largest UK conurbations; Greater London, Greater Manchester and the West Midlands

2.4 Objective four:

Whilst the systematic review under objective 2 determined approaches to understanding changes in susceptibility to heat and cold over time and whether there was evidence for this over a number of high/middle income countries, it found no studies specifically examining changes in susceptibility in heat and cold risk within UK conurbations in recent years. This represented an important gap in knowledge: changes which have occurred over longer periods of time could plausibly be related to wider societal factors and phenomena, such as the epidemiological transition, and are less likely to be as a result of recent adaptive policy actions such as heat and cold weather plans, fuel subsidies etc. In addition, understanding changes in vulnerability in recent years can inform adaptation assumptions used in climate health impact assessments.

Since publication of the review (though after undertaking the work for this results paper), there have been a few further studies which have examined changes in risk of heat or cold related mortality in the UK as a whole as part of a larger study (Vicedo-Cabrera et al., 2018) and specifically examining changes in cold risk since the introduction of the cold plan (Murage et al., 2018). However, no study has undertaken this analysis at a conurbation level or using YLL as an outcome.

Research question:

Is there any evidence for changes in susceptibly (risk of mortality and YLL) to ambient heat and cold in recent years in the three largest English conurbations?

Objective(s):

Examine the epidemiological evidence for a change in the RR of heat and cold related mortality and YLL in recent years in the three largest English conurbations

2.5 Objective Five:

The most recent risk assessment of the temperature effects of climate change undertaken specifically for the UK, used the UKCP09 projections (Hajat et al., 2014). These gave probabilistic projections for regions of England in 2020, 2050 and 2080. Multi-country studies have also included UK data when assessing the impact of climate change on temperature-related mortality using climate change projections driven by the RCPs (Gasparrini et al., 2017). However, few studies have examined the impacts of climate change on health outcomes specifically under the conditions of the UNFCC 2015 Paris agreement and this represents a significant gap in knowledge across many locations.

Research question:

What is the range of projected heat-related mortality burdens for Greater London, Greater Manchester and the West Midlands, if average global warming is limited to 2°C or 1.5°C, as laid out in the Paris agreement?

Objective(s):

Model the impact of climate change under scenarios compatible with the Paris agreement (limiting warming to 1.5°C or 2 °C compared to pre-industrial levels) on heat related mortality in the three largest English conurbations.

Secondary objectives:

- Quantify the probability of extreme heat (heat wave) events under baseline (current) conditions and under scenarios of 1.5°C or 2 °C of global warming (relative to a pre-industrial baseline)

2.6 Summary

The overall framework for the PhD, including how research objectives map to each chapter and research paper is summarised in Table 1 below. Of note, almost all studies of temperature-related health outcomes in the UK have been conducted at the regional level and few studies have been carried out at conurbation level. However with the majority of the UK population living within cities (Office for National Statistics), effects such as the Urban Heat Island (UHI) (Heaviside et al., 2017) and the degree of devolvement of power and climate change action being undertaken at city level, conurbation level assessments of temperature related health risks are important and represent a gap in current knowledge. Therefore, where health effects have been quantified, this PhD uses conurbation level data to address the specific gaps in knowledge. Ethics permission for the research carried out in this thesis was granted by the LSHTM observational research ethics committee in November 2013. The methods used for each research study are detailed in the individual papers and are not repeated here to avoid repetition.

Table 1: Overall PhD framework

Aims and objective(s)	**Methods Used to address research objective**	**Which (if any) other parts of the PhD did this inform?**	**Chapter/Results paper**
1.To develop an informed approach to cold threshold selection, by specifically: a. Examining current key issues around cold threshold selection, e.g., the differences in temperature threshold choices between key London-based studies and the influence of threshold on the cold related mortality burden b. appraising and integrating evidence for causality across the different temperature ranges and time-periods used in studies using the Bradford Hill considerations c. discussing whether the above can inform appropriate temperature threshold placement and interpretation of health impact assessment results, and to examine the policy and research implications of this.	Time series regression analysis to illustrate temperature-mortality risk relationship and sensitivity of risk to threshold selection: Bradford Hill considerations used as a framework	Informs cold threshold selection for epidemiological models used for objectives 3 and 4 (assessing current and recent temperature effects)	Chapter 4 Paper 'what is cold related mortality? A multi-disciplinary perspective to inform future climate change assessments' (Arbuthnott et al., 2018)
2. Determining how 'adaptation' to temperature is understood and represented in epidemiological literature and how this can inform future Climate change risk assessments (CCRAs). Specifically, the chapter aimed to systematically review changes in mortality in response to: a. general temperature increases or decreases and b. to extreme weather events, such as heatwaves and cold snaps.	Systematic literature review	Appreciating the range of approaches used to assess 'adaptation' in the epidemiological literature and critiquing these informed methods for objective 4 (determining whether sensitivity Understanding whether there have been changes in vulnerability to temperature over time informs	Chapter 5 Results paper: 'Changes in population susceptibility to heat and cold over time: assessing adaptation to climate change' (Arbuthnott et al., 2016)

		adaptation assumptions in future impact assessments	
3. Estimate current effects of temperature in Greater London, Greater Manchester, West Midlands. Specifically to: a. Quantify the risk of mortality for every 1 °C above or below the heat or cold threshold b. Quantify the risk of YLL for every 1 °C above or below the heat or cold threshold	Time series regression analysis	Originally performed to provide baseline co-efficient for impact assessment	Chapter 6 Results paper: ‘Years of life lost and mortality due to heat and cold in the three largest English cities’ (Arbuthnott et al., 2020)
4. Determine whether there have been changes in sensitivity to temperature effects in these conurbations in recent years a. Analyse cold and heat related risks for mortality and YLL over discrete time bands and yearly to assess whether this has changed	Time series regression analysis	Informs whether adaptation can be assumed based on recent empirical evidence from the UK	Chapter 6 Results paper: ‘Years of life lost and mortality due to heat and cold in the three largest English cities’ (Arbuthnott et al., 2020)
5. Determine impact of climate change under scenarios compatible with the Paris agreement (limiting warming to 1.5 or 2 Degrees Celsius) on heat related mortality in the three conurbations. Specifically, I set out to investigate: a. the change in frequency of heat wave events under global warming scenarios of 1.5 or 2 degrees b. the change in heat related mortality under global warming scenarios of 1.5 or 2 degrees	Health impact assessment methods		Chapter 7 Results paper: ‘Heat Related Mortality in the three largest English Conurbations under the Paris Agreement’ (in preparation)

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3 Background Literature Review

3.1 Introduction

This chapter places the thesis in context and summarises the past, current and potential future effects of increased temperatures/heat on health outcomes in the UK. It is split into three parts – the first, is a background review of the health effects of increased temperature, which has since been published and is therefore included in its published format. The supplementary materials that accompanied the publication (e.g. the results tables that summarise included studies) are included in Appendix 1. The second, is a post-script to the literature review, which highlights findings from the Environmental Audit Committee's consultation on resilience to heatwaves and a recent review of England's heatwave plan, both important to UK policy but published after the literature review. The third section of this chapter, summarises literature on the effects of cold and is kept very brief because the effects of cold in the UK have been reviewed extensively and recently elsewhere, and because the literature is reviewed as part of the background to chapter 4.

3.2 Research Paper

Cover sheet and research paper on subsequent pages

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	310970	**Title**	Dr
First Name(s)	Katherine		
Surname/Family Name	Arbuthnott		
Thesis Title	Temperature related effects on mortality and years of life lost in the UK for current and future climates		
Primary Supervisor	Dr Shakoor Hajat		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Environmental Health		
When was the work published?	05 December 2017		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	Choose an item.

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I undertook the literature searches, reviewed the literature, wrote the first draft of the manuscript and responded to reviewers' comments

SECTION E

Student Signature	[redacted]
Date	12/08/2020

Supervisor Signature	[redacted]
Date	24/08/2020

Arbuthnott and Hajat *Environmental Health* 2017, **16**(Suppl 1):119
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Environmental Health

REVIEW **Open Access**

The health effects of hotter summers and heat waves in the population of the United Kingdom: a review of the evidence

Katherine G. Arbuthnott[1,2*] and Shakoor Hajat[1]

Abstract

It is widely acknowledged that the climate is warming globally and within the UK. In this paper, studies which assess the direct impact of current increased temperatures and heat-waves on health and those which project future health impacts of heat under different climate change scenarios in the UK are reviewed.

This review finds that all UK studies demonstrate an increase in heat-related mortality occurring at temperatures above threshold values, with respiratory deaths being more sensitive to heat than deaths from cardiovascular disease (although the burden from cardiovascular deaths is greater in absolute terms). The relationship between heat and other health outcomes such as hospital admissions, myocardial infarctions and birth outcomes is less consistent. We highlight the main populations who are vulnerable to heat. Within the UK, these are older populations, those with certain co-morbidities and those living in Greater London, the South East and Eastern regions.

In all assessments of heat-related impacts using different climate change scenarios, deaths are expected to increase due to hotter temperatures, with some studies demonstrating that an increase in the elderly population will also amplify burdens. However, key gaps in knowledge are found in relation to how urbanisation and population adaptation to heat will affect health impacts, and in relation to current and future strategies for effective, sustainable and equitable adaptation to heat. These and other key gaps in knowledge, both in terms of research needs and knowledge required to make sound public- health policy, are discussed.

Keywords: Climate change, Heat, Summer, Heat-wave, Temperature, Mortality, Morbidity, United Kingdom, Adaptation

Background

There is a well-established link between increased ambient temperatures and adverse health outcomes. This has been demonstrated for the United Kingdom (UK) and across a range of settings [1, 2]. It is also unequivocal that the global climate is warming and the consensus is that this is largely due to anthropogenic causes [3]. Recent probabilistic projections [4] using a medium emissions scenario estimated that summer mean temperatures in some locations in southern England are very likely to rise between 2.2 and 6.8 °C (10% and 90% probability levels respectively), with a central estimate of 4.2 °C (50% probability level) by 2080 relative to a 1961–1990 baseline [4]. The frequency of extreme heat events or heat waves is also projected to increase [5, 6]. Therefore, understanding both the current and future impact of hot weather on health and the measures which can be taken to reduce these impacts is important for planning and carrying out effective public health action.

The aim of this narrative review is to bring together evidence from epidemiological studies and health impact assessments to provide an overview of what is known about current and projected effects of heat on population level health in the UK. We review only those impacts directly related to increased ambient heat exposure (i.e. evidence of the indirect impacts of temperature changes such as changing patterns of infectious diseases are not included). This review focuses on UK studies, though evidence from other high-income settings has occasionally been included for illustration and discussion where evidence from the UK is lacking.

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Lastly we discuss what is known about the potential for adaptive measures to reduce the impact of heat on health and identify key gaps in knowledge.

Methods

Studies were included which used data from the United Kingdom, aggregated to regional, conurbation (e.g. Greater London) or national level. These could have been as part of a larger study including data from other countries. We included studies in the epidemiological and impact assessment part of the review which estimate:

- current or past associations between a) patterns of hot weather (time series or case-crossover studies) and health outcomes (see below) and b) heat waves (studies using episode analysis) and health outcomes
- impacts of warming under climate change (past and projected) on health.

All outcomes related to health and well-being were considered (e.g. mortality, indicators of morbidity – use of health services e.g. hospital admissions, NHS direct calls, GP visits, specific outcomes such as myocardial infarction etc.). Where outcomes for specific sub-groups of the population (e.g. older persons) were available, these were included to further understand potential vulnerable sub-sets of the UK population.

In order to locate the relevant epidemiological studies we searched the database Ovid Medline using terms relating to two main concepts: one relating to climate and high temperatures/heat waves/climate and one relating to health outcomes. The search terms were combined using appropriate Boolean operators and results limited to the English language and humans. No date restrictions were applied and searches were updated in January 2017. Searches were not initially restricted by geographical region, as many studies included data from multiple countries. However, from these multi-country studies we specifically review results from the UK. In order to capture relevant articles not indexed in the databases, we also snowballed references.

Epidemiological studies of the effect of heat on health

The effects of ambient heat on mortality and morbidity

Study design

In general, the relationship between mortality (and morbidity) and changes in ambient temperature has been assessed using time series regression models or case crossover designs, which have been shown to yield similar results [7, 8]. UK based studies have generally shown a U,V or J shaped relationship between temperature and health outcomes, with an increased risk of mortality or morbidity above and below a given thresholds or minimum mortality temperatures (MMTs). Results are presented as the increased risk of outcome (relative risk (RR) for time series studies, odds ratios (OR) for case-crossover studies) for every 1 °C increase above that threshold.

Studies presented here have controlled for a combination of potential time varying confounders, such as pollution – typically ozone or PM_{10} (though the precise role of pollutants in analysis is currently under debate [9]), public holidays and day of the week, in addition to season and long term trends. Most studies have used a lag of between 0 and 2 days to analyse the relationship between exposure and outcome as, in contrast to the effect of cold, the effect of heat on health generally occurs within a few days of exposure [10].

The specific aspects of each study, including details of methods, exposure and outcomes and threshold selection are summarised in Additional file 1: Table S1 (UK based studies examining the effects of increased temperatures on mortality and Additional file 2: Table S2 (UK based studies examining the effects of increased temperatures on morbidity).

Effect of ambient heat on mortality

Across the UK there is an increased risk of all-cause mortality with increasing temperature above threshold values [10–30](see Additional file 1: Table S1 for details), a finding consistent with studies from a variety of global settings [1, 2]. The size of the effect varies between regions and also between studies, which may be partly driven by modelling choices such as the choice of the threshold but also due to local population differences in climate, demography and social factors. Modelled above the 93rd percentile of maximum daily temperatures, one recent study found the increase in all-cause mortality is 2.1% for each 1 °C increase in temperature (95% CI:1.6%, 2.6%) for England and Wales [22]. Some UK based studies have examined the attributable deaths due to heat exposure. For example, Gasparrini et al. [22] found that 1.0% of all summer deaths in England and Wales were attributable to temperature and Armstrong et al. [21] found a similar figure.

Most UK studies examining cause-specific mortality [13, 20, 22], have categorised deaths as cardiovascular, respiratory or external (to retain power). Within these categories, respiratory and external causes of mortality have been demonstrated to be most sensitive to heat in terms of RR (though due to the total larger number of deaths occurring from cardiovascular disease, a greater portion of heat attributable deaths are due to cardiovascular causes). However, a more detailed breakdown of causes of death [22] (see Additional file 1: Table S1 for further details) found that within these general categories (e.g.

cardiovascular, respiratory deaths) some causes of death were much more sensitive to heat (in terms of magnitude of RR) than others (for example the RR of death from atrial fibrillation or pulmonary heart disease was much greater than for cardiovascular disease in general) and also that endocrine, nervous system and genitourinary causes of death are sensitive to heat . The risk of suicide is also increased by heat [17].

Baccini et al. analysed Years of Life Lost (YLL) due to heat in a multi-city European study [24]. An average of 1914 heat-related YLL per year in London was estimated, not adjusted for harvesting or mortality displacement (see below).

Mortality displacement

Mortality displacement ("harvesting") refers to the process by which some deaths which occur in an already frail population are brought forward by a few days or weeks. The effect of mortality displacement on the estimated risk of mortality caused by increased ambient temperatures has been specifically examined for London.

For example, the 1914 heat-related YLL in London, estimated by Baccini et al. [24], reduced by 81% to 356 per year when adjusted for short-term harvesting. One study specifically examined the effects of mortality displacement across a range of settings [14] and found that for London, the RR of all cause and cardiovascular mortality did not persist past 2 days and that by day 11 the sum of the effects for all-cause mortality was 0 (the risk for respiratory cause mortality, however, remained over the 28 day period tested). In contrast, the excess risk of heat on mortality persisted for 3 weeks in Delhi. This was attributed to heat causing death in children or people who are not usually at risk of imminent death. More recently, annual time series were used to examine longer time mortality displacement for London. However, the study was unable to draw any firm conclusions about how long heat deaths may have been brought forward by, due to the imprecision of estimates [31].

Of note, the harvesting evaluation could be sensitive to modelling choices. For example, most studies use a threshold fitted from data from the general population, whereas the threshold may be lower for those at risk of harvesting.

Effect of ambient heat on morbidity and other indicators of health and wellbeing

In the UK, there is no clear evidence of an association between total emergency hospital admissions and raised ambient temperatures [32]. However a significant increase for respiratory admissions (5.4% (95% CI: 1.9%, 9.1%)) increase per 1 °C above the 23 °C threshold (and for renal disease admissions (1.3% increase per 1 °C above the 18 °C threshold (95% CI: 0.3%, 2.4%)) has been demonstrated [32]. These findings have been supported by other work [33]. The contrast between mortality and hospital admissions may in part be due to heat causing a rapid deterioration in those who are vulnerable, meaning they do not present to medical attention before death. There is evidence from two studies of an association between paediatric emergency trauma admissions and increasing ambient temperature in England [34, 35]. For example, Atherton et al. report an 11% increase (95% CI: 12%, 38%) in paediatric trauma admissions for every 5 °C increase in maximum temperature (and larger increases using minimum temperatures as an exposure variable) [34]. This association for paediatric admissions was greater than for adult trauma admissions, which was found to be non-significant in the study by Atherton et al. and of smaller magnitude the study by Parsons et al. (1.8% increase in adult trauma admissions for 5 °C increase in temperature, significance not reported) [35].

At a daily resolution, there has been no demonstrated increased risk of myocardial infarction (MI) admissions with increasing temperatures in the UK [36]. However, an increased risk in MI (1.9% (95% CI: 0.5%, 3.3%) per ° C above the threshold) has been demonstrated 1–6 h after heat exposure [37]. This excess-risk at shortest lags was followed by reduced risk at 24 h leading to the hypothesis that the reduction at longer time intervals is due to short term displacement.

A recent study in Birmingham [38] demonstrated correlation between increased temperatures and poorer ambulance category A response times. Further work is needed to quantify the risk, for example using time series regression, to include better confounder (e.g. number of ambulances on duty in a day, air pollution etc.) and seasonal control in the analysis.

In London, although the odds of preterm birth were affected by seasonality (increased odds in winter months), no association between premature birth and increased or decreased temperatures up to six days before birth was found [39]. Studies examining different exposure timings and neonatal outcomes of interest (e.g. birth weight, pre-term birth) within the UK would be welcome as results from other settings have yielded mixed outcomes [40].

The effects of heat on these indicators of health and wellbeing are summarised in Table S2 in the supplementary materials.

Heat waves

The effect of heat waves or defined periods of high temperatures on health has been mostly examined using episode analyses, where the outcomes over an identified heat-wave period are compared to an expected baseline. There is no consensus around the definition of a heat wave used within the UK, though most studies include a duration and severity component. For example, the World Meteorological Organization define a heatwave as "when the daily maximum temperature of more than five consecutive days exceeds the average maximum temperature by 5°C, the normal period being 1961-1990" [41]. However, criteria used to trigger public health warnings in Public Health England's heat wave plan, use region-specific thresholds based on maximum daytime and minimum night-time temperatures to trigger different alert levels [42].

Given the lack of a consistent definition of a heatwave (leading to the use of different duration and severity components used in analysis), differences in baseline selection for episode analyses, differences of heatwave timing within the summer season (heatwaves and hot days occurring earlier in the summer may have a greater effect on mortality [43, 44]) and differing characteristics of the preceding winter (there is evidence that winter mortality may affect heat related mortality of the following summer [45]), the effects of heatwaves between years within the UK is difficult to compare.

Mortality and heat wave episodes

Estimates of excess mortality have been made for many of the notable heatwave periods in the UK in recent years [11, 46–49].

The most severe single heat wave (HW) of recent times was in 2003, for which the health effects were greatest in continental Europe [50]. In England between 4-13th August 2003, the Central English Temperature (CET) exceeded average values (from 1871 to 2000) by 8 °C. This HW period in 2003 HW has been calculated to have led to 2091 excess deaths in England - a 17% increase (95% CI: 15%,19%) above the expected baseline [48].

Recently Green et al. used consistent definitions (any period that would trigger a Met Office heatwave alert of level 1, or a single day when mean Central England Temperature was greater than 20 °C) to compare total daily excess deaths occurring during all the defined heatwave periods over each summer between 2003 and 2013 [49]. The estimated excess mortality of all heatwave periods occurring in 2013 was considerably lower than in preceding years. For example, in 2013 there were an estimated total 195 excess deaths (95% CI: -87,477) across all heatwave days in those older than 65 years, with an excess of 10 deaths per heatwave day (95% CI: -4, 24). By comparison, for the same age group (65 plus years) the number of excess deaths for all heatwave days in 2003 was 2234 (95% CI: 1936, 2532) with 102 excess deaths per heatwave day (95% CI: 88,115) and in 2006 was 2323 (95% CI: 2008,2638) for all heatwave days with an average of 89 excess deaths (95% CI: 77,101) per heatwave day. There are many possible explanations for the decrease in later years. It is possible that the population has become less vulnerable to the effect of HWs (for example the Heatwave Plan was introduced in 2004 in England). In addition, the lower peak temperatures occurring in 2013 compared to 2003 and 2006, the timing of heatwaves in the season (see above) and differences in other environmental exposures such as pollution and humidity may have contributed.

In separate studies, notable increases in mortality have also been demonstrated for the 1995 and 1976 heatwaves [11, 47]. The 1995 heatwave is estimated to have caused an increase in mortality of 8.9% (95% CI: 6.4%, 11.3%) over England and Wales (and a 16% increase in Greater London) and the 1995 heatwave is estimated to have led to a 30.7% (95% CI: 25.8%, 35.8%) increase in mortality in Greater London.

Mortality displacement

Whilst none of the studies described here undertook a formal analysis of harvesting for UK data, estimates attributed less than 10% and 25% of the excess deaths to harvesting in the Paris 2003 [51] and Chicago 1995 [52] heat-waves respectively. Of note, there is current debate about how best to calculate mortality displacement for heatwave periods [53].

Heat waves and other health outcomes

In contrast to the large number of excess deaths in the 2003 heatwave, the proportional increase in hospital admissions over the whole of England was small – just 1% (95% CI: 1%,2%). This is consistent with findings that ambient heat increases mortality risk, but not all cause hospital admissions. London suffered a higher increase in admissions compared to the rest of the country in the 2003 heatwave (with a 6% proportional increase across the age groups, though this too was smaller than the 42% increase in mortality seen in London during the same heatwave period) [48]. A similar pattern has been demonstrated for the 1995 heatwave, where an excess mortality of 10.8% (95% CI: 2.8%, 19.3%) was calculated, but the increase in hospital admissions of 2.6% (95% CI -2.2%, 7.6%) was not significant [32].

Recently the use of syndromic surveillance demonstrated an increase in a range of selected indicators during heatwave periods in July 2013 [54]. These indicators included calls to NHS direct and GP services and visits to the emergency department for heat/sun stroke symptoms. A moderate increase in NHS direct calls was seen in the 2003 heatwaves, but was only significant for the younger age groups (0–4 years and 4–14 years) [55]. Other indicators for GP consultations and emergency department attendance for asthma, severe wheeze, myocardial infarction and cerebrovascular accidents showed no increase during the 2013 heatwave [56]. Indeed, the number of GP consultations over this period decreased for myocardial infarctions.

During the 1976 HW in Birmingham [57] there was no significant increase in sickness benefit claims but a modest increase was seen in GP consultations.

Work productivity and heat

Although the impact of hot weather has not been assessed in terms of productivity or occupational health outcomes in the UK, there is evidence that these outcomes are affected by heat elsewhere. A review of occupational health impacts of heat exposure, including data from a range of countries, found that manual workers exposed to extreme heat or working in hot environments and especially those in tropical low-middle income countries are at increased risk [58]. At risk occupations included farming, construction work, firefighters, manufacturing (where workers are exposed to heat generation) and those in the military. A recent review of all the heat related occupational fatalities in the US between 2000 and 2010 found a yearly death rate of 0.22 per million workers. Those most at risk included men, those working in agriculture and construction and Hispanics [59].

Distribution of health impacts by geographical region, age, gender and socio-economic status

Geographical/regional differences

A consistent finding, is that the increase in risk of heat related mortality is greatest for London, the South East and the East of England. Typically London, the South East and East of England have the highest RR per °C rise in temperature (typically thresholds for these studies have been set at a given percentile of the regional temperature distribution, so that all effects are estimated above say the 93rd percentile but the absolute value of this varies between locations, with hotter regions having higher absolute values) [20–22, 26, 60]. Bennet et al. [25] examined geographical vulnerability at greater resolution (district level) for England and found the same general pattern of risks of heat related mortality being higher in the South of England but also identified districts at particular high risk, for example the London borough of Tower Hamlets.

London, the South East and East of England also have the highest proportion of excess mortality calculated during heat waves. During the 2003 heat wave, the largest increase in proportion of deaths was seen in London (42%), followed by Eastern England (27%) compared to lowest proportional increases of 4% in the North West and 2% in the North East [48].

Reasons for the difference in risk between regions are not known, but differences in demographics, social and economic factors may play a part, as may the hotter temperatures experienced – particularly during heatwaves. It is likely that for cities such as London, the Urban Heat Island (UHI) has a role. The UHI refers to the increased temperature within built-up urban areas compared to surrounding suburban rural areas [61, 62], due to alterations in the energy balance as a result of surface properties (e.g. albedo etc.), land use and city design. Estimates from the West Midlands attribute around 50% of the deaths in the 2003 heatwave to the UHI effect [63] and it is likely to become increasingly important as we see an increasing proportion of the population living in cities [64].

Age

In the UK, older age groups are more at risk of heat-related morbidity and mortality [19, 25, 65]. This may be due to diminished ability to thermo- regulate, increasing medical co-morbidities or use of medications, and social factors which may limit behavioural adjustments to the increased temperatures. Vulnerability in older age groups is increasingly important, as demographic projections show an ageing UK population [66]. The exception to this is within populations with chronic psychiatric conditions (including psychoses, dementia and alcohol and substance misuse). In this subgroup of the population, those under the age of 65 were at increased risk [23].

Sex

In UK based studies females (in particular older females) appear to have a higher risk of dying at hotter temperatures and in a heat wave [16, 19, 57, 67]. However, it is possible that many of these results for females are confounded by age as this finding is not consistent across countries [68, 69].

Underlying co-morbidities and medications

In the UK, patients with neurological and psychiatric diagnoses, such as dementia and substance misuse and those prescribed antipsychotics, antidepressants and hypnotics have been shown to be at increased risk of heat related mortality [23]. An increased risk of hospitalisation and mortality from use of prescribed medication and recreational substance use has been found elsewhere [70, 71]. Plausible mechanisms underlying this include decreased thirst and decreased sweating [72]. No UK studies have examined heat related risk of mortality (or morbidity) in those with cardiovascular, respiratory, renal disease and diabetes, though evidence from other settings suggests they may be more vulnerable to the effect of heat [73, 74].

Socio-economic status

UK studies have not found a consistent relationship between socio-economic status (SES) (quintiles of deprivation analysed) and an increased vulnerability to heat or heat waves, analysed with data aggregated to regional or district level [16, 25]. However, analysis even at district level, could mask potential differences in vulnerability between socio-economic groups occurring at the individual level.

Studies in other countries, most notably North America have found some linkage with SES [73, 75]. This relationship may be partially explained or related to access to air conditioning, which is much more prevalent in the US compared to the UK or by differences in access to healthcare which are less prevalent in the UK (due to universal coverage provided by the National Health System).

Other factors affecting vulnerability

In the UK, place of residence (nursing or residential home) has been associated with an increased risk of heat-related mortality [16, 46], though this may simply reflect that those populations are likely to be more frail. There is little evidence of the effect of heat being modified by living alone or in a flat [16].

Current heat related impacts attributable to climate/weather and observed climate change

Despite observed warming of the climate over recent years [4], there is no evidence of a substantial increase in heat related mortality in the UK. Indeed, studies would suggest that there has either been a decline in heat related mortality in the UK over the last century [15] and between 1971 and 1997 in South East England [12], or that heat related risk has remained unchanged in London between the two time periods of 1996–2002 and 2004-2010 [28] and between 1993 and 2006 [30]. One study demonstrated a marginal increase in heat related mortality between 1977 and 2005 (of 0.7 deaths per million population per year [76], see below). Potential explanations for the decrease or lack of change in heat related mortality, despite an ageing population and observed warming, include a contribution from both specific adaptive policies (such as the introduction of the heatwave plan in 2004 [42]) and spontaneous changes not specifically aimed at adapting to heat but which may reduce vulnerability to it, such as improved healthcare and improved standards of living (this may be particuarly relevant to the decrease in heat related mortality observed over the early part of the last century [15]).

Christidis et al. [76], using optimal detection, investigated the contribution of climate (anthropogenic and natural influences) and adaptation (reduced population vulnerability to heat, rather than specific adaptive measures) to changes in mortality occurring between 1976 and 2005 in England and Wales. Results indicated a small increase in heat related mortality over the time period (of 0.7 deaths per million population per year) but they estimated this increase would have been higher (1.6 deaths per million population per year) if no adaptation had taken place. Results of the optimal detection analysis also demonstrated that if no adaptation had taken place, then anthropogenic influences on climate would have been the main influence on heat related mortality.

Recently, Mitchell et al. demonstrated that anthropogenic climate change increased the risk of excess heat-related mortality in the 2003 heatwave by around 20% in London [77].

Projected future health impacts of heat

Health impact studies estimating future heat-related mortality in the UK [26, 60, 78–82] have projected increases in heat related mortality throughout the twenty-first century. Health impact studies for a wide range of countries have been reviewed elsewhere [83].

These health impact studies typically take an epidemiological relationship, as described in the studies above, and apply future temperature projections (often derived from regional climate projections), to this relationship. To our knowledge, no current published estimates use temperature projections based on the more recent Representative Concentration Pathways [84]. Uncertainty in these health impact studies is introduced at many levels including uncertainty in the baseline coefficient (see above sections), future emissions, the parameters, processes and initial conditions included in climate change models, and a populations adaptive capacity [79]. Regarding the uncertainty introduced by climate projections, mortality estimates for London were found to be most sensitive to climate model physics uncertainty compared to emissions scenario choice and downscaling uncertainty [80]. Some [85] have suggested that future health impact projections are more sensitive to the choice of climate projections rather than uncertainties in the baseline exposure-response relationship or demographic projections.

The most recent projections of future impacts of climate change on UK mortality, estimate an increase in heat related mortality from a baseline of 1974 deaths per year in the 2000s, to 3281 deaths per year (66% increase) in the 2020s, 7040 deaths per year (257% increase) in the 2050s and 12,538 deaths (535% increase) in the 2080s. These projected deaths are attributable both to increased temperature and the increased projected population size. This study [60], based partially on the UK Health Protection Agency (HPA) climate change risk assessment [78], used a baseline co-efficient from the time series analysis of historic weather and mortality data in England and Wales from 1993 to 2006. The climate data was based on the UKCP09 climate projections for a medium emissions scenario. These medium emissions scenario UKCP09 projections used the Met Office Hadley Centre Regional Climate Model (HadRM3-PPE-UK) to dynamically downscale Global Climate Model (GCM) results for historical emissions and the Special Report Emissions Scenario (SRES) A1B. Though demographic changes were considered for the risk assessment, assumptions about adaptation were not. The regions projected to be most at risk are the East and South of England, the West Midlands and London. The additional heat-wave effect was significant only for London, where it was estimated to add an extra 58%, 64%, 70% and 78% to heat-related mortality in the 2000s, 2020s, 2050s and 2080s [60].

Of studies that have projected heat-related mortality for European or global cities which include London [26, 79, 81, 82], one included estimates which accounted for population adaptation [79]. The GCM used was the UK HadGM3 (with no downscaling) and emissions scenarios were A2 and B2. Adaptation assumptions included an assumption that the population would not adapt, adapt to a 2 °C or to a 4 °C increase in mean temperatures (achieved by shifting the dose response curve so that the heat-slope remained unchanged but the threshold temperature is increased). The projected mortality for London roughly halved for each 2 °C adaptation assumed.

In another study the proportion of respiratory hospital admissions attributable to heat for Northern Europe was projected to increase from 0.13% (lowest estimate 0.10%, highest estimate 0.15%) to 0.27% (lowest estimate 0.19%, highest estimate 0.32%) in the period 2021–2050 [86]. One less recent Department of Health report [87] projected in-patient hospital days associated with increased temperatures to increase to 285,000 per year by 2050 under a medium emissions scenario (using the UKCIP98 climate projections) compared to the baseline of 81,000 per year in 1995 and 1996 for England and Wales. Up to date projections using more recent data, climate projections and taking advantages in improved statistical techniques for modelling the underlying baseline associations between hospital admissions and heat, however, are lacking.

Potential for impacts of heat to be avoided by adaptation measures

Adaptation has often been used to refer to planned and unplanned structural and policy level actions which may reduce a population's vulnerability to heat. The extent to which adaptation can be achieved will depend upon the local context, vulnerabilities and adaptive capacity [88]. Acclimatisation more commonly refers to increased short term physiological tolerance to heat. It is outside the scope of this review to present evidence on physiological acclimatisation.

There is evidence that populations residing in areas with a warmer climate have increased thresholds for heat sensitivity [18, 89, 90] and that vulnerability to heat has decreased over time in several locations [12, 30, 91, 92]. However, identifying specific adaptive measures which have contributed this, and distinguishing the role of these from demographic or socio-economic background factors which may decrease sensitivity to heat, is challenging (though some studies have indicated a correlation between decreasing vulnerability and increased prevalence of air conditioning [91]). Further, the evidence of efficacy for given planned and implemented policies or interventions to specifically reduce negative health outcomes such as mortality and morbidity, using robust methods, is scarce [93, 94].

Potential adaptive strategies range from interventions and actions at an individual and housing level, health systems and infrastructure level through to national policy and plans. However there are complex interactions between impacts of many given policies. It is important to consider whether any of policies could be 'maladaptive' or have unintended consequences (e.g. [95, 96]). It would be most desirable if strategies reduced health effects of both heat and cold (for example through improved building design, which may also be useful for climate change mitigation [97–99]) and had other health co-benefits (e.g. urban greening – see below).

Adaptive measures with the potential to reduce the health impacts of heat are briefly considered here from the individual level to National Policy level.

Behavioural measures

Behavioural measures to protect against the effect of heat such as use of cool clothing, increasing intake of non-alcoholic fluids, and restricting strenuous activity to cooler parts of the day, are often advised [42, 100]. However there is a lack of studies that have fully quantitatively evaluated the impact of behavioural measures on heat related outcomes.

The efficacy of behavioural measures will depend both upon the effectiveness of the intervention to reduce heat exposure and also the willingness of individuals to take up these behaviours: one recent survey examined a number of protective behaviours carried out during the 2013 heatwave and home characteristics (e.g. prevalence of air conditioning) in a sample of the UK population [101]. It found that the elderly were less likely to partake in some personal and home protective measures but were more likely to open their windows at night. Higher income earners were also more likely to engage in personal and home protective measures. It therefore highlighted groups for further targeting of health messaging.

Interventions at an individual or place of residence level

Air conditioning and electric fans

Prevalence of air conditioning in the UK is low (estimated at 3% in a recent survey [101]) and evidence for its efficacy in reducing heat-health impacts is not available within the UK. However, there is evidence, mostly from Northern America, that air conditioning offers protection against the impacts of heat on health [74, 102] and that seeking a public space with air conditioning can be protective [103]. Indeed this is a measure included in many heat wave plans. However, there are potential disadvantages to promoting this as an adaptive strategy. For example there may be equity issues in terms of both the prevalence and availability of air conditioning units. Access to shared air-conditioned space may remove some of these concerns. Extensive use of air conditioning could increase energy demands and itself contribute to the urban heat island effect [96]. There are also examples of power grid outages (which can occur during extreme weather events such as heat waves), which would limit the protection that air conditioning could offer [104]. Further evidence is required in order to be able to effectively weigh the benefits of air conditioning against its environmental, energy and health costs. Passive cooling measures may reduce the need for air conditioning.

A systematic review [105] of the evidence on use of electric fans found no studies which met its inclusion criteria (study type of randomised controlled trials or other experimental designs, such as interrupted time series studies). It therefore concluded that there were not enough high quality studies to assess the evidence. Where case control studies were found, results for the protective effect of fans were inconclusive with some studies showing a protective effect and others the opposite.

Community, services and Urban Design level adaptations

Many interventions have been postulated that may improve adaptation at an urban design level, for example increased use of green spaces [106], improved insulation of housing against heat and cold [98], improved surface properties of buildings (e.g. increasing albedo) [107] etc. Some of these, such as increased green spaces can provide co-benefits to health [108, 109] in addition to adapting to climate change [106]. Unintended consequences of interventions should also be considered (e.g. indoor air quality concerns in more air tight houses etc. [110], exposure to allergens and volatile organic compounds released from urban trees [111]). Further, health services will also need to adapt to ensure comfortable and reliable care in warmer temperatures (e.g. indoor temperatures, power supply in heat waves, ability to cope with potential increased demands during hot weather [112]). These measures will require multi-sectorial working and planning.

Policy level interventions

Heat warning systems (heatwave plans)

Public Health England publishes an annual heatwave plan [42], which has been operational since 2004, following the 2003 European heatwave. The plan details actions that individuals and organisations can take to reduce the risk of heat to public health. These include both high level preparations and actions for health and social care organisations in England and advice for the general public on health protection and specific measures to protect vulnerable groups. As such there are several core parts of the plan ranging from strategic planning and preparedness to the alert system and advice on communication with the public. It details cascades of heatwave alerts and specific advice on protective measures (for example key messages for the public include keeping out of the heat, taking measures to cool down and keeping the environment cool and monitoring others who are vulnerable). The heat health alert service detailed in the plan splits heatwave alert levels into 5 categories: level 0 (long term planning which is to take place all year round) to level 4 (a major incident – severe or prolonged heatwave which affects several National level sectors in addition to health). Temperatures used to trigger heatwave alerts are set at regional specific thresholds and use daytime and night time maximum temperatures. For example the daytime maximum temperature which would trigger an alert in London is 32 °C compared to 28 °C for the North East of England.

A recent systematic review has examined the effectiveness of Heat Warning Systems (HWS) [113] (any action plan based on meteorological and demographic information typically including early alerts and public health protection measures, tailored to local contexts). The review found that research in this area is limited. Six out of the 15 studies included found some evidence of effectiveness of HWS, but were unable to robustly establish a causal relationship between HWS implementation and reduced mortality and morbidity. Further evidence to evaluate both the individual recommendations within the plans and the effectiveness of the plans overall would be useful for improvements to these.

National level frameworks for adaptation

Under the Climate Change Act of 2008 [114], a framework was established for the UK to respond to climate change. As part of this, government is required to assess the risks from climate change to the UK and prepare strategies to address these (e.g. through the National Adaptation Plan) and to increase resilience to climate change.

Targeting policy

Attention should also focus on ensuring the adaptation needs of the most vulnerable populations are met. However, this may be complex to achieve.

Identifying those at risk has the potential to improve targeted prevention policies. Some UK studies have sought to incorporate known vulnerabilities into spatial heat health risk assessments combining geographical information on the heat hazard, exposure and vulnerability of small area populations within cities. Examples include the development of a vulnerability index for London [115], a spatial heat health risk assessment for Birmingham [116] and a conurbation-scale heat risk assessment undertaken for Greater Manchester [117], combining projected temperature rises with urban vulnerability indicators. These vulnerability mapping studies are often undertaken to support decision and policy making. However, one recent systematic review, demonstrated that although this is often the authors stated intention, there is currently little demonstrable evidence of their use to influence policy [118]. This highlights the importance of ensuring that research is both useable and relevant to policy makers.

Identification of vulnerable populations can also be difficult to translate into the social and medical support required. Firstly, whilst front-line responders feel they know those individuals who are at increased risk at a given time, vulnerabilities such as co-morbidities and social isolation fluctuate rapidly and keeping a systematic record of these is difficult [119]. Further, barriers to implementation of protective policies may result from the low priority given to heat risk by practitioners and also by the vulnerable populations themselves [119]. The picture may in fact be made more complex by reinforcement of social norms within at risk populations. For example increased contact in social networks may perpetuate views amongst the elderly that they are not at risk [120].

Conclusions

This review has discussed the key findings of UK studies illustrating the association between increased temperatures and heat waves and mortality. Results for other health outcomes are less consistent. Vulnerable populations include the elderly and those with certain co-morbidities. Future projections all predict an increase in heat related deaths throughout this century, the magnitude of which depends on assumptions used within models.

However, key gaps in our knowledge remain and warrant further investigation. These include knowledge gaps around the relationship between health outcomes and more extreme temperatures not yet experienced in the UK, a better understanding of certain vulnerabilities to heat (for example, the effect of UHIs and different individual and local level factors which increase or decrease risk within the UK) and the effect of high temperatures on other well-being outcomes (such as economic productivity).

Considering future impacts, the use of temperature projections based on the newer Representative Concentration Pathways (RCPs) [84] could be examined for future health impact assessments. Further work on impact by certain groups such as by age and socio-economic status in addition to location would be useful. There are also many gaps in our knowledge about adaptation. For example, what works now and what may work in the future? How can past specific adaptive measures be identified and evaluated? And how might adaptive strategies translate from one setting to another? How can we best model adaptation in future heat-health impact assessments? There are gaps in our knowledge around adaptive measures that might have multiple health benefits and how public health can best work with other sectors to promote integrated research and policy development in this area. The design and use of suitable indicators for adaptation and ensuring equity components are reflected in these, is important in order to evaluate progress.

Addressing these knowledge gaps will be paramount to ensure that evidence can inform policy for appropriate actions and use of resources to minimise future health impacts of heat, and to improve health under a changing climate.

Additional files

Additional file 1: Table S1. UK based studies examining the effects of increased temperatures on mortality. (DOCX 27 kb)

Additional file 2: Table S2. UK based studies examining the effects of increased temperatures on morbidity. (DOCX 19 kb)

Additional file 3: Open peer review. (PDF 50 kb)

Abbreviations

CET: Central England Temperature; CI: Confidence Interval; DOH: Department of Health; GCM: Global Climate Model; GDP: Gross Domestic Product; IPCC: Inter-governmental Panel on Climate Change; MI: Myocardial Infarction; MMT: Minimum Mortality Temperature; ONS: Office for National Statistics; PM: Particulate matter; RA: Risk assessment; RCP: Representative Concentration Pathways. These represent four greenhouse gas trajectories and describe used in the fifth IPCC report (AR5). Rather than describing emissions scenarios (e.g. like the SRES), the product is a set of four pathways that lead to a range of radiative forcing levels from 2.6–8.5 W/m2. These endpoints are compatible with the range of previous emissions and climate policy scenarios; SRES: Special Report Emissions Scenarios. Produced by the IPCC, these are baseline scenarios and include the A1 family (an integrated world with rapid economic growth) A1F1 (emphasis on fossil fuels) A1B1 (balanced emphasis on all energy sources) A1T (emphasis on non -fossil energy sources). A2 (more heterogeneous world, self-reliant nations, increasing populations, regionally orientated economic development). B1 (rapid economic growth but towards a service and IT economy, population rises then declines past 2050, introduction of clean and efficient technologies) B2 (world more divided/heterogeneous but more ecologically aware); UHI: Urban Heat Island; UK: United Kingdom; UKCP09: UK Climate ProjectionsUKCP09 represent the 5th generation of climate projections for the UK. These provide probabilistic projections for three different future emissions scenarios, representing low, medium and high emissions (chosen from scenarios in the Special Report on Emissions Scenarios (SRES)); UKCP98: UK Climate ProjectionsUKCP98 represent the 3rd generation of climate projections for the UK. These used the HadCM2 model. They presented four scenarios 'low' (low forcing, low climate sensitivity), Medium-low, medium-high and high (high forcing, high climate sensitivity); YLL: Years of Life Lost

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Peer review reports for this article are available in Additional file 3.

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3.3 Postscript to the "Health effects of hotter summers" review

Since the publication of this review, two important and national level reports relevant to heat and adaptation policy have been published: the Environmental Committee's consultation and report on resilience to heatwaves (House of Commons Environmental Audit Committee., 2018) and an evaluation of Public Health England's heatwave plan (through the LSHTM Policy Innovation Research Unit - see (Williams L., 2020)). The relevant findings from the reports are summarised here.

The consultation and report on resilience to heatwaves (House of Commons Environmental Audit Committee., 2018), demonstrates the recognised societal and political importance of the current and future impacts of heatwaves. The report incorporated findings from a number of sectors, including public health, health and social care and bodies involved in the buildings and the built environment and also drew attention to the lack of evidence presented to this particular enquiry, from local authorities and Local Health Resilience Partnerships. It highlighted a number of areas in which governance and systems based/cross-sectoral approaches to mitigate the effects of heat waves on health could and should be improved going forward, given the current and projected impacts of heat across England summarised in the background literature review. For example, it acknowledged the burden of heat related deaths occurring outside of the most "extreme" heatwave periods, and identified actions from PHE and NHS England, that could help to address this alongside specific actions relating to planning for summer pressures for NHS services, over-heating of nursing homes and hospitals. Relevant to conurbation level adaptations, were the recognition of the key role of local authorities and recommendations on how the long term risks of climate change might be considered through local plans and existing national frameworks (for example by inclusion of a target for urban green infrastructure in the metrics of the 25 Year Environment Plan and the National Planning Policy Framework to help reduce the Urban Heat Island effect).

The recent evaluation of the Heatwave Plan (HWP) for England comprises three main components: a time series analysis of hot weather and adverse health outcomes; research to understand how the HPW is implemented comprising five local case studies of local implementation of the HWP and; a national survey of nurses across care home, community and hospital settings and research to understand attitudes and behaviours of the general public in response to the HWP (Williams L., 2019). These areas of evidence complement those presented in the Environmental Committee’s consultation on resilience to heatwaves report.

The HWP evaluation, like the Environmental Committee’s report, highlighted that the largest number of excess deaths currently occur outside heatwave alert periods and the ensuing need to place more emphasis on general preparedness strategies. This is in contrast to insights gained from stakeholders, that heatwave planning was largely viewed as emergency preparedness rather than long term and strategic planning. The evaluation also found that heatwaves were often assessed as lower risk than other weather-related hazards (e.g. floods, cold weather), and that regional variation in temperatures has meant that the temperature alert thresholds (above which actions are triggered) do not feel relevant across all local areas within a given larger region. In terms of HWP implementation, some of the main findings included the need for a clearer role for CCGs (which aligns with the increased need for oversight and governance highlighted in the Environmental Committee’s consultation). The evaluation also found that frontline staff, including nursing staff, were often unaware of local heatwave plans and specific HWP guidance, often worked in environments not adapted for climate change and without the resources to implement the HWP actions. The evaluation further highlighted that many high risk groups are difficult to reach. Engagement with the public as part of the evaluation largely supports findings summarised in the chapter literature review with most not considering themselves to be at risk, including older adults and those with long term medical conditions. Despite promotion of heat protection messages, more is needed to increase knowledge of some protective behaviours (e.g. closing windows) especially within some vulnerable populations.

Both the Environmental Audit Committee and the HWP Evaluation made a number of specific recommendations to help reduce the impact of heatwave son public health. Some of these are discussed in later sections of the PhD (e.g. in chapter 8).

3.4 The effects of ambient cold on health

The effects of ambient cold on health in the UK have been extensively and recently reviewed (Hajat, 2017). Therefore in the paragraphs below only a brief summary is provided for context of the thesis. The impacts of cold on health are assessed in Chapter 4 which follows and in which literature cold effects and causality specifically is discussed in more detail.

The U or V shaped relationship between mortality and temperature which is described in the above literature review of heat and health indicates that as for the increase in effects above a given threshold for heat, there is an increase in the number of adverse health effects below a given cold threshold. This too has been shown across a number of locations (Gasparrini et al., 2015) and varies depending on climatic, demographic and socio-economic factors (Hajat, 2017). Notably, within one study of 15 European countries, the risk of cold to mortality in London was higher than in Helsinki, Prague and Stockholm, though lower than most of the other cities studied (Analitis et al., 2008). Compared to epidemiological studies of heat, however, the thresholds below which cold effects are modelled vary widely, and this affects the risk of attributable cold related mortality (and cold attributable burdens) derived from the estimates ((for further exploration of this topic, see chapter 3 and (Arbuthnott et al., 2018)). For example, one recent study estimated a 6% increase in all-cause deaths in England and Wales (Hajat et al., 2007), for each 1°C fall in daily mean temperature for the coldest 5% of days of the year, whereas another study used the 60th percentile of the year round distribution as the cold threshold (Vardoulakis et al., 2014).

Ambient low temperatures are also associated with increased indicators of morbidity, such as emergency respiratory hospital admissions (McGregor et al., 1999) and GP consultations (Hajat and Haines, 2002) and myocardial infarctions (Bhaskaran et al., 2010). They can affect health service delivery, for example, through delayed ambulance response times (Thornes et al., 2014).

Compared to heat, effects of cold are delayed by longer – often by up to weeks, and respiratory effects are thought to occur at longer lags compared to cardiovascular effects (Analitis et al., 2008).

As for heat, certain groups are more vulnerable to the effect of cold in the UK. These include those of increased age (Wilkinson et al., 2004, Conlon et al., 2011) and those with pre-existing co-morbidities such certain cardio-vascular (Bhaskaran et al., 2010) or respiratory conditions (e.g. COPD). Females may have a slightly increased risk of cold related mortality compared to males, including in studies which have accounted for differences in age structure in male and female populations (Wilkinson et al., 2004). The relationships between socio-economic status, housing and cold related health outcomes are more complex (Hajat, 2017). For example although poverty and cold housing affect winter health (Tanner et al., 2013) and fuel poverty is likely to affect wellbeing and quality of life (Hills, 2012, Liddell and Morris, 2010) other UK studies have not shown a consistent modification of the ambient cold mortality relationship by socio-economic status (Hajat, 2017).

Regional differences exist for cold risk across the UK: in a recent study, the North East, North West and London were those areas with the greatest RR of cold related mortality above a regional threshold and these differences are likely to be partially explained by differences in demographic, socio-economic and environmental characteristics (Hajat et al., 2016).

Despite much research being focused on heat related health outcomes, given the context of climate change, prevention of cold related illness and mortality is important: the burdens of cold related mortality in the UK currently higher than for heat related mortality. UK specific projections have demonstrated that under projections of temperature related mortality under climate change, if demographic changes (increased population size and ageing) are factored into analysis then under a medium emissions scenario (SRES A1B, as detailed in the background review of heat-health effects in section 3.2) the decrease in cold related mortality is only 2% by the 2050s compared to the baseline period for the study (Hajat et al., 2014) . However if demographic factors were not included then the decrease in cold related mortality by the 2050s was 26% under the same set of climate projections. Notably, however, as with current studies of temperature related health effects, the projected burdens of cold related mortality (including, where they have been studied in relation to burdens of heat related mortality under climate change) are sensitive to threshold choice, and this issue is explored further in chapter 3.

Lastly, it should be noted that it is cold related mortality that is the outcome of interest (along with heat related mortality) in this PhD, rather than Excess Winter Mortality (EWM), which refers to the seasonal distribution of health effects. This distinction has been discussed elsewhere, but cold related mortality is more appropriate here, as in brief: it is the equivalent measure to heat related mortality – i.e. both account for temperature effects after controlling for seasonal changes, but also not all cold related deaths occur in the winter and not all of the excess winter mortality is due to cold (see (Hajat and Kovats, 2014) for a more in depth discussion). In the context of climate change, understanding the effects specifically related to changes in temperature is important.

3.5 References

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PART II: RESULTS

4 A multi-disciplinary perspective on Cold Related Mortality

4.1 Introduction

This paper forms the first results chapter of the PhD. On undertaking initial reviews of the literature on heat and cold related health effects, it became apparent that the cold thresholds below which effects are modelled are highly variable between UK studies, but that there was little discussion in the epidemiological literature on how thresholds are selected and whether causal relationships can be assumed across the spectrum of temperatures used to define cold within epidemiological models. This is important, because defining cold thresholds is an integral step in linking temperature to health effects, and as examined further in the paper, quantified cold effects are sensitive to threshold choice. Exploration of these issues was an important first step to undertake, before going on to quantify heat and cold effects for each of the conurbations in chapter 6.

This chapter addressed the first research objective of the PhD, and three subsidiary objectives detailed below, and is included in the form a research paper, published in Environment International in 2018.

Research Objective:

Assess the implications on of cold threshold placement on quantified cold related burdens and assess whether causal pathways that link low ambient temperature to mortality and morbidity.

Specific objectives:

- Determine the range of cold thresholds used in previous UK studies and use London as a case study to model the sensitivity of relative risk (RR) and attributable burdens to cold threshold placement.
- Determine an appropriate framework and method of integrating knowledge from different disciplines to inform whether the relationship between temperature and mortality over the range of temperatures in UK studies can be deemed causal

4.2 Research Paper

Cover page and research paper on subsequent pages

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	310970	**Title**	Dr
First Name(s)	Katherine		
Surname/Family Name	Arbuthnott		
Thesis Title	Temperature related effects on mortality and years of life lost in the UK for current and future climates		
Primary Supervisor	Dr Shakoor Hajat		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Environment International		
When was the work published?	December 2018		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
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SECTION E

Student Signature	[redacted]
Date	12/08/2020

Supervisor Signature	[redacted]
Date	24/08/2020

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What is cold-related mortality? A multi-disciplinary perspective to inform climate change impact assessments

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ABSTRACT

Background: There is a growing discussion regarding the mortality burdens of hot and cold weather and how the balance between these may alter as a result of climate change. Net effects of climate change are often presented, and in some settings these may suggest that reductions in cold-related mortality will outweigh increases in heat-related mortality. However, key to these discussions is that the magnitude of temperature-related mortality is wholly sensitive to the placement of the temperature threshold above or below which effects are modelled. For cold exposure especially, where threshold effects are often ill-defined, choices in threshold placement have varied widely between published studies, even within the same location. Despite this, there is little discussion around appropriate threshold selection and whether reported associations reflect true causal relationships – i.e. whether all deaths occurring below a given temperature threshold can be regarded as cold-related and are therefore likely to decrease as climate warms.

Objectives: Our objectives are to initiate a discussion around the importance of threshold placement and examine evidence for causality across the full range of temperatures used to quantify cold-related mortality. We examine whether understanding causal mechanisms can inform threshold selection, the interpretation of current and future cold-related health burdens and their use in policy formation.

Methods: Using Greater London data as an example, we first illustrate the sensitivity of cold related mortality to threshold selection. Using the Bradford Hill criteria as a framework, we then integrate knowledge and evidence from multiple disciplines and areas- including animal and human physiology, epidemiology, biomarker studies and population level studies. This allows for discussion of several possible direct and indirect causal mechanisms operating across the range of 'cold' temperatures and lag periods used in health impact studies, and whether this in turn can inform appropriate threshold placement.

Results: Evidence from a range of disciplines appears to support a causal relationship for cold across a range of temperatures and lag periods, although there is more consistent evidence for a causal effect at more extreme temperatures. It is plausible that 'direct' mechanisms for cold mortality are likely to occur at lower temperatures and 'indirect' mechanisms (e.g. via increased spread of infection) may occur at milder temperatures.

Conclusions: Separating the effects of 'extreme' and 'moderate' cold (e.g. temperatures between approximately 8–9 °C and 18 °C in the UK) could help the interpretation of studies quoting attributable mortality burdens. However there remains the general dilemma of whether it is better to use a lower cold threshold below which we are more certain of a causal relationship, but at the risk of under-estimating deaths attributable to cold.

1. Introduction

Recently there has been much attention focused on the current and future effects of temperature on health. This has included debate around projected reductions in cold-related mortality burdens due to future climate warming and how these compare to increases in heat related health burdens (Woodward, 2014). Many epidemiological studies have demonstrated an increased risk of death as temperatures drop below a threshold across a number of locations (Bunker et al., 2016; Yu et al., 2012; Gasparrini et al., 2015). Within these studies, however,

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there are two distinct but linked issues which are rarely discussed, but which are integral to results obtained and their interpretation: temperature threshold choice (i.e. how 'cold' is defined) and whether the cold effects summarised in studies are indeed causal across the range of temperatures used to quantify health impacts. These are important issues. Understanding causal mechanisms can help identify downstream policy options and opportunities to prevent 'avoidable' deaths, and the magnitude of mortality burdens attributable to cold is dependent upon the threshold used in calculations. Implicit in any calculation of current or future attributable burden of mortality is that the exposure-response co-efficient used describes a causal relationship. This has particular importance for discussions regarding the extent to which reductions in future cold-related mortality will offset expected increases in mortality associated with hot weather – where impacts tend to be more direct and heat-thresholds better defined.

In this paper we explore these two related issues (and issues which inform these, such as the lagged (delayed) effect of cold on mortality), and, by integrating evidence from other disciplines, we aim to initiate a discussion around how best to interpret results from epidemiological and health impact assessment studies using a variety of cold thresholds. Of note, the metrics used both for cold exposure (e.g. mean temperature, apparent temperature, minimum temperature etc.) and for health outcomes (all-cause mortality vs cause-specific mortality or different causes of morbidity) are complex and vary across studies. For example, there is debate about whether the duration of low temperatures may be important (Barnett et al., 2012) and whether variability is important, both short term (e.g. diurnal variation in temperatures) or long term (e.g. deviation from a long-term average for that location) (Zhang et al., 2018). A wide range of health outcome measures are also used in epidemiological studies (e.g. falls and injuries, healthcare consultations such as hospital or primary care visits, acute respiratory illness in certain population groups etc.) which may have relevance to particular policy decisions but also different thresholds, time to effect and mechanisms of action.

Here, however, we focus on mean temperature as the exposure and all-cause mortality as the outcome metric, primarily because these are frequently used in both epidemiological studies of association between temperature and health outcomes (mortality is generally a more sensitive outcome in epidemiological studies) and in assessments of the potential health effects of temperature changes under climate change scenarios.

We have three main objectives:

1. To highlight some key issues around cold threshold selection – for example, the differences in temperature threshold choices between key London-based studies and the influence of threshold on the cold related mortality burden, using our own London dataset to illustrate this relationship. In doing this, we are not aiming to illustrate cold-mortality relationships for every context (we recognise that the exact relationship between temperature and mortality differs between regions and contexts (Gasparrini et al., 2015)), but aim to provide an illustration as a reference point for the evidence synthesis and discussion that follows.
2. To investigate and integrate evidence for causality across the different temperature ranges and time-periods used in studies using the Bradford Hill considerations (Hill, 1965) as a framework to do this. We appraise the range of evidence which suggests there are different health effects from extreme cold and more moderate cold conditions, with manifold mechanisms and operating over different (non-exclusive) time scales.
3. To discuss whether integrating this evidence from different disciplines can inform appropriate temperature threshold placement and interpretation of results, and to examine the policy and research implications of the preceding discussion. We consider the extent to which cold-related effects are likely to reflect causal mechanisms, and therefore how appropriate their use is in climate change risk assessments.

To address each of these objectives we use a range of different methods, described briefly below and divide our results and discussion into 3 main sections, which in turn address each of these objectives.

2. Methods

2.1. Objective 1

In order to highlight differences in common strategies used for threshold placement, we first summarise studies that analysed the relationship between daily temperature and all-cause mortality using data from Greater London. Given the aim here is not to provide a comprehensive review of the literature on the effects of cold in the UK (which has been done elsewhere (Hajat, 2017)), papers were identified through one database – Ovid Medline and were searched for combining terms for cold/low temperature and mortality. Studies which estimated the relationship between low temperature and all-cause mortality using Greater London data were selected from these, and the temperature threshold below which cold effects were estimated plotted in Fig. 1. Information about the lag period used was also noted (and summarised in Fig. 1).

In order to demonstrate the relationship between temperature and all-cause mortality in Greater London, we used mortality data provided by the Office for National Statistics (ONS). All deaths occurring in England between 1st January 1996 and December 2013 were used. We aggregated data to the Greater London conurbation level, as defined by the ONS Built-up Area codes from the 2011 census (Office for National Statistics (ONS), 2013). We used daily mean temperature (average of the daily maximum and minimum temperatures) between January 1996 and December 2013 as our main exposure variable, obtained from the UK Met Office UKCP09 gridded observation datasets (The Met Office, n.d). This dataset has the advantage of using observations from all available UK temperature stations, interpolated using inverse-distance weighting (using a regression model which includes information on longitude, latitude and importantly for Greater London, urban land use) to provide daily temperatures for 5 km^2 gridded areas.

We used a time series regression framework to analyse the risk of all-cause mortality for each 1 °C temperature decrease below a cold threshold. We controlled for the effect of season and secular trends using a cubic spline function with 7 degrees of freedom per year

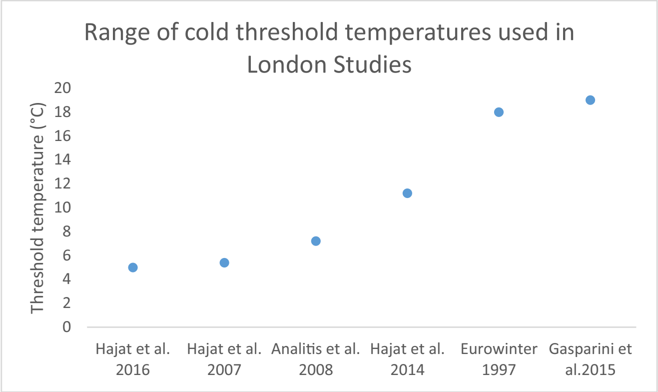

Fig. 1. Range of ambient (outdoor) cold threshold temperatures used in studies of cold related mortality in Greater London (where studies reported the threshold as a percentile of the temperature distribution, this has been converted to degrees Celsius using temperature distributions reported in the study). All studies used daily mean temepratute as the main exposure variable, with the exception of the Analitis et al. study (which used daily minimum apparent temperature). Lag periods for the included studies are as follows: Hajat et al., 2016 – 28 days, Hajat et al., 2007 – 14 days, Analitis et al., 2008 – 15 days, Hajat et al., 2014 – 28 days, Eurowinter, 1997 – 3 days, Gasparrini et al., 2015 – 21 days.

(Bhaskaran et al., 2013) and adjusted the model for over-dispersion, auto-correlation and other time varying factors such as day of the week (flu and air pollution have not been included in the model as their specific roles are addressed in Section 2 of the paper). In order to demonstrate the nature of the relationship between temperature and risk of mortality, we visualised the relationships using natural cubic splines of the temperature function, whilst controlling for time-varying factors and plotted graphs at different time lags.

To assess the impact of a change in threshold on the proportion of deaths attributable to cold, we used a distributed lag (28 days) linear model. We set the threshold at 2° intervals between 2 °C and 18 °C (to include the range of thresholds used in papers reporting the relationship between cold and mortality in Greater London). For any given threshold, the RR each 1 °C drop in temperature below that threshold was estimated. The attributable fraction of cold related deaths over the time period was calculated for each selected threshold. This was done using previously documented methods (Vardoulakis et al., 2014; Hajat et al., 2014). We made use of the specific RR from the time-series model run for each threshold and used this to calculate the risk of mortality for the number of degrees below the cold-threshold on any given day. This was used with the corresponding day's baseline mortality to calculate the cold-attributable deaths and these were totalled over the time period to give the cold-related mortality burden. Therefore changing the cold threshold changes not only the specific RR derived from the time series model, but other key inputs to the attributable mortality calculation – e.g. the number of days over the time period that are below the threshold and the change in temperature below the threshold for any given day.

2.2. Objective 2

In order to integrate information and knowledge from multiple disciplines, we used the Bradford Hill considerations as a framework to evaluate a breadth of evidence that could help determine potential causality. These were first described in 1965, when Sir Bradford Hill described nine useful considerations that can help determine whether an observed relationship is causal: coherence, plausibility, strength of association, consistency, specificity, temporality, biological gradient, experiment and analogy (Hill, 1965). Over time, these have been informally adopted as ‘criteria’, though Bradford Hill himself didn't intend for them to be used as such – in the original paper they are set out to allow a systematic approach to consider causality based on information and considerations in addition to the statistical measure of association. It has been argued that the considerations differ in relevance depending on context and that a nuanced approach should be taken when using them (Hofler, 2005; Phillips and Goodman, 2004), but also that the framework is still useful as a tool for data integration (Fedak et al., 2015). In this paper, we use the considerations as a framework (as opposed to a set of criteria) to investigate evidence for causality across different temperature ranges and time-periods used in studies, and discuss whether this can inform appropriate threshold placement and interpretation of results. We place more emphasis on the considerations that are most relevant to considering causality and threshold placement in this context.

Relevant literature for this section was located using the Ovid Medline database and combining appropriate search terms for two main concepts – cold (low temperature) and health outcomes (including physiological outcomes and markers along pathways that commonly lead to cardiovascular or respiratory mortality - such as increased blood pressure). We limited our search to English and to studies conducted in humans or mammals (further details available on request).

For both objectives, we have focused on mean temperature and on ‘all-cause’ mortality as the main exposure and outcome metrics as these are frequently used in epidemiological studies and health impact assessments of climate change. Given the majority of cold-attributable deaths are cardiovascular or respiratory deaths, we primarily consider these when integrating evidence on causality. We limit the analysis and summary of epidemiological studies to Greater London, as the aim is to provide an illustrative example of how temperature thresholds can change between studies even within one limited location, and then to use this as a reference point to interrogate causality. Further, it also removes the complication of differences in thresholds being attributed to differences in susceptibility between populations as a result of adaptation to lower temperatures.

3. Results

3.1. Current approaches to cold threshold selection and the nature of the temperature-mortality relationship

The epidemiologic relationship between ambient (outdoor) temperature and mortality is usually estimated using time–series regression (or case-crossover) analysis. These approaches require certain modelling choices, for example accounting for the length of the possible lagged effects of temperature and selection of heat and cold thresholds above or below which health effects are demonstrated. The V or U-shaped relationship between ambient temperature and daily mortality is usually characterised either by assuming a single value of temperature where mortality risk is lowest – a ‘minimum mortality temperature’ (MMT), which places a V-relationship constraint upon models - or by using separate thresholds for heat and cold. Typically, the risk of heat related mortality begins at a more clearly defined threshold temperature and at shorter time lags compared to cold-related mortality. The use of a single threshold in MMTs adds a further constraint to models and therefore tends to identify cold thresholds towards the upper end of the temperature distribution (i.e. cold thresholds will be influenced by the heat threshold). The rise mortality risk associated with decreasing temperature occurs more slowly compared to heat-related mortality and with a less obvious inflexion point, resulting in larger variation in threshold identification compared to for heat. The wide range of ‘cold’ thresholds used between studies is illustrated for papers using UK data in Fig. 1, with cold thresholds or MMTs ranging from the 5th percentile of the overall mean temperature distribution, to as high as the 90th percentile (Gasparrini et al., 2015; Analitis et al., 2008; The Eurowinter Group, 1997; Hajat et al., 2016; Hajat et al., 2007; Hajat et al., 2014) (with the higher thresholds occurring in models using an MMT value).

Fig. 2 illustrates the relationship between ambient temperature and relative risk (RR) of mortality in Greater London from all-causes over the range of (outdoor) year-round daily mean temperatures experienced during 1996–2013 (all-cause mortality) The relationship is shown at lags 0, 2 and 7 days and cumulatively at 28 days.

These data illustrate that in London, the RR of all-cause mortality associated with low temperatures becomes steeper at lags greater than zero. As the lag increases, it appears that the temperature above which cold effects appear generally increases. For example at lag 0 in Fig. 2, the ‘cold’ threshold (above which the RR of mortality increases) shown on the graph is between 3 and 4 °C, whereas by lag 7 it is around 8 °C. i.e. a plausible hypothesis might be that of an initial cold effect, occurring at lower temperatures and shorter lag periods and an effect which occurs at longer lags and milder temperatures; the longer the lag period, the higher the threshold above which effects occur is seen to be. This raises the question as to whether the choice of threshold selection is also dependent on the lag period considered. We do not address this point in more detail, although studies have previously reported a difference in lag structure between cardiovascular and respiratory deaths (Analitis et al., 2008), with respiratory deaths persisting over longer lag periods.

The variation in thresholds used across studies, as illustrated in Fig. 1, is important. It has an impact on the magnitude of cold-related mortality burdens since this is dependent on the number of days with temperatures below the assumed threshold. This is illustrated for Greater London data in Fig. 3. Given health burden estimations are so

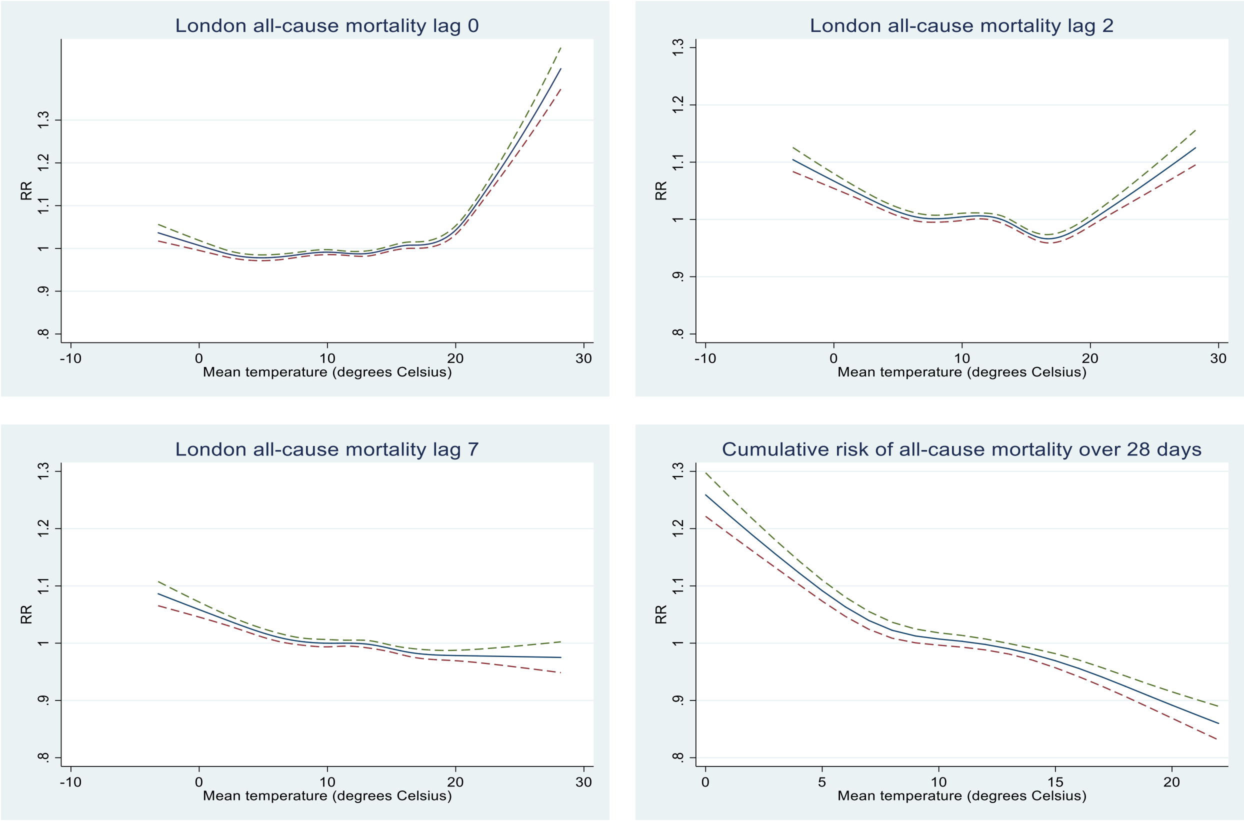

Fig. 2. Relative risk (RR) of temperature related mortality at 0, 2, and 7 day lags and over 28 days for Greater London. The solid lines represent the estimated RR of mortality, and dashed lines the upper and lower confidence intervals.

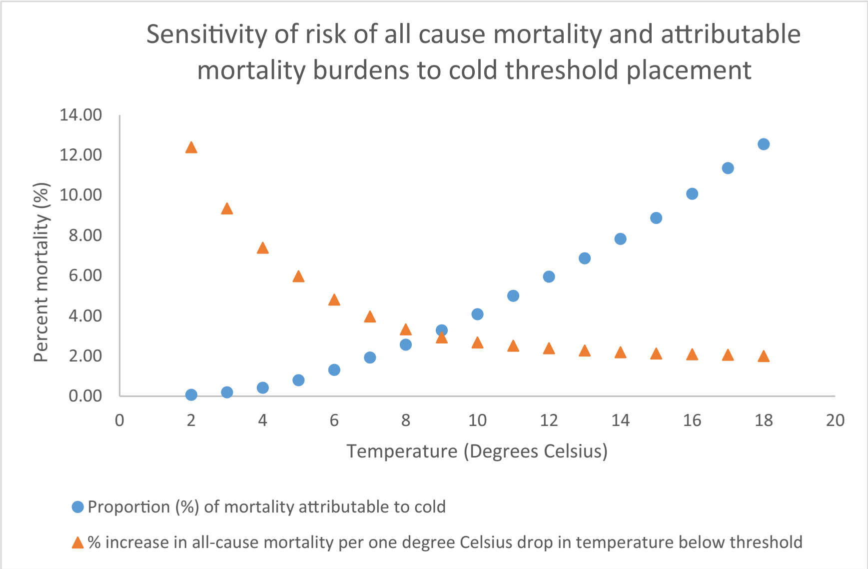

Fig. 3. Attributable fraction (AF) (%) of all-cause mortality and % increase in deaths ($(RR - 1) * 100$) per one degree Celsius drop in temperature below a given cold threshold. Results are based on time series regression analysis of Greater London data.

highly sensitive to the choice of threshold temperature, it is notable that the rationale for the choice of threshold is often not addressed more fully in publications. Where described, most studies have taken an empirical approach to determining a threshold (e.g. by comparing model deviance). Conceptual arguments about causality are rarely used when considering implications of threshold selection and interpretation of results. Since the proportion of deaths attributable to cold deaths determines the relative importance of cold as a risk factor to health, attributable burdens influence political and economic decisions on how much to invest in policies to reduce cold-related deaths in relation to other public health strategies. Attributable burdens also contribute to the debate in the literature of the importance of climate change on heat and cold-related deaths and the 'net' effect of temperature changes due to climate change (some studies have projected a net increase in overall temperature-related mortality as heat deaths outweigh cold-related deaths under climate change projections, but others have found the

Box 1

Questions arising around cold threshold selection.

Some important questions arising around cold threshold placement:

How should we define a cold effect? And is this the same as where we place a 'cold' threshold?

- Is the effect of cold the same occurring across all temperatures, or are there different causal mechanisms occurring at different temperatures (e.g. 'extreme' and 'moderate' cold). How is this reflected in different choices of threshold placement?
- Why do we define cold thresholds? And should the purpose of the modelling affect threshold choice? E.g. are certain thresholds more useful for policy actions (e.g. defining levels at which to instigate actions or for looking at preventable deaths). Are these the same thresholds as we would use to quantify the impact of cold on mortality? I.e. should we distinguish between epidemiological thresholds and thresholds for action?

Box 2

The Bradford Hill considerations.

Bradford Hill considerations

Originally proposed by Sir Bradford Hill in 1965, these considerations are widely used in the field of epidemiology, to assess the evidence for causality for an observed association between exposure and effect. In brief they are:

- Coherence – between laboratory, physiological and epidemiological studies increases evidence for causality
- Plausibility – a plausible mechanism for the effect of the exposure would increase the evidence for causality
- Strength of association – a stronger association/larger effect of size supports evidence of causality
- Specificity – the more specific the association between exposure and effect, the more likely it is to be causal
- Temporality – the effect must occur after the exposure
- Biological gradient – generally speaking, the greater the exposure, the greater the effect within a population. However this may not always be the case
- Experiment – reversal of exposure leads to reversal of effect
- Analogy – similar factors or exposures cause similar effects

opposite) (Li et al., 2013; Doyon et al., 2008; Martens, 1998; Martin et al., 2012).

The range of cold thresholds we have demonstrated used in studies and the sensitivity of attributable burdens to threshold selection leads to a number of interesting questions (Box 1). For example, to what extent is threshold selection dependent upon regression modelling choices? Are these studies describing the same 'cold' effect or are there different 'cold' effects e.g. of 'moderate' (approximately 9–18 °C) and more 'extreme' (below 9 °C) cold, which may have different causal mechanisms and policy implications? We next explore the latter of these possibilities and examine whether threshold placement should be justified from a causal perspective. We propose that definitions of cold and interpretation of results for use in policy and risk assessments should reflect the different causal mechanisms operating.

3.2. A multi-disciplinary perspective on cold and causation

Before considering evidence of causality across a range of temperatures used as cold thresholds, some consideration should be given to whether the relationship between cold and mortality could be biased or confounded by certain time-varying factors.

There has been discussion as to whether the demonstrated association at longer lags between temperature and mortality is affected by collinearity between season and low temperatures within models (Kinney et al., 2015). This co-linearity is particularly pertinent for cold effects at longer lag periods and does not present an issue for heat estimates where effects are typically estimated at much shorter lags. However, this co-linearity between season and long lag periods would likely mean that cold effects are under-estimated rather than over-estimated. Results using simulated data (Gasparrini, 2016) indicate both distributed lag linear and non-linear models give estimates of mortality with minimal bias even at longer lag periods (models using moving averages, however, were reliable to investigate the temperature-mortality relationship only at shorter lags). This suggests that the cold effect does indeed operate at longer lags although does not help determine whether there are different mechanisms of causality operating at different lag periods.

Stanisic Stojic et al. (2016) have suggested that when controlling for the effect of air pollution (SO_2, NO_2 and soot) in a study in Belgrade, not only was the magnitude of the cold-related mortality risk reduced, but any increased risk between −5 °C (the temperature at which risk increased dramatically) and 20 °C disappeared. However, further analysis is required across different contexts and cities to determine whether this is a generalizable result. Other studies have found effect sizes in London unaltered by inclusion of air pollution in epidemiological models (Hajat et al., 2014). However, regardless of whether the effect estimate is altered by controlling for pollution is the question of where on the causal pathway pollutants lie. The potential complexity of causal pathways for specific pollutants has been discussed elsewhere (Buckley et al., 2014).

One confounder which is often included in epidemiological models, and which may have an impact on the effect of cold on mortality, is influenza. However, its potential role as a confounder again depends on where it lies on the causal pathway (see Section 2.1 for the direct effect of temperature on influenza transmission).

Assuming that the general association between cold and mortality is not due to bias or confounding, we use the Bradford Hill criteria (Box 2) as a framework to integrate evidence from different disciplines, and consider whether this supports a causal relationship across the range of temperatures used in studies of cold and mortality. In the discussion, we explore whether this can be used to inform better description of cold effects and more transparent use of epidemiological evidence to inform policy.

3.2.1. Bradford Hill criteria: plausibility and coherence

At the most extreme, cold exposure can lead to hypothermia. The drop in body temperature has a direct physiological effect on most organs, including inducing bradycardia (due to the effect on cardiac pacemaker cells) with a resulting reduction in cardiac output and blood pressure (BP) or other cardiac arrhythmias and depression of the central nervous system. However, few deaths associated with low ambient temperatures are caused directly by hypothermia. The majority of cold-attributable deaths are cardiovascular or respiratory deaths. For this reason, we focus on plausible direct and indirect causal mechanisms and coherence between studies that relate to these causes. We consider the criteria of coherence and plausibility together, first for cardiovascular and then for respiratory mortality.

3.2.1.1. Direct and indirect mechanisms for cardio -vascular mortality. There is coherent evidence from a range of disciplines, that cold exposure can lead to an increase in cardiac risk factors (RFs) (Fig. 4).

Animal studies have demonstrated exposure to cold induces hypertension through a variety of mechanisms (Liu et al., 2015; Sun, 2010). These include cold-induced activation of the sympathetic nervous system and renin-angiotensin system in rats (Sun, 2010; Papanek et al., 1991; Fregly et al., 1989; Sun et al., 2002; Sun et al., 2003; Sun et al., 1997; Sun et al., 1995). A decrease in endothelial Nitric Oxide Synthase (eNOS) production (nitric oxide is a vasodilator involved in the regulation of BP and endothelial function) may also play a role in cold- induced hypertension in mice (Wang et al., 2005). These animal studies are typically conducted with cold exposures of 5–7 °C. Of note, one study found that mice exposed to 9 °C did not display the same increase in BP as those exposed to 5 (± 2) °C (Shechtman et al., 1990). However, other studies have found increases in cardiac RFs, including BP at temperatures of around 11 °C in mice (Luo et al., 2012).

Cold exposure has also been shown to result in a significant BP increase in human subjects. This has been demonstrated across a number of study settings and in general, the studies have shown larger increases in BP, the lower the temperature subjects were exposed to (Hintsala et al., 2013; Komulainen et al., 2000; Jevons et al., 2016; Shiue and Shiue, 2014; Leppaluoto et al., 2001; Collins et al., 1985; Inoue et al., 1992). For example, in a randomised controlled study set in Japan, Saeki et al. (Saeki et al., 2013) demonstrated that healthy adults with intensive room heating (to 22 °C), had significantly lower morning systolic and diastolic BP when compared to an experimental group with overnight heating to only 12 °C, and suggested that night-time heating could reduce the incidence of stroke by 25.5% and of mortality (all-cause) in the elderly by 12.4%. In a Scottish cross-sectional study (Shiue and Shiue, 2014), households that were heated to less than 18 °C had increased odds (OR 2.08) of increased blood pressure (compared to those heated to above 18 °C) and in those heated to less than 16 °C the odds of increased BP were higher again (OR 4.92). Leppaluoto et al. (2001) demonstrated that in healthy males exposed to temperatures of 10 °C for 2 h on 11 consecutive days, there was a significant increase in BP and Collins et al. (Collins et al., 1985) found subjects exposed to 4 h of low temperatures (6 °C, 9 °C or 12 °C), experienced significant increases in blood pressure, with the most marked effects with the coldest (6 °C) exposure.

Epidemiological studies have also established that populations have a significantly higher BP in winter months compared to summer (Modesti, 2013). Although this could in part be due to seasonal factors, such as daylight exposure and vitamin D, an increased BP has also been associated with decreased temperatures (after control for seasonal effects) (Modesti, 2013; Halonen et al., 2011a; Li et al., 2016; Madaniyazi et al., 2016; Madsen and Nafstad, 2006; Alpérovitch et al., 2009), though typically this has been seen over a broader range of temperatures than those used in physiological experimental protocols.

Human subjects exposed to low temperatures (5 °C for 3 h) have demonstrated increased activation of norepinephrine release and increase in the relative number of SP1 platelet subtypes (increasing the tendency for blood to clot) (Opper et al., 1995). Increased coagulability, mild inflammation and vasoconstriction have also been demonstrated in humans after exposure to temperatures of 11 °C for an hour, but not at pathological levels (Mercer et al., 1999). Again, these results from physiological experiments are largely supported by epidemiological biomarker studies in human populations (Schneider et al., 2008; Halonen et al., 2011b). For example, Wu et al. grouped biomarkers to represent mechanistic pathways ('indices') of systemic inflammation (e.g. coagulation, systemic oxidative stress etc.) and found an inverse association between the biomarker indices and decreasing temperature (Wu et al., 2017).

Some specific risks of cold exposure in animals have been demonstrated. Rats with reno-vascular hypertension exposed to 4 °C for 3 days were shown to have increased rates of cerebral infarction or haemorrhagic stroke (Li et al., 2014), likely linked to release of important neuro-transmitters. Cold is also known to induce cardiac hypertrophy (Liu et al., 2015; Sun, 2010; Roufai et al., 2007).

Cardiovascular events may also be brought about by a number of indirect mechanisms and events may be precipitated by preceding infection (Estabragh and Mamas, 2013; Warren-Gash and Udell, 2017; Barnes et al., 2015; Corrales-Medina et al., 2013; Smeeth et al., 2004; Wang et al., 2017). For instance, Meier et al. found an increased risk of acute myocardial infarction (AMI) in subjects with a preceding acute respiratory tract infection 10 days before (Meier et al., 1998). Plausible mechanisms for this include a number of pro-inflammatory, pro-coagulant and haemodynamic effects induced by infections, which may lead to cardiac complications. For example, increased concentrations of C reactive protein (CRP) are associated with increased risk of AMI (Kuller et al., 1996; Ridker et al., 2000)) and the systemic inflammation associated with an acute respiratory tract infection (or directly as a result of cold exposure) can result in altered endothelial function or be

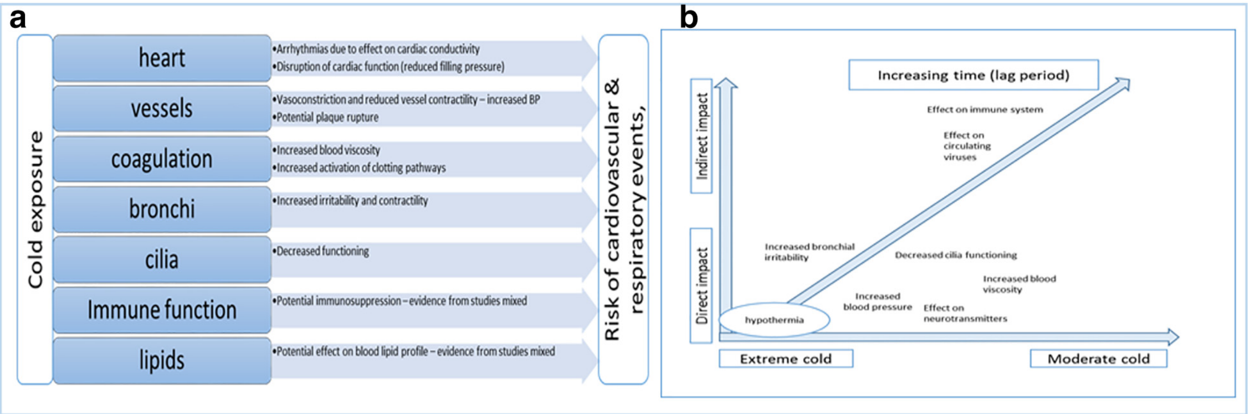

Fig. 4. a) (left) summary of coherent and plausible mechanisms for cold related cardiovascular and respiratory mortality b) (right) plausible time frames and temperatures over which these effects may occur.

associated with plaque rupture (Vallance et al., 1997). Cardiovascular events may also be triggered by indirect behavioural mechanisms, such as reduced mobility (e.g. brought about by people being less mobile in the cold, or being unwilling to move outside heated areas of homes) which can lead to deep vein thrombosis and pulmonary embolisms.

3.2.1.2. Direct and indirect mechanisms for respiratory mortality. The direct and indirect mechanisms by which cold causes an increase in respiratory mortality have not been widely discussed in the epidemiological literature and a number of plausible mechanisms exist (Fig. 4).

Facial cooling of −5 to −20 °C has been shown to reduce Forced Expiratory Volume (FEV1 – a measure of lung function) in healthy humans and those with asthma or chronic obstructive pulmonary disease (COPD) (Gavhed et al., 2000; Koskela and Tukiainen, 1995; Koskela, 2007; Koskela et al., 1996). However, the effects of breathing cold air in healthy subjects (and in animal experiments) on lung function have been mixed, with some demonstrating a positive relationship between inhalation of cold air and bronchoconstriction and others not (Koskela, 2007). In people with asthma, cold air can trigger bronchoconstriction (Deal Jr et al., 1980; Koskela et al., 1997; Nielsen and Bisgaard, 2005). Further studies have indicated the presence of cold sensitive channels in lung epithelium, that when activated (below 18 °C) increase pro-inflammatory (IL-6, IL-8) cytokine secretion (Sabnis et al., 2008). Release of these cytokines may contribute to the pathogenesis of cold-induced asthma. These findings are coherent with population based studies that have demonstrated exacerbation of symptoms in those with COPD and asthma when temperatures decrease (Tseng et al., 2013; Guo et al., 2012; Huang et al., 2015; Donaldson et al., 1999).

Studies at a population level that have examined the association between respiratory tract infections and temperatures have also demonstrated an increased risk of upper and lower respiratory tract infection with decreasing temperature (Mäkinen et al., 2009; Hajat et al., 2004). This is likely to be due to a multitude of factors, such as the effect of cold on the immune system and on pathogen transmission and reproduction within the host, and infections that follow cold-induced bronchoconstriction.

For example, decreasing temperature may result in a direct reduction on cilia motility and mucociliary clearance (and hence reduction in clearance of pathogens from the nasal passages) (Mwimbi et al., 2003). An effect of cold on the immune system (which may in turn affect mortality from respiratory and other infections) has also been demonstrated in some physiological experiments, though this has not been a consistent finding across all studies (Castellani et al., 2002).

Respiratory infection, however, also depends on exposure and rate of transmission of infective agents and their capacity to cause disease within the host. There is evidence that certain viruses (EBV, parainfluenza) persist within humans for longer in cold conditions (Mourtzoukou and Falagas, 2007). In guinea pigs, both viral shredding and transmission of influenza were increased at 5 °C compared to 20 °C (Lowen et al., 2007). Pneumococcal transmission between humans is increased in cold and dry conditions (Numminen et al., 2015) and rhinovirus replication is increased within mouse hosts at lower temperatures (Foxman et al., 2015). Further, within cold seasons, some populations may spend more time within confined spaces, which may also increase the chance of pathogen spread. This hypothesised increased exposure risk is likely to happen at any range of temperatures below which populations spend more time indoors – i.e. in the 'more moderate' temperature range.

3.2.2. Bradford Hill criteria: specificity and consistency.

Whilst the Bradford Hill criteria include specificity of effect for a given exposure, it could be argued that this is less relevant for direct temperature effects - ultimately all biological processes are affected by temperature. However, we have demonstrated that there are specific mechanistic effects of cold temperatures on the cardiac, respiratory and immune system. Some of the indirect mechanisms by which cold affects mortality (e.g. though increased respiratory illness) may also cause deaths at longer lags. Some indirect causes of mortality may also occur at milder temperatures. There is some evidence of this in population-based studies (Analitis et al., 2008), where respiratory deaths occur at longer lag periods. Cardiovascular effects could plausibly occur at short or more prolonged time frames – a quick increase in cardiac risk factors (e.g. BP, arrhythmia) may be enough to trigger a fatal cardiac event. It could be hypothesised that more extreme cold temperatures have severe enough short-term physiological effects to trigger an event. However, cardiac events could also occur due to a cumulative/prolonged effect of raised BP or at longer time periods due to the effect of inflammation or infection.

Even though the exact nature of the temperature-mortality relationship changes by location, in almost all settings and populations there is an increase in the risk of mortality below a given temperature (Gasparrini et al., 2015). Consistent findings observed in different places with different samples strengthen the evidence for a common physiological pathway, especially at lower temperatures. However, commenting on consistency as support for causality across the full range of 'cold' temperatures used is complex. The different thresholds or MMTs demonstrated between locations are often interpreted as evidence that populations differ in their susceptibility to cold and may be 'adapted' to different temperatures through a variety of mechanisms. These adaptations may range from behavioural mechanisms, to more societal level mechanisms such as the existence of public health messaging for colder weather (Public Health England, 2016), improved insulation and housing design. However, a difference in thresholds between locations may also be due, in part, to different indirect causal mechanisms between locations. For example one would expect the physiological mechanisms underlying increased mortality to remain largely consistent between locations, but that mortality related to circulating pathogens (such as influenza etc.) for example, may vary from location to location due to differences in endemic diseases which may respond differently to temperature. Another possibility is that the more consistent effects at very low temperatures are causal, but the difference in the pattern of effects at 'more moderate cold' temperatures are due to differences in confounding structures or modifying factors such as the proportion of vulnerable individuals (e.g. older adults, those with underlying co-morbidities) and behavioural differences between locations. For example, there is evidence that older populations are less able to tolerate cold and therefore may experience physiological effects at less extreme temperatures.

Generally consistent, however, is that a greater increase in risk occurs in most (but not all) locations below a lower threshold than the 'optimum' temperature (where this has been demonstrated in studies) or that the increase in mortality follows a 'double' threshold pattern, with an obvious additional upturn in risk at very low temperatures (in some settings). Consistent too is that there is a longer lag period for the mortality risk associated with cold than for heat. These two observations may support evidence that there are both direct physiological impacts of cold which occur at lower temperatures occurring across all locations (and which can occur at both short and longer time lags) and indirect (both as a result of infections and the delayed effects of immobility) affects occurring at longer lags.

3.2.3. Bradford Hill criteria: experiment, effect size and gradient, temporality and analogy

Given the multiple pathways of potential causality and variety of ways in which populations can be exposed to cold (e.g. through short exposure to decreased ambient temperatures outside or through exposure within adequately heated or insulated homes), interventions to reduce exposure to cold or its effect are varied and complex in nature.

However, a number of studies have examined the effect of interventions (in particular in the area of improved energy efficiency of housing) to reduce cold exposure on health outcomes and these have been systematically reviewed (National Institute for Health and Care Excellence (NICE), 2014; Thomson et al., 2009).

One review found some evidence that housing interventions to improve thermal comfort (e.g. through heating, insulation, fuel poverty interventions) improve a variety of respiratory and mental health outcomes in study populations (Thomson et al., 2009). More specifically, a randomised control study investigated the effect of intensive room heating (compared to 'weak room heating') on ambulatory BP. Systolic morning BP and sleep-trough morning BP surges were significantly reduced in the intensive heating group (Saeki et al., 2013). This corroborates evidence from animal studies that one of the potential mechanisms for cardiovascular effects of cold exposure is its effect on BP. Whilst mortality is rarely an outcome in studies of this kind (due to rarity of the end point), there is evidence that respiratory morbidity can be reduced by interventions to improve housing, though the pathways through which interventions improve outcome may be multifactorial (e.g. could be a direct effect of increasing temperature or related to humidity, changes in indoor air quality or mould growth etc.) Evaluations of the effect of a telephone alert system using meteorological reports to communicate times of increased risk to patients with COPD ("Healthy Outlook") produced mixed results. Some concluded it reduced hospital admissions (Sarran et al., 2014) or mortality (Steventon et al., 2014) and some that admissions and GP visits were either unaffected or increased with the scheme (Steventon et al., 2014; Maheswaran et al., 2010; Bakerly et al., 2011). One pilot randomised controlled study examined the effect of providing thermal clothing to vulnerable groups of patients over the age of 50 (Barnett et al., 2013). However, the study was too small to determine whether the intervention was of benefit.

In some settings, the effect size at more extreme ends of the temperature distribution is observed to be larger than at more mild temperatures (Gasparrini et al., 2015), lending more support to causal mechanisms at lower temperatures. Studies in animals have also shown increased effects on cardiac risk factors with increasing intensity of cold exposure (Luo et al., 2014).

Lastly we consider temporality and analogy. In epidemiological studies of the effect of cold exposure on mortality, the criterion of temporality is easily fulfilled - reverse causality between cold temperatures and mortality cannot feasibly exist. Lagged effects of cold exposure are also seen, as previously discussed.

Analogy seems less applicable to cold exposure, compared to other environmental exposures and is not likely to be helpful in determining causation or in considering threshold choice.

4. Discussion

4.1. Can using evidence from different disciplines help in the placement of cold thresholds?

We have demonstrated the range of temperature thresholds used in studies of cold – mortality effects in Greater London, the sensitivity of attributable burdens to threshold selection, and examined evidence for a causal relationship between cold and mortality. An important question is whether the physiological and experimental evidence supports threshold temperature choices for cold-related mortality (Fig. 5) and how it can aid interpretation of evidence from epidemiological studies. Most of the experimental evidence of the direct effect of cold is from animal studies, and the exposure used is between 4 and 7 °C. This may support a lower threshold, but only if thermoregulation and body temperatures in rats and mice is deemed to be similar to humans. Some experiments in humans have used a more 'moderate' cold exposure (above 11–18 °C) – for example, one study demonstrated increases in BP in houses heated below 18 °C (Shiue and Shiue, 2014), but the majority of studies showed that effects were largest at lower temperatures, for example with exposures to indoor temperatures below 12 °C. The paucity of experiments performed at more moderate cold temperatures (taken here to mean up to 18 °C, or the 'optimum/minimum mortality' temperature used in some studies) in humans and animals does not mean that physiological effects do not occur at higher temperatures – it may just reflect experimental protocols.

It is plausible that indirect mechanisms, operating through infective pathways (Fig. 4b), may start at higher temperatures depending on how air temperature affects droplet survival and behaviour related to

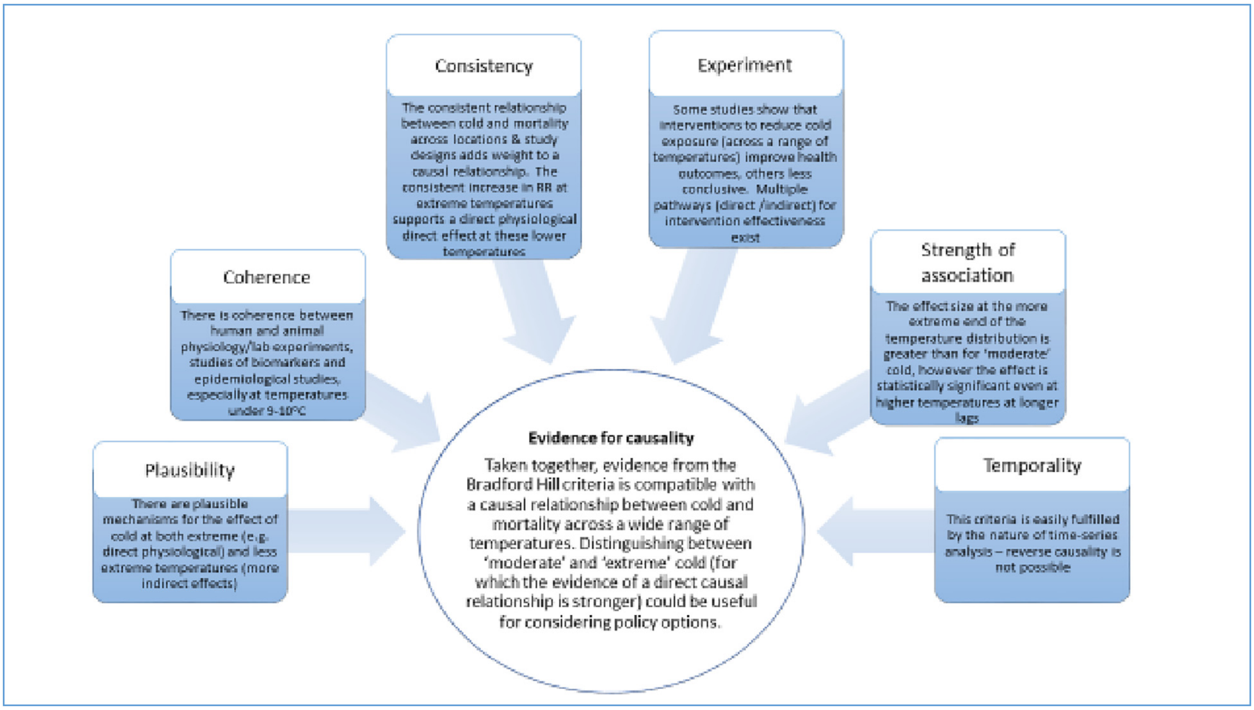

Fig. 5. Use of the Bradford Hill criteria as a framework to summarise evidence for a causal relationship across the range of low temperatures used in studies of cold related mortality.

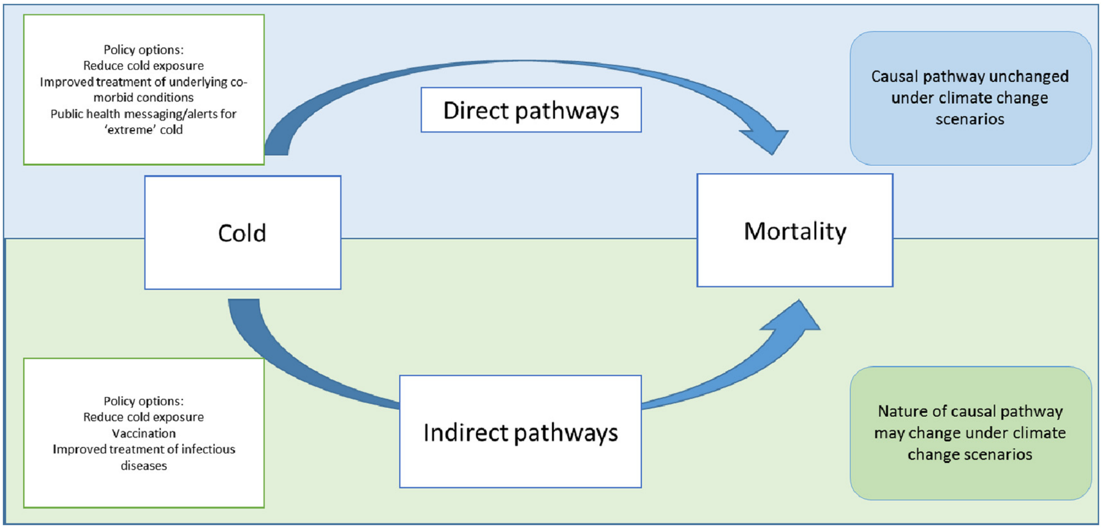

Fig. 6. Direct and indirect pathways of cold related mortality.

transmission (time spent indoors and contact with others etc.). Some indirect effects of cold due to behaviour change (e.g. reduced activity and staying in one (heated) room, increasing the risk of DVTs for example, may occur across a range of temperatures depending on affordability of heating and quality of housing stock.

One further complicating factor is that the thresholds set in epidemiological studies are usually related to outdoor air temperatures. In reality, the temperatures that populations are exposed to will vary with the amount of time spent indoors and access to heating etc. There is evidence across the UK that heating of homes is variable and depends on a number of factors (Tod et al., 2012) and also that in some settings indoor and outdoor temperatures are poorly correlated at cooler temperatures (Nguyen et al., 2014; Vadodaria et al., 2014). However, there is a paucity of studies which examine the correlation between indoor and outdoor temperatures and more work in this area would be welcomed.

4.2. Relevance to risk assessment and policy setting and conclusions

In order for attributable mortality fractions of 'cold' deaths to be valid, the underlying association between cold temperatures and mortality must be causal. Evidence from a range of disciplines appears to support a causal relationship across a range of temperatures and lag periods, although evidence is more consistent for a causal effect at lower temperatures. It is also plausible that 'direct' mechanisms for cold mortality are likely to occur at lower temperatures and 'indirect' mechanisms (e.g. via increased spread of infection) may occur at milder temperatures.

This is important when thinking about policy and future adaptation (Fig. 6). For example, if a substantive proportion deaths are attributable to moderately cold temperatures (Gasparrini et al., 2015) then alongside policies which focus on keeping active, keeping warm and reducing exposure to extremely low temperatures, policies which include reduced disease transmission (such as vaccination programmes, public health campaigns about reducing influenza spread) are also important to consider. This could be achieved by a mixture of policies including improvement of housing and affordability of heating, by activating emergency responses such as those in Public Health England's cold weather plan at relevant cold thresholds (Public Health England, 2016) and by policies which reduce infectious disease transmission. Understanding the causal mechanisms behind cold related mortality also highlights the importance of general management of risk factors for cardiac and respiratory disease within the population; improvement here may substantially reduce cold related mortality. For policy purposes it is not realistic to issue cold warnings or have policies for ambient daily mean temperatures as mild as say 18 °C (similar to 'minimum mortality temperature used in some studies). For example, Public Health England's cold weather plan (Public Health England, 2016) advocates background prevention policies are in place year-round with winter preparedness measures between November and March but more focused public health messaging and alerts are only triggered when temperatures drop below 2 °C for a period of 48 h.

Care must be taken when using epidemiological baseline estimates for projections of mortality under different climate scenarios - the validity of future estimates relies upon assumptions that the causal relationship will remain. This seems valid for mortality attributable to direct physiological mechanisms (though population adaptation to temperature extremes may negate some of this effect). However, where indirect infectious mechanisms lead to an increase in mortality, the assumption that these pathways do not change in the future is harder to justify – circulating pathogens and infections may change. Separating the effects of 'extreme' and 'moderate' cold in any given setting, may help better describe these effects and make interpreting results of studies quoting attributable mortality burdens easier. The increased evidence for causality at more extreme or increasingly cold temperatures does raise the dilemma of whether it is better to use a lower threshold (e.g. in London below 8–9 °C) to estimate cold related mortality burdens, below which we are more certain of a causal relationship, but at the risk of under-estimating deaths attributable to cold. We conclude that as a minimum, the choice of threshold be justified in this type of research, and that where appropriate (e.g. in cases where an MMT is used or where there appears to be distinct increase in risk at lower temperatures and a smaller risk at more moderate temperatures) attributable burdens are given separately for extreme cold in addition to 'moderate' or the overall cold effect. This would enable those using the research to take a more nuanced and critical approach to using the results informed by likely causal mechanisms, and for policy makers to better determine future risks of temperature to health and appropriate policy actions.

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Competing Financial Interests Declaration

The authors declare they have no actual or potential competing financial interests.

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5 Changes in population susceptibility to heat and cold over time: assessing adaptation to climate change

5.1 Introduction

This systematic review paper forms the second results chapter of the PhD and laid the foundations for some of the analysis in Chapter 6 which follows. At the time of undertaking this review, adaptation was widely mentioned in temperature and health studies but there was a gap in the literature for a synthesis of studies which brought together results from epidemiological studies of heat and cold effects in terms of changes in susceptibility of these effects over time in a given location. This review set out clear research objectives to determine whether there was evidence of decreasing susceptibility to heat and cold in epidemiological studies, discussed some of the methodological aspects of these analyses and then how the results of these studies relate to the broader understanding of adaptation and acclimatisation in the context of climate change. Specifically the review sought to address the second research objective of the PhD, to systematically review the epidemiological literature on evidence for changes in susceptibility to health-related temperature effects over time by assessing studies which;

- quantified the risk of health-related events with changing ambient temperature in one location over a given time period (not limited); and
- compared the health outcomes between two different discrete extreme temperature events (>1 day, for example, usually defined by the context specific definition of a heatwave or cold spell) in one location

The review was published in Environmental Health in 2016. Since the time of publication, further studies relevant to this body of literature have been published. A postscript is included after the review paper, which summarises evidence from the most salient of these. However, this is kept brief, as many are reviewed in the background and discussion section of chapter 6. The supplementary materials for this review can be found in Appendix 3.

5.2 Research paper

Cover page and research paper on subsequent pages

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	310970	**Title**	Dr
First Name(s)	Katherine		
Surname/Family Name	Arbuthnott		
Thesis Title	Temperature related effects on mortality and years of life lost in the UK for current and future climates		
Primary Supervisor	Dr Shakoor Hajat		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Environmental Health		
When was the work published?	08 March 2016		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

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SECTION C – Prepared for publication, but not yet published

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SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I designed the review and undertook the literature searches, reviewed the included papers, wrote the first draft of the manuscript and responded to reviewers' comments

SECTION E

Student Signature	[redacted]
Date	12/08/2020

Supervisor Signature	[redacted]
Date	24/08/2020

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Changes in population susceptibility to heat and cold over time: assessing adaptation to climate change

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From The 11th International Conference on Urban Health
Manchester, UK. 6 March 2014

Abstract

Background: In the context of a warming climate and increasing urbanisation (with the associated urban heat island effect), interest in understanding temperature related health effects is growing. Previous reviews have examined how the temperature-mortality relationship varies by geographical location. There have been no reviews examining the empirical evidence for changes in population susceptibility to the effects of heat and/or cold over time. The objective of this paper is to review studies which have specifically examined variations in temperature related mortality risks over the 20th and 21st centuries and determine whether population adaptation to heat and/or cold has occurred.

Methods: We searched five electronic databases combining search terms for three main concepts: temperature, health outcomes and changes in vulnerability or adaptation. Studies included were those which quantified the risk of heat related mortality with changing ambient temperature in a specific location over time, or those which compared mortality outcomes between two different extreme temperature events (heatwaves) in one location.

Results: The electronic searches returned 9183 titles and abstracts, of which eleven studies examining the effects of ambient temperature over time were included and six studies comparing the effect of different heatwaves at discrete time points were included. Of the eleven papers that quantified the risk of, or absolute heat related mortality over time, ten found a decrease in susceptibility over time of which five found the decrease to be significant. The magnitude of the decrease varied by location. Only two studies attempted to quantitatively attribute changes in susceptibility to specific adaptive measures and found no significant association between the risk of heat related mortality and air conditioning prevalence within or between cities over time. Four of the six papers examining effects of heatwaves found a decrease in expected mortality in later years. Five studies examined the risk of cold. In contrast to the changes in heat related mortality observed, only one found a significant decrease in cold related mortality in later time periods.

Conclusions: There is evidence that across a number of different settings, population susceptibility to heat and heatwaves has been decreasing. These changes in heat related susceptibility have important implications for health impact assessments of future heat related risk. A similar decrease in cold related mortality was not shown. Adaptation to heat has implications for future planning, particularly in urban areas, with anticipated increases in temperature due to climate change.

Keywords: Climate change, Adaptation, Temperature, Heat, Cold, Heatwave, Mortality, Health

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Background

The global climate is projected to warm although to what extent depends on future greenhouse gas emissions and socioeconomic and land use changes. Global surface temperatures are likely to warm by between 0.3 °C and 4.8 °C by the end of this century relative to the end of the last, depending on modelling choices which reflect differences in the amount of anthropogenic forcing in different scenarios [1]. It is anticipated that there will be increasing variability in future temperatures and extreme weather events over most geographical regions [1–4]. For example, heatwaves are likely to increase in frequency and severity and this, combined with projected demographic changes, will lead to an increase in population exposure to extreme events [5, 6]. However, the same locations may still experience (extreme) low temperatures. These are important considerations for public health, as both heat and cold exposure lead to increased risk of mortality [7–21].

Adequate public health responses to temperature related effects of climate change require a sound risk management process, informed by the use and synthesis of relevant evidence. A framework for such a public health approach for climate change adaptation is outlined by Hess et al. [22]. In considering the future impact of temperature on health, knowledge about past and current risks to health from changes in ambient temperature is essential: it informs the baselines used for future risk assessments upon which management strategies may be based. Changes in temperature related health outcomes over time could give valuable insight into whether populations have adapted to hot and/or cold temperatures in more recent times. Understanding what has caused changes in susceptibility to temperature related mortality can help inform current public health policy and protection of vulnerable communities. Alternatively, if temperature related mortality remains unchanged this gives further weight to the need for specific planned adaptive strategies to address the health risks of future climate change. For the purpose of this review, adaptation and acclimatisation have been defined as in Fig. 1 below, with the definition of adaptation based upon that of the Intergovernmental Panel on Climate Change [23]. However, a distinction between evidence of decreasing susceptibility to heat and cold and evidence that adaptation or acclimatisation have occurred should be made. For example, a decrease in temperature related mortality may have arisen through general improvements in health or social care rather than specific planned adaptations to the effects of heat or cold: to attribute decreasing heat or cold related mortality solely to planned adaptive measures would be misleading.

Epidemiological evidence for the effect of temperature on health outcomes is typically based on observational studies. The relative risk of mortality per unit change in temperature (e.g. per degrees Celsius (°C)) is generally estimated using a time series or case-crossover approach. This is usually denoted by 'U','V' or 'J' type curves, with adverse health effects appearing below or above a given range of temperatures [11]. Where a threshold temperature is set, above or below which health effects occur (and can be estimated using a log-linear or non-linear approach), this point is often referred to as the Minimum Mortality Temperature (MMT). The effect of individual heatwaves is often estimated using episode analysis, where observed numbers of deaths during the heatwave period are compared to expected deaths estimated using an appropriate baseline.

A number of epidemiological studies [24–26] have examined how temperature-mortality relationships vary by geographical location. The geographical variation in this relationship is also the subject of a review by Hajat and Kosatsky [27], who explored possible explanations for the differences in temperature related susceptibility between countries. In a random-effects meta-regression of studies, the relative risk of heat related mortality was found to be strongly related to heat thresholds. Heat thresholds (and RR of heat-related mortality) were higher in countries closer to the equator (with higher summertime mean temperatures). It was proposed that the higher thresholds seen in countries closer to the equator, may indicate some level of population adaptation to heat. The risk of heat-related mortality was also found to increase with increasing urban density, decreasing city level GDP and increasing age of the population.

No review, however, has examined how or whether temperature-related mortality varies over time in one location. This paper seeks to address this gap in knowledge. Specifically we review the evidence for changing population susceptibility (in terms of mortality) to ambient heat and cold and heatwaves or cold snaps over different time points over the last century and more recently. Understanding changing temperature-related mortality, the time scales over which this has occurred, and its possible causes could make important contributions to managing future risk. We discuss the extent to which changes in susceptibility are attributed to planned adaptive measures within the selected studies and consider how this evidence could be used in assessments of future temperature related health impacts. Both heat and cold related mortality are reviewed, as in many parts of the world studies suggest cold related mortality currently has and will continue to have a substantial contribution to temperature related mortality, even under warming projections [28, 29].

We review both changes in mortality in response to general temperature increases or decreases and to extreme weather events, such as heatwaves and cold snaps. Extreme events are included since the specific adaptive measures

Adaptation:

The IPCC have defined adaptation as "*Adjustment in natural or human systems to a new or changing environment. Adaptation to climate change refers to adjustment in natural or human systems in response to actual or expected climatic stimuli or their effects, which moderates harm or exploits beneficial opportunities. Various types of adaptation can be distinguished, including anticipatory and reactive adaptation, private and public adaptation, and autonomous and planned adaptation.*" [23]

For the purpose of this review, we define population adaptation to heat and/or cold as adjustment(s) which reduce the harmful effects on the health of a population or its health system in response to actual or expected temperature changes, as measured by reduction in mortality or morbidity (contact with health services may be used as a proxy for this). This can be anticipatory, spontaneous or planned. For example, in this context, planned adaptation would include specific structural or policy interventions which reduce a populations susceptibility to the effect of experienced heat.

Acclimatisation : A physiological protective response to changes in temperature, occurring over a short time period (within one season).

In practice, acclimatisation and adaptation are likely to be difficult to separate within epidemiological studies.

Fig. 1 Definition of Adaptation (based on the Intergovernmental Panel on Climate Change (IPCC) definition [23]) and Acclimatisation

and policies relating to these may differ to those for general temperature effects. For example, there are many specific measures, such as heat health warning systems (HHWS) that are only fully activated during an extreme event [30, 31]. Political will to react to extreme events, such as the 2003 heatwave (commonly stated as the trigger for many European countries' HHWS) may be greater [32], as although considered low probability they have an immediate and high impact compared to slowly changing environmental risk.

Only the direct effects of ambient temperature on health (all cause and cause specific mortality – for example mortality due to cardiac or respiratory disease) are considered in this review. A review of individual and specific adaptive measures (e.g. the effectiveness of electric fans, or heat health warning systems) is beyond the scope of this paper and has, in part, been undertaken in previous works [33–35].

Methods

All populations, analysed/aggregated at either city, regional or national level, were included in this review. We included observational studies (time series, case-crossover or period analysis design) which:

- quantified the risk of health related events with changing ambient temperature in one location over a given time period (not limited); or
- compared outcomes between two different discrete extreme temperature events (>1 day, for example, usually defined by the context specific definition of a heatwave or cold spell) in one location.

Where studies compared the effect of temperature extremes but by individual days (e.g. risk at the 98th percentile of temperatures compared with average temperature but as part of a heatwave) these were categorised as the first type of study – assessing the effect of ambient increased temperature on health.

The primary outcome assessed was mortality (all cause or by type), as estimations of this are not sensitive to changes in organisation of care (whereas, hospital admission rates for example, may change over time, not as a function of morbidity but related to changing expectations or access to care). Studies which only examined deaths coded as due to heat or temperature disturbances (e.g. heatstroke, hypo/hyper-thermia) were excluded as these deaths are comparatively rare, the coding of such death may vary and they may also be associated with occupational or working conditions unrelated to ambient temperature (e.g. heat stroke may occur in military recruits in training etc.). Studies were excluded if there were no quantitative results available that compared mortality (risk or rates or attributable burden) over time.

Five electronic databases were searched (Ovid MEDLINE, Ovid EMBASE, CINAHL, Psych- info and Global Health) using three main concepts: temperature, health outcomes and changes in vulnerability or adaptations. Search terms were combined using the appropriate Boolean operator terms and limited to English and to humans. Further articles were identified through snowballing of references and hand searching of relevant journals not indexed in the databases (e.g. Nature Climate Change).

Data from studies was extracted on location and duration of the study, exposures studied, health outcome measures, methods used for estimating the effect and methods used to assess changes in mortality at the time points recorded. Where available, subgroup analysis was also recorded (e.g. by age category or by cause of death). Contextual information, for example whether protective measures had been introduced during the study time period, was recorded even if the description of these was qualitative rather than quantitative.

Due to the heterogeneity of approaches to defining and assessing changes in temperature related mortality risk (for example, changes in relative risk (RR) or attributable mortality burdens over time) a meta-analysis was not deemed appropriate. Where complete results from more than one statistical model were presented, those that were reported in full or stated to be the main model by the authors are included. When results from more than one model were given, those judged to have the best control for confounders or best fit to data were chosen. Where estimates were made over a period of time the mid-point of this time period was used when representing the information.

Results

Eleven studies met the inclusion criteria examining changes in susceptibility to heat and cold over time and six studies of heatwaves met the inclusion criteria.

Changes in vulnerability to ambient heat and cold over time (non- heatwaves)

Types of study and methods used

Eleven studies [36–46] were identified that had quantitatively analysed changes in the effects of either ambient heat, cold or both on mortality over time. The key information about study populations, outcomes and methods is summarised in Table 1. The majority of studies used data from the US or Europe. The time periods studied ranged from 18 to 150 years. Eight studies focused only on urban populations [36–40, 43, 46], eight analysed all age groups of which four reported trends in time also by age category [36–39] and two papers only analysed older age groups [43, 45]. Five studies examined the effects of both high and low temperatures [39, 41–44], whilst all others only examined the effect of heat. Ten papers examined all-cause mortality, of which three also analysed trends in heat related cardiovascular and/or respiratory deaths [37, 38, 44] and one paper only analysed cardiovascular mortality [43].

A variety of health outcome measures were used within the time series studies to analyse the effect of temperature on health and how this varied with time (see Tables 1 and 2). Results were either presented as the RR of mortality per 1 °C (or 10 °F) increase in temperature [36, 38, 39, 43, 44], the RR of mortality at one temperature compared to another (e.g. 29 °C vs 22 °C) [36] or the 98th centile vs average temperature [39] or as the (average) annual number of excess heat or cold related deaths as a proportion of the population [45, 46] or of deaths [37]. The most common approach used to examine changes in susceptibility over time was the comparison of RR or excess temperature related deaths from the models on an annual or decadal basis or between two defined time points. The extent to which trends could be identified or were quantified varied, with some studies also analysing year or decade as a modifying factor in the relationship or using regression to examine the effect of time on heat/cold related health outcomes [36, 45].

Where the time series models used a linear-threshold approach to estimate the effect of temperature on mortality, different decisions were taken regarding setting the threshold above or below which temperature effects were estimated. In some cases [42, 45] a change in threshold or MMT was used to support evidence for or against changes in susceptibility (i.e. an increase in threshold represents a decrease in susceptibility to heat). Even if not specifically analysed, a change in threshold is important as it relates to the slope of the regression line. One paper fixed the threshold [44] across the entire analysis period but noted that it increased in later years and two papers [42, 46, 47] allowed the threshold to vary between decades. These approaches are commented on further in the discussion section.

The amount of control for time varying factors within the epidemiological models varied. For example, only one paper specifically reported including air pollution control in the main model [44] and this was only for the last part of the century due to limited data availability (see Table 1). One study [37] reported control for air pollution as part of their sensitivity analysis and supplementary materials. In those studies reporting cold effects over time, control for influenza varied (see section on varation in effect by study design and metrics used).

Temporal changes in susceptibility to ambient heat

The effect of increased temperature on mortality was examined in eleven studies [36–46]. Of these, ten found evidence of some decrease in susceptibility to heat (see Table 1). Seven reported a measure of statistical significance – either a test for trend or included confidence intervals for estimates at two discrete time points. Of these seven, five found the decrease over time or between two time periods to be statistically significant at the 5 %

Table 1 Characteristics and results of studies analysing temporal changes in temperature related mortality

Study	Location time period population	Exposure(s) and outcomes	General modelling approach and methods to assess change in susceptibility over time	Results: changes in (RR) of heat/cold related mortality (HRM, CRM) over time (all CI/PIs and significance are for 5 % level unless stated otherwise)
Bobb et al. 2014 [37]	105 US cities 1987–2005 All ages & age stratified	Heat (only summer months) All-cause mortality & CVD / Respiratory mortality	Time series regression (daily series) model. Control for time varying factors. Estimated excess heat related deaths for each year (1987 and 2005 results compared). Each year allowed a separate coefficient for daily temperature.	Heat related deaths per 1000 deaths (all cities):51 (95 % PI: 42,61) in 1987 compared to 19 (95 % PI: 12,27) in 2005. Decline observed for all ages & significant for heat related respiratory & CVD mortality. Cities with larger increases in AC had larger decreases in mortality (not significant).
Petkova et al. 2014 [36]	New York (US) 1900–1948 & 1973–2006 All ages & age stratified	Heat (only summer months) All-cause mortality	Time series regression (daily series). Control for time varying factors. Modelled risk of mortality at 29 °C vs 22 °C for each decade. Decadal averages of RR at 29 °C vs 22 °C compared. Used random effects meta-regression, including linear term for decade.	Decrease in RR at 29 °C vs 22 °C of 4.6 % (2.4,6.7) per decade (all ages) >65 years: highest initial risk and most decline in RR over time. Also found a change in lag structure over time - harvesting effect more prevalent in earlier part of century.
Astrom et al. 2013 [39]	Stockholm, Sweden 1901–2009 All ages & stratified by age and sex	Heat and cold 'extremes' (Defined in model 1 as above/ below the 98th percentile for entire period) Daily mortality	Time series regression (daily series). Control for time varying factors. Examined trend in RR of mortality at extremes of temperature over time of mortality at 98th percentiles of temperature compared to mortality at average temperatures.	Significant decline in mortality risk for elderly and combined age categories for heat but non-significant for cold. Patterns similar for men & women Significant declining trend in temperature related mortality risk for 0-14 s for hot and cold. In last decades, upward trend in the heat risk for the 15–64 age group observed.
Ha et al. 2013 [38]	Seoul, S. Korea 1993–2009 (1994 excluded: extreme HW) All ages & age stratified	Heat All-cause mortality (excluding accidental deaths) and CVD mortality	Time series regression (daily series). Linear threshold model to estimate quantitative effects. Control for time varying factors. Compared results from two periods (1993 and 1995–2000, and 2001–2009). Used common threshold throughout study period.	% increase in all-cause mortality per 1 °C increase in temperature above threshold (changes not significant): All-cause mortality (pattern similar for >65s) 1990s 4.73 % (all ages) 2000s 6.05 % (all ages) CVD mortality (pattern similar for >65s) 1990s 8.69 % (all ages) and 2000s (all ages) 5.27 %
Matzarakis et al. 2011 [40]	Vienna, Austria 1970–2007 All ages	Heat (Physiological Equivalent Temperature (PET)) All-cause mortality	Time series analysis (daily series). Modelled daily excess mortalities, calculated as deviations from average annual mortality. Linear regressions fitted to mortality rates per 10000 to give % change in heat related mortality per decade (1970–2007) for given ranges of PET.	% change per decade from 1970 to 2007 in mortality: PET range <29 °C - 0.15 %: (reported not significant) PET range 29-35 °C −0.83 % (−0.68,-0.97) PET range 35-41 °C −0.96 % (−0.77,-1.16) PET range > =41 °C −1.32 % (not significant - low numbers)
Christidis et al. 2010 [41]	England and wales 1976–2005 All ages	Heat and cold All-cause mortality	Daily excess HRM/CRM obtained by comparing to the average mortality within a 3 °C 'comfort zone'. Compared: 1.yearly regression slopes (1976–2005) 2.Change in HRM/CRM obtained using regression slopes from different time periods (1976 compared to 2005) to demonstrate no adaptation or early adaptation.	Slope of regression lines for heat and cold related mortality risk (SE) decreased in magnitude over time. CRM decreased by 85 deaths/million/year from 1976–2005. "No adaptation" scenario (1976 regression slope) CRM reduction less 47 deaths/million/year. HRM increased by 0.7 deaths/ million/ year. "No adaptation" scenario (1976 slope) HRM increased more (by 1.6 deaths/million/year).

Table 1 Characteristics and results of studies analysing temporal changes in temperature related mortality *(Continued)*

Ekamper, 2009 [42]	Zeeland, Holland 1855–2006 All ages & age stratified	Heat and cold All-cause mortality	Times series analysis (daily series) Compare: a) regression co-efficient from model between 25 year periods (thresholds allowed to vary between time periods) b) MMT value in each 25 year time period analysed.	Regression coefficients for HRM reported as decreasing over time (no test for significance). Pattern unclear for cold. Found shift in MMT to higher temperatures in later time periods analysed: MMT slightly below 15 °C for 1855–1897 and around 17 °C for 1905–1929 and 1930-1954
Barnett, 2007 [43]	107 US cities 1987–2000 'Elderly' (age range not given)	Increases in temperature in both summer and winter (effects of heat & cold) CVD mortality	Case-crossover design Time stratified Compare the % increase in of cardiovascular deaths per 10 °F increase in temperature within a given season and across the time period 1987–2000.	% increase in risk per 10 °F rise in temperature summer Winter 1987 4.7 % (3.0, 6.5 %) 1987–4.2 (−5.1,-3.2) 2000–0.4 % (−3.2,2.5) 2000–4.9 (−6.8,-3.1) Variation between geographic regions (e.g. biggest declines in heat risk in NW, NE, Industrial MW and California)
Carson et al. 2006 [44]	London (UK) 1900–1996 All ages	Heat and cold All-cause mortality and CVD and respiratory mortality	Time series regression (weekly series). Linear hockey stick model. Controlled for time varying factors. Threshold set at 15 °C. Compared a)decadal RR for heat and cold related mortality b)proportion of deaths attributable to heat/cold.	RR (for heat related mortality above threshold) and % attributable deaths: increased between 1910 and 1937 then decreased for last 2 time points.
Davies et al. 2003 [46]	28 major US cities 1964–1998 Age standardised population	Heat only All-cause mortality	Time series analysis (daily series) using HRM: daily mortality anomalies estimated using median mortality for given month as a baseline. Analysed daily fluctuations in excess mortality with temperature variation. Compared decadal HRM. Threshold varied by decade.	Mean decadal HRM in standard population of 1 million for all cities declined over time. 12 cities showed no evidence of threshold AT above which heat related mortality begins to appear in the 1990s. Most decline in 1980s in the South in NE cities. Seattle and Washington show increased HRM in latest decades compared to the 1960s.
Donaldson et al. 2003 [45]	North Carolina (NC), South East England (SEE) South Finland (SF) 1971–1997 Age: > 55 yrs	Heat only All-cause mortality	Time series analysis using HRM (daily mortalities at daily temperatures exceeding a 3 °C threshold band, minus daily mortalities in that 3 °C band for the given month. Summed to give annual heat related mortality) Compared a) Change in temperature at which minimum mortality occurs (MMT) b) Change in excess heat related mortality per 10^6 between 1971 and 1997.	Changes in MMT (between 1971 and 1996): Increase in MMT significant for NC and SEE but not for SF Change between 1971–1996 in HRM per 10^6 population (unadjusted for age & sex and adjusted): NC 228 in 1971 decreased to 16 in 1996. Change of 212 (59,365). Adjusted change 552 (significant) SF 382 in 1971 decreased to 99 in 1996. Change of 282 (66–500). Adjusted decrease 414 (significant) SEE 111 in 1971 decreased to 16 in 1996. Change of 2.1 (−119, 114). Adjusted decrease 53 (significant)

Table 2 Characteristics and results of studies comparing effects of heat-waves on mortality

Study	Population: location & study time periods	Definition of heat wave (HW)	Outcome measure	Methods used to compare effect of heat waves	Standardisation of HW characteristics?	Results: health outcomes	Comments and explanations given for changes in mortality between events
Kysely et al. 2012 [51]	Czech Republic 1986-2006	≥2 days with temperature >95th quartile of distribution for given part of the year	All-cause and CVD mortality	Determined whether the deviation of observed deaths significant compared to expected deaths estimated by Monte Carlo method using data drawn from summers between 1986–2006.	Within common definition, length & intensity of HW allowed to vary between years.	Linear test for trend for deviation of mortality for hot spells between 1986 and 2009. Decrease in mortality over time found (significant at $p = 0.05$ level). Decline of around 0.4-0.5 % deaths per year.	Hypothesised decreasing mortality due to acclimatisation to heat within a summer season in later years and/or increased adaptive measures such as improved living, health & building standards and increased heat awareness
Kysely et al. 2008 [52]	Czech Republic 2003 HW compared to period 1986-2006	≥3 days with average daily heat index exceeding 95 % quartile of distribution and ≥ 1 day exceeding 98 % quartile	All-cause and CVD mortality	Observed and expected mortality compared. Expected deaths over April-September period computed using smoothed 15 day running means corrected for weekly cycle and annual changes in mortality .	Within common definition, length & intensity of HW allowed to vary between years.	Taken together, the HW effects of 2003 were weaker than HW effects in previous years	Hypothesised that decreased effects of 2003 HW could be due to: factors unrelated to adaptation – e.g. influenza epidemic affecting European countries in spring 2003 reducing number of susceptible individuals or improved response to heat
Feuillet et al. 2008 [53]	France (all regions) 2006 compared to previous 29 years	2006 HW defined as period with consecutive days of alert in at least one (of 96) departments of France	All-cause mortality	Observed and expected mortality compared. Expected mortality derived from baseline deaths predicted by model using data from previous 29 years: model included seasonal control and long-term mortality trend.	Modelled expected deaths from 2006 HW using model & actual deaths from 2006 HW using mortality figures.	4388 fewer deaths than estimated by predictive model for the 2006 HW Larger decrease in the over 75 years	Hypothesised heat wave plans instigated post 2003 led to a decrease in heat wave related mortality.
Tan et al. 2007 [54]	Shanghai 2003 and 1998	≥3 days where daily maximum temperature exceeds 35 °C	All-cause mortality	Average number of deaths on heat days and non-heat days compared. Linear regressions run for 1998 and 2003 summers including mortality, temperature and air pollution concentrations to assess effect of length of HW, timing in summer and pollution.	Within common definition, length & intensity of HW allowed to vary between years.	Absolute deaths: 1998: Average number deaths on non-heat days 244, heat days 358 2003 Average number deaths on non-heat days 223, heat days 253 Not adjusted for population size/age	Hypothesised decreased HW effects could be due to: Urban green area increasing from 19.1 % to 35.2 % over the time period. Increased use of air conditioning and implementation of heat/health watch warning system in 2002
Rey et al. 2007 [55]	France (all regions) Six Heat Wave periods between 1971 and 2003	≥3 days where max and min temp simultaneously greater than respective 95th percentile	All-cause and cause-specific mortality	Observed and expected mortality ration (O/E) compared for each HW Expected mortality calculated from observed mortality in previous 3 years using log-linear Poisson model of mortality rates (by month, year, age, gender, cause of death).	Within common definition, length and intensity of HW allowed to vary between years.	Observed-Expected (O-E) mortality (all cause) 1975 2952 1976 5116 1983 1473 1990 1624 2001 1330 2003 13734	In all six heatwaves, age >75 years were most vulnerable. Mortality standardised by age and gender

Table 2 Characteristics and results of studies comparing effects of heat-waves on mortality *(Continued)*

Smoyer et al. 1998 [56]	St Louis, Missouri 1980 and 1995 heat waves	Days with Apparent Temperature > 40.6 °C (cut off for US National Weather service warnings)	All-cause mortality	Mortality –heat relationship modelled using Poisson regression, including terms for HW duration, temperature and interaction between heat wave duration and timing in season. Best models for 1980 and 1995 selected Only > 65 years studied.	Simulated severe HW using 2 models: Model 1: deaths estimated using 1980 weather data and 1980 model parameters (adjusted for 1995 population size) Model 2:deaths estimate using 1980 weather data and 1995 model parameters	For a simulated HW: vulnerability increased using 1995 model parameters (estimated number of deaths using 1980 parameters 446 (419,465) compared to 1995 model parameters (estimated number of deaths 481 (319,822)	Imprecise estimates make the difference between 1995 and 1980 models difficult to assess .Between 1980 and 1995 the numbers of persons in the eldest age category and of older persons below the poverty line increased. Air conditioning prevalence: 1980 64.1 %, 1991 86.7 %

confidence level. Given the different approaches to analysis and quantitative formulation of the outcomes, changes in RR over time are brought together graphically only for those papers which used similar methods and the same outcome metric (Figs. 2 and 3).

In those studies that examined changes in heat related mortality over the last century, most change appears to occur between the first (where risks appear substantively higher) and last part of the last century [36, 39, 44] (Fig. 2). Petkova et al. [36], appeared to show a slowing of the decrease in risk from the 1980s onwards (as the RR also approaches 1). Ha et al. [33] only analysed two points in time – both after 1990, and did not find a significant difference between RR of heat related mortality between the time points. Carson et al. [44] used larger time frames to compare risk and therefore results past 1980 cannot be visualised, however it appears that the decrease in risk after 1927 was substantial. The authors hypothesised that the large decrease seen in heat related mortality risk could be due to heat related deaths being caused by infectious diseases (such as diarrheal disease or septicaemia) in the first part of the century, but that with the epidemiological transition (the shift in burden of disease from infectious diseases to chronic non-communicable disease over time, due to improved sanitation and healthcare [48]), these have become less prominent over time. Of note, this study was the only one to use a weekly time series for the analysis of effect, which may explain some of the difference in pattern seen between this and other studies. Interestingly, Petkova et al. [36] specifically examined the effect of short term mortality displacement, and found it contributed less to heat related mortality over the last part of the century despite an ageing population.

In all studies where the proportions of deaths attributable to heat were analysed, deaths were decreased at the latest compared to earliest dates (see Table 1 and Fig. 3a and b). Two of these papers [37, 45] only presented risks for two dates, making it difficult to comment on trend. Bobb et al. [37] found the overall (combined average of all 105 US cities analysed) attributable proportion of deaths to excess heat to be significantly (5 % confidence level) less in 2005 compared to 1981. Carson et al. [44], using the same metric, also found the proportion of deaths attributable to temperatures above a given threshold to be significantly lower in the last time period compared to all others, though the pattern over the first 3 time periods is less clear. Two studies analysed deaths attributable to excess heat per million of the population (Donaldson et al. [45] and Davis et al. [46, 47]). Donaldson et al. [45] compared two specific time periods in three locations. In North Carolina and South Finland the decreases in vulnerability were significant (5 % confidence level) in all models. In South East England, the decrease was only significant in the model with control

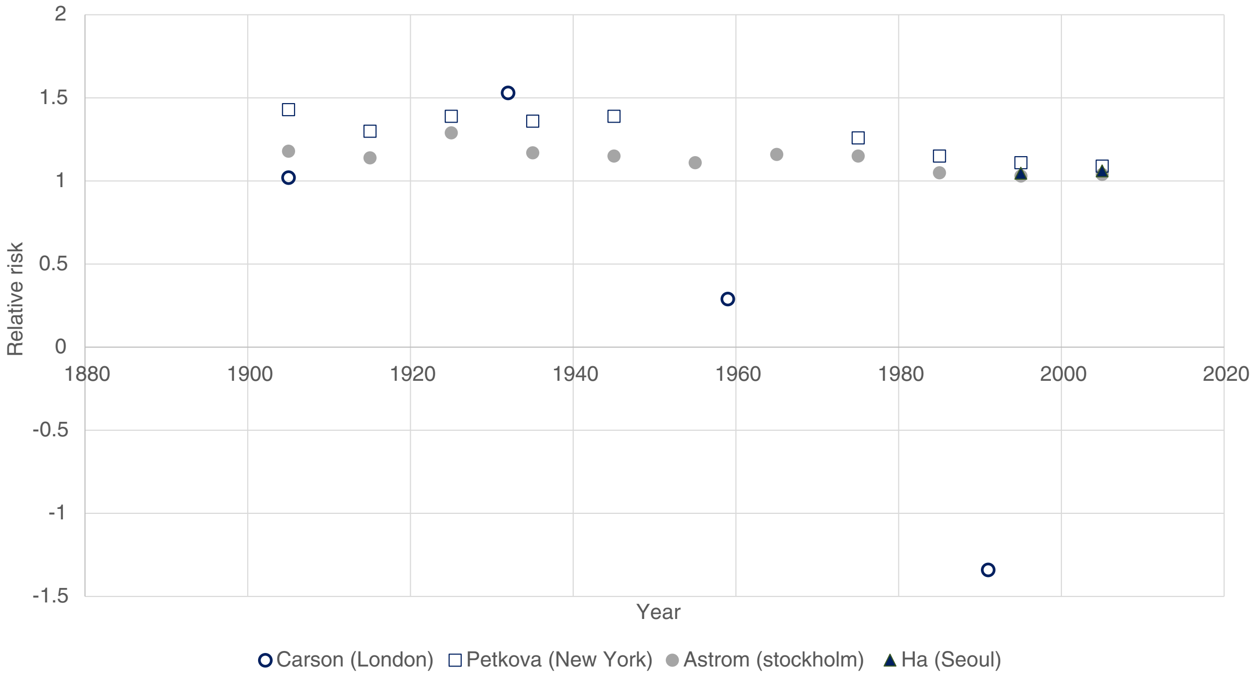

Fig. 2 Studies reporting relative risk of heat related mortality over time. This figure shows the relative risk associated with a 1 °C increase in temperature above a common threshold (Carson et al. and Ha et al.) and the relative risk associated with extremes of high temperature compared to average temperatures (Petkova et al. and Astrom et al.). Note due to the different thresholds used, this graph is only illustrative of trends and not differences in magnitude of risk between cities

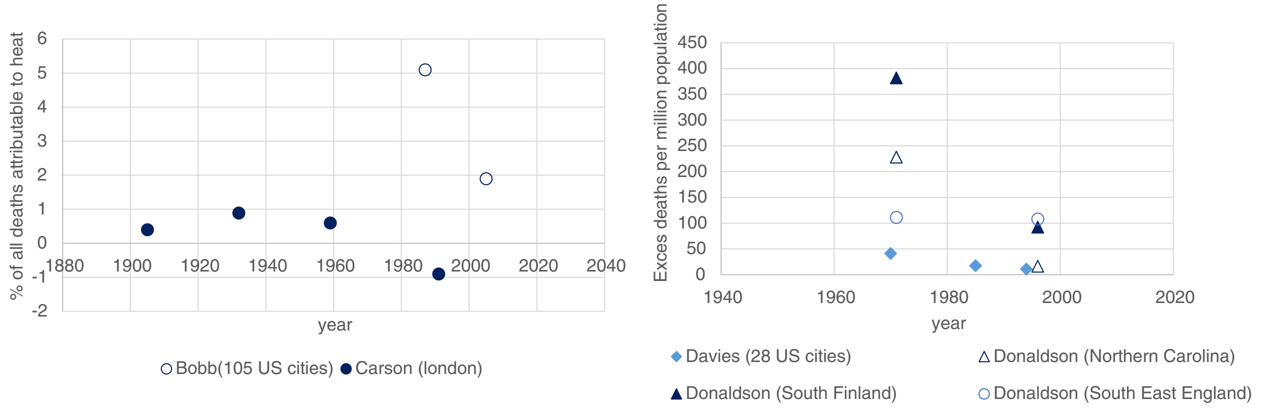

Fig. 3 Studies reporting heat related deaths over time. This figure shows studies comparing excess heat related mortality as a proportion of all deaths (left) and studies where excess heat related mortality was reported per million population (right)

for age and sex. However, it was not possible to represent the results from the adjusted models graphically as only the changes in excess deaths were reported (i.e. no baseline or final figures) Davies et al. examined heat risk in 28 US cities [46] and showed a decreasing trend across the three time points but included no information on significance.

Four papers analysed results using different methods/outcomes to any other study and therefore are not represented graphically: Christidis et al. [41], Matzarakis et al. [40], Barnett [43] and Ekamper et al. [42].

Christidis et al. [41] investigated the hypothesis of 'adaptation' by comparing heat and cold related mortality estimates obtained by using regression slopes from either earlier or later years in the study. Regression slopes from earlier time periods in the study (1976) were used with weather data for the whole period to calculate heat and cold related mortality to demonstrate mortality with 'no adaptation'. Results obtained using the slope of the regression line from later years (2005) with the same weather data as a comparison were used to demonstrate deaths accounting for 'early adaptation'. These scenarios were compared to the actual heat and cold related mortality calculated with slopes and weather data from over the entire time period. They found actual heat related mortality increased by 0.7 deaths per million per year (using data from the whole time period) but if no adaptation had occurred heat related mortality would have increased by a larger amount (1.6 deaths per million per year over the period 1976–2005, calculated using regression slopes from the earlier time period with weather data from the whole period).

Matzaraki et al. [40], examined the change in excess mortalities attributable to different temperatures in 1970 and in 2007. For two of these ranges of temperature (29 °C to 35 °C and 35 °C to 41 °C) the excess mortality significantly decreased between the two time points. The last temperature range (>41 °C) was reported as non-significant but had low numbers of deaths.

Barnett [43] used a case-crossover approach to examine the increase in risk of cardiovascular mortality with temperature in the US. Combined estimates for all the cities showed a significant decrease in vulnerability between the two time periods analysed (1987 and 2000).

Ekamper et al. [42] reported both shifts in the MMT (which increased over time) and slopes of regression analysis. They reported a decrease in vulnerability over time but did not test significance.

Temporal changes in susceptibility to ambient cold

Only five studies [39, 41–44] analysed the risk of cold related deaths over time, all as part of an overall analysis of temperature related mortality (i.e. none examined cold effects alone). Results of the two of these studies which reported the RR of cold related mortality below a given threshold over time are illustrated in Fig. 2 below.

Three of the five studies examining cold effects reported decreased susceptibility over time [39, 41, 44]. Carson et al. found that this decrease was significant (at the 5 % level) in a London based study [44] (see Fig. 4 below). In a second UK based study, Christidis et al. [41], found that actual cold related mortality decreased by 85 deaths per million population per year over the period 1976–2006 (significance not reported). Using the same methods as described in the above section (on heat) to examine changes in cold related mortality under actual, 'adaptation' and 'no adaptation' scenarios they found that the decrease would have been smaller (47 deaths per million population per year) with 'no adaptation' (see also Table 1). Although Astrom et al. found a decrease in cold related mortality over time, it was found to be non-significant [39] except in the 0–14 year age category.

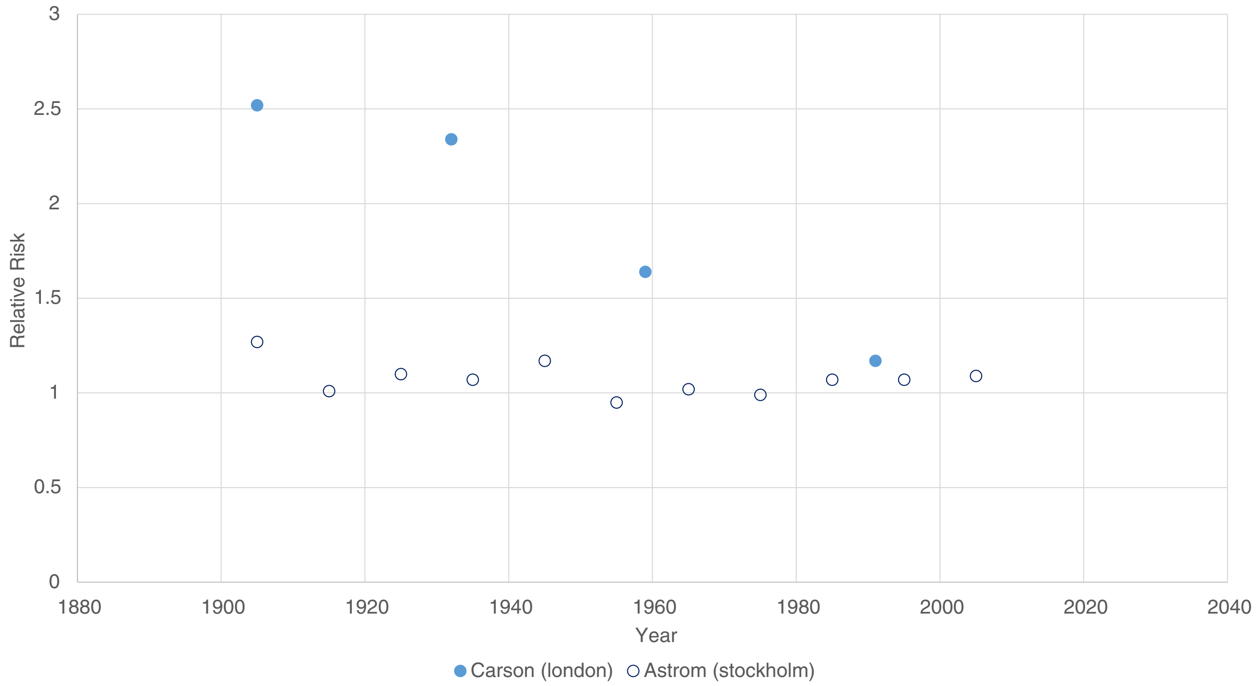

Fig. 4 Studies reporting the relative risk of cold related mortality over time. This figure illustrates the relative risks associated with a 1 °C decrease in temperature below a common threshold

The study based in the US no clear evidence of any trend in cold related mortality over time [43] and a trend in cold related vulnerability was not clear in the study by Ekamper et al. [42].

Of note, all five studies had found a decreasing trend in heat related mortality.

One study exclusively examined the effects of cold temperatures on mortality in Spain by examining shifts in threshold for effects, but did not report quantitative results and so has not been specifically discussed in this review [49].

Variation of results of heat and cold mortality by study characteristics

Variation of effect by study design and metrics used

It does not appear that the overall direction of effect over time was influenced by study design (time series, case crossover) or by the amount of time varying factors (e.g. seasonality, temporal trends, holidays etc.) controlled for by studies (see Additional file 1: Table S1a). Studies also used different approaches in either fixing the thesholds above which effects were modelled, or allowing these to vary across each time period analysed. This did not appear to alter the direction of effect demonstrated by studies (which consistently demonstrated decreasing susceptibility to heat effects regardless of precise design). However, the implications of these different choices are considered in the discussion section and in Table 3. Where sensitivity analyses were carried out, allowing definitions of extreme temperatures to vary by time periods analysed, small differences in results were seen within studies [39] (see Additional file 1: Table S1b) although the overall direction of effect remained unchanged.

Using excess heat or cold related deaths as an outcome includes many factors: the risk of mortality related to changes in temperature for the given time period, baseline mortality in the population and also the number of days at different temperatures above or below the threshold (where used) within that time period. In studies which used this metric [37, 41, 45, 46], the number of heat-related deaths decreased over time in three studies. However, this could reflect changes in any of the factors mentioned above (e.g. RR, baseline mortality or temperature). It could be expected (though not always reported in these studies) that temperature has been increasing over the last century [1] and therefore the decreasing trend in excess deaths over time in these studies illustrates a decrease in vulnerability despite the increased temperature. One study [41] found that the number of heat related deaths did not decrease over time, but that the regression slope used to calculate these did.

Given that few studies included control for ambient air pollution in the main model it is difficult to know how this would have affected trends. It should be noted that the confounding role of air pollution is currently under debate [50]. In the study by Carson et al. [44], controlling

Table 3 Advantages and disadvantages of approaches used to assess changes in susceptibility to temperature effects over time

Approach to assess change in vulnerability	Comments: advantages, disadvantages and implications of method to consider when interpreting results	Example of study using this approach
Compare minimum mortality temperature or thresholds above or below which heat/cold effects occur over time.	Simple metric for comparison. Can be determined from models using maximum likelihood estimation. Does not give information on how the RR is changing over time - an important factor in determining deaths attributable to heat or cold. The slope of the regression line is often related to the MMT or threshold. For heat effects, steeper slopes are often seen with higher thresholds. Quoting only the MMT/threshold would not include this relevant information. MMTs/thresholds can be difficult to establish with data, especially for cold – models may not always select the most appropriate threshold.It would be helpful to quote changes in MMT along with changes in RR. For example, when modelling heat effects, if there is both an increase in MMT over time and a decrease in RR despite the higher heat threshold, then this would give convincing evidence of a shift in susceptibility over time.	No included study used this approach in isolation, Carson et al. [44]. and Donaldson et al. [45] both give report MMT changes over time in addition to the changes in RR.
Compare the RR for heat or cold effects over time allowing: a) Fixing the thresholds above/below which effects are modelled over time b) Allowing thresholds above/below which effects are modelled to vary with time (e.g. allow for a shit in MMT)	Approach a:If the threshold is fixed then the changes in RR are simple and easy to interpret – i.e. allows comparison of 1 parameter only. Fixing the threshold whilst fitting a linear relationship, however, may influence results: If the threshold is fixed at a lower temperature than that at which it actually occurs, the modelled heat slope may be biased towards being more shallow. If thresholds are fixed, then giving information on how they have varied over time could help capture some information (as Carson et al. did). Approach b: Allows a better fit with the data series. However, this may lead to results which are difficult to interpret: If both measures vary then interpreting the two measures is difficult, as they are inherently related. Further, if thresholds vary by time period and only the RR is reported, this will not capture the full change in susceptibility occurring. For example, a situation may arise where both the threshold and slope have increased in a later period, but it is unclear whether the slope is artificially raised due to the higher threshold placement. Conversely, if the shape of the temperature-mortality relationship remained the same but the threshold /MMT shifted to the right over time, reporting only the RR would under-estimate the change in vulnerability. This could be misinterpreted as there being no change in susceptibility over time.	Approach a) used by Carson et al. [44] Approach b) used by Ekamper et al. [42]

Table 3 Advantages and disadvantages of approaches used to assess changes in susceptibility to temperature effects over time *(Continued)*

Compare the RR for heat or cold effects at two defined temperatures (e.g. a) At 29 DC vs 22 DC or b) At a given percentiles of the temperature distribution.	Allows for risk from relationships modelled non-linearly to be compared. Gives information on how the population are responding to more 'extreme' temperatures. If RR compared are derived from percentiles of the temperature distribution then these can be calculated relative to the whole time period of data (in which case similar to fixing an exact temperature as in a) or allowed to shift (defined relative to each time period analysed). If the percentiles shift according to the time period analysed, this will implicitly include some information about changing susceptibility or 'adaptation'. If the temperatures used for comparison of RR across the time period are fixed then interpretation of the results is simpler. Results would need to be interpreted with this choice in mind. For example, if the RR at the 98th percentile compared to the average temperature has not changed over time, but the 98th percentile has been calculated according to each time period (i.e. if temperatures have risen, the 98th percentile temperature increases) then this demonstrates some decrease in susceptibility despite no change in RR. Approach a) fixed temperatures or temperatures fixed at a given percentile relative to the entire time period, allows changes in susceptibility to heat/cold to be more easily judged as only one parameter is changed. If approach b) is taken and percentiles used are allowed to vary by time period, then care should be taken in interpreting results. A sensitivity analysis could be undertaken either using approach a) for comparison or by allowing the percentiles used for approach b) both to be fixed across the entire period and allowed to vary.	Approach a) used by Petkova et al. [36] Approach b) used by Astrom et al. [39] who included sensitivity analysis allowing for percentiles at which RR were compared to either vary by time period or be defined relative to the whole time period of data analysis.
Compare deaths attributable to heat or cold over time.	The calculation of attributable deaths takes into account both the threshold above/below which effects are seen and the RR for each temperature above/below the threshold. The calculation of deaths attributable to heat/cold also uses number of days at which the temperature was above/below the threshold for the given period and the baseline mortality for each time period. Therefore the change in outcome could be related to any of these factors which are independent of the temperature-mortality relationship. For example, the RR of heat related mortality may have decreased over time, but the number of days above the threshold increased with as temperatures warm. This may lead to the number of attributable deaths staying constant or increasing over time, despite a decrease in susceptibility compared to the earlier time period. Providing information on the number of days above/below the given threshold or on temperature trends and on trends in baseline mortality may ease interpretation – for example, if the temperature has been increasing but there is a decreasing trend in excess heat-related deaths this gives more weight to evidence of decreasing population susceptibility to heat.	Bobb et al. [37], Carson et al. [44]

Table 3 Advantages and disadvantages of approaches used to assess changes in susceptibility to temperature effects over time *(Continued)*

Use transfer function (e.g. RR from modelled relationship between temperature and mortality) from later or earlier years with the weather series from whole time period to assess whether there has been a change in attributable deaths.	This approach gives results which are easy to interpret. However, it would need to be made clear whether both the changed RR and potentially changed threshold above/below which effects have been modelled have been used to calculate the burdens. Although using the temperature-mortality relationship from each time period with the same series of weather data seems to give an easily comparable result, clarity should be provided on whether the baseline mortality used for calculations has also been consistent. As for any of the above scenarios, the modelled RR may be influenced by outlying extreme temperatures and therefore taking a number of years as a basis for 'transfer' functions may be more reliable.	Christidis et al. [41]

for air pollution did not affect the overall trend over time in cold related mortality, indeed individual RRs for each time period for cold-related mortality were higher after controlling for air pollution. Bobb et al. [37] provided information about models with pollution control as part of a sensitivity analysis. In this paper, when fine particulate matter was included in a linear model, the reduction in heat related mortality between the two time points was no longer significant at the 5 % level (though the reduction remained significant in the non-linear model when air pollution was included).

Influenza is often thought to be a confounding factor when estimating the effects of cold (although whether it is considered a confounder in this relationship will depend on how much influenza survival and transmission rates are affected directly by ambient air temperature (i.e. placing it on the causal pathway between lower temperatures and mortality) as opposed to seasonal and behavioural factors such as school opening times (which occur independently of day to day variation in temperatures)). Three of the five papers reporting cold effects attempted to control for influenza, for example with the inclusion of an indicator for influenza within the models [39] or where flu data was not available by excluding years of known influenza epidemics [42, 44].

Variation of effect by subgroup analysis

Where studies examined temperature related mortality by specific subgroups such as cardiovascular or respiratory mortality [37, 38, 43, 44], decreases in these subgroups were seen for the effect of heat and in three of the studies this was significant [36, 37, 43]. Of interest, in the study by Ha et al. [38], there was a (non-significant) decrease in risk of cardiovascular mortality above the temperature threshold in contrast to a (non-significant) increase in all-cause mortality. Carson et al. [44] reported decreases in cardio-vascular and respiratory deaths were less prominent than for all-cause mortality. However, this study analysed a much longer time period than others examining outcome specific mortality and therefore factors such as the epidemiological transition may explain some of the differences. As previously mentioned, this study used weekly data which may also affect the patterns in results seen between different causes of death.

Where results were analysed by age group, the majority of studies found that the largest temporal reductions in mortality were in the older age groups [36, 37, 39]. Barnett [43] and Donaldson et al. [45] only analysed the results in the elderly and over 55s respectively and both found decreases in vulnerability to heat.

Variation of effect by location: between and within studies

The variety in approaches used for analysis makes it difficult to compare the variation between studies of effects seen across geographical areas. However, results presented so far have been for area or national level aggregated estimates. Four papers [37, 43, 45, 46] included multiple cities or areas within the same paper (i.e. same methods used). For those which analysed multiple cities within the US [37, 43, 46] some heterogeneity in results was seen. Bobb et al. [37] found that 74/105 cities displayed a significant decrease in excess heat related mortality between 1987 and 2005 and that cities with cooler climates had a larger decline in heat related mortality risk, though these cities also had the highest heat related mortality at the start of the time period. The cities with the largest increase in prevalence of air conditioning over the time period also had the largest declines in mortality, though this was not a statistically significant association. For one city in Southern California, susceptibility increased over time (not statistically significant at the 5 % confidence level). Davies et al. [46] examined 28 US cities over an earlier time period. They found heat related mortality rates had declined in 42 % of the cities but that two cities on the West coast (Seattle and Washington) had an increased number of excess deaths in the later time periods. They also reported that 12 cities (in the South) no longer displayed evidence of a threshold temperature above which heat mortality occurred (see Table 1 for details). Barnett [43] found the largest declines in heat related mortality risk in the US were in the North West, North East, Industrial West and Southern California. The reason for the difference in regional declines seen between these two papers cannot be conclusively determined, though some may be attributable to the difference in levels of aggregation of data (for example, Barnett uses regions, whereas Davies et al.. examine metropolitan areas), the different time periods analysed between studies and potentially the difference in methods used.

Donaldson et al. [45] analysed three different geographical areas (Southern Finland, Northern Carolina and Southern England) and found that the decrease in heat related mortality was smallest in South East England.

Susceptibility to extreme temperature events

Six papers were identified that examined differences in all-cause mortality between two different heatwaves or between heatwaves occurring over a number of years in the same location [51–56] (see Table 2 for details). All studies were from high or middle-high income countries. Most of these papers use an episode analysis approach to compare the expected and actual deaths during heatwaves. The approaches taken to selecting an appropriate baseline (for the expected deaths) varied between studies (Table 2) from using a moving 15–30 day average [52] to using more complex models over longer time periods (e.g. [51, 53, 55]). One study compared the absolute number of deaths occurring in two heatwave periods [54]. In comparing different heatwaves, some papers (e.g. [56]) made allowances for the different characteristics of various heatwaves by using model parameters from previous years with weather data from a heatwave in later years and vice versa. Other papers did not make such allowances, but two reported a decrease in heatwave related mortality despite a general increase in the maximum temperature encountered in later heatwaves.

Four papers reported decreased heatwave related mortality in later years [51–54], of which two reported a measure of statistical significance for this. Using a test for linear trend, Kysely et al. [51] found a significant decrease in the effects of heatwaves over the years. Fouillet et al. [53] found the number of deaths to be significantly fewer than those expected when derived from a predictive model based on previous years data.

One study reported no pattern in effects of heatwaves over time [55] and one found a non-significant increase in expected heatwave related deaths in a later year, despite there being an increase in air conditioning over this time and having made allowances for differences in heatwave characteristics [56]. This study used data from Chicago and it was hypothesised that this could be due to the increase in number of persons in the eldest age category between the two events and the number of older persons living below the poverty line (in the US, socio-economic status has been associated with heat related outcomes [57, 58], possibly because it relates to access to working air conditioning which is predictive of reduced heat related mortality [59–61]).

Where a decrease in mortality was seen, potential explanations included the introduction of heat health warning systems (HHWS), increased prevalence of air conditioning, improved urban design and living standards (Table 2). No study attempted to quantify these relationships.

No studies were located that specifically examined the effects of cold snaps over time.

Discussion

Of the eleven papers that examined variations in the RR of, or heat related mortality over time, all except one [38] found some evidence of decreasing susceptibility. In five of these, this decrease was significant at the 5 % confidence level (either analysed as trend over time or the difference between two discrete time points). Susceptiblity to heat appeared to stabilise over the last part of the century in those studies which covered that time period and in studies analysing more than one location, the magnitude of the decrease varied according to region or city. Where examined, studies found a decrease in cardio-vascular and respiratory heat related mortality.

Comparison of the magnitude of the changes in RR or temperature related mortality between studies is difficult, due to the variety of outcome measures and approaches used to model the temperature-mortality relationships. For example, where thresholds have been used, some studies have fixed temperature thresholds across the whole time period [44] and others have allowed them to vary within time periods analysed [42, 46]. This is important due to the inherent link between the temperature at which the threshold is set and the slope of the exposure-response regression line. There are further inherent limitations of approaches used by individual studies. For example, results of studies which use heat related mortality as an outcome (rather than the RR of death at different temperatures) are also affected by changes in baseline mortality and temperature over time. This can make it difficult to ascertain how much susceptibility to temperature itself is changing over time. Table 3 discusses in more detail the approaches used by individual studies included in this review to assess changes in vulnerability. Whilst we have not gone so far as to recommend one specific approach be used, we do highlight specific aspects of each study design that have implications for the interpretation and comparability of results obtained from these studies (see Table 3). Residual confounding is likely in many of the studies – although the importance of air pollution as a confounder is currently under debate [50], studies examining year round risk also had incomplete control for influenza and other seasonal trends or trends in mortality over time. The results of studies examining temperature related health risks are also aggregated to at least city level, which may lead to a masking of differences in vulnerability of certain population subgroups. It would be important to ascertain, for example, whether different sections of society (e.g. age groups, rural vs. urban populations or groups of different socio-economic status) display differences in their changes in risk of heat related mortality over time. For example, the urban heat island is likely to alter heat related risk and with increasing urbanisation, understanding how urban populations can and have adapted to heat will be important to inform future planning of cities.

There are also limitations of the body of literature reviewed as a whole. For example, there are no studies specifically from low income settings, where planned adaptive measures may be different to or less prevalent than those used in high income settings. Changes in temperature related mortality over time could be different in these contexts. Secondly, the number of studies is small and, due to differences in outcome measures and approaches used, is difficult to draw conclusions from. Also, many studies [38, 39, 42–45] have not analysed factors contributing to changes in risk over time. Although studies have controlled for general long-term trends in mortality (which should, for example, pick up long term trends in all-cause mortality), whether cause-specific (e.g. cardiovascular) mortality has changed specifically due to adaptation to heat or due to reduced cardio-vascular risk factors in general cannot be determined from the models. Only two papers made an attempt to quantitatively attribute changes in vulnerability to specific adaptive measures [37, 46]. Each found non-significant associations between air conditioning prevalence (see Additional file 1: Table S1b) changes over time and heat related mortality within cities [37] and overall [46]. Other studies included qualitative explanations for the reduction in heat related mortality over time, for example improved urban planning and building design [36, 39, 44, 46], increased living standards and a reduction in risk factors for conditions such as cardiovascular or respiratory morbidity [36]. These possible modifiers of the heat-mortality relationship have been summarised in Fig. 5. Identifying factors which have contributed to such changes could be used to inform environmental and health policy and future urban planning.

The possible slowing of the decline in heat related mortality over the latter part of the last century is interesting. This may, in part, be related to the epidemiological transition (for example, in the later part of the last century, declining susceptibility due to fewer heat related deaths from infectious causes would have occurred but heat-related cardiovascular mortality, for example, may be harder to prevent) but it also potentially demonstrates a limit to 'adaptation'. For example, there may be limits to both physiological adaptation and adaptive changes in infrastructure. Further studies which examine trends over time and in particular in more recent years are necessary to better understand this. Better integeration of physiological and epidemiological research would enable improved understanding of the importance that physiological adaptation can play within populations.

Overall, studies which have examined the effects of specific heatwave events on mortality over time, have found a reduction of heat-related mortality in later years [51–54]. These studies are not as robust in design as time-series or case-crossover approaches, and particular effects of a given heatwave may vary due to factors not captured in all definitions (e.g. intensity, temperature related to previous days etc.), that is to say that no two heatwaves are the same and have different characteristics which can modify the temperature-mortality relationship [62].

Despite a decreasing vulnerability to heat over time, there is little consistent evidence for decreasing cold related mortality, especially over the latter part of the last century. This may be unexpected, given advancements in housing design and in medical care. However, this should be considered in the context of the small number of studies that examined cold, and fewer that included information on the statistical significance. The lack of reduction in vulnerability to cold remains important as there is some evidence that maximum temperatures are rising faster than minimum temperatures [63]. Conversally, it might be expected by some, that as the climate has warmed over the last century, populations would become less vulnerable to heat and potentially more vulnerable to cold. However, there is no evidence of increased vulnerability to cold, either in terms of cold related mortality or

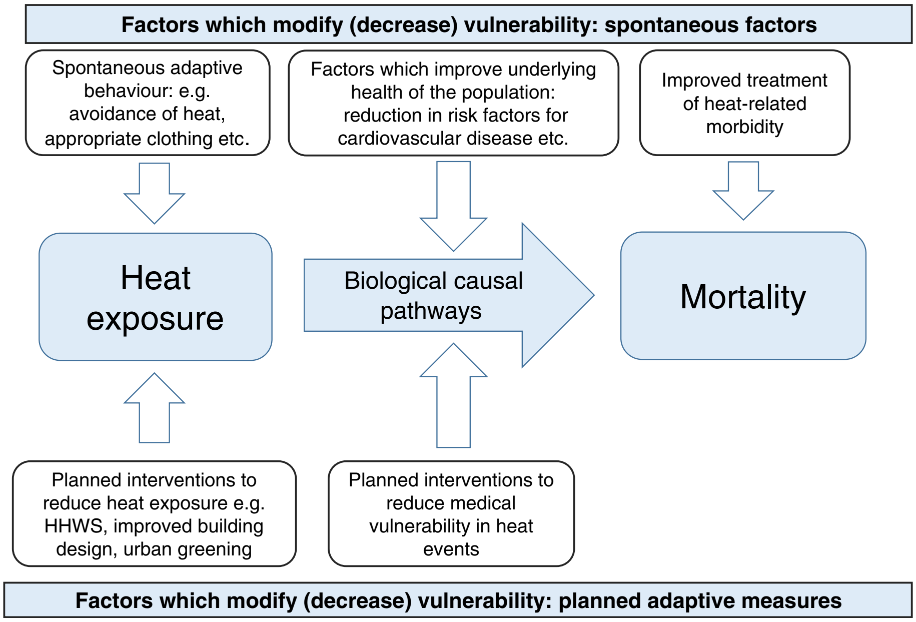

Fig. 5 Factors accounting for changes in vulnerability to heat over time

relative risk. This does suggest that, at least at an ecological level, there is no current evidence that 'maladaptation' has led to an increased vulnerability to cold over time.

Reasons for the differences over time between heat and cold related mortality have not been quantitatively explained in any papers. Therefore, different explanations should be examined: if improvements in the standard of living and reduction in risk factors for co-morbidities/improved medical care have contributed to some of the temporal decline in heat related mortality, it is reasonable to expect similar reductions in cold related mortality if similar pathways of causation exist. Some of the difference in trend may be due to different causal pathways for heat and cold exposure, for example, cold related mortality is known to occur over longer lag periods and mortality displacement (harvesting) is thought to be less important. It is also hpossible that physiological acclimatisation contributes more substantially to decreasing heat related mortality than to cold related mortality. For example, in their paper, Kysely et al. [51] specifically look at late summer versus early summer mortality from heat waves and find that this decreases over time. Physiological acclimatisation and changes in this over time have not been specifically evaluated in this review and would be an interesting area of further research. As the climate has warmed, the use of air conditioning and heat warning systems/health messaging are also offered as hypotheses for decreased heat related mortality, where these interventions are present. There have also been substantial changes in building design over time. However, whilst some of these might reduce vulnerability to heat specifically, others, such as the increased proportion of people living in flats might be expected to have the opposite effect [64]. Understanding differences in trends between heat and cold related vulnerability represents an important gap in knowledge.

Evidence from other studies and cities

Studies of differing vulnerability to temperature across geographical regions [21, 24, 26, 65] are often cited as potential evidence for adaptation. A review of these studies [27] used meta-regression to establish city-level characteristics associated with the heat-mortality relationship, demonstrating thresholds were generally higher in communities living closer to the equator. It also found that decreasing GDP, increasing age and population density were associated with increased relative risks of mortality from heat. This evidence is generally consistent with the findings of this review: many of the studies in this review hypothesised that improved standards of living and healthcare would reduce risk factors for disease and also heat exposure, therefore reducing susceptibility to heat over time. It is possible, however, that some cities have become more densely populated which may have increased vulnerability to heat, for example due to higher proportions of the population living in flats and risks of building overheating. However, while comparing results across cities or regions may implicitly include adaptation to temperature over time, it cannot give an estimate of how quickly or by how much community vulnerability can change.

This review provides suggestive evidence of decreasing susceptibility to heat over time. Due to the information included in the studies it cannot, however, determine how much specific adaptive measures (such as the use of cooling systems or HHWS) have contributed to changes compared to general improvements in healthcare and wellbeing in the population. The importance of air conditioning has, however, been demonstrated in other studies [57–61]. Studies, such as one undertaken in migrants which showed reduced vulnerability to heat in those who were born in Southern compared to Northern Italy [66] lend some evidence that physiological and behavioural adaptations to heat could be important and last over population lifespans. Examining trends in cities over time either within the same country or across countries with similar life expectancies and level of development could help further understand the role of adaptation. For example, vulnerability to heat across the US over time was shown to differ by city in the three multi-city studies presented here [37, 43, 46]. Whilst there are likely to be differences in patterns of risk factors and mortality across the US, the overall trend in these factors over time might be broadly expected to be the same. Differences in heat related vulnerability, compared to other specific trends over time by city could support the hypothesis that adaptation to heat specifically has occurred in these areas. Further studies would be required to substantiate this and differentiate different levels of underlying vulnerability across regions.

Implications for future climate change assessments and policy

A systematic review of future temperature related mortality projections synthesised evidence from 14 studies [67]. Of these, it was found that only half included assumptions about adaptation or changes in vulnerability in future estimates. Methods used to account for adaptation varied from the use of analogue cities [68, 69] analogue summers [70] and assuming adaptation to heat for a pre-determined number of degrees Celsius [71, 72]. The merits and limitations of each of these approaches have been discussed elsewhere [73–75]. Whilst the comparison of vulnerability to temperatures across regions can be used to inform the 'analogue cities' approach and differences in early versus late summers can be used to inform how much short term acclimatisation can achieve, the use of past declines in vulnerability has not been used, to our knowledge, to inform any future risk assessments. It could be argued that past trends cannot be used to inform future estimates of adaptation – the climate is projected to warm faster over the next century than in the past [1] and it is uncertain whether future populations will be able to adapt at the same rate (for example, some 'markets' for air-conditioning in the US were already thought to be saturated [46]). It is also unknown whether general health gains which lead to reduced vulnerability have been achieved. Nonetheless it is important to recognise that baseline vulnerability to heat in particular has changed across a number of settings. Baseline periods used in a number of studies projecting future temperature related risk studies published over the last decade span a period from the 1960s/70s to the 1990s/2000s [71, 76–78], though some studies - especially those published most recently, have used a more recent baseline period which is likely to improve future estimates [28, 79–81]. Given the trends in mortality observed, estimates of future risk could be improved to better reflect contemporary temperature related health risk. Where this has not been done, projections of future heat related mortality may have been over-estimated.

Conclusions

There is evidence that the risk of heat related mortality has changed over the last century and more recently. Further studies would be required to improve knowledge in this area, for example to understand the rate of changes in susceptibility more recently and whether changes are occurring at equal rates across sectors of society. Attribution of decreases in mortality to planned adaptive measures may help to inform future actions or policy, as would studies that specifically examine the effectiveness of certain adaptive actions. There are potential policy implications in the lack of decreasing vulnerability to cold. Adaptive efforts should not focus on heat alone, despite warming temperatures. Recent climate change risk assessments (e.g. [28]) show that the risk from cold is expected to account for most of the temperature related risk until late in the century (this is because of the magnitude of the RR and because there remain many more days below cold thresholds until this time). Therefore, any adaptive strategies would ideally reduce the risk from both heat and cold in order to prepare for both short and longer term temperature related risk, and urban and housing design with other co-benefits to health should be emphasised (e.g. [82]). Given the additional risk in urban areas due to the urban heat island effect [83] understanding the risk that future temperatures are likely to pose to health, and how populations can adapt equitably using solutions with co-benefits, is especially important in urbanised societies to plan for healthy and sustainable cities.

Lastly, when considering adaptation in impact assessments of future temperature related risk, sensitivity analyses which include differences in baseline vulnerability could improve understanding of future risk, as would assessments which could include, where possible, effects of certain specific adaptive measures on future heat related risk.

Additional files

Additional file 1: Table S1a. Features of Studies Examining Changes in Heat and Cold Susceptibility over Time. **Table S1b.** Results of studies examining the change in heat/cold susceptibility over time. (ZIP 50 kb)

Additional file 2: Peer review reports. (PDF 62 kb)

Abbreviations

CRM: Cold related mortality; DF: Degrees of freedom; GDP: Gross domestic product; HRM: Heat related mortality; HW: Heatwave; MMT: Minimum mortality temperature; PAT: Physiological apparent temperature; PM10: Particulate matter ≤10 μm in diameter; RR: Relative risk.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

KA conceived the idea for review and drafted the original manuscript. All authors contributed to the design of the review. CH, SH and SV provided critical input to the paper, tables and figures. All authors read and approved the manuscript.

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Declarations

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Peer review

Peer review reports for this article are attached as Additional file 2.

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5.3 Postscript to research paper

Since the time of publication of the review paper included as Chapter 5 of this thesis, there have been additional studies and one further review published, which examine whether there have been changes in heat and cold risk in any given location over time. One additional review of temporal trends in heat risk has been published, which summarised information on any paper where the risk of general ambient heat or of heatwave events over time was reported (Sheridan and Allen, 2018). The review by Sheridan et al. included many additional studies published after acceptance of the review paper in this chapter (Fechter-Leggett et al., 2016, Gasparrini et al., 2015, Green et al., 2016, Hess and Ebi, 2016, Kim et al., 2017, Li et al., 2017, Linares et al., 2015, Ragettli et al., 2017, Ruuhela et al., 2017, Yang et al., 2015, Barreca et al., 2016, Benmarhnia et al., 2016, Chung et al., 2017, Davis et al., 2016, De'Donato et al., 2015, Nordio et al., 2015, Onozuka and Hagihara, 2017, Kim et al., 2015). The ultimate conclusions of this second review paper are similar to those in this results chapter – namely that there is evidence of decreasing sensitivity to ambient heat and heatwave events in many countries, but that there is spatial heterogeneity in temporal trends. In some studies, while overall vulnerability to heat decreased in a given country, this was not the case in all regions demonstrating the importance of reporting results at a sub-national level (e.g. (Linares et al., 2015)) and in some locations studies demonstrated increased vulnerability to heat in later time periods (Li et al., 2017). Some studies reported a mixed picture, depending on the outcome studied (e.g. (Kim et al., 2015)). The review also included papers from more diverse locations but highlighted that studies including data from more low-income settings would be useful.

Four studies that have been published since the time of this review are particularly relevant to this PhD, as they include assessment of temporal variation in heat or cold risk in the UK (Gasparrini et al., 2015, Murage et al., 2018, Vicedo-Cabrera et al., 2018, Williams et al., 2019). These studies are discussed further in the introduction and discussion sections in the next chapter (chapter 6) of this thesis.

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6 Years of life lost and mortality due to heat and cold in the three largest English cities

6.1 Introduction

This paper forms the penultimate results chapter of the PhD and combines results of the analysis undertaken to address research objectives 3 and 4 of the PhD. A gap in knowledge around the use of alternate metrics such as potential years of life lost (YLL), which take into account population life expectancy and age at which mortality occurs in UK studies was identified. Quantifying this relationship could help with understanding the priorities of temperature related risk compared to other exposures/health risks and is important in the context of climate change and an ageing UK population.

The first part of the paper looks to address the research objective 3: to quantify the relationship between temperature, mortality and YLL in three major UK conurbations.

The second part of analysis in the paper addresses the fourth research objective of the PhD and builds on the results of the systematic review included as chapter 5. The review demonstrated a lack of studies undertaken in the UK in recent years which examine changes in heat and cold risk to public health, and studies which have analysed changes in risk to YLL or at a conurbation level.

The review also critiqued some of the methods used to examine changes in risk over time. In this results paper, I have built on the understanding developed in the previous chapter, for example by undertaking sensitivity analyses to examine whether methodological changes such as keeping the temperature thresholds constant or allowing them to vary with each time period analysed substantively alter the conclusions reached. Therefore, the second stream of analysis in this results paper addresses the fourth objective of the PhD: to examine the epidemiological evidence for a change in heat and cold RR of mortality in recent years in the three largest English conurbations and place the results in the context of relevant literature.

The paper included as this results chapter was accepted for publication by Environment International in July 2020. The supplementary materials for this paper can be found in Appendix 4.

6.2 Research paper

Cover page and research paper on subsequent pages

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	310970	**Title**	Dr
First Name(s)	Katherine		
Surname/Family Name	Arbuthnott		
Thesis Title	Temperature related effects on mortality and years of life lost in the UK for current and future climates		
Primary Supervisor	Dr Shakoor Hajat		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Environment International		
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SECTION E

Student Signature	[redacted]
Date	12/08/2020

Supervisor Signature	[redacted]
Date	24/08/2020

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Years of life lost and mortality due to heat and cold in the three largest English cities

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ABSTRACT

There is a well-established relationship between temperature and mortality, with older individuals being most at risk in high-income settings. This raises the question of the degree to which lives are being shortened by exposure to heat or cold. Years of life lost (YLL) take into account population life expectancy and age at which mortality occurs. However, YLL are rarely used as an outcome-metric in studies of temperature-related mortality. This represents an important gap in knowledge; to better comprehend potential impacts of temperature in the context of climate change and an ageing population, it is important to understand the relationship between temperature and YLL, and also whether the risks of temperature related mortality and YLL have changed over recent years.

Gridded temperature data derived from observations, and mortality data were provided by the UK Met Office and the Office for National Statistics (ONS), respectively. We derived YLL for each death using sex-specific yearly life expectancy from ONS English-national lifetables. We undertook an ecological time-series regression analysis, using a distributed-lag double-threshold model, to estimate the relationship between daily mean temperature and daily YLL and mortality between 1996 and 2013 in Greater London, the West Midlands including Birmingham, and Greater Manchester. Temperature-thresholds, as determined by model best fit, were set at the 91st (for heat-effects) and 35th (for cold-effects) percentiles of the mean temperature distribution. Secondly, we analysed whether there had been any changes in heat and cold related risk of YLL and mortality over time.

Heat-effects (lag 0–2 days) were greatest in London, where for each 1 °C above the heat-threshold the risk of mortality increased by 3.9% (CI 3.5%, 4.3%) and YLL increased by 3.0% (2.5%, 3.5%). Between 1996 and 2013, the proportion of total deaths and YLL attributable to heat in London were 0.50% and 0.40% respectively. Cold-effects (lag 0–27 days) were greatest in the West Midlands, where for each 1 °C below the cold-threshold, risk of mortality increased by 3.1% (2.4%, 3.7%) and YLL also increased by 3.1% (2.2%, 3.9%). The proportion of deaths and YLL attributable to cold in the West Midlands were 3.3% and 3.2% respectively. We found no evidence of decreasing susceptibility to heat and cold over time.

The addition of life expectancy information into calculations of temperature-related risk and mortality burdens for English cities is novel. We demonstrate that although older individuals are at greatest risk of temperature-related mortality, heat and cold still make a significant contribution to the YLL due to premature death.

1. Introduction

There is a well-established relationship between heat and cold and all-cause daily mortality (Gasparrini et al., 2015; Basu, 2009) which has been demonstrated globally, across varying climates. The relationship typically follows a U, V or J shape with increased mortality above and below location-specific thresholds. In general, the size of effect varies between regions and studies, in part driven by epidemiological modelling choices and differences in climate, but also by differences in local population, such as demographic or socio-economic factors affecting vulnerability to the effects of heat and cold. In the UK (and other locations), older age groups are most at increased risk of temperature related mortality (Hajat et al., 2007), though as temperatures continue to rise, other age-groups may become increasingly vulnerable.

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However, results are rarely presented using a metric which takes the length of life shortening into account. This is important, both to better understand the current impact of temperature on population health and also to appreciate the potential impacts of climate change in an ageing population, where some degree of mortality displacement may account for a proportion of temperature related mortality.

Potential years of life lost (YLL) is a composite indicator, which summarises information on both mortality and life expectancy, providing information on potential life lost as a result of premature mortality. First used as a concept in the 1940s (Dempsey, 1947), YLL gives greater weight to deaths occurring at younger ages. Taking life expectancy and age of death into account gives a metric which is a more instructive summary statistic, allowing for comparison of how health risks and conditions can shorten life. YLL can therefore be helpful to define policy and research priorities (Romeder and McWhinnie, 1977). In the area of environmental health, YLL are widely used to assess the burden of air pollution (e.g. (Broome et al., 2015; Cohen et al., 2005; Huang et al., 2018) and more generally have been used as an outcome metric to reflect premature mortality in the Global Burden of Disease studies (Lopez et al., 2006; Murray and Lopez, 2013). In England, the National Institute for Health and Care Excellence (NICE) uses a metric for health technology assessment which combines information both about the length and quality of life (the QALY) to make funding decisions (Sassi, 2006).

Despite the large number of studies that have described the association between temperature and mortality, there are relatively few studies that have used YLL as an outcome measure (Baccini et al., 2013; Egondi et al., 2015; Huang et al., 2012a, 2012b; Yang et al., 2015; Sewe et al., 2018; Bunker et al., 2017; Luan et al., 2017; Zhang et al., 2018, 2017; Urban et al., 2020). For high income settings specifically, Huang et al. demonstrated a relationship between YLL due to cardiovascular disease and heat in Brisbane, Australia (Huang et al., 2012), and more recently Sewe et al. (2018) demonstrated a relationship between YLL and temperature across a range of settings including low income countries (Burkina Faso), low-middle income countries (Kenya and India) and high income countries (the US and Sweden). To our knowledge, there have been no studies that have focused on the effect of temperature on YLL in the UK, and this represents a gap in knowledge that may be useful to inform policy decisions. Further, understanding temperature related health risks in cities is important. In England, recent estimates indicate that over 80% of the population live in cities (Office for National Statistics. Rural population, 2014). Cities are likely to be at greater risk from the negative health impacts of increased temperatures under climate change, due to factors such as the Urban Heat Island (UHI) (Heaviside et al., 2016) (the phenomenon whereby temperatures in cities or urban areas are generally higher than those in surrounding rural areas) and much adaptation planning in relation to climate change in the UK is starting at city level (e.g. C40, Greater London, Manchester and Birmingham climate change plans (Mayor of London, 2018; Manchester City Council, 2010; Birmingham City Council, 2012).

A second concept, which has important implications for understanding potential impacts of climate change and policy, is that of changing susceptibility of populations to the effects of heat and cold. It is often assumed that populations will ‘adapt’ to some extent to the effects of heat and/or cold and therefore be less vulnerable to temperature effects in the future. There is some evidence that in a number of locations, populations have become less vulnerable to the effects of heat due to a potential number of influences – some of which may be planned adaptive measures (such as heat wave plans, air conditioning) and some unrelated to climate such as improved healthcare (leading to decreased susceptibility to heat) (Arbuthnott et al., 2016; Vicedo-Cabrera et al., 2018). However, changes in the mortality risk associated with cold over time are less well studied and effects are less consistent between studies (Arbuthnott et al., 2016). For the UK specifically, reductions in vulnerability to temperature were in evidence throughout the last century (Carson et al., 2006). One recent study found little temporal change in the heat risk in the UK over recent years (Gasparrini et al., 2015), and a second study examining changes in heat and cold attributable fractions (AFs) over recent years at the regional level (with results presented at the aggregated national level) found that AFs for heat and cold related mortality remained stable over time (Vicedo-Cabrera et al., 2018). To our knowledge, however, there has been no study which examines temporal changes in heat and cold related YLL or in the UK at conurbation (rather than regional or national) level. The introduction of heat and cold weather plans in England (operational from 2004 and 2011 respectively), combined with a national level commitment to understanding the risks of and adaptation to climate change (Arbuthnott and Hajat, 2017), mean that understanding recent temporal variation in heat and cold risk and the effect of temperature on premature mortality, are both important to inform policy in the UK.

In this paper, we aim to address the gaps in knowledge around heat and cold related premature mortality and changes in this risk in English conurbations over recent years. Using time series regression, we analyse data from three major English conurbations chosen to represent the north, south and middle of England – Greater London, Greater Manchester and the West Midlands (including Birmingham) to determine the relationship between heat, cold and YLL and changes to this relationship over recent years.

Specifically, this study has three main objectives: (a) to determine the nature of the relationship between YLL and temperature in the studied conurbations, (b) to estimate (and compare) the proportion of total yearly mortality and YLL attributable to heat and cold and (c) to examine whether the risk of mortality and YLL due to heat and cold has changed over the study period.

2. Methods

2.1. Data

We used two main health outcomes: YLL (primary outcome) and all-cause mortality (for comparison). Mortality data were obtained from the Office for National Statistics (ONS). All deaths occurring in England on each day between 1st January 1996 and mid December 2013 were used. YLL for the same period were derived by matching each death to the age specific yearly life expectancy for males and females obtained from period lifetables provided by the ONS (Office for National Statistics, 2017) based on the years in the mid-point of our time-series (2004–2006) and extended up to age 110 years. For example, according to these 2004–2006 tables, a 90-year-old male had a life expectancy (and hence YLL in the event of death) of 3.89 years and a 70-year-old female had a life expectancy of 15.88 years.

Data were aggregated by conurbation, as defined by the ONS Built-up Area codes from the 2011 census (Office for National Statistics., 2011). We created time-series of total daily deaths and potential YLL for Greater London, the West midlands and Greater Manchester by summing the individual deaths and/or numbers of YLL for all male and female deaths on any given day. As life expectancy is sex-specific, the time series were also stratified by sex.

We used daily mean temperature (the average of the daily maximum and minimum temperatures) as our main exposure variable, since this has been shown in previous UK studies to be an effective predictor of temperature related health effects (Hajat et al., 2016). Daily mean temperature was obtained from the UK Met Office UKCP09 gridded observation datasets (UK Met Office, 2017). This dataset was created using input from all available temperature stations within the UK, interpolated using inverse-distance weighting (based on a regression model with information on longitude, latitude, coastal influence, altitude, and urban land use) by the UK Met Office to provide daily temperatures for 5 km^2 gridded areas (Perry, 2009). We took the value represented by the 5 km^2 gridded cell that overlapped with the centre of each conurbation (identified using ArcGIS) to provide the daily mean temperature for each conurbation.

In our analysis, we also included regional data on weekly laboratory confirmed influenza A counts, obtained from Public Health England, as a potential time-varying confounding factor of cold effects. Daily mean PM_{10} and ozone counts for London from the UK-AIR (Air information resource data archive) were also collected as confounding factors (DEFRA, 2018).

2.2. Statistical analysis

We undertook an ecological time series regression analysis to determine the risk of YLL and mortality for each 1 °C temperature rise or fall above or below a given heat or cold threshold.

We assumed a Poisson distribution for the outcomes, corrected for over-dispersion and autocorrelation. It is well established that the effects of heat and cold on health can be delayed (lagged), and we used previously published lag periods of 0–2 days for the heat effect and four weeks for cold. We controlled for the effect of season and secular trends using a cubic spline function with 7 degrees of freedom per year (Bhaskaran et al., 2013) and included a term for day of the week. Relationships were visualised using natural cubic splines of the average temperature function, having controlled for time varying factors and confounders. These indicated the presence of heat and cold thresholds, above or below which the risk of YLL (and mortality) increased. Therefore, in order to quantify the effects of heat and cold, a distributed lag double-threshold model was used. Best model fit was used to select the heat and cold thresholds: the model was run across the three conurbations with the heat and cold thresholds fixed separately at temperatures corresponding to all percentiles of each conurbation's annual mean temperature distribution. The percentiles with the lowest summed model deviance across the three conurbations were selected as the heat and cold thresholds for the primary analysis. This corresponded to the 91st percentile of the annual temperature distribution for heat effects (18.9 °C for London, 17.6 °C for the West Midlands and 16.8 °C for Greater Manchester), and the 35th percentile of the year round temperature distribution for cold effects (9.0 °C for London, 8.0 °C for the West Midlands and 7.9 °C for Greater Manchester). These thresholds are consistent with those seen when the data are represented graphically.

Results are presented as the relative risk (RR) or percentage increase in risk for each 1 °C rise or fall above or below the specified threshold and attributable burdens of heat and cold related YLL and mortality (calculated using previously published methods) (Vardoulakis et al., 2014; Hajat et al., 2014) as a proportion (%) of total YLL and mortality over the time-period studied. We used STATA v 15 for all statistical analyses. To aid interpretation of results, heat and cold related mortality analysis was also undertaken by age categories (0–65 years, 65–74 years and 75 years and over) and is included in the supplementary materials (Table S1).

2.3. Changes in YLL and mortality risk over time

A number of approaches have been used previously to analyse the change in risk of heat and cold related mortality over time, each with advantages and disadvantages (Arbuthnott et al., 2016). In order to assess whether the risk of heat and cold exposure on YLL and mortality had changed over time we divided our data into discrete 4 year bands (summer 1996-winter 1999/00, summer 2000-winter 2003/4, summer 2005-winter 2008/9, summer 2008-winter 2011/2). Within each band we estimated the risk of YLL and mortality above and below the given temperature threshold. Cold and heat thresholds were maintained at 35th and 91st percentiles (see above) of the temperature distribution for each particular 4 year band within each given conurbation, to allow the best model fit with the data and the number of hot and cold days contributing to the analysis to remain consistent between time periods. However, we also undertook a sensitivity analysis using absolute thresholds fixed at the 35th and 91st percentiles of the temperature distribution for the whole time period (rather than allowing thresholds to vary with each time band).

2.4. Sensitivity analysis

We undertook a number of analyses to determine the sensitivity of our main modelling approach to certain methodological choices. In addition to using lifetables from the middle of the time period to calculate YLL, we used lifetables based on years at the beginning and end of the times period to calculate YLL as part of our sensitivity analyses. We also carried out analyses using lifetables adjusted for regional differences in life expectancy. As we did not have air pollution data for all three conurbations (series for Greater Manchester and the West Midlands contained large sections of missing data), we used a model which included PM_{10} and ozone as a sensitivity analysis for London. We also carried out year by year (June-May to include a summer/whole winter season) analysis of heat and cold risk to ensure that the overall trend observed using 4 year bands was not sensitive to the time bands chosen for analysis and a sensitivity analysis using absolute thresholds (see Section 2.3 above).

3. Results

3.1. Descriptive statistics

Table 1 summarises the descriptive statistics for our dataset. Greater London had the highest number of all-cause daily deaths and YLL, followed by Greater Manchester, then the West Midlands. We analysed over a million deaths in Greater London and more than 400,000 deaths in each of the West Midlands and Greater Manchester. This is equivalent to more than 15 million YLL analysed for Greater London and more than 5 million YLL each for the West Midlands and Greater Manchester. The mean temperature over the time series was highest in Greater London and similar in the West Midlands and Greater Manchester. For each conurbation, the number of days above and below the heat and cold thresholds respectively are summarised in Table 1. Of note, there was no consistent increase in temperature over the time period analysed (see Fig. S1), which is consistent with temperature trends over this time period published elsewhere (Brohan et al., 2006). In all the conurbations, the number of daily male YLL is greater than daily female YLL (but daily female all-cause mortality is higher than male all-cause mortality in all conurbations) (Table 1).

3.2. Results from regression models

3.2.1. Risk of heat and cold related YLL and mortality: Pattern across the conurbations and differences in risk by sex

For all conurbations, there was an increased risk in total mortality and YLL for each 1 °C rise or fall in temperature above or below the threshold value (Table 2). The relationship between the RR of YLL and daily mean temperature is shown in Fig. 1. This illustrates that the RR of YLL associated with mean temperature follows a similar pattern to that seen using mortality as an outcome.

The RR of YLL per degree above threshold temperature was higher in London than for the West Midlands or Manchester (Table 2). The RR of heat related mortality also varied between conurbations, and was also higher for London, compared to the West Midlands and Manchester (Table 2). In all conurbations, the RR for total heat-related YLL was lower than for total heat-related mortality (though confidence intervals for YLL and mortality risk estimates overlap). In Greater London and Manchester, the RR of heat related YLL and mortality was higher in females compared to males. This difference was significant for the risk of heat related mortality in Greater London. In the West Midlands, however, the risk of both heat related YLL and mortality were higher in males compared to females (but not substantially) and in males the RR

Table 1
Descriptive data.

	Mean temperature (°C) (min, 25th percentile, 75th percentile, max)	Cold threshold (°C) Days below threshold: total over whole time period and average number per year	Heat threshold (°C) Days above threshold: total over whole time period and average number per year	Average (mean) daily values for daily YLL and all-cause mortality (minimum, 25th percentile, median, 75th percentile, maximum)					
				Daily male YLL	Daily female YLL	Daily total YLL	Daily male all-cause mortality	Daily female all-cause mortality	Daily all -cause mortality
Greater London	11.5 (−3.2 ,7.3, 16.0, 28.2)	9.0 Total: 2276 days Average: 126 days	18.9 Total: 604 days Average: 34 days	1277 (563, 1098, 1263, 1437, 2599)	1139 (541, 966, 1120, 1286 2580)	2416 (1261, 2112, 2391, 2677, 5016)	90 (44, 79, 89, 99, 197)	96 (49, 82, 94, 105, 227)	186 (107, 164, 182, 203, 412)
Greater Manchester	10.2 (-6.5, 6.3, 14.3, 24.3)	7.9 Total: 2288 days Average: 127 days	16.8 Total: 600 days Average: 33 days	461 (132, 372, 451, 540, 1117)	420 (106, 336, 409, 484, 1113)	881 (299, 747, 867, 998, 2055)	32 (13, 27, 32, 36, 85)	35 (13, 29, 34, 40, 94)	67 (33, 58, 66, 74, 169)
West Midlands	10.4 (-7.4, 6.4, 14.8, 25.4)	8.0 Total: 2280 days Average: 127 days	17.6 Total: 591 days Average: 33 days	428 (114, 343, 420, 505 1007)	374 (81, 298, 365, 440, 1055)	802 (285, 678, 792, 910, 1767)	30 (11, 26, 30, 35, 76)	31 (10, 26, 31 36, 101)	61 (30, 54, 61, 68, 154)

of heat related YLL was greater than for heat related mortality.

The RR of cold related YLL and mortality varied across conurbations, though not substantially (Table 2). The RR was highest in the West Midlands where the RR of YLL per degree Celsius below the threshold was 1.031 (1.024, 1.037). The RR for cold-related YLL and mortality was most similar in the West Midlands. In general, the RR of cold-related mortality in females was slightly higher than in males (though confidence intervals overlapped). However, in Greater Manchester for cold-related YLL, the RR was lower in females compared to males.

3.2.2. *Risk of heat and cold related YLL and mortality: Differences in heat and cold related burdens depending on metric (YLL vs mortality) used*

We hypothesised that the proportion of total YLL attributable to heat or cold would be lower than for mortality, due to older people being more vulnerable to the effects of heat and cold. The percentage of year-round YLL attributable to heat was 0.391% for Greater London, 0.309% in the West Midlands and 0.206% in Greater Manchester (Table 2). By comparison, the percentage of year round mortality attributable to heat was 0.498% for Greater London, 0.301% for the West Midlands and 0.262% for Greater Manchester. The results for cold related YLL and mortality are shown in Table 2 and similarly indicate a lower proportion total YLL attributable to cold compared to mortality. In the West Midlands, however, the percentage of total YLL attributable to heat and cold were similar for mortality and YLL. Results for heat and cold related mortality analysed by age category are included in the supplementary materials (Table S1 – some results have lower precision due to the small number of daily deaths in some categories). In contrast to London, where as expected the risk of heat and cold related mortality is significantly higher in the oldest age group compared to the youngest, the risk of cold related mortality appears more consistent across the age categories in the West Midlands. This may in part explain the smaller difference in temperature related risk and burdens between mortality and YLL in this conurbation.

3.2.3. *Changes in temperature related YLL and mortality over time*

We divided the time series into four discrete time periods to investigate whether the effect of cold and heat on YLL and mortality changed between 1996 and 2012. The RR of heat and cold related YLL and mortality for each of these time periods are illustrated in Fig. 2a (heat risk) and Fig. 2b (cold risk) and Table S2 (see supplementary materials). Graphs of the sensitivity analysis performed on time periods obtained by dividing data at yearly intervals are included in the supplementary Figs. (S2a and S2b), but overall patterns observed did not change depending on whether yearly series (less precise estimates) or each of the four year bands were used and there was no difference in patterns observed when thresholds were fixed across the entire time period for analysis (Table S3 supplementary materials).

The RR of heat related YLL and mortality did not show any consistent increase or decrease over time within or between the conurbations, both for results of analysis in 4 yearly time bands (Fig. 2a) or by yearly time bands (see Supplementary materials Fig. S2a). For Greater London, the RR of heat related YLL and mortality followed the same path, with no discernible increase or decrease in heat related risk over time. There was, however, a spike in risk for the years 2000–2003 for both YLL and mortality (where the temperature series includes the 2003 heatwave which had a large impact on mortality over Western Europe and particularly London and the South East in the UK (Johnson et al., 2005; Kovats and Kristie, 2006). This spike in risk is also clearly seen in the yearly series in 2003 but over the entire time period there is no increasing or decreasing risk over time (Fig. S2a, supplementary materials). In Greater Manchester and the West Midlands there is no clear spike in risk for the period containing the 2003 heatwave, likely reflecting both that the 2003 heatwave was less severe outside the south of England and also that the 2006 heatwave had greater health impacts in the West Midlands (National Statistics, 2006).

Table 2
Results from time series regression analysis (with control for time varying factors and confounders).

		Mortality RR (95% CI)	Percentage (%) of total mortality attributable to heat or cold (%)	Years of Life Lost (YLL) RR (95% CI)	Percentage (%) of total YLL attributable to heat or cold (%)
Greater London					
Heat (Threshold 18.9 °C)	Total	1.039 (1.035, 1.043)	0.498	1.030 (1.025,1.035)	0.391
	Male	1.029 (1.024, 1.035)	0.377	1.026 (1.019, 1.032)	0.338
	Female	1.049 (1.043, 1.054)	0.619	1.035 (1.027, 1.042)	0.454
Cold (Threshold 9.0 °C)	Total	1.029 (1.026, 1.033)	3.266	1.025 (1.020, 1.030)	2.675
	Male	1.027 (1.022,1.032)	2.991	1.022 (1.016, 1.029)	2.370
	Female	1.032 (1.027, 1.037)	3.521	1.028 (1.021, 1.035)	3.000
Greater Manchester		Mortality		YLL	
Heat (Threshold 16.8 °C)	Total	1.020 (1.014, 1.027)	0.262	1.015 (1.007,1.024)	0.206
	Male	1.017 (1.008. 1.026)	0.220	1.0140 (1.003, 1.025)	0.188
	Female	1.024 (1.015, 1.032)	0.303	1.017 (1.005, 1.029)	0.228
Cold (Threshold 7.9 °C)	Total	1.026 (1.019, 1.032)	2.685	1.021 (1.012, 1.030)	2.150
	Male	1.026 (1.017, 1.035)	2.658	1.028 (1.016, 1.040)	2.761
	Female	1.026 (1.017, 1.035)	2.703	1.014 (1.004, 1.026)	1.436
West Midlands					
Heat (Threshold 17.6 °C)	Total	1.025 (1.018, 1.031)	0.301	1.024 (1.016, 1.033)	0.309
	Male	1.025 (1.014, 1.037)	0.310	1.030 (1.018, 1.043)	0.387
	Female	1.021 (1.012, 1.031)	0.256	1.017 (1.004, 1.030)	0.218
Cold (Threshold 8.0 °C)	Total	1.031 (1.024, 1.037)	3.298	1.031 (1.022, 1.039)	3.213
	Male	1.028 (1.019, 1.036)	2.921	1.030 (1.019, 1.042)	3.142
	Female	1.034 (1.025, 1.042)	3.706	1.032 (1.019, 1.043)	3.295

The RR of cold related YLL and mortality did not show any consistent increase or decrease over time within or between the conurbations (Fig. S2b). Whilst in the West Midlands, there is a possible increase in risk from the first to the third time-bands for both cold related YLL and mortality, the yearly estimates (Fig. S2b) do not demonstrate a pattern of increasing risk and it is likely that the first time band of the 4 yearly estimates was sensitive to the very low cold risk in the winter of 1998/1999 in this conurbation. Of note, in the yearly estimates (supplementary materials, Fig. S1b), a peak in cold related risk can be seen in 1999/2000 in Greater London and Greater Manchester, which may be related to high flu deaths that year (Hardelid et al., 2013), not adequately controlled for in the model using laboratory influenza A counts. Tables S2 and S3 (supplementary materials) detail the relative risks and burdens of heat and cold related mortality and YLL (as a percentage of mortality or YLL for each time period). The increased percentages of cold related deaths and YLL attributable to cold in later time periods (Tables S2 and S3) are likely due to the colder winters during these times (reflecting the contribution of greater extremes in cold temperatures where the threshold temperature is exceeded by a greater amount, to the attributable mortality for these time periods).

4. Discussion

We investigated the association between heat, cold and YLL and

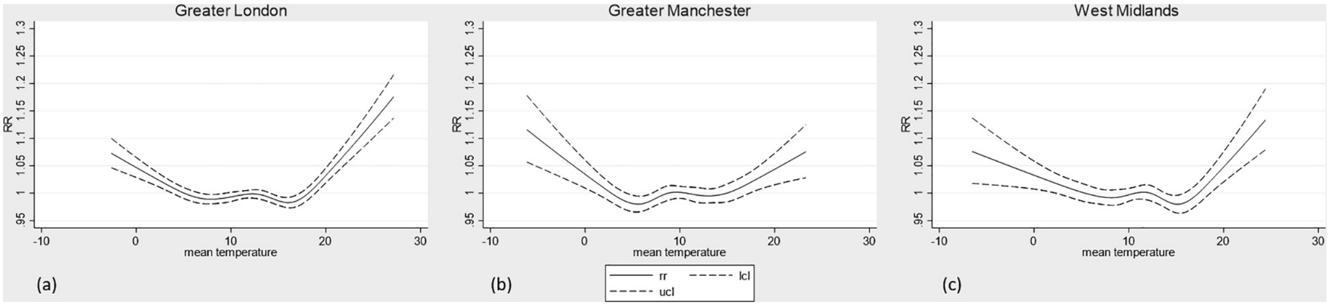

Fig. 1. The RR of temperature related YLL at lag 0–2 days for (a) Greater London, (b) Greater Manchester and (c) the West Midlands (including Birmingham).

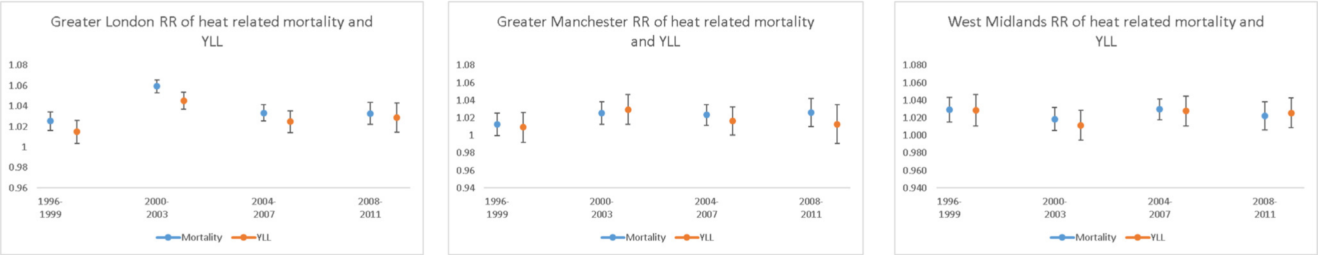

Fig. 2a. Changes in heat related RR of YLL and mortality over time.

mortality and whether these associations have changed in magnitude over recent years. We found an increased risk in YLL for each 1 °C increase or decrease in temperatures above and below identified temperature thresholds in Greater London, the West Midlands and Greater Manchester. We demonstrate that in these conurbations, the nature of this relationship between YLL and temperature is similar to that between mortality and temperature. We found no evidence for a trend of decreasing risk (RR) of heat or cold related mortality or YLL over time in the conurbations, and therefore no evidence of population adaptation to ambient heat or cold over this time period. Heat risks were highest in Greater London, and cold risks were highest in the West Midlands, though variation in risk between conurbations was less pronounced for cold effects. This is broadly consistent with findings from previous studies (Vardoulakis et al., 2014; Hajat et al., 2007; Arbuthnott and Hajat, 2017; Hajat, 2017), though cold effects have not been specifically examined at conurbation level for the UK. This geographical variation in heat and cold effects may be due to social, demographic, built environment and economic factors. For example, the West Midlands has the highest proportion (13.5% of households) of fuel poverty across England (Office for National Statistics, 2017) which may contribute to the increased risk in cold mortality.

Although the effects of temperature on YLL have to date not been specifically studied within England, our results are consistent with those from other high-income settings which have used YLL as an outcome, and have demonstrated an increased risk of YLL with increased temperatures (Huang et al., 2012; Sewe et al., 2018). The percentages of overall YLL attributable to heat and cold related YLL were lower compared to those for mortality in Greater London and Greater Manchester but similar in the West Midlands. However, the overall similarity in RR between temperature related mortality and YLL in all conurbations may imply that the results are mostly dominated by the large number of deaths occurring in older people. This is consistent with existing knowledge that in the UK, older people are at increased risk from temperature related mortality (Arbuthnott and Hajat, 2017; Hajat, 2017).

We found that over the studied time period, there was no consistent decrease in heat or cold related risk across the conurbations based on four yearly and yearly estimates. Importantly, this result remained unchanged when heat and cold related risks were analysed using an absolute threshold value (fixed at the 35th and 91st percentiles of the temperature distribution for the entire time period). This means possible adaptation denoted by an undetected increase in heat thresholds but masked by a lack of increase in the RR, is unlikely for this time period. Across a number of other settings, however, the risk of heat related mortality has been shown to decrease over time, including in studies using data over short (less than 20 years) time periods and in recent years, though this has not been the case in all locations (Sheridan and Allen, 2018). Trends in cold related health outcomes over time are less well studied, and results have been more heterogeneous (Arbuthnott et al., 2016). Some of these studies of changes in heat and cold risks over time have included English data in their analysis. Carson et al. (Carson et al., 2006) found that between 1900 and 1996 there was a decrease in both heat and cold related deaths in London. The time period for this study does not overlap with ours and by contrast includes the period over which England underwent the epidemiological transition, meaning that temperature related deaths may have declined rapidly due to rapid improvements in health and social care. Donaldson et al. (Donaldson et al., 2003) also found a significant reduction in heat related mortality in South East England in an earlier (but similar in length) time period to ours - between 1971 and 1996. However, our results are broadly consistent with more recent UK studies. For example, Gasparrini et al. did not find any attenuation in heat related mortality risk in the UK (Gasparrini et al., 2015). A recent analysis by Vicedo-Cabrera et al. (2018) showed no attenuation in heat and cold related AFs over the time period 1990–2011. However the study did find some attenuation in the relative risk of mortality at a national level when comparing the risk at the 99th or 1st temperature percentile with the minimum mortality temperature, though this may highlight changes in risk of mortality at 'extreme' temperatures (Vicedo-Cabrera et al., 2018). Our study adds to this body of evidence, and contributes information on changes in YLL over time and disaggregated by conurbation.

It is not surprising that vulnerability to heat and cold is context specific and will depend on a number of factors from individual to societal, city and national level influences – the age structure of the population, potentially the rate of recent temperature change, health and social care and also more specific factors which could be adapted to modify the heat or cold risk (e.g. availability of air conditioning, individual behaviour, housing fabric and ventilation and urban design). The similar pattern over time in risk of YLL and mortality would imply that the population age structure over the period is not contributing to an increase in risk. However, in our study, the lack of any decrease in temperature (hot or cold) related risk in these conurbations (compared to other global locations which have seen decreases in risk over similar

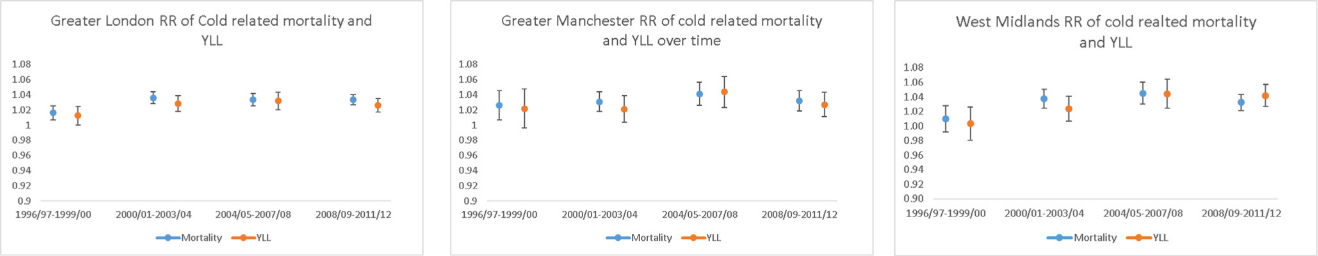

Fig. 2b. Changes in cold related RR of YLL and mortality over time.

time periods) may be due to several factors. For example, regarding specific 'heat adaptation', a recent survey (Khare et al., 2015) indicated that the prevalence of air conditioning is still low in the UK (< 3%) and also that populations at high risk, such as the elderly, were less likely to engage in personal and home-related protective behaviours. Regarding specific 'cold adaptation', there have also been a number of UK housing improvements made (12.2 million UK homes have undergone some energy efficiency retrofit since 2000 (Hamilton et al., 2016) to reduce energy demand, which may improve indoor air temperatures in the winter and the proportion of energy efficient homes rose from 2% in 1996 to 18% in 2012 (NICE, 2015). Despite this and winter fuel payments, one in-depth survey suggested that in the previous winter those whose income was less than 60% of the national average had trouble paying fuel bills (Anderson et al., 2010). The absence of any decreasing risk of cold related mortality highlights that policies to reduce the effect of cold weather on public health (e.g. Public Health England's Cold weather plan and the NICE recommendations on cold homes (NICE, 2015)) in the UK remain important, and should not be overlooked in the context of climate change.

England does, however, have heat and cold weather plans (Public Health England, 2020), introduced in 2004 and 2011 respectively. The time period of our analysis would mean that any beneficial effects of the cold weather plan would not be adequately captured, though one recent study suggests that since the introduction of the cold weather plan, cold related mortality has decreased in the under 65s but increased in the over 75s and that geographical variability in cold related mortality has increased since the introduction of the plan (Murage et al., 2018). Importantly, we found no reduction in mortality risk in the time periods after the introduction of the Heatwave Plan (HWP) compared to before its introduction. Whilst the outcomes used in this study may be too narrowly defined to adequately capture all the beneficial effects of the HWP, our findings are broadly consistent with a recent evaluation of the HWP for England. The evaluation found that although mortality during extreme events or heatwave periods has reduced in recent years, there was little evidence since its introduction for a reduction in the risk of annual heat related mortality outside heatwave events (and consequently for those more moderately hot days which contribute to the largest public health burdens) (Williams et al., 2019). It highlighted that in accordance with previous studies, most adults at risk of heat related mortality did not perceive themselves to be at personal risk and that further work around public health messaging (amongst other recommendations) is needed (Williams et al., 2019). Whilst the HWP has motivated the implementation of an alert and response system for high temperatures, many activities could go beyond this acute response (for example into longer term planning such as in levels 0 and 1 of the plan). There are many interventions which may be introduced at the housing or urban/conurbation level to reduce ambient heat exposure, such as those which reduce the effect of the urban heat island effect through reflecting solar radiance or increasing evaporative cooling through increased urban green and blue spaces (Heaviside et al., 2017). For example, a recent modelling study suggested cool roofs could reduce UHI intensity and the associated mortality during heatwave events in the West Midlands (Macintyre and Heaviside, 2019), and well-designed urban greenspaces, have the potential for multiple and varied additional health co-benefits in addition to those from reducing ambient temperatures (though specifics depend on a number of contextual factors) (van den Bosch and Nieuwenhuijsen, 2017; Wheeler et al., 2015; Rojas-Rueda et al., 2019; Twohig-Bennett and Jones, 2018).

To our knowledge, this is the first study to specifically examine the effects of heat and cold on YLL in the UK, and to assess changes in these risks over time at conurbation level. One strength is the assessment of both heat and cold effects: in the context of climate change, many studies have focused on increased temperature effects, while significant cold burdens remain (Almendra et al., 2019). Examining YLL in different English conurbations can reveal differences in risk and trends over time (which may be masked in a larger scale analysis) and contributes to specifically understanding urban temperature risks. Additional strengths include the use of life expectancies specific to each individual year of age (many previous studies have used life expectancy for 5 year age bands), which is especially important for the majority of deaths which occur in older age categories, and the different approaches taken to analysing changes over time. We also made use of gridded temperature data (Perry, 2009), which is more likely to provide an accurate reflection of urban temperatures than previous datasets based on interpolations which have not taken into account urban land use.

However, our study has a number of potential limitations. The method of deriving YLL from the age at death and English life expectancy assumes that those dying from the effects of heat and cold have the same life expectancy as others of their age. Some evidence of mortality displacement in high income settings has previously suggested that a proportion of deaths, due to heat at least, are likely to have been brought forward by only a short amount of time (Hajat et al., 2005; Baccini et al., 2013). More recently, however, methods of quantifying mortality displacement such as those based on displacement ratios from short term Poisson regression analyses have been shown to be unreliable (Armstrong et al., 2014) and a number of more recent studies suggest that deaths are displaced by at least one year (rather than a few weeks as suggested in previous analyses) (Armstrong et al., 2017; Goggins et al., 2015). If this is the case, then the assumptions made when calculating YLL are less likely to have affected our results; the similarity between risk of mortality and YLL would indicate the majority of deaths due to heat and cold occurring in those with close or less than a year's life expectancy, less than the amount by which deaths have recently been shown to be brought forward. We used England-wide life expectancy rather than city-specific life expectancy, which was not available. However, to account for this, we undertook a sensitivity analysis using YLL corrected for regional differences in life expectancy (produced by ONS), which did not significantly alter results. We also matched deaths to life expectancy values from the mid-point of the time period analysed, meaning that for the years early in the series, life expectancies could be over-estimated, with the opposite being true for the latter part of the study. Consequently, it is possible that upward trends in risk of temperature related YLL may be overlooked. However, we would expect this to be more consequential if changes in susceptibility over time were presented as total attributable burdens or if there was an observed downward trend in risk which may have been exaggerated.

We did not include relative humidity or air pollutants as potential confounders or effect modifiers in our primary analysis (though inclusion of air pollution in our sensitivity analysis for London did not significantly alter the estimates), and note that previous analyses did not find a significant contribution of humidity or air pollution when assessing the relationship between temperature and health within the UK (Hajat et al., 2006). There is also a methodological question as to whether air pollution is indeed a confounder or in fact lies on the causal pathway in the relationship between temperature and health – this has been well considered for ozone (Buckley et al., 2014) and a similar argument could be made for PM being on the causal pathway, for example combustion is likely to be higher on cold days and there may be less dispersion of air pollution on cool still days in the winter. A limitation of our study is that the time-period over which changes in RR of heat or cold related mortality or YLL were examined was relatively short, which has two implications. Firstly, the period may be too short to examine population 'adaptation' (and of note, no consistent increase in temperature was seen over the time period), though it does include time-periods over which changes in heat and cold risk have been observed in other settings. Secondly, splitting the time series into 4-year time-bands increases the sensitivity of the analyses to particularly hot or cold winters within each time-band. However, a sensitivity analysis was undertaken splitting the data yearly and results from this have been discussed and presented (supplementary materials Fig. 2a and 2b).

5. Conclusions and implications for policy and research

We have demonstrated a positive association between YLL and temperatures above and below a given threshold, in the three largest conurbations in England – Greater London, Greater Manchester and the West Midlands. The risks of YLL and mortality due to heat and cold were largely similar, though the percentages of total YLL attributable to heat and cold were lower than for mortality in Greater London and Greater Manchester, likely indicating a proportion of deaths are occurring in those with less than one year of life expectancy. Despite this, there remains a significant burden in terms of YLL attributable to heat and cold across all conurbations, indicating that heat and cold remain an important public health concern, warranting attention both now and in the consideration of adaptation to the effects of further climate change. Additional research, using further outcomes relevant to public health and planning, such as those that take into account health losses that are not fatal (for example Disability Adjusted Life Years) would also make an interesting area of study. We did not find evidence of any changes in the risk of heat and cold related mortality or YLL over the course of our study. This is in contrast to studies in other locations and is important, since it has implications for assumptions that are often made (for example in the context of climate change risk assessments) that populations will ‘adapt’ to heat. We highlight that adaptation is context specific, and will not occur without active policy or structural changes in the UK. There is a growing evidence base of urban adaptation measures that can reduce heat related mortality, for example urban greening, improved architectural and urban design. Whilst the increased use of some interventions such as air conditioning is problematic and can result in anthropogenic warming and increased GHG emissions, many interventions at conurbation level could serve to both reduce heat related mortality and have additional health co-benefits. Further research is needed to better evaluate the specific and contextual adaptive measures to heat and cold which have already been undertaken within UK cities and to better understand how cities can best adapt and mitigate the effects of climate change using measures that will be beneficial to health. Improved integration of research and policy development in this area would be of great benefit.

CRediT authorship contribution statement

Katherine Arbuthnott: Conceptualization, Investigation, Formal analysis, Writing - original draft. **Shakoor Hajat:** Conceptualization, Methodology, Writing - review & editing. **Clare Heaviside:** Conceptualization, Data curation, Writing - review & editing. **Sotiris Vardoulakis:** Conceptualization, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2020.105966.

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7 Heat Related Mortality in the three largest English Conurbations under the Paris Agreement

7.1 Introduction

This paper forms the final results chapter of the PhD. Given the context of climate change, global efforts under the Paris agreement to try and limit warming to well under 2 degrees and the increased risk of mortality associated with high temperatures (demonstrated in previous chapters, and in other research papers), this chapter sets out to project heat-related mortality under two global warming scenarios – a 1.5-degree world and a 2 degree world. I used temperature projections, modelled as part of the HAPPI (Half a degree Additional warming, Prognosis, and Projected Impacts) project to model mortality in the three major UK conurbations: Greater London, West Midlands and Greater Manchester. The heat related mortality co-efficient was derived for summer months, using time series methods similar to those described in previous chapters. As it is currently unknown when exactly we will reach 1.5 or 2 degrees Celsius (though according to the IPCC's special report on Global warming of 1.5°C, it is thought we are likely to reach 1.5 degrees Celsius of warming between 2030 and 2052 (V. Masson-Delmotte, 2018)) and because we wish to isolate the impacts of temperature changes on health, we do not factor societal factors such as population growth, urbanisation and ageing into this analysis.

This research paper aims to address the gap in research around changes in heat related mortality in UK cities (and indeed in most other locations), under the Paris agreement targets (i.e. under climate scenarios consistent with average increases of global mean temperature of 1.5 °C and 2 °C from the pre-industrial baseline). This is important, because for scenarios consistent with global climate stabilisation at these temperatures, projected temperatures and therefore impacts will vary spatially and across climate simulations used.

In this chapter, I looked to answer two questions relating to the effect of heat on mortality under climate change:

1. How would the frequency of extreme heat events change in Greater London, Greater Manchester and the West Midlands between current conditions, 1.5 °C and 2 °C climate warming scenarios?
2. How would heat related mortality (HRM) change under the conditions of the Paris agreement? (i.e. how would heat attributable mortality change under current climate conditions, and temperatures consistent with a global mean of 1.5 °C and 2 °C higher than pre-industrial times?) if socio-economic or structural factors (e.g. population size and age, etc.) were the same in future years as for now?

This chapter only examines the impact of warming on heat related (i.e. not cold related or differences in net) mortality. This is for two reasons:

The first is that the purpose of this work is not to examine the net effect of temperature changes under warming scenarios on mortality. As demonstrated in chapter 4, cold attributable mortality is highly sensitive to threshold choice, so that the choice of threshold has the potential to affect whether the net effect of global temperature rises on mortality is positive or negative (i.e. net effects are dependent on the temperature threshold). The mechanisms for, and drivers of, heat and cold related mortality are different. However heat and cold related mortality are both - in part - preventable, and as such require different preventative/adaptive measures. Grouping effects together to produce 'net' effects removes focus from public health action to avoid preventable deaths and to maximise opportunities for health co-benefits within climate mitigation and adaptation policy.

The second, is due to the way in which the climate HAPPI data has been modelled. For each scenario (baseline, 1.5 degrees and 2 degrees warming), the 450 years of modelled temperature data are not consecutive (i.e. there are no runs of 10 years of data). Due to the lagged effect of cold, and that individual year model runs are from January to December, effects for the days at the beginning of January would not be adequately able to take into account lagged temperature.

The work in this research chapter is currently being prepared for journal submission and the supplementary materials can be found in appendix 5.

References for research paper introduction

V. MASSON-DELMOTTE, P. Z., H. O. PÖRTNER, D. ROBERTS, J. SKEA, P.R.SHUKLA,A. PIRANI, W. MOUFOUMA-OKIA, C.PÉAN, R. PIDCOCK, S. CONNORS, J. B. R. MATTHEWS, Y. CHEN, X. ZHOU, M. I. GOMIS, E. LONNOY, T. MAYCOCK, M. TIGNOR, T. WATERFIELD(EDS.)., 2018. Global warming of 1.5°C. An IPCC Special Report on the impacts of global warming of 1.5°C above pre-industrial levels and related global greenhouse gas emission pathways, in the context of strengthening the global response to the threat of climate change, sustainable development, and efforts to eradicate poverty. *In:* IPCC. (ed.).

7.2 Research paper

Cover page and research paper on subsequent pages

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	310970	**Title**	Dr
First Name(s)	Katherine		
Surname/Family Name	Arbuthnott		
Thesis Title	Temperature related effects on mortality and years of life lost in the UK for current and future climates		
Primary Supervisor	Dr Shakoor Hajat		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	Choose an item.	Was the work subject to academic peer review?	Choose an item.

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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	**Nature Climate Change**
Please list the paper's authors in the intended authorship order:	Katherine Arbuthnott, Clare Heaviside, Shakoor Hajat, Dann Mitchell, Peter Uhe, Sotiris Vardoulakis
Stage of publication	**Not yet submitted**

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I designed study with supervisors and collaborators, carried out the epidemiological and health impact analysis and wrote the first draft of the manuscript

SECTION E

Student Signature	[redacted]
Date	12/08/2020

Supervisor Signature	[redacted]
Date	24/08/2020

Projected heat related mortality in the UK in line with Paris Climate Agreement targets

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Abstract

The relationship between heat and mortality is well established, and provides a direct pathway through which climate change impacts public health. In the 2015 Paris Agreement, the parties of the United Nations Framework Convention on Climate Change set out to limit increases in global average temperature to well below 2°C (preferably below 1.5°C) compared to pre-industrial levels. However, temperature increases are likely to vary spatially within and across countries, and research that specifically addresses how heat related mortality (HRM) will change in UK cities under this agreement is lacking.

We used gridded temperatures and mortality data provided by the UK Met Office and the Office for National Statistics to undertake an ecological time-series regression analysis of the relationship between ambient heat and mortality in 3 major UK conurbations. We analysed a total of 790,132 deaths to estimate heat related mortality based on current climate conditions in 3 major UK conurbations: Greater-London, the West

Midlands and Greater-Manchester. Coefficients from these models were applied to temperatures from local climate projections from the Half a degree Additional warming, Prognosis and Projected Impacts (HAPPI) project, to understand how HRM might change under the Paris agreement – i.e. under current climate conditions, 1.5 °C and 2 °C climate scenarios, whilst holding all else constant.

Regarding heat wave frequency, we found that if the climate stabilises at 1.5 degrees, there is between a 230-250% increase in the 'more extreme' 1 in 100 year heat wave events and under the HAPPI 2 degree simulations, there is a 400-440% increase in 1 in 100 year heat wave events. We projected general HRM (excess HRM on all days above the heat threshold and not limited to heat wave events) to increase by 60-68% under a 1.5°C scenario and by 100-110% under a 2°C scenario (depending on location), from a current annual baseline of around 400 heat-related deaths across the conurbations. Even if warming is limited to 1.5 degrees compared to pre-industrial times, this research demonstrates the continued need for public health heat adaptation measures to address both current and future temperature related risks to health. The avoided mortality when warming is limited to 2 degrees, compared to 1.5 degrees, provides additional motivation for increased climate change mitigation.

Introduction

Anthropogenic warming of the climate is estimated to have been increasing by 0.2 °C per decade and in recent years is thought to have reached 1°C (likely between 0.8°C and1.2°C) compared to pre-industrial baselines (V. Masson-Delmotte, 2018). In England, 2018 was the hottest summer on record (Kendon et al., 2019) and the observed increases in the annual mean Central England Temperature (CET) are consistent with those expected from increased GHG concentrations (Karoly and Stott, 2006).

In 2015, the parties of the United Nations Framework Convention on Climate Change (UNFCCC) set out the Paris agreement - a new global framework for addressing climate change to keep "*the increase in global average temperature to well below 2°C, and to pursue efforts to limit the temperature increase to 1.5°C above pre-industrial levels*" (United Nations / Framework Conventionon Climate Change., 2015). Central to this agreement, the Intended Nationally Determined Contributions (NDCs), form a series of bottom-up commitments from countries to reduce their national emissions and adapt to climate change impacts. Modelled emissions based on the original NDCS, however, are consistent with 2.6-3.1 °C warming by the end of the century (Rogelj et al., 2016). In 2021, the UK, jointly with Italy, will host Conference of the Parties (COP26), when all parties are expected to increase the ambition of their NDCs under the Paris agreement.

Complementary to this, the national basis of the UK response to climate change is set out in the 2008 climate Change Act(HM Government., 2008) , which now commits the UK government to a net-zero GHG target by 2050 (Committee on Climate Change., 2019, 2019), consistent with the country's "highest possible ambition" under Section 4 of the Paris agreement.

The direct relationship between high ambient temperatures and health outcomes (mortality and morbidity) is well established (Basu, 2009). However, estimating future heat impacts under different climate scenarios is important not only for public health and adaptation planning (Arbuthnott and Hajat, 2017a, Hess et al., 2014) but also in demonstrating the direct societal consequences of failure to achieve the ambitions of the Paris agreement (V. Masson-Delmotte, 2018). Regional impact assessments are essential. Under conditions consistent with global average warming of 1.5 or 2 degrees there will be differences in projected temperature rise regionally, and local temperature changes can be very different to global mean projections (e.g because land areas warm more than the ocean – for further details see (Stott et al., 2017)).

A number of studies have reviewed potential health outcomes as a result of increased temperatures under climate change (Huang et al., 2011b, Sanderson et al., 2017). Typically, these health impact studies have sought to project heat related mortality (HRM) at given timepoints in the future (Gasparrini et al., 2017, Hajat et al., 2014, Huang et al., 2011b, Sanderson et al., 2017, Vardoulakis et al., 2014) and there is a general paucity of research on the regional impacts of global conditions consistent with the Paris agreement. The majority of research included in the recent IPCC impacts of 1.5 degrees of warming special report (V. Masson-Delmotte, 2018) was not from impact assessments from climate projections specifically relating to degrees of global warming once the global climate has stabilised at 1.5 or 2 degrees (i.e. impact as associated with an end temperature point, irrespective of the emissions path followed), but from studies of future time periods using a ‘time sampling’ approach and assessing impacts of a transient climate response under given emissions scenarios (Ebi et al., 2018).

For the UK specifically, projections of heat related mortality have used UKCP09 climate projections based on the Special Report on Emissions Scenario (SRES) A2 scenario to estimate mortality at specific future timepoints at regional level (Hajat et al., 2014) and have estimated net differences in temperature related mortality under climate change for different global regions (with the Northern European regional estimates including data for the UK) (Gasparrini et al., 2017). Another study estimated temperature related mortality aggregated at national level from climate projections driven by Representative Concentration Pathways (RCPs) and used relevant time slices to link to expected different degrees of warming (Vicedo-Cabrera et al., 2018a). Only one study has used data from climate experiments specifically designed to produce regional data consistent with a global climate stabilised at 1.5 and 2 degrees (Mitchell et al., 2017) to estimate how mortality attributable to extreme heat, such as the summer of the European 2003 heat wave, would change in Paris and Greater London (Mitchell et al., 2018). Our paper builds on this work, providing a more comprehensive assessment to include all heat-related mortality, not just the summer of 2003 and for the three largest UK conurbations: Greater London, the West Midlands and Greater Manchester.

This study contributes to the much needed evidence of local level impacts under conditions consistent with the Paris agreement (Mitchell et al., 2016b). It adds to our understanding of future heat-health impacts, an area prioritised by the 2017 UK Climate Change risk assessment (HM Government., 2017) and UK National Adaptation Programme (Department for Environment, 2018). Presenting results at the conurbation level for the UK is vital for planning for climate change: the majority of the population live in cities in England (Office for National Statistics., 2018) and many plans for climate action are undertaken at city level (Mayor of London., 2018, Birmingham City Council., 2012, Manchester City Council., 2010).

We aim to answer two specific questions related to the Paris agreement, setting UK climate change impacts within the national and global policy context. These are:

1. How will the frequency of extreme heat events change in Greater London, Greater Manchester and the West Midlands between current conditions, 1.5 °C and 2 °C climate scenarios?
2. How would heat related mortality change (HRM) under the conditions of the Paris Agreement, holding all else constant?

Methods

Statistical methods for deriving the baseline temperature-mortality coefficient:

Data sources

Mortality data for all deaths occurring in England on each day between 1st January 1996 and mid-December 2013 were obtained from the Office for National Statistics (ONS). Data were aggregated by conurbation, as defined by the ONS Built-up Area codes from the 2011 census (Office for National Statistics) and we created time-series of total daily deaths for Greater London, the West Midlands and Greater Manchester by summing the individual deaths on any given day.

We used daily mean temperature (the average of the daily maximum and minimum temperatures) as our main exposure variable, obtained from the UK Met Office UKCP09 gridded observation datasets (UK met office). At the time of analysis, these represented the most up to date observational temperature data from the met office and were used only to provide historical observations for the epidemiological analysis (so that even if updated gridded data become available, their use is unlikely to change estimates. This is in contrast to updated climate projection data, for which estimates would be expected to change between UKCP09 and UKCP18 and for which the newer UKCP18 are now available. The climate projection data for this paper is from the HAPPI project, described below).

This dataset provides daily temperatures for 5km^2 gridded areas and takes into account urban land use, meaning it will capture some urban heat effects (Perry MC, 2009). We used the value represented by the

$5km^2$ gridded cell that overlapped with the centre of each conurbation (identified using ArcGIS) to provide the daily mean temperature for each conurbation.

Daily mean PM_{10} and ozone counts for London from the UK-AIR (Air information resource data archive) were also collected to include as confounding factors in a sensitivity analysis for Greater London heat effects (Department for Environment, 2018).

Statistical analysis

We undertook an ecological time series regression analysis to determine the risk of mortality for each 1°C temperature rise above a given heat threshold during the summer months, defined here as May-September (to adequately capture days above the threshold temperature in any given year).

We assumed a Poisson distribution for the outcomes and corrected for over-dispersion and auto-correlation. We controlled for time-varying confounders and secular trends using a cubic spline function with 4 degrees of freedom per year (in line with previous studies (Bhaskaran et al., 2013)), a linear term for date and a term for day of the week. Increasing the degrees of freedom or using a term for year rather than date did not improve model fit or significantly change the estimates. We used previously published lag periods of 0-2 days (Arbuthnott and Hajat, 2017b) for the heat effects. The heat thresholds were determined by best model fit: we ran the model across the three conurbations with heat thresholds fixed at each percentile above the 85th centile of the year-round temperature distribution and also with no threshold. The heat threshold was set at the percentile which corresponded to the lowest summed deviance across all the conurbations – the 94th percentile. Heat thresholds were therefore set at 19.7 °C for Greater London, 18.5 °C for the West Midlands and 17.8 °C for Greater Manchester.

As a sensitivity analysis, we also quantified the relationship with an included heat wave term in the model, which was coded as 3 or more consecutive days above the 99th percentile of the year-round temperature distribution.

In this paper, we first examine whether and to what extent heat waves are likely to increase in frequency under the two climate change scenarios and also as a sensitivity analysis we add a heat wave term to our epidemiological model (as described above) to test whether accounting for the non-linear change in risk seen at temperature extremes affects our estimates.

In scientific and policy literature, a number of different heatwave definitions have been used (Xu et al., 2016). However all contain a component of severity (temperatures above a specified threshold, which may vary according to the background climate) and duration (number of days).

To examine changes in heat wave frequency, we defined and identified “heat wave events” which are 1, 2 or 3 days in duration, occurring with a probability of 1 in 100 years, 1 in 50 years and 1 in 20 years using the baseline (current) climate data. The definition of these events is then applied to the future 1.5 degree and 2 degree worlds of the modelled Half a degree Additional warming, Prognosis and Projected Impacts (HAPPI) climate data and returned probabilities of such events occurring in the future. The large number of climate years analysed here (450) allows for extreme events to be examined probabilistically.

In the epidemiological model, we take an approach used in health impact literature (Xu et al., 2016), defining the heat wave in relation to background climate for each of the three conurbations, as more than 3 days above the 99th percentile of the mean temperature distribution. It was not possible to use the same definition of rare events as for the return periods above (e.g. the conditions consistent with 1/100 year events) as these would not occur with enough frequency in baseline time series datasets to derive a reliable or precise heatwave effect.

HIA methods

Climate Data

We used climate projection data from the Half a degree Additional warming, Prognosis and Projected Impacts (HAPPI) project (Mitchell et al., 2017). This project was designed to specifically address the challenge of separating the impact of the additional 0.5 °C warming from climate model response uncertainty and internal climate variability that dominate other experiments (e.g. Coupled Model Intercomparison Project

Phase 5 (CMIP)) under low emissions scenarios. The large number of ensembles used in the study allows for comprehensive sampling of the climate space under conditions consistent with current temperatures and with the Paris temperature goals after climate stabilization. We used daily mean temperature from 450 member ensembles of simulations (to account for internal climate variability states) from the atmosphere only HadRM3P general circulation model (Pope et al., 2000, Jones et al., 2004) run using donated computing resources through the citizen science weather@home project (Guillod et al., 2017) following the HAPPI protocol for the 1.5 °C and 2 °C experiments. This methodology is based on sea surface, sea ice and well mixed concentrations of GHGs from weighted sums of RCPs from CMIP5 (Taylor et al., 2012), such that the multi-model mean global mean temperature from CMIP5 experiments between 2091 and 2100 was around 1.5 or 2 degrees higher than the 1861-1880 baseline. This meant that RCP2.6 was used for the model boundary conditions for the 1.5 scenario (the multi-model mean across climate simulations under the RCP2.6 forcing scenario submitted to CMIP5 was 1.55 °C greater than baseline) and a weighted combination of RCP2.6 and RCP4.5 (0.41xRCP2.6 + 0.50xRCP4.5) for the model boundary conditions for the 2 degree scenario (calculated so that the global mean temperature response is 2.05°C - i.e. half a degree warmer than 1.5°C experiment, for which it was 1.55°C).

The mean temperature data from the climate experiments was bias corrected to the same time series of data used for the calculation of the heat related mortality co-efficients – i.e. the UKCP09 gridded data for the time period used in the epidemiological assessment (see above). The data was bias-corrected using the Inter-Sectoral Impact Model Intercomparison Project 2 (ISI-MIP2) bias correction method (Frieler et al., 2017, Lange, 2018). Table S1 and Figure S2 (supplementary materials) show that the modelled HAPPI baseline scenario is well calibrated with the UKCP09 data.

Application of epidemiological risk to climate data

We used daily mean temperatures from each of the 450 climate model runs for the three scenarios (baseline, 1.5 degrees and 2 degrees) to calculate the temperature above the heat threshold for each HAPPI model run, in each of the three conurbations. For each day with a daily mean temperature above the heat-threshold, excess mortality risk was derived from the conurbation-specific temperature-mortality co-efficient and baseline mortality rate. This is summarised as:

$$EM_j = \sum_{i=1}^{N} BM_{ij}\left(\frac{RR_{ij} - 1}{RR_{ij}}\right)$$

$$RR_{ij} = e^{(b_j \Delta T_{ij})}$$

Where EM_j gives the total estimated excess temperature related deaths over time period N in conurbation j. BM_{ij} is the base line daily mortality for all causes for conurbation j on day i.

RR_{ij} is the calculated relative risk of mortality for heat effects for day i, in conurbation j and b_j is the slope of the temperature-mortality relationship for heat for each region j, which reflects the change in all-cause mortality per 1^{o}C change in daily mean temperature above the conurbation-specific threshold for heat, and ΔT_{ij} represents the change in temperature (°C) above the heat threshold for conurbation j on day i. An estimate of future burdens due to more extreme events – i.e. the additional heat-waves effect is also investigated.

The temperature-mortality risk function and baseline mortality rates were held constant over the decades considered. We acknowledge that baseline mortality rates are likely to change in future as a result of socioeconomic and other changes and that the risk function may also change in future as populations potentially adapt to higher temperatures (Huang et al., 2011a). However, our interest is in estimating the contribution of achieving the Paris agreement goals on future mortality burdens, and therefore we hold other parameters constant.

Uncertainty analysis

To demonstrate the range of uncertainty associated with the climate models, we ran the mortality burden calculations over each of the 450 climate 'model runs' and presented results as the average (arithmetic mean) of these, and as probability density functions (PDFs) to demonstrate the spread of the results over the climate ensembles for each of the scenarios. The upper and lower bounds for the uncertainty analysis in tables are based on the upper and lower confidence intervals (CI) of the derived epidemiological relationship between heat and mortality, run over 450 model runs for each HAPPI scenario.

Results

The Modelled current relationship between heat and mortality

To derive the current risk of heat-related mortality, we analysed 466,508 (Greater London), 169,260 (West Midlands) and 154,364 (Greater Manchester) deaths from all causes occurring in summer months between 1996-2013.

The RRs of heat related mortality for each degree above the threshold temperature (94th percentile of the year-round temperature distribution for each conurbation, as selected by best model fit) were greatest in London, where the risk of all-cause mortality is of 4.7% (4.3%, 5.2%) for each degree Celsius above the threshold. Heat risks in the West Midlands and Greater Manchester were 3.0% (2.2%, 3.8%) and 2.4% (1.6%, 3.2%) respectively for each degree above the heat threshold. Inclusion of air pollution (PM_{10} and Ozone) in the model for Greater London did not significantly change the risk - from 4.7% (4.3%, 5.2%) to 4.5% (3.9%, 5.1%). The additional heatwave effect (where temperatures have exceeded the 99th percentile of the year round temperature distribution for any given conurbation for at least 3 consecutive days) was 8.9% (4.6%, 13.4%) for Greater London and 9.7% (0.9%, 19.5%) for Manchester (see supplementary materials, S3). However, the heatwave effect in the West Midlands was much smaller and non-significant.

The change in mean temperature under 1.5 degree and 2 degree scenarios

Across the model runs, the annual mean temperature for London is 11.38 °C for the HAPPI baseline scenario, 12.13 °C for the 1.5 degree scenario and 12.59 °C for the 2 degree scenario. For the West Midlands, the mean temperature for the baseline HAPPI scenario is 10.37 °C, for the 1.5 degree scenario is 11.08°C and for the 2 degree scenario is 11.54 °C. In Greater Manchester, the temperatures across the HAPPI baseline, 1.5

and 2 degree scenarios are 10.08°C, 10.75°C and 11.18 °C respectively (see also supplementary materials, table S1). For the conurbations investigated, scenarios consistent with 1.5°C warming (compared to pre-industrial levels) globally, give an average projected temperature increase of around 0.7°C in Greater London and the West Midlands (and 0.6 °C for Greater Manchester) and scenarios consistent with 2 °C warming globally, give an average projected temperature rise of 1.2°C for Greater London and the West Midlands and 1.1°C for Greater Manchester (see also supplementary materials, table S3). Figure 1 summarises the number of days above the 94th percentile of the year-round baseline temperature distribution across the scenarios, representing the days where there is increased risk of heat related mortality and therefore relevant to the health impact assessment.

Figure 1 shows the average (arithmetic mean) number of days above the 94th percentile (the centile above which deaths attributable to heat are calculated) of the baseline temperature data for each of the conurbations in each of the HAPPI data ensembles (the HAPPI baseline simulations, HAPPI 1.5 simulations and HAPPI 2.0 simulations). These data are also summarised in Table S3 (supplementary materials). For London, the number of days above the 94th percentile increased by 47% in the 1.5 degree world (compared to baseline) and by 79% in a 2 degree world. For the West Midlands, the increase in ‘hot’ days compared to baseline is 51% under a 1.5 degree world and 82% in a 2 degree world. For Greater Manchester, the increase is 43% and 70% for the 1.5 and 2 degree scenarios respectively.

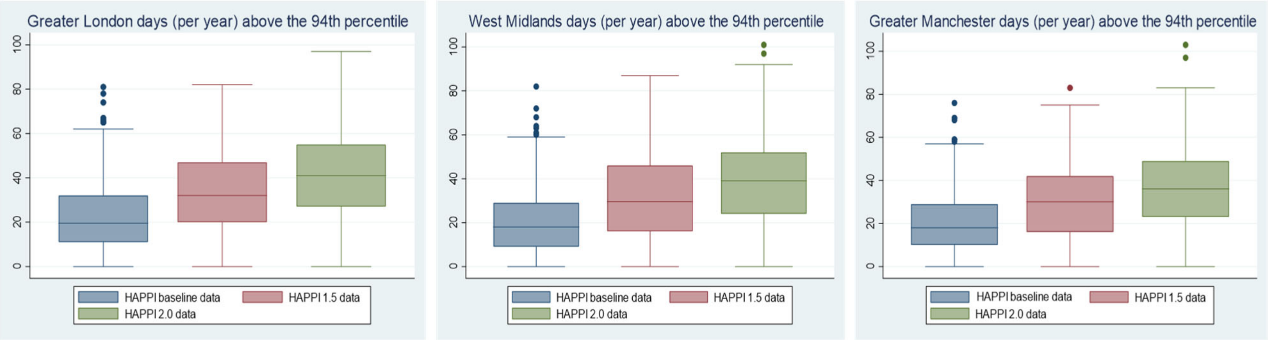

Figure 1: Number of days above the 94th percentile of the year round baseline temperature distribution in each of the scenarios (baseline, 1.5 degrees and 2 degrees)

The Increase in frequency of heat wave events under each scenario

Heat wave events are projected to increase under scenarios consistent with 1.5 and 2 degrees of warming globally (Table 4). For the 1.5 degrees scenario, 1 in 20 year heat wave events (minimum duration 3 days) are projected to occur around once every 10 years and those that were 1 in 100 year occurrences, are projected to occur once every 22-30 years (depending on conurbation). Under the HAPPI 2.0 warming scenarios, 3-day heat wave periods occurring once every 20 years are projected to increase in frequency to around one in every 6 - 7.5 years (depending on conurbation) and those occurring every 100 years to increase to one in every 15-18 years (depending on conurbation). That is to say, if the climate stabilises at 1.5 degrees, there is between a 60-100% increase in frequency of "1 in 20 " year events and a 230-250% increase in the 'more extreme' 1 in 100 year events. Under the HAPPI 2 degree simulations, there is a 167-233% increase in 1 in 20 year events and a 400-40% increase in 1 in 100 year events. Therefore, the largest increase in heat wave events occurs for the 'more extreme' events across both scenarios and there is a substantive increase in events between the 1.5 and 2 degree scenarios. A more detailed summary of heat wave events is available in Table S4 (supplementary materials).

Table 1: Return periods for heat wave events

Conurbation and Duration of event	Historical HAPPI series : frequency of event across all simulations (nearest half year)	HAPPI 1.5 degrees: frequency of event across all simulations (nearest half year)	How many times more likely for 1.5 degrees compared to baseline	HAPPI 2 degrees: frequency of event across all simulations (nearest half year)	How many times more likely for 2 degrees compared to baseline
Greater London					
3 days > 27.2	1 in 20 years	1 in 10 years	2.00	1 in 6 years	3.33
3 days > 28.6	1 in 100 years	1 in 30 years	3.33	1 in 18 years	5.56
West Midlands					
3 days > 25.9	1 in 20 years	1 in 10 years	2.00	1 in 6 years	3.33
3 days > 27.4	1 in 100 years	1 in 22 years	3.41	1 in 15 years	5.00
Greater Manchester					
3 days > 25.2	1 in 20 years	1 in 12.5 years	1.60	1 in 7.5 years	2.67
3 days > 26.5	1 in 100 years	1 in 28 years	3.57	1 in 18 years	5.56

Projected Heat Related Mortality in a 1.5 and 2 degree world

Estimated heat- related mortality under each of the three HAPPI scenarios (baseline, 1.5 degrees and 2 degrees) is summarised in Table 6 and in Figure 2. It should be noted that the larger excess HRM is much higher in London partly due to population size (at the 2011 census, conurbation population sizes were 9,787,426 for Greater London, 2,440,986 for the West Midlands and 2,553,379 for Greater Manchester (Office National Statistics (ONS).). Here we present results modelled without an added heat wave effect, as the modelled heat-wave effect for the West Midlands was not significant. Therefore to ensure consistency across conurbations and between scenarios, main results for all analyses are presented without the epidemiological heatwave term. Results modelled with added heat-wave effect are given in the supplementary materials for Greater London and Greater Manchester (See table S5). However, it should be noted that the addition of the heat wave effect did not substantially alter either the proportional increase in heat related mortality across warming scenarios for Greater London or Greater Manchester (see supplementary materials table S5).

For Greater London, there is a projected 63% increase in HRM under the 1.5 degree scenario and an 107% increase of HRM under the 2 degree scenario, from a baseline of 297 excess heat-related deaths per year (summer). In the West Midlands, HRM is projected to increase by 68% under the 1.5 degree scenario and by 110% under the 2 degree scenario, from a baseline of 59 excess annual heat related deaths. In Greater Manchester, on average HRM increased by 60% under the 1.5 degree scenario and by 97% under the 2 degree scenario, from a baseline of 51 excess annual heat related deaths

Therefore, estimates indicate that stabilising the climate at 1.5 degrees rather than 2 degrees would avert a further 27% increase in excess HRM in London, a 25% increase in HRM in the West Midlands, and a 23% increase in HRM in Greater Manchester.

Table 2: Excess heat related mortality under each scenario

Conurbation	HAPPI baseline	HAPPI 1.5 degrees	HAPPI 2.0 degrees	Further increase (%) in excess heat related mortality if warming is stabilised at 2.0 rather than 1.5 degrees
Greater London				
Average (mean) number of annual/summer excess heat related deaths across all simulations (LCI, UCI)	297 (274, 323)	486 (444, 528)	618 (566, 668)	
Proportion(%) increase in excess deaths compared to HAPPI baseline		63%	107%	27%
West Midlands				
Average (mean) number of annual/summer excess heat related deaths across all simulations (LCI, UCI)	59 (45, 74)	100 (75, 124)	125 (94, 146)	
Proportion(%) increase in excess deaths compared to HAPPI baseline		68%	110%	25%
Greater Manchester				
Average (mean) number of annual/summer excess heat related deaths across all simulations (LCI, UCI)	51 (35, 67)	82 (56, 108)	101 (69, 132)	
Proportion(%) increase in excess deaths compared to HAPPI baseline		60%	97%	23%

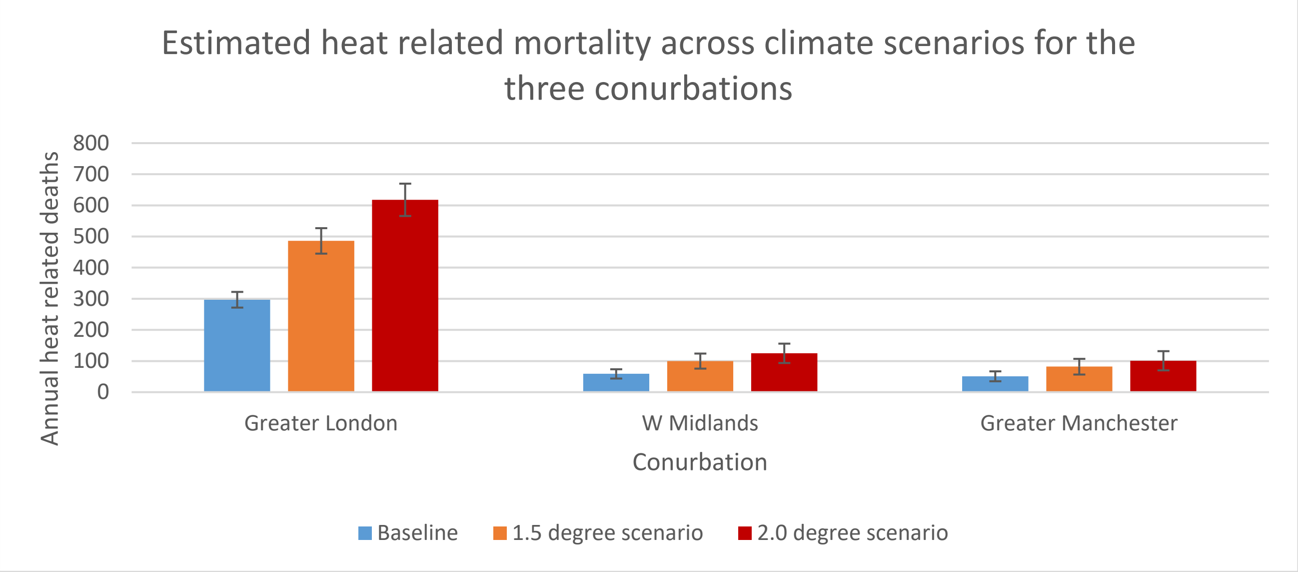

Figure 2: Estimated Heat related mortality in each of the three scenarios – current day baseline, 1.5 degrees of global warming and 2 degrees of global warming. Note: the upper and lower limits represent averaged mortality across the climate simulations using the LCI and UCI of the epidemiological co-efficient; Conurbation population sizes at the 2011 census – Greater London 9,787,426, West Midlands 2,440,986, Greater Manchester 2,553,379.

Excess heat related mortality is also expressed as a probability density function plot in Figure 3. This indicates that, for Greater London, under baseline conditions, the probability of excess HRM exceeding around 250 deaths per summer drops off rapidly, whereas under a climate stabilised at 1.5 or at 2 degrees, the probability of HRM exceeding 1000-1500 deaths per summer exists across more model runs. Therefore for the 1.5 and 2 degree scenarios, the probability of excess HRM for London tails off less rapidly than for the baseline scenario. For the West Midlands and Greater Manchester, the shape of the PDF is more similar across all three scenarios (baseline, 1.5 and 2 degrees of warming), but is shifted to the right in the 1.5 and 2 degree scenarios.

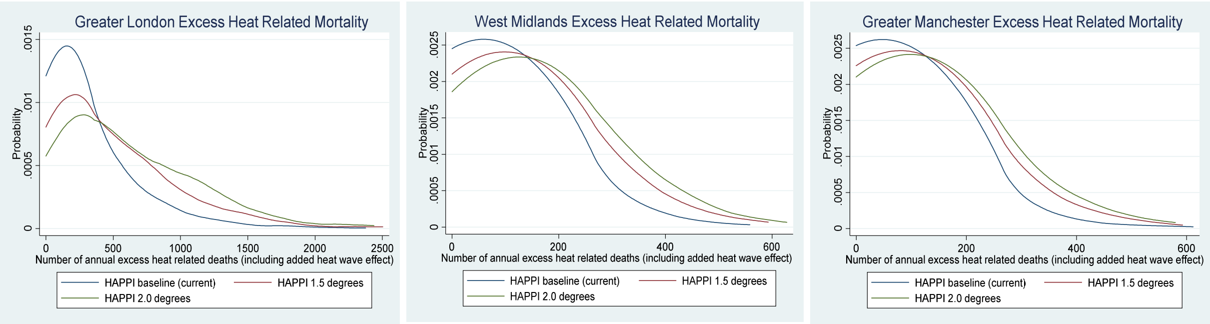

Figure 3: Cumulative excess heat related mortality in Greater London (left), the West Midlands (centre) and Greater Manchester (right) across the baseline, 1.5 degree and 2 degree scenarios. Note excess HRM is much higher in London partly due to population size - Conurbation population sizes at the 2011 census – Greater London 9,787,426, West Midlands 2,440,986, Greater Manchester 2,553,379.

Discussion

We modelled the baseline relationship between ambient temperature and mortality and found increased risk of mortality for each degree Celsius above the 94th percentile of the temperature distribution to be 1.047 (1.043,1.052) for Greater London, 1.030 (1.022,1.038) for the West Midlands and 1.024 (1.016,1.032) for Greater Manchester. Applying these co-efficients to local climate projections, we found heat-related mortality is projected to increase by 60-68% under 1.5°C scenarios and by 97%-110% under 2°C scenarios (depending on location), from a current annual baseline of around 400 heat-related deaths across the conurbations in total. Therefore, the absolute increase in heat related mortality between the 1.5 degree and 2 degree scenarios compared the baseline scenario is between 37% and 44% depending on the conurbation. This implies that for these conurbations, stabilising warming at 1.5 degrees compared to 2 degrees, could avoid a further increase in HRM of up to 27% for Greater London, 25% for the West Midlands and 23% for Greater Manchester.

We also found that rare heat wave events, such as those occurring with a 1/100 year probability in the baseline series, increased by over three times for some conurbations under a 1.5 degree scenario and over five times for a 2 degree scenario. Events with a 1/20 year probability in the baseline series increased by slightly less – around twice as likely across 1.5 degree scenarios and just over 3 times as likely across 2 degree scenarios. The proportional increase in heatwave events when defined as 1 in 100 or 1 in 20 year events, is not matched by a similar proportional increase in mortality across simulations. Whilst it is possible our standard models do not adequately capture the heatwave effect, especially the more ‘extreme’ heat waves which were calculated under the return periods, it more likely reflects the existing knowledge that most HRM occurs on ‘hot’ days rather than during heatwave periods and therefore mortality wouldn’t be expected to increase by a similar proportion to heatwave frequency. Our time series used for the baseline risk calculation includes a long period after the introduction of PHE’s heat wave plan (HWP) in 2004 which may have specifically reduced heat wave related mortality in our baseline series, as has occurred in other settings (Arbuthnott et al., 2016), although there is little evidence for a decline in general HRM in the UK after introduction of the HWP (Williams et al., 2019). In addition, we did undertake a sensitivity analysis including a heatwave term in our models, which did not substantially alter the mortality figures (but note that definitions of the heat wave terms calculated under the return periods and those used in the epidemiology models and for the HIA varied by necessity: heatwave terms in the epidemiological models captured three days above the 99th percentile of each conurbations year round temperature distribution, whereas the temperatures used for the heat wave analysis in return periods (e.g. 1/100 year events) were much higher, but would not have been captured adequately in in the baseline epidemiological models).

We specifically didn’t include population, socio-economic and structural factors, which can be expected to change the magnitude and uncertainty associated with climate projections (Gosling et al., 2017). This is because it is currently unknown when we will reach 1.5 or 2 degrees Celsius (though it is currently thought that mean global warming is likely to reach 1.5 degrees Celsius between 2030 and 2052 (V. Masson-Delmotte, 2018)) and also because the climate projections are not matched to a specific time-point. Additionally, isolating the impacts of temperature changes from societal factors such as population growth, urbanisation and ageing allows for a clear and more easily interpretable assessment of the impacts of the climate contribution of the Paris agreement to be made at a local level (Stott et al., 2017, Ebi and Rocklov, 2014). Previous work has indicated that projected ageing in the UK will contribute substantially to future heat related mortality (Hajat et al., 2014). Inclusion of generic population adaptation assumptions – for example through assumed modification of the exposure-response co-efficient or heat-threshold, would lower future estimates (Huang et al., 2011b). However, there is no clear evidence that the general heat-mortality relationship has been decreasing in recent years in the UK (Gasparrini et al., 2015, Vicedo-Cabrera et al., 2018b, Williams et al., 2019), questioning whether such generic adaptation assumptions are currently valid in this setting. The Urban Heat Island (UHI) effect has been shown to contribute to heat related mortality in the UK (Heaviside et al., 2017, Heaviside et al., 2016) and may also change in future, as will urban characteristics and socio- economic factors which can modify temperature-mortality relationships (Sera et al., 2019). That said, the introduction of specific planned adaptive measures could further reduce heat related mortality (Macintyre and Heaviside, 2019).

It is also widely acknowledged that there are a number of different pathways leading to stabilisation of the global climate at 1.5 or 2 degrees, including the likely possibility of 'overshoot' of temperature goals in the shorter term before temperatures reach equilibrium (Rogelj et al., 2015, Schleussner et al., 2016, Seneviratne et al., 2018) and the different mitigation and socio-economic development paths consistent with these goals (Seneviratne et al., 2018, Riahi et al., 2017). Therefore although not assessed in this paper, the cumulative heat-related mortality over the time period taken to reach these end points and the end distribution of population factors which modify the HRM relationship are likely to differ depending on the pathway taken, with implications for policy and adaptation planning.

Strengths and limitations

This study had a number of strengths. The spatial and temporal resolution of health, weather and climate data was consistent throughout the assessment from baseline co-efficients through to the climate projections. Climate data, for example, was downscaled to the 25km^2 level geographically closest to the area used for the estimation of epidemiological co-efficients; baseline simulations were bias corrected using the same weather data and time period used to calculate the underlying epidemiological relationships for each conurbation; and daily temperature series were derived from the climate projections for the health impact assessments. This improves on the methods used in many health impact assessments, which have been criticised for the small number of climate simulations used, which may bias projections high or low or inadequate downscaling of climate data to fine enough resolution (Sanderson et al., 2017). Further, the HAPPI projections (Mitchell et al., 2017) use a large number of initial ensemble members which better account for uncertainty associated with different internal climate variability states, allows for assessment of rare extreme events and for a probabilistic assessment of future health impacts. Both the climate and the gridded weather data have an urban scheme which is important in this context, given the impact of the urban heat island effect on mortality, and the spatial resolution and number of model runs improve on climate data used in past UK health impact assessments (Gasparrini et al., 2017, Hajat et al., 2014, Vardoulakis et al., 2014) and allow a more comprehensive assessment of climate uncertainty.

Lastly, the study sets to answer a topical and relevant policy question. The IPCC requested further research to understand the impacts of implementing the Paris agreement and this paper adds to this much needed body of evidence (Mitchell et al., 2016a), using projections specifically designed to assess the impact of an extra half degree of warming (Mitchell et al., 2017).

We have not assessed impacts under warming scenarios of more than 2 degrees compared to pre-industrial levels. Whilst an estimate of health impacts at higher levels of warming was not the objective of this study, current evidence shows likely warming between of 2.6-3.1 °C by the end of the century if emissions are limited to current NDCs (Rogelj et al., 2016). Recent evidence demonstrates total global Greenhouse Gas (GHG) had reached 55.3 GtCO2e in 2018, their highest recorded level to date (UNEP., 2019). Without the commitment of reducing emissions to meet 1.5 or 2 degree targets by 2030 respectively the direct heat mortality impacts here are likely to have been underestimated.

One limitation of all studies of future heat related mortality is the use of temperatures in future scenarios outside the temperatures used to construct baseline co-efficients (Rocklov and Ebi, 2012). Estimating relationships at the extremes lacks precision in current observed baseline temperature series and fitting a log-linear relationship above a threshold may under-estimate mortality at the extremes, leading to an under-estimation of future heat related mortality and especially in hotter future scenarios.

Lastly, the HAPPI projections are based on CMIP5 climate models. More recent CMIP6 climate models (World Climate Research Programme., 2016) have a higher climate equilibrium sensitivity suggesting higher projected warming for given GHG increases. This means that running the same experiment using projections based on CMIP6 models may show higher HRM under future warming.

Results in context of other literature

This paper takes forward work from previous climate related impact assessments, by setting questions related to climate change impact within the global policy context and by considering urban populations, important for adaptation planning. The projected impacts are difficult to contextualise within most previous climate projection literature for the UK, as the methods used have differed substantially. For example, previous health impact assessments for the UK considered impacts by region and have typically presented estimates for future time periods using different climate models and scenarios. For example, Hajat et al. (Hajat et al., 2014) presented results for the 2020s, 2050s and 2080s using the UKCP09 projections (based on one medium emissions scenario – SRES A1B) and projected an increase of 257% in heat related mortality across the whole of the UK by the 2050s. However, this figure also contains the increase in HRM attributable to increased population size and ageing and uses an emissions scenario resulting in expected mean temperature rises greater than that of RCP2.6 or RCP4 (resulting in levels of warming by 2090-2099 somewhere between those arising from experiments using RCP6.0 and RCP8.5) (Rogelj et al., 2012), therefore we would expect our estimates to be lower. Other studies have also presented results at a UK-wide level, and used different methods to derive epidemiological co-efficients and downscale climate data (Gasparrini et al., 2017, Vicedo-Cabrera et al., 2018a). The most recent projection study, however, does allow a comparison of results as it examined heat related mortality under the Paris agreement in London and in Paris for future events based on the 2003 heatwave. Mitchell et al. found that in London heat-wave related mortality would increase by a further 22% if the climate stabilised at 2 degrees compared to 1.5 degrees (Mitchell et al., 2018). Our results for London are broadly consistent with this (we find 27% averted

HRM for climate stabilisation at 1.5 degrees compared to 2 degrees). However, we would expect our results to differ slightly as we examine all heat related mortality, rather than projections constrained by the single hot summer of 2003, different epidemiological methods for calculating the baseline heat-related mortality co-efficient and also new model runs of HAPPI climate data.

Meaning of the study and implications for policy makers

Our study is consistent with others from the UK and other locations that demonstrate heat related mortality can be avoided through greater action to achieve the Paris agreement goals (Lo et al., 2019, Mitchell et al., 2018). This is especially relevant at a time when policy makers are being asked to increase the ambition for their NDCs. Currently there is political support for a 'green recovery' from the COVID-19 pandemic. This, alongside the growing recognition of the need to live within planetary boundaries provides a window of opportunity for action (Haines and Ebi, 2019, Kingdon and Stano, 1984, Rockström et al., 2009, Rose et al., 2017) and in line with achieving the ambitions of the sustainable development goals (SDGs). In addition to the direct heat related mortality averted through stabilising the climate at lower temperatures, there are many additional potential gains – in terms of reduced heat related morbidity (Åström et al., 2013, Hajat et al., 2017, Michelozzi et al., 2009), potential morbidity and mortality related to indirect temperature effects (such as impacts on disease and vector distribution), and the many co-benefits to public health that can be achieved if mitigation policies are also optimized for improvements in wellbeing (Chang et al., 2017, Gao et al., 2018). The co-benefits to health and wellbeing (with the implicit effect on productivity, economic benefit of reduced burden of disease) are a strong motivator for ambitious reductions in GHG emissions. Some interventions to reduce emissions are more likely to provide health co-benefits , for example increasing walking and cycling in urban areas (transport emissions are estimated to be responsible for around a quarter of the UKs GHG emissions (Department for Business, 2018)) could lead to savings of around £17 billion to the NHS within a 20 year timeframe, through reduced costs related to Type 2 diabetes, dementia, cerebrovascular disease and cancer (Jarrett et al., 2012). However, there is a risk of unintended consequences, a widening of health inequalities and missed opportunities to improve health and wellbeing with policies that are not optimised for health benefits, due to the multiple interactions between intervention components and the complex nature of cities (Chapman et al., 2016, Proust et al., 2012, Rydin et al., 2012). Taking a system wide approach to reducing GHG emissions would allow for co-benefits and unintended consequences of policies at an urban level to be better anticipated, allowing progress on net zero targets, whilst optimising achievement of the sustainable development goals (SDS) (Gomez-Echeverri, 2018, Ramirez-Rubio et al., 2019).

Regarding heat related mortality specifically, this study highlights the continued need for planned adaptative actions to reduce heat related mortality in the UK, even if the ambitious Paris targets are met. In the UK, Public Health England have a specific heat wave plan aimed at reducing the negative health effects of extreme heat (Public Health England., 2015). A recent evaluation of this plan has made specific recommendations for improvement (Williams et al., 2019) and this study adds weight to the need for continuing action to reduce heat related mortality into the future.

Unanswered questions and future research

This work has implications for future research and has highlighted further questions that would be both interesting and relevant to investigate. Given that under current NDCs global warming is unlikely to stabilise below 2°C, it would be interesting and pertinent to explore HRM averted by achieving 2 °C of warming compared to higher degrees of warming. In this study, we held future socio-economic conditions constant to allow for clear interpretations of the effects of 1.5 and 2 degrees of warming. However, it would be relevant to consider an integrated health impact assessment of heat-health impacts factoring in socio-economic dimensions, for example, using Shared Socio-economic Pathways (SSPs) compatible with achieving the goals of the Paris agreement. Further, whilst this assessment focused on mortality as an outcome, for public health planning and a full appreciation of the impact of the Paris agreement, impact assessments considering both the direct impacts of heat on other health outcomes (e.g. indicators of morbidity), indirect impacts (e.g. on vector borne disease transmission, food systems etc) and economic implications will make a further valuable contribution. Undertaking the assessment of health burdens at the conurbation level has been particularly pertinent, given that plans for climate action exist at the level of the cities studied (Birmingham City Council, Manchester City Council., 2010, Mayor of London, 2018) and the multiple challenges and opportunities for climate mitigation and adaptation in urban settings. In order to take effective action, an understanding of local policies which will make progress towards the UK's net zero target whilst improving public health will be vital. Whilst many of these have been identified (see section on policy above), understanding policy interactions between different sectors and anticipating potential dis-benefits at a local level will be important, and many have advocated taking a systems approach in order to better understand this (Chapman et al., 2016, Proust et al., 2012, Rydin et al., 2012). Lastly, whilst we have projected future heat risks in the three largest English cities, extending this analysis to other locations Is important, given the regional variation of projected warming.

Conclusions

We demonstrated a 23-27% reduction in excess heat related mortality for selected UK conurbations, if the global climate can be stabilised at 1.5 degrees compared to 2 degrees. We also found that rare heat wave events, such as those occurring with a 1/100 year probability in the baseline series, increased by over five times under a 2 degree warming scenario. Better understanding of the societal impacts of climate mitigation can improve motivation and commitment to climate mitigation actions, but care now needs to be taken to ensure that mitigation measures are equitable (and not regressive) and a health in all policies approach used to maximise population wellbeing so that cities are able to take climate change action in line with the sustainable development goals (SDGs).

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PART III: DISCUSSION

8 Discussion

8.1 Context of the Thesis

The many risks that climate change poses to health have been recognised as one of the largest public health challenges of our time (Costello et al., 2009). The breadth and scale of projected impacts on health are vast and likely to be brought about by both direct impacts, such as adverse effects of rising temperature on a population's health, wellbeing and productivity, and indirect impacts including those mediated through natural systems, through socio-economic pathways or combinations of both (Haines and Ebi, 2019). It is widely acknowledged that the climate change which has occurred over recent decades has already impacted on health (Smith et al., 2014). For example, anthropogenic climate change increased the risk of heat-related mortality by around 20% in London in the summer of 2003 (Mitchell et al., 2016a).

Climate change is occurring alongside many other large-scale changes with rapid urbanisation in many locations (United Nations., 2014), ageing populations (Lutz et al., 2008) and the rising prevalence of many non-Communicable diseases (NCDs) (Allen, 2017, Miranda et al., 2008, Wang et al., 2011) being just a few examples. There is also an increasing recognition that populations will need to live sustainably and within planetary boundaries (Rockström et al., 2009) and that this can be done with positive effects for health and wellbeing (Cheng and Berry, 2013, Haines, 2017, Patz et al., 2014).

In 2015 the United Nations Framework Convention on Climate Change (UNFCCC) Paris agreement was introduced, setting out a new global framework for addressing climate change and marking a commitment to climate change mitigation and adaptation (United Nations / Framework Conventionon Climate Change., 2015). The UK's specific response to climate change, legislated in the 2008 Climate Change Act, commits the UK government to a net-zero GHG target by 2050 (Committee on Climate Change., 2019, HM Government., 2019). This is consistent with the countries' "highest possible ambition" under Section 4 of the Paris agreement. In 2021, the UK jointly with Italy, will host the United Nations climate change summit – the 26th Conference of the Parties (COP26, delayed one year due to the COVID-19 pandemic), when countries are expected to re-submit their Nationally Determined Contributions (NDCs) under the Paris agreement. This, along with the UK's government recent pledge to 'grow back greener' from the COVID-19 pandemic and the strong levels of public support for this (Climate Assembly UK., 2020), mark an important opportunity for increased ambition to mitigation and adaptation commitments.

Many of the health challenges that our and future populations face are determined by our social and environmental context (van den Bosch and Nieuwenhuijsen, 2017a). Improved understanding of how climate change will impact upon health and how global, national or local policies can affect this is critical. It not only provides an important understanding of the risks important for planning and allocation of resources, but additional motivation for an increased commitment to climate change mitigation and adaptation.

Broadly this thesis set out to investigate the current and future relationship between ambient temperature and mortality in the UK and to place the quantitative risk analysis of temperature related health impacts into a broader public health paradigm.

An initial review of the literature for this PhD identified important gaps in knowledge that affect both our understanding of current and future impacts of temperature on population health. Through a series of integrated research questions and objectives, it set out to address over-arching and specific gaps in knowledge. It contributes to a more comprehensive and policy-relevant understanding of current and potential future temperature related effects under future warming scenarios in the UK consistent with the Paris agreement, for the three largest English conurbations; Greater London, Greater Manchester and the West Midlands

The research in this PhD sought to make novel contributions to knowledge in five main areas (see Table 1, Chapter 2 for more details):

- Understanding the importance of temperature threshold placement in epidemiological models, and specifically cold thresholds in relation to use in health impact assessments and policy decisions, in order to develop an informed approach to cold threshold selection (Chapter 3)
- Understanding the degree of life shortening associated with temperature exposure, specifically by analysing the relationship between ambient heat and cold potential Years of Life Lost (YLL) (Chapter 5)
- Understanding the epidemiological evidence for population level adaptation to heat and cold, and whether changes in susceptibility to temperature effects have occurred in the UK (Chapters 4 and 5)
- Projecting temperature-related mortality under the conditions of the Paris agreement and understanding the implications of maintaining climate change mitigation and adaptation ambitions (Chapter 6)
- Providing estimates for current and future impacts at conurbation (rather than regional) level (Chapters 5,6)

This discussion chapter of the PhD summarises the main results, provides a critical assessment of the major findings of the research and reviews their implications for research and policy. In order to avoid repetition, this chapter discusses the strengths and limitations of the body of work taken as a whole, because the strengths and limitations of each study's specific methods are discussed within chapter individually.

8.2 Summary of PhD Main Findings

The main results of each of the PhD chapters are summarised below. Within each individual chapter, the results are discussed in the context of previous studies/work (see Chapters 3-6) and therefore this is not repeated at length here.

8.2.1 Chapter 3: "What is cold related mortality? A multi-disciplinary perspective to inform health impact assessments"

This chapter addressed three research objectives: to demonstrate the range of temperatures used for cold threshold selection in UK studies and how sensitive estimates of cold related relative risk (RR) and attributable fractions (AFs) are to this threshold choice using London as a case study; to improve understanding of causality across the range of temperatures used in studies of cold related mortality and; to understand how this can inform threshold placement and the implications for policy.

The paper demonstrated that temperature thresholds below which cold effects are modelled in published studies of London vary widely and that the magnitude of RR and attributable burdens are indeed sensitive to cold threshold choice, with the proportion of mortality attributable to cold in Greater London approximately doubling if the threshold is placed at 11°C compared to 8°C or at 16 °C compared to 11°C (reflecting the change in RR modelled and the greater number of days contributing to the cold related burden).

The chapter explored whether reported associations across the range of studied cold temperatures reflect causal relationships, and the implications of this for estimated future health impacts. I integrated knowledge from multiple disciplines and identified potential causal mechanisms for cold related mortality across the range of temperatures used in epidemiological studies, demonstrating that 'direct' mechanisms for cold mortality are more likely to occur at (extreme) lower temperatures and 'indirect' mechanisms (e.g. via increased spread of infection) at milder temperatures. This has implications for policy and estimated future impacts (see section 7.8).

8.2.2 Chapter 4: "Temporal changes in vulnerability to temperature related mortality"

The main research aim of this chapter was to systematically review the epidemiological evidence for changes in susceptibility to temperature-related health effects over time. A subsidiary aim was to evaluate methods used to assess evidence for past adaptation in the epidemiological literature.

There was some evidence across different geographical locations for reductions in heat related mortality (HRM) over time (measured using a variety of metrics – the RR of HRM and in attributable burdens of HRM), but no consistent evidence for cold related mortality (again measured using a variety of metrics):

Ten out of the eleven papers that quantified the risk of heat related mortality over time, found a decrease in susceptibility, though the magnitude of this varied by location and time period studied. Four of the six papers examining effects of heatwaves found a decrease in expected mortality in later years. Two studies attempted to attribute changes in susceptibility to specific adaptive measures and found no significant association between the risk of heat related mortality and air conditioning prevalence within or between cities over time. Five studies examined the risk of cold. In contrast to the changes in heat related mortality observed, only one found a significant decrease in the risk of cold related mortality in later time periods.

8.2.3 Chapter 5: "Years of Life Lost and Mortality due to heat and cold in three UK Conurbations"

There were two main research objectives for this chapter: to determine the relationship between temperature, mortality and YLL in three major UK conurbations - Greater London, Greater Manchester and the West Midlands (including Birmingham) and to use empirical data from these conurbations to assess whether there had been any temporal changes in heat or cold related risk of YLL or mortality in recent years.

Heat-effects (lag 0-2 days) were greatest in London, where for each 1 °C above the heat-threshold the risk of mortality increased by 3.9% (CI 3.5%, 4.3%) and of YLL increased by 3.0 % (2.5%, 3.5%). Between 1996-2013, the proportion of deaths and YLL attributable to heat in London were 0.50% and 0.40% respectively. Cold-effects (lag 0-27 days) were greatest in the West Midlands, where for each 1 °C below the cold-threshold, risk of mortality increased by 3.1% (2.4%, 3.7%) and of YLL increased by 3.1% (2.2%, 3.9%). The proportion of deaths and YLL attributable to cold in the West Midlands were 3.3% and 3.2% respectively. Though there are no previous UK studies that have quantified the effects of temperature on YLL, the findings are broadly in line with studies from other locations, where a positive relationship between YLL and increasing or decreasing temperatures has been found (e.g. (Huang et al., 2012, Odhiambo Sewe et al., 2018, Yang et al., 2015).

We did not find any evidence of changing susceptibility to heat and cold effects in the population over our study period (1996-2013). This is in contrast to some other locations (see results of chapter 4 above), but broadly consistent with other UK studies which have not shown an attenuation in heat related mortality risk in recent years following the introduction of the heat wave plan (Williams L., 2020) or heat risk (Gasparrini et al., 2015), or heat and cold related mortality burdens (Vicedo-Cabrera et al., 2018b). For example, one study showed a decrease in cold related mortality in the under 65s after the introduction of the cold weather plan (CWP) but an increase in risk in the over 75s over time (Murage et al., 2018). The work demonstrated that although older individuals are at greatest risk of temperature-related mortality, heat and cold still make a significant contribution to the attributable burden of YLL in all three conurbations.

8.2.4 Chapter 6: “Heat related mortality avoided under the Paris agreement”

This chapter had two main research objectives: to understand how the frequency of heat wave events could change under the conditions of the Paris agreement in Greater London, Greater Manchester and the West Midlands, and to estimate/derive probabilistic projections of heat related mortality burdens under current and Paris agreement (1.5 °C and 2 °C climate scenarios) conditions for these conurbations, whilst holding all else constant.

We found that HRM is projected to increase by 60-68% under 1.5°C scenarios and by 100-110% under 2°C scenarios (depending on location), from a current annual baseline of around 400 heat-related deaths across the conurbations. This implies that for these conurbations, stabilising warming at 1.5 °C compared to 2 °C, could avoid a further increase in HRM of up to 27%. Though there hasn’t been a previous study that has projected general HRM under the Paris agreement for the UK, these results are broadly consistent with one study examining the increase in heat wave related mortality in London under conditions of the Paris agreement (Mitchell et al., 2018).

8.3 Strengths of the research and contribution of this PhD to the field

Across the four chapters identified above, the research has made an important contribution to empirical and policy relevant knowledge in this area of environmental public health.

Through the work on cold thresholds, a methodological contribution to the field, with implications for future research, has also been made.

One strength of the work as a whole has been the integration of knowledge across disciplines and the placing of quantitative risk analysis into a broader public health paradigm, for example by defining research questions with policy relevant outcomes at the fore – such as, linking the health effects of climate change to the 2015 UNFCCC Paris agreement, examining evidence for existing adaptation to heat or cold, and defining outcomes of current temperature related health risk in different policy relevant metrics (see below).

There have been previous calls from researchers for better integration of climate science and epidemiology when producing health risk assessments (Sanderson et al., 2017). From the perspective of climate data use, this can help avoid the potential of certain biases introduced by inadequate handling of climate data for use in impact assessments (e.g. with respect to bias correction and downscaling of modelled data). Undertaking all aspects of the climate health impact assessment, from the epidemiological modelling, determining whether there had been any local changes in risk in recent years and modelling projected burdens under warming scenarios, allowed for a full integration of information across disciplines and a true consistency in the approaches taken (for example, the use of consistent exposure data, such as use of climate data bias corrected to exposure data used for epidemiological assessment and a consistent approach to setting and using thresholds in epidemiological and health impact studies). The collaboration with climate scientists for the last chapter of the PhD enabled use of policy relevant, novel and appropriately bias corrected temperature data for the UK conurbations studied.

Likewise, a full understanding of the epidemiology of how temperature effects are modelled is critical to the interpretation of health impacts (see sections on chapter 3). In general, how effects are measured and designed defines not only what issues are seen to be important (Parkhurst, 2017), but can also promote or limit potential policy options (e.g. see (Garnett et al., 2019)). The choice of temperature thresholds, i.e. how 'cold' is defined by those generating epidemiological evidence, has rarely been discussed in the literature despite the high sensitivity of cold burdens (and therefore future projections and also net temperature related mortality in some studies) to threshold choice: defining cold thresholds is an integral step in linking temperature to health effects and influences how cold risk is understood. Integrating the discussion on threshold choice with multi-disciplinary evidence on causal pathways, promotes a more refined approach to interpretation of studies for policy consideration.

Both a strength and novel component of the work in comparison to previous UK studies is that all analysis has been carried out at conurbation level. Most UK studies of temperature effects (on health) have used regional level data (Arbuthnott and Hajat, 2017, Hajat, 2017). Whilst this allows assessments for the whole of the English population (i.e. including rural areas), it has left gaps in knowledge at a more local level. Understanding risk at the urban level is important as cities face a number of distinct challenges, from specific socio-economic factors through to physical phenomena, such as the Urban Heat Island effect – whereby temperatures in cities are higher than those in surrounding areas (Oke, 1982) (in general, night time temperatures can be on average 2-4 °C higher compared to rural areas, but can be as much as 5-10°C higher in the centre of larger cities such as London, Birmingham and Manchester (Heaviside et al., 2017a)). In addition, studies have demonstrated that local level analysis has more salience for policy makers responsible for local policy development in public health and climate change ((Williams L., 2020, McGill et al., 2015, Adger et al., 2018, Howarth and Painter, 2016)). Understanding conurbation-level climate impacts – an important first step in any risk management process or evidence-policy cycle (Hess et al., 2014) – assesses the scale of impact and current adaptation measures required at a policy relevant level. Each of the conurbations investigated has a specific city level climate change adaptation plan (Birmingham City Council, Manchester City Council., Mayor of London, 2018) and elected mayoral leadership. Now that public health sits within local authorities in England (2012), there is the opportunity for analysis that is undertaken at this level to inform policy decisions across sectors.

This PhD has made specific contributions to knowledge across three further areas: understanding the relationship between temperature and YLL in the three conurbations, adding to knowledge of changes in susceptibility to temperature over time, and producing novel heat related mortality projections.

To our knowledge, whilst there have been studies which have examined the relationship between YLL and temperature in different locations (e.g. (Huang et al., 2012, Odhiambo Sewe et al., 2018, Yang et al., 2015)), this is the first research which specifically examines this in the UK (though there are studies which examine the relationship between YLL and air pollution e.g. (Cohen et al., 2005, Smith et al., 2013)). As discussed in more detail in Chapter 5, YLL is an important metric in policy making, as it takes account of premature mortality and is often used in decision making by improving comparison of risks, for example, in comparison to attributable deaths which is a relatively blunt metric. In fact, there have been calls for YLL to be used much more widely in temperature-health studies for these reasons (Liu and Ma, 2019). Whilst YLL can be more informative as a metric, YLL are also less straightforward to communicate and when used in temperature related studies, a number of assumptions are made around the life expectancy of those dying from heat and cold: the specific strengths and limitations of methods used in Chapter 5 on YLL are discussed therein.

Chapters 4 and 5 of the PhD contributed to empirical knowledge of historical population changes in susceptibility to heat and cold. The systematic review (Chapter 4), was one of the first papers in the field to synthesise evidence across geographical locations on changes in both heat and cold risk over time, highlighting that the extent of the decrease in vulnerability to heat varied by location and time period analysed. The review set out a framework for the different mechanisms for changes in susceptibly, examining whether these could be attributed to spontaneous or planned adaptation, and provided a critique of the methods used to assess changes over time, building on our understanding of how results from studies can be interpreted (Kinney et al., 2008). Since publication, the review has been cited (>75 times[1]) in relation to: the empirical evidence it presented for HRM declining over time (e.g.(Domingos et al., 2018, Hoegh-Guldberg et al., Organization, 2017)); highlighting the need for further evidence of CRM trends (e.g. (Liu and Ma, 2019, Vicedo-Cabrera et al., 2018b)); the need for further evidence from different locations and time periods and; highlighting the importance of understanding historic evidence in the context of adaptation assumptions made in climate change health impact assessments (e.g. (Gosling et al., 2017b, Liu and Ma, 2019, Vicedo-Cabrera et al., 2018b)).

Having demonstrated a gap in evidence around changes in susceptibly to heat and cold in recent years in the UK specifically, Chapter 5 examined data from the three largest English conurbations for evidence of changes in susceptibility to heat or cold over the past two decades. The analysis made an important contribution by adding to evidence on temperature related mortality heat risks in recent decades (e.g. (Gasparrini et al., 2015, Vicedo-Cabrera et al., 2018b)), and also by using YLL as an outcome. In demonstrating the similar pattern over time in risk of YLL and mortality, results most likely reflect that any changes in the population age structure over the period are not contributing to an increase in risk. Lastly, results are disaggregated by conurbation so that any differences between

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[1] As referenced in google scholar, as of July 2020

conurbations could be highlighted, in contrast to many analyses that have presented results at a national level (e.g. (Vicedo-Cabrera et al., 2018b)).

The third main area in which the PhD makes a novel contribution to empirical knowledge is in quantifying the effects of heat related mortality in the three largest conurbations under conditions of the Paris agreement. To our knowledge, these are the latest UK projections for heat related mortality and the only projections which specifically examine averted mortality under a 1.5 °C world compared to a 2°C world for all heat related mortality, responding to calls for evidence on the effects of the Paris agreement (Mitchell et al., 2016b, Tschakert, 2015) and providing important evidence for policy makers on the implications of achieving NDCs under the Paris agreement. One strength of this chapter is the use of a large number of climate modelling experiments (an ensemble of 450 members) to give results of local climate after global warming has stabilised at 1.5 or 2 degrees. Both the large ensemble and the use of climate data specifically modelled to analyse the effects of the Paris agreement is an improvement on many previous studies, where either smaller climate ensembles have been used (e.g. (Hajat et al., 2014)) or where impacts of the Paris agreement have been estimated from temperature end points derived from approximate time slices of when given RCPs reach a given level of warming, rather than after results of experiments to project climate stabilisation at 1.5 or 2 degrees (e.g. (Ebi et al., 2018, Vicedo-Cabrera et al., 2018a)).

8.4 Limitations of the thesis

Within this section, only limitations of the PhD as a whole are discussed, as the limitations of each approach and research for each paper/chapter are discussed within each of the relevant chapters.

8.4.1 Limitations of geographical scope

The analysis for this PhD was limited to the UK, and specifically to the three largest English conurbations. Whilst inclusion of more locations would allow for comparison of temperature related mortality across geographical locations (e.g. between conurbations in different countries) and undertaking analysis at the regional would allow for a more comprehensive HIA of temperature effects throughout the UK, there were both advantages and practical reasons for limiting the geographical scope. For example, there are already projects, such as the Multi-country, Multicity project where the specific aim is to compare temperature related mortality across locations (but where UK analysis has traditionally been undertaken at the region rather than city level – e.g.(Guo et al., 2016)) and previous health impact assessments have been undertaken for the whole UK, albeit using different climate data (e.g.(Hajat et al., 2014, Vardoulakis et al., 2014)). The decision to focus on three conurbations was in part practical: climate data is costly to produce and downscale and this project relied upon a non-funded collaboration with the climate modelling team producing the bespoke projections (Mitchell et al., 2017), requiring a balance of feasibility within limited timescales and budgets.

8.4.2 Limitations of exposures and outcomes studied

The temperature exposure studied in this thesis was limited to daily mean temperature. Whilst a variety of metrics have been used to quantify heat and cold exposure (e.g. mean, apparent, minimum, night-time temperature etc.), previous work has not shown one temperature metric (including composite measures) to be an overall better predictor of outcome in the US (Barnett and Astrom, 2012) and there is some evidence that mean temperature is a good predictor of temperature related mortality across the range of geographical, demographic (age) and seasonal periods assessed in Europe (Hajat et al., 2006) (though for heat related mortality alone, maximum temperature may be a better metric (Armstrong et al., 2011)). Within this PhD, the quantification of effects of both heat and cold and the use of mean temperature in many UK studies of current and future risk (Arbuthnott and Hajat, 2017) justifies mean temperature as the exposure variable. Many studies have also included humidity in models of temperature related health effects (or used a composite exposure measure which includes humidity, such as apparent temperature). Humidity data at the same gridded resolution as the temperature data was not available for this study, which would have limited its use. However previous UK estimates of temperature related all-cause mortality have not been substantively changed by the inclusion of humidity in epidemiological models, and recently a large multi-centre study found no association between mortality and humidity in summer months (Armstrong et al., 2019).

In all studies of temperature related risk where exposure is assessed using fixed-point measurements, there is likely to be some misclassification bias. Whilst the gridded data used in this PhD to assess exposure is likely to be an improvement compared to that taken from meteorological stations (often located in rural areas outside cities and therefore less good at estimating urban temperature exposure (Heaviside et al., 2017a)), personal temperature exposure is dependent on a number of factors including indoor temperature, microclimate variability and social and behavioural factors (Kuras et al., 2017), which are likely to be important in evaluating health effects (Modesti and Parati, 2014, Saeki et al., 2014). However, in the case of this study, the classification bias is likely to be non-differential and therefore bias the results towards the null (rather than over estimate effect size). The extent to which misclassification affects results of this type of study would benefit from further evaluation (e.g. using personalised exposure assessment) (Kuras et al., 2017).

The temperature-mortality time series used in the primary research ran until the end of 2013, which represents the mortality data that was available at the time the epidemiological analysis was undertaken. However, in the UK, 2014, 2017, 2018 are included in the top 10 hottest years (all since 2002). It would be interesting in further research to examine whether any changes in risk are apparent over more recent years - understanding whether temporal patterns have changed more recently would be of interest in understanding heat adaptation. Of note, the recently published evaluation of PHE's Heatwave plan contains an epidemiological analysis of heat-mortality risks, using data until the end of 2015 (Williams et al., 2019). This more recent research found patterns of risk across geographical areas similar to those in this study and did not find any change in temperature health risk functions in the years studied since the HWP's introduction (though in recent years heatwaves specifically have not been associated with high numbers of excess deaths – not researched in this PhD). This has been discussed in more detail in chapter 6.

In this thesis, air pollution was controlled for only as part of a sensitivity analysis for Greater London, though including PM_{10} and ozone in the models did not affect the results significantly (consistent with other UK studies). This was due to limited availability of air pollution data. However, there is also the ongoing debate, referred to in more detail in Chapters 3 and 5 as to whether specific air pollutants are indeed a time varying confounder or lie on the causal pathway between temperature and health effects (Buckley et al., 2014).

The health outcomes studied in this thesis were limited to all-cause mortality and YLL, for a number of reasons. The objectives for the PhD were designed to be inter-linked. The overall aim was to examine the current and future health impacts of temperature in terms of an integrated HIA using methods and analysis that would build on or address evidence gaps relevant to public health and policy. There exists a wealth of studies which have examined the relationship between other health outcomes, such as emergency hospital admissions (Kovats et al., 2004), ambulance response times (Thornes et al., 2014), cause specific mortality (Gasparrini et al., 2012) and GP consultations for specific conditions (Hajat et al., 2017). Within this PhD, focusing on mortality and YLL allowed important gaps in knowledge, such as understanding the impact of temperature on premature mortality, to be addressed. Choosing all-cause mortality as the outcome for the projections made use of an indicator for which there is a strong relationship with current temperature (compared, for example, to urgent hospital admissions for which the strength of relationship is less strong (Kovats et al., 2004)) and where the pathway to impact in the future is less likely to change: even before the COVID-19 pandemic and the manifold ways in which this could change patterns of healthcare delivery there was an increasing move towards more integrated and community based care pathways (Charles et al., 2018, Imison et al., 2017, Kendall et al., 2009, Young and Philp, 2000). Therefore, impact assessments of future temperature-related hospital admissions, would not only be based on risk functions where the signal is less clear but also on the premise that healthcare delivery patterns remain the same, despite current policy pressures to change this.

For the thesis, temperature effects were modelled using a time-series regression approach and a double threshold (for year round data in Chapter 5) distributed lag model (and use of a single heat threshold when heat risks were modelled for the summer period only in Chapter 7) (Armstrong, 2006, Bhaskaran et al., 2013). Whilst the case-crossover approach would have presented a suitable modelling alternative when using individual post-coded mortality data, the use of aggregate exposure data in this thesis meant that time series regression and case-crossover designs are likely to yield similar results (Basu et al., 2005, Tong et al., 2012). Therefore for this purpose, one method was not felt to be more advantageous and using a time series framework provided consistency between approaches taken in this thesis and previous analyses in the UK and those analyses which have been used in previous health impact assessments (Hajat, 2017, Arbuthnott and Hajat, 2017). The use of a double threshold model for modelling the effects of temperature, compared to use of a minimum mortality temperature (MMT - above and below which effects are estimated) has been discussed in Chapter 4, and has also been a topic of recent discussion in the literature in other locations (Longden, 2019). In this thesis, a double threshold model was chosen to allow both heat and cold threshold selection based on best model fit (rather than constraining the model to a single threshold or MMT, which would likely result in cold effects being modelled at higher temperatures with implications for causality, discussed in Chapter 4). The advantage of using distributed lags to model delayed temperature effects (compared to moving averages) has been extensively discussed elsewhere, and has been demonstrated to capture temperature effects well even at long lags (Gasparrini, 2016, Armstrong, 2006). Of note, models were corrected for auto-correlation (checked by plotting Partial auto-correlation functions (PACFs) of the deviance residuals from the models) and over-dispersion. Season and trend were captured in the models using a cubic spline with 7 degrees of freedom per year, as in previous studies (Bhaskaran et al., 2013). This was chosen to represent a balance between sufficient control for unmeasured confounders and allowing sufficient variation to estimate temperature effects. Specific limitations of approaches used for each given research objective and sensitivity analyses undertaken are discussed in more detail in each individual chapter.

8.5 Reflections on the HIA approach: Modelled representation of a complex problem

8.5.1 Framing of the HIA (limitations of scope) and dealing with uncertainty

Climate change, by its very nature, creates inter-dependent and cascading risks across all systems, all of which interact with additional socio-economic dimensions. In quantifying the potential effects of climate change on health any model will, by necessity, represent a simplification of impact pathways and include a number of assumptions and be subject to uncertainty from many sources. Clarity in objective setting for any health impact/risk assessment is paramount: different models are useful for answering different public health questions (Ebi and Rocklöv, 2014). There is a fundamental difference in the framing and interpretations of assessments where, for example, the objective is to better understand the impact of a specific policy, compared to assessments where the aim is to project future heat related mortality having accounted for as many inter-related aspects as possible, many of which involve assumptions around information which is subject to deep uncertainty. Both have relevance – the latter, for public health planning, understanding adaptation and resource needs e.g. at a local level, and the former for understanding specific aspects of policy change. Chapter 6 of this thesis set out clearly to examine potential impacts of future temperature rises under the Paris Agreement on heat related mortality, whilst holding all else constant. i.e. to the examine the outcome of the largest global policy development (specifically the GHG mitigation targets within the Paris agreement) in the area of climate change, at a relevant local level. This approach has been used in other studies (Mitchell et al., 2018). However, even within this simplified framework there are extensions of the analysis which would represent useful information. For example, it appears increasingly unlikely that the target of limiting global warming to 1.5 degrees will be met (Rogelj et al., 2016). Understanding how limiting warming compared to our current trajectory may be useful to key decision makers and whilst the climate data to do this was not available at the time of study, it will be examined as part of the UK's 4th Climate Change Risk Assessment. Even within the justifiably simplified framework used in the thesis, results are subject to uncertainties – around climate model outputs and the baseline co-efficient used. These were partially accounted for by running each of the 450 climate simulations with the baseline co-efficient and its upper and lower bounds, an approach which has been used in previous health impact assessments (Hajat et al., 2014, Mitchell et al., 2018), although other approaches such as Monte-Carlo simulations have also been used (Lo et al., 2019). Approaches to quantifying and communicating uncertainty are important, not least as uncertainty can be interpreted as a barrier to action or lead to multiple interpretations or normative judgements being justified/made on the basis of risk assessments (Adger et al., 2018).

8.6 Areas for future research

8.6.1 Representing population level 'Adaptation'

By examining adaptation or changes in susceptibility to heat and cold in the literature and in UK data, this PhD has highlighted multiple areas for future research. These range from further work to increase our understanding of past adaptation trends and how this can inform climate change risk assessments, to work understanding potential future adaptation needs. There is also the question as to whether different approaches to modelling could make valuable contributions to health policy and planning when considering adaptation needs within a given (complex) system, including taking a more practical perspective starting with understanding needs of policy makers and communities. Both of these areas are discussed below.

8.6.2 Understanding past and current population level adaptation

The literature review in this PhD demonstrated that across a number of locations, there is evidence for reduced susceptibility to heat. Understanding the factors that have contributed to this to further understand past adaptation trends remains important. Some studies have partially addressed this - there are studies which have examined how heat risk varies with the prevalence of air conditioning (especially in the US (Anderson and Bell, 2009, Barreca et al., 2016, Bobb et al., 2014, Curriero et al., 2002)) and with other socio-economic and geographical factors (Hajat and Kosatky, 2010). However, studies comparing changes in risks across a number of settings using a consistent epidemiological approach may help identify potential adaptation interventions and also inform whether and how adaptation assumptions can be included in climate risk assessments (see below).

8.6.3 Inclusion of adaptation with Health Impact Assessments of climate change

Whether and how to include adaptation assumptions in health impact assessments remains a topic of discussion and area for future work, and highlights some important considerations for interpretation of results from more simple health impact models. The first is around the use of historical risk functions in projecting future risk: in the UK where there is limited epidemiological evidence of recent adaptation (including results from this work) the use of historical risk functions may be easier to justify, though results from such models risk over-estimating future burdens (Arbuthnott et al., 2016, Kinney, 2018).

A number of previous health impact assessments have therefore included assumptions about population level adaptation to heat (Huang et al., 2011). However, justification of a given approach is rarely given, despite results being sensitive to the approach used (Gosling et al., 2017a). Approaches have ranged from assuming populations adapt to a certain number of degrees, that populations in one location will behave like those in another hotter locations exhibiting less heat sensitivity in years to come (analogue cities), or that minimum mortality temperatures will shift to the right as the climate warms (Kinney et al., 2008). In general, these are not informed by current/past trends of changes in susceptibility (with the exception of some, e.g. (Petkova et al., 2017)). Even when past trends are used to inform future assessment, there is no way of knowing whether recent trends in changes in risk (if any) will continue into the future: limits to the extent and the pace of adaptation are largely unknown and are likely to depend on a wide range of societal and context dependent factors – for example, the pace of adaptation may slow as the relative risk of heat related mortality approaches 1, or for areas with higher initial risks the pace of adaptation may be faster if local planned adaptive measures put in place.

Therefore, one pertinent remaining research need is considering how adaptation could best be included in future health impact assessments of climate change. Pathways or scenarios can play an important role in helping researchers to explore possible futures within the context of deep future uncertainties, as illustrated by the RCPs (Van Vuuren et al., 2011) and the more recent “Shared Socioeconomic Pathways” (SSPs), in which five scenarios of how the world may evolve with regards to socio-economic drivers such as population, economic activity and urbanization are described (Riahi et al., 2017). These two complementary approaches (pathways for GHG concentrations and the context in which any reduction in emissions could be achieved) could form a basis for considering adaptation HIAs in the future. For example, ‘adaptation pathways’ could consider endpoints of population adaptation for inclusion within health impact assessments, or ‘adaptation scenarios,’ could consider different adaptation options within a modelling framework internally consistent with the narratives within the SSPs (where possible). To inform these, further research would be needed to understand how shared socio-economic drivers (e.g. GDP, urbanisation etc) could affect adaptation within populations.

In addition to the problem of how best or indeed whether to include population adaptation within health impact assessments, there are few health impact projections which make use of the new SSPs to allow projections taking an integrated and internally consistent approach to climate data, population projections and other socio-economic factors. This represents an additional important area for future work.

8.6.4 Adaptive measures within complex systems

A large part of this PhD and discussion has focused on quantifying the current and projecting future risk of heat and cold to population health along with discussing future research needs in these areas. However, the thesis also demonstrated a lack of evidence for decreasing susceptibility to heat and cold in recent years in the UK, highlighting the need for (evidence to inform) adaptive policies to reduce current and future temperature related risk in UK cities. Whilst research characterising the effect of specific adaptive policies to reduce adverse outcomes related to heat or cold continues to be important (e.g. the use of cool roofs to mitigate the UHI effect (Macintyre and Heaviside, 2019), improvements to housing (National Institute for Clinicale Excellence (NICE). 2016), evaluation of heat and cold weather plans and their implementation (Chalabi et al., 2016, Hajat et al., 2016) etc.), many policies relating to urban adaptation needs, are likely to be trans-disciplinary in nature. The wider determinants of physical and mental health and wellbeing are linked to policies made in other sectors (e.g. transport, environmental policy etc) and integration of knowledge across sectors and disciplines will be essential in order to maximise wider public health gains and to avoid potential maladaptive outcomes (for example, increased inequities, negative path dependencies or increased GHG emissions (Barnett and O'Neill, 2010)). The move of UK public health into local authorities after 40 years of being situated within the National Health Service (NHS), brings with it the opportunity to advocate/influence for a health in all policies approach. However, studies have also suggested that the type of evidence used in this environment can differ from the traditional evidence hierarchies favoured in evidence-based medicine models with contextual local evidence and expertise also being important (Garnett et al., 2019, Parkhurst, 2017, McGill et al., 2015).

The use of systems approaches has gained much attention in recent public health literature (Carey et al., 2015, Petticrew et al., 2019). Through an increased shared understanding and co-production of evidence with local stakeholders (for example through developing collaborative conceptual models or causal loop diagrams), the approach allows for the production of evidence that is of relevant and contextual for use in city level planning. It has also been argued that a collaborative process of model construction allows for an improved collective understanding of the system in question and in itself can increase adaptive capacity (Carey et al., 2015).

Cities can be recognised as complex self-organising systems (Chapman et al., 2016, Proust et al., 2012, Rydin et al., 2012). Interaction between and integration of their multiple parts at multiple scales (e.g. geographical scales of infrastructure, governance at multiple scales, institutions etc.) leads to emergent properties (such as city identity, economic productivity). The dynamic interaction and feedback processes between a cities components over time determines much of the health and wellbeing of its citizens, and in potentially unanticipated ways.

Research to improve health and wellbeing within cities could benefit from insights gained from systems approaches. For example, Proust et al. (Proust et al., 2012), used systems approaches and collaborative conceptual modelling workshops to consider maladaptive technology dependence - in particular individual dependence on private motorised transport and the (dynamic) links between this, air quality climate change and health and wellbeing. Their conceptual model highlighted both potential downstream leverage points (such as capping car parking in city centres) and upstream leverage points (such as examining mind-sets from which systems arise) which could be used to reverse the dependence on cars in cities, by examining the drivers of path dependence and lock in).

Whilst a comprehensive understanding of any city's complexity may be too costly to be feasible for policy makers, systems approaches focusing on key aspects of cities or policy experimentation can crystalize connections and pathways for urban transformation (Chapman et al., 2016) and allow a more integrated approach to improving health and wellbeing. Through making interactions transparent, multiple policy effects can be considered, and allow for a more comprehensive consideration of important social, ethical or contextual components of any given policy (such as effects on health equity (Rydin et al., 2012, Carey et al., 2015)). Making co-benefits and unintended consequences of policies clear can enable shared understanding and political alliances sometimes necessary to effect change (Rutland and Aylett, 2008). However, as with any approach it is important to ask appropriate questions of the methods and is likely to be complementary to more traditional methods, which remain important.

8.6.5 Areas for future epidemiology work

In addition to the different approaches and methods which could contribute to policy relevant knowledge in the area of climate change, adaptation and health there are still a number of fundamental questions relating to the epidemiological relationship between temperature and health which would make interesting areas for future research, a few of which are outlined below.

For example, considering exposure assessment, integrating personal ambient temperature exposure into health studies could improve estimates and understanding of vulnerability, as could further studies exploring the relationship between indoor and outdoor temperatures. Considering causal relationships, further work on the role of air pollution in temperature health relationships would be useful, including work on the potentially confounding role or synergistic effects (Analitis et al., 2018) between air pollution and temperature in the UK specifically, and in extreme weather events. This could complement potential important research on the role of multiple climate hazards and stressors on health outcomes and how this affects vulnerability.

Building on the research in this PhD, further exploration of the association between ambient temperature and cause-specific YLL would be interesting and could give insight into the comparative burden of certain causes of mortality (e.g. cardiovascular, respiratory) commonly associated hot and cold temperatures in terms of premature mortality. It would also would be interesting to investigate whether temporal changes in vulnerability to heat and cold risk are apparent and differ by cause of mortality. In some studies, observed trends in heat related mortality have differed by cause of death, but not in all. For example, some research has demonstrated declines in cardiovascular mortality in recent years but not in respiratory or all-cause mortality (Miron et al., 2015, Ha and Kim, 2013), some studies have found finding that cardio-respiratory mortality has declined faster than all-cause mortality (Chung et al., 2017) and others have demonstrated variable patterns in cardio and respiratory causes according to location (De'Donato et al., 2015).

In addition to this, there are many outcomes for which further studies would be beneficial in the UK, including improving understanding of: temperature effects on the workforce and productivity; of some specific health outcomes (such as cerebrovascular events, mental health); and other composite indicates, such as Quality Adjusted Life Years (QALYs). Additionally, studies examining the relationship between biomarkers and temperature could add further understanding to causal pathways (e.g. see chapter 3) and would be possible with use of UK biobank data (Allen et al., 2012). Lastly, analysis of health outcomes at a more granular level would help improve understanding of vulnerability and inequitable effects of temperature on health.

8.7 Policy Implications of the thesis

The policy implications of this thesis fall into two broad categories: those areas where the work contributes to understanding the nature of current and future temperature related risk and the implications of the quantified temperature related health risks for current and future mitigation and adaptation policy. There are both high level policy implications, and implications for local authorities and the conurbations studied in this work – both are discussed here.

The 2008 UK Climate Change Act, with its mandated 5 yearly cycles of Climate Change Risk Assessments (CCRAs e.g. (Sub-Committee, 2016)) and National Adaptation Programmes

(NAP e.g. (DEFRA., 2018)), and the IPCC through its structured scientific assessments on climate change, provide frameworks for formally assessing the risk that climate change poses to our society at national and international levels. The understanding of risks and vulnerabilities is vital in order to understand the necessity for climate change mitigation and adaptation and to prioritise the effective use of (often limited) public resources (Hess et al., 2014). The 2017 UK CCRA highlighted the effects of temperature on health as a priority area for the UK government. Work from this thesis has been cited in both recent IPCC reports (Hoegh-Guldberg et al., Roy et al., 2018) and the previous UK CCRA (Kovats and Osborn, 2016).

The hosting of COP26 by the UK in 2021, when countries are expected to increase the ambition of their NDCs, marks an important window of opportunity for policy making. The specific work on both current heat-health related risk (in terms of both mortality and YLL) and future heat related risk (Chapter 4) under the conditions of the Paris agreement (Chapter 5) in this thesis provides timely and relevant evidence that increasing ambition of Nationally Determined Contributions (NDCs) to cut carbon emissions can reduced heat related mortality. The current commitment to net zero could in itself bring about further public health benefits, if gains in health, wellbeing and equity are prioritised within GHG reduction policies (Cheng and Berry, 2013, Haines, 2012, Haines, 2017, Mayrhofer and Gupta, 2016, Patz et al., 2014), and provide further motivation for achieving the Sustainable Development Goals (SDGs) and prioritising public health in the post 2030 agenda.

The work from this thesis also has implications for current adaptation and mitigation policies. For example, in the chapter on thresholds, the consideration of the wide range of causal pathways operating across temperature at which cold deaths occur highlights the importance of a range of policies to reduce cold related mortality – from population level influenza vaccination programmes and the general management of risk factors for cardiac and respiratory disease within the population, through to improved thermal comfort in buildings or policies addressing fuel poverty. In 2011, Public Health England (PHE) introduced the cold weather plan (Public Health England.), with the aim of reducing adverse effects of the winter and cold on health through a series of levels of preparedness (from 0-4, with the weather alerts developed in conjunction with the UK Met Office issued at levels 2 and above) aimed at health and social care organisations and professionals (including the NHS, GPs, national level actors and the voluntary sector), communities and individuals. The results from Chapter 4 on cold thresholds and 5, along with other research in this area on current risk of cold temperatures to YLL and mortality (Hajat et al., 2016), highlight the importance of year round planning and winter preparedness (levels 0 and 1) to address some of the structural drivers of cold related effects on health (e.g. fuel poverty, ensuring flu vaccinations are taken up). These are especially important, given that the greatest burdens of cold weather occur outside temperatures used to trigger alerts in the CWP (where alerts are triggered for mean temperatures below 2°C). Additionally, in the conurbations studied here (Greater London, Greater Manchester and the West Midlands), cold effects on mortality started to appear at temperatures around 7-9°C depending on location. This, along with the sensitivity of the relative risk and cold burdens to threshold choice illustrated in chapter 4, raises questions about how to best define cold effects. For example, the question remains as to whether the same thresholds used to quantify the impact of cold on mortality are also useful for policy actions (e.g. defining levels at which to instigate actions or for looking at preventable deaths) - i.e. should we distinguish between epidemiological thresholds and thresholds for public health action? Thresholds for policy action and triggering cold or indeed heat alerts require a degree of practicality – if they are triggered too often (i.e. at warmer temperatures for cold thresholds) they may be less impactful or have implications for resources. However, set at lower temperatures, they are activated after the largest proportion of cold deaths have occurred. Therefore, a major implication of this work is that in addition triggering cold alerts, there is more that needs to be done across the UK to reduce cold related risks to health at temperatures outside alert periods

Importantly, the thesis did not demonstrate a decline in susceptibility to heat and cold in recent years. This has implications for the continued need for policies to address heat and cold adaptation both now and in the future. Regarding cold risk, it is possible that beneficial effects of the CWP weren't captured in the time period of the analysis in the thesis, though recent studies have suggested that whilst cold related mortality has decreased since the introduction of the CWP in the under 65s it has increased in the over 75s, and that geographical variability in cold related mortality has also increased (Murage et al., 2018). Taken together, these stress the importance not only of improved measures to reduce cold related mortality and morbidity but also measures to address inequities in this, such as policies on fuel poverty and housing standards, even within the context of climate change. Given other northern European countries have lower excess winter deaths by comparison (Fowler et al., 2015), there may be opportunities to learn from policies in other contexts. For the specific conurbations studied, this thesis has demonstrated the continuing high burden of cold related deaths and YLL. It has highlighted the need for local government commitment to improving indoor thermal comfort, addressing fuel poverty and the continuing need for embedding long term cold weather planning and preventative measures relating to the wider determinants of health across local authorities and within local public health strategies (such as highlighting fuel poverty and environmental health in Joint Strategic Needs Assessments, Director of Public Health reports and finding local solutions demonstrated in local Health and Wellbeing strategies). Taking effective preventative action requires working across local community partners, voluntary sectors, clinicians, citizens and local government through health and wellbeing boards, to bring about place based health plans to serve local populations (National Health Service (NHS). 2015).

This thesis also did not demonstrate a reduction in heat related mortality risk in the time periods analysed, which included time after the introduction of the Heatwave Plan (HWP). This is consistent with a recent evaluation of the HWP for England, which found little evidence for a reduction in the risk of annual heat related mortality outside heatwave events since the HWP's introduction (Williams L., 2019). The evaluation made further specific recommendations for the HWP, for example around public health messaging (amongst other recommendations) and implementation of the plan by service providers. The lack of reduction in current heat related risk, taken together with results from Chapter 5 of projected increases in mortality under conditions of the Paris agreement, demonstrate the need for system wide adaptation measures to heat both now and in the future and have implications at a more local level for public health and urban planning (in addition to national level policies). There are many interventions which may be introduced from the individual behavioural level, through to housing adaptations and interventions at a conurbation level to reduce ambient heat exposure, such as those which reduce the effect of the urban heat island effect through reflecting solar radiance (e.g. with cool roofs (Macintyre and Heaviside, 2019)) or increasing evaporative cooling through increased urban green and blue spaces (Heaviside et al., 2017). In the context of the three conurbations that are the focus of this research, the findings of this thesis (persistent heat related risks and projected increases in heatwave frequency and mortality, even under a 1.5 °C scenario) align with recommendations from the HWP evaluation to support and a review of capacity of local authorities and health and social care organisations to implement protective measures against heat-health impacts. As for cold related risks, commitment in local public health to addressing long term environmental risks, through inclusion of their importance in Joint Strategic Needs Assessments, Director of Public Health reports and understanding and implementing local public health solutions is important. Research has also highlighted the importance of behavioural, social and communication insights to reduce the health impacts of heat (Howarth et al., 2019). Local authorities and organisations are well placed to work with the local communities they serve to understand climate risks from a local populations perspective and to improve public health communication and messaging around the health risks of heat-waves, ensuring that these are locally and culturally relevant. Additionally, within local authorities and across organisations many opportunities exist to work across sectors and take a “health in all policies” approach and embed planning for heat-related risks across sectors and into business as usual. The need for sustained and committed action to mitigate current and potential future heat related risks demonstrated in this thesis supports joined up climate, environmental and health planning in local areas (i.e. healthy place shaping). For example, the London Environment strategy (Greater London Authority., 2018) highlights the inter-dependencies of climate risks and the increasing risk of heat-health impacts under climate change. It sets out specific actions to reduce risks of over-heating in existing and new housing developments and reducing heat exposure across the city, through minimal heat generation from buildings and a hierarchy of cooling mechanisms such as passive and mechanical building cooling, green and white roofs. It also highlights the importance of tree shading and green infrastructure. The London Plan (Spatial Development Strategy for London) highlights the need to create a healthier city, through tackling inequalities in the wider determinants of health and bringing health into spatial planning and reduction of future climate risks (Greater London Authority., 2020).

The UK’s commitment to rapid decarbonisation combined with the multiple public health challenges faced by the UK (such as rising levels of obesity, mental health challenges etc.), mean interventions with multiple co-benefits and those which also reduce health inequities would be the most desirable from a public health perspective (for example, well designed urban greenspaces (van den Bosch and Nieuwenhuijsen, 2017b, Wheeler et al., 2015, Rojas-Rueda et al., 2019, Twohig-Bennett and Jones, 2018)). Understanding the implications of many of these policies would benefit from a systems approach (see section 7.7.4) and allow for urban areas to make better progress towards the SDGs and in line with UN Habitat's New Urban Agenda (UN Habitat., 2016). Understanding contextual barriers and facilitators to adaptation within the local context will be important in translating this into concerted public health action, and taking a "health in all policies" is important where many health co-benefits are brought about through interventions outside the public health sector.

8.8 Concluding Statements

This PhD has quantified the current effects of ambient temperature on mortality and YLL in the three largest English conurbations. A systematic review demonstrated that in some locations the risk of heat related mortality has declined in recent years, though no consistent evidence for a reduction in cold risk was found. By contrast, analysis in this thesis did not support an attenuation in cold or heat related risk to mortality and YLL in recent years in the conurbations studied. This, along with the current burdens of heat and cold related YLL and mortality, has direct implications for the importance of public health planning and urban interventions to reduce preventable temperature related mortality. Projections of heat related mortality in these conurbations and the avoidable deaths under 1.5 degrees compared to 2 degrees of global warming is not only important for public health planning, but adds timely evidence to motivate increased ambition of NDCs under the Paris agreement. Many policies aimed at mitigating and adapting to climate change can have multiple co-benefits to public health, in addition to the direct benefits of reduced exposure to heat. The UK's current commitment to net zero emissions by 2050 and a green recovery from the COVID-19 pandemic, alongside hosting the COP26, could provide an important and unique window of opportunity to improve public health.

8.9 References

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APPENDICES

Appendix 1 - Supplementary material for Chapter 3

Table S1: Studies which examine the impact of heat on mortality in the United Kingdom

Study	Study Population (time period, region, age)	Methods and where reported threshold (either absolute °C or percentile of temperature distribution) and lag period	Exposure	Outcome(s)	Time varying confounders included in model	Results: % increase in mortality every 1 °C above threshold value (unless stated otherwise)	Comments
Hajat et al. 2002 [11]	1976-1996 London All ages	Time series regression Threshold was varied between 90th-99th percentiles of temperature distribution with little effect on the estimated RR. Results reported here are for the 97th percentile (21.5 °C). Lag 0	Daily mean temperature	All-cause mortality	Season, trends over time, day of week, public holidays, influenza.	All-cause mortality 3.34%(2.47, 4.23) Respiratory mortality 5.46% (3.43,7.52) Cardiovascular mortality 3.01% (1.73,4.32)	Threshold choice did not appear to affect estimate of RR but threshold choice will affect number of hot days included in analysis. Different lag periods tested (from 0-3).
Donaldson et al 2003 [12]	1971-1997 South East England All ages	Time series analysis Comparison of change in risk over time and threshold was allowed to vary between time periods.	Daily Apparent temperature	All-cause mortality: Daily mortality data converted into excess mortality compared to the monthly median mortality count.	Use of monthly mean as a baseline will have captured some monthly fluctuations in death rate, but no explicit control mentioned for other time-varying factors/confounders	Decrease in excess heat related mortality per 10^6 : 111(41,180) in 1971 decreased to 108 (41,176) in 1997. After adjusting for age and sex the decrease was larger (decrease of 53 excess heat related deaths).	
Pattenden et al. 2003 [10]	1993-1996 London (study also included data from Sofia) All ages	Time series regression Used 90th percentile of temperature distribution (21°C)to estimate heat effects and also produced estimates assuming a V shaped mortality-temperature relation (MMT) – where threshold for heat and cold days at 18°C Lags up to 25 days assessed	Daily mean temperature	All-cause mortality	Season, trends over time, day of week, public holidays, relative humidity, particulate matter.	All-cause mortality using 90th percentile as threshold 1.86% (1.36,2.36) All-cause mortality using 18°C threshold 1.30% (0.99, 1.62) Proportion of heat attributable deaths using 90th percentile as threshold – 0.44% (0.33,0.56) Proportion of heat attributable deaths using 18 °C as threshold – 0.82% (0.63,1.01)	
Goodman et al. 2004 [13]	1980-1996 Dublin All ages	Time series regression Threshold not reported Lag 0	Daily minimum temperature	All-cause mortality (excluding external causes) and cardiovascular and respiratory mortality	Season, trends over time, humidity, particulate pollution	All-cause mortality 0.4% (0.1,0.6) Cardiovascular mortality 0.0% (-0.4, 0.4) Respiratory mortality 0.8% (0.1,1.5)	Effect was also larger in older age groups

Hajat et al., 2005 [14]	1991-1994 London (study also included data from Delhi and Sao Paulo) All ages and by age category	Time series regression Threshold 20 °C Lag 0-1 but then examined deficits of deaths at longer lags to examine mortality displacement	Daily mean temperature	All-cause mortality and split by cause (cardiovascular, respiratory)	Season, trends over time, humidity, rainfall, particulate pollution, influenza A	Lag 0 All-cause mortality 1.4 (0.8, 2.0) Lag0-1 week All-cause mortality 0.9 (-0.2,2.0) Lag 0-4 weeks -1.6 (-3.4,0.3)	Sum of the heat effects by day 11 was 0
Carson et al. 2006 [15]	1900-1996 Time periods analysed in 10 year bands to assess the change in heat related risk over time London All ages	Time series regression Threshold 15°C	Mean weekly temperature	All-cause weekly mortality and by cause: cardiovascular and respiratory mortality	Trends over time and seasonality. excluded years of war and influenza pandemic For later period also included air pollution (PM10)	RR of all-cause mortality and % attributable deaths 1900-1910 1.02(-0.16,.21) 0.4% (-0.06,0.86) 1927-1937 1.53(0.152.93) 0.89%(0.09,1.69) 1954-1964 0.29(-1.95,2.59) 0.06% (-0.39,0.5) 1986-1996 -1.34(-1.94,-0.75) -0.9%(-1.31,-0.5)	Risk of heat related death decreased over time. Was highest in the period 1927-1937 and lowest between 1986-1996 The weekly data used meant that results may have been attenuated for heat affects
Hajat et al 2007. [16]	1993-2003 10 governmental regions of England and Wales Mortality data linked to census data to investigate sub-groups at risk (by, deprivation, persons living alone or nursing homes, sex etc.)	Time series regression Lag 0-1 Region specific thresholds selected.	Daily mean temperature	All-cause mortality	Season, trends over time, day of week, public holidays, ozone, influenza. PM10	All-cause mortality 3% (2.0,3.0)	Little effect modification by deprivation (as tested by quintile of deprivation) Effect stronger in urban compared to rural locations Those in nursing homes were at increased risk Women over 65 yrs at increased risk Deaths from respiratory and external causes most strongly associated with heat exposure
Page et al. 2007 [17]	1993-2003 England and Wales All ages	Time series regression used for overall heat effect. Also episode analysis for the effect of heat waves. Threshold 18°C	Daily mean temperature (Central England Temperature)	Suicide	Season, trends over time, day of week, public holidays, length of daylight	Suicide 3.8 % (2.1,5.6)	The increase in violent suicide was greater than non-violent suicide. Percentage increase of male and female suicide above the threshold was similar.
Baccini et al. 2008 [18]	1990-2000 (Dublin) 1992-2000 (London) London, Dublin (study included data from 14 European studies) All ages and by age category	Time series regression Warm season only Threshold: London 23.9 °C (22.6,25.1) Dublin 23.9 °C (20.7,27.1) Lag 0-3	Apparent temperature	All-cause mortality (excluding external causes)	Holidays, day of the week, calendar month, barometric pressure, wind speed, NO2	London 1.54 % (1.01, 2.08) Dublin -0.02 (-5.38, 5.65)	Harvesting was assessed – the cumulative effect of heat was only 30% of that at lag 0-3 compared to at lag 25
Ishigami et al 2008 [19]	1993-2003 London (study included 3 European cities)	Time series regression	Daily mean temperature	All-cause mortality and by cause (cardiovascular,	Season, trends over time, day of week, PM10, O3	Age <75 years: All cause 3% (2.0 ,5.0) CVD 3% (1.0,4.0) Respiratory 5% (1.0,8.0)	Heat effects greater in females across age categories

	All ages, split also into age category	Threshold 95th percentile Lag 0-1		respiratory and external)		External 6% (2.0,10.0) Age > 75 years: All cause 6% (5.0,7.0) CVD 6% (5.0,7.0) Respiratory 8% (6.0,10.0) External 10% (2.0, 18.0)	No obvious effect modification by deprivation (assessed by deprivation quintile)
Pattenden et al. 2010 [20]	1993-2003 15 conurbations in England and Wales All ages	Time series regression Summer only (May-Sept): Risk at 97.5th percentile of summer temperatures compared to 75th percentile 2 day mean of daily max temperature used	maximum temperature		Season, trends over time, day of week, PM10, O3	All ages: All cause: 7% (5.0,9.3) CVD 5.5% (2.5,8.7) Respiratory 13.9% (7.9,20.2) All cause: Age 65-74 6.7 (3.1,10.3) Age 75-84 9.2% (6.3,12.1) Age >85 12.4% (9.3,5.5)	Risk increased with age. There was an interaction between the effect of heat and ozone in London .
Armstrong et al. 2011 [21]	1993-2006 10 governmental regions of England and Wales All ages	Time series regression. Thresholds allowed to vary by region but also results presented for threshold at the 93rd percentile Lag 0-1	Daily mean temperature	All-cause mortality	Season, trends over time, day of week, humidity	Overall effect 2.1% (1.6,2.6) NE 0.8% (0.2,1.3) NW 1.3% (1.0,1.6) Yorks & Humberside 1.7% (1.3,2.1) Wales 2.0%(1.5,2.5) W Mids 2.2% (1.9,2.6) East Mids 2.3% (1.9, 2.8) SW 2.1% (1.7,2.5) SE 2.6% (2.2, 2.9) East 2.4% (2.0,2.8) London 3.8% (3.4,4.1)	Regions with higher temperatures had higher thresholds (in absolute °C – the threshold was at the 93rd percentile of the regional temperature distribution across the regions) Regions with higher summer temperatures showed greater increases in risk above the threshold
Gasparrini et al. 2012 [22]	1993-2006 10 governmental regions of England and Wales All ages	Time series regression Summer months Threshold 93rd percentile of temperature distribution Lag 0-1	Maximum daily temperature	Mortality by cause: cardiovascular mortality, endocrine mortality, respiratory, neurological mortality and genito-urinary causes	Trends over time, day of the week, within summer seasonal variation	% increase per °C increase above threshold: All cause 2.1 % (1.6,2.6) Selected causes: Cardiovascular diseases 1.8% (1.2,2.5) Stroke 2.5% (1.6,3.4) Ischaemic heart disease 1.7% (1.2,2.2) Myocardial infarction 1.1% (0.7,1.5) Pulmonary heart disease 8.3% (2.7,4.3) Respiratory deaths 4.1% (3.5,4.8) COPD 4.3%(3.6,5.1) Asthma 5.5% (2.8,8.3) Respiratory infections 4.2% (3.5,5.0) Endocrine 2.9% (1.7,4.2) Genito-urinary system 3.8% (2.9,4.7) Nervous system 4.6% (3.7,5.4) Heat deaths attributable to specific causes (n and %) : Cardiovascular 8005 (33.9%)	Heat slopes higher for London and other regions with higher mean temperatures.

						Stroke 2864 (12.1%) Ischaemic heart disease 3725 (12.1%) Myocardial infarction 1121 (4.1%) Pulmonary heart disease 37 (0.2%) Respiratory deaths 5841 (24.1%) COPD 1821 (7.7%) Asthma 133 (0.6%) Respiratory infections 3194 (13.5%) Endocrine 446 (1.9%) Genito-urinary system 732 (3.1%) Nervous system 1118 (4.7%)	
Page et al 2012 [23]	1998-2007 UK patients registered on the UK General Practice Research Database (GPRD) with psychoses, dementia, alcohol misuse and other substance misuse All ages	Time series regression Threshold 93rd percentile of temperature distribution Lag 0	Average daily temperature	Mortality (all-cause) in this subgroup of patients)	Trends over time, season, humidity, day of week	Overall effect 4.9% (2, 7.8)	Effect modifiers – age and diagnosis: those under 65 were at greatest risk and those with primary diagnosis of alcohol misuse or other substance misuse Effect size was largest in the South East and East midlands
Baccini et al 2013 [24]	1990-2000 (Dublin) 1992-2000 (London) London, Dublin (study included data from 14 European studies) All ages	Attributable deaths from the PHEWE study (Baccini et al 2011) were translated into Years of Life Lost (YLL)	Daily maximum apparent temperature	YLL	As per Baccini et al 2008	YLL attributable to heat before accounting for harvesting (across all ages): London 1914 (1033,2841) Dublin 7 (1,15) YLL attributable to heat after accounting for harvesting (across all ages): London 356 (219,498) Dublin 1 (0,2)	Estimates were adjusted for the 'harvesting' effect. Study found that harvesting had a greater effect on results in the North continental than Mediterranean cities. This could reflect differences in frailty between populations, or a lack of further recruitment of frail individuals into the high risk pool in the North continental region. Also, the thresholds for models were lower in North continental regions – more frail individuals could be more sensitive to lower threshold and therefore harvesting in the Mediterranean could have been under-estimated.
Bennet et al. 2014 [25]	2001-2010 376 local authority districts in England and Wales All ages and by age category	Time stratified case-crossover District specific thresholds at 85th percentile of temperature distribution (based on summer temperatures – range of thresholds used from 15.4 °C to 19.9 °C)). Results also analysed using a common threshold of 18 °C.	Daily Mean Temperature	Cardio-respiratory mortality	Control days on same day of week selected for each death and same calendar month. PM10 controlled for	National level increase in OR of cardiorespiratory mortality: Men: <75 yrs 2.7 (1.6,3.8) 75-84 yrs 2.2 (1.1,3.2) >85 yrs 2.4 (1.2,3.6) Women: 2.4 (1.0,3.9) 3.4 (2.3,4.6) 3.9 (3.0,4.8)	Deprivation measure on the Carstairs score – combines indicators of unemployment, crowding of housing, social class and vehicle ownership. Variables of greenspace and of urban/rural residence also assigned to deaths.

						Effects of hot weather varied across districts#; London, South and South East were most affected	
Vardoulakis et al. 2014 [26]	1993-2006 10 governmental regions of England and Wales All ages	Time series regression Threshold 93rd percentile Summer months only analysed Lag 0-1	Daily mean temperature	All-cause mortality (including external causes)	Trends over time, season, humidity, day of week	All-cause mortality 2.5% (1.9,3.1)	
Guo et al. 2014 [27]	1993-2006 10 governmental regions of England and Wales (study included data from 12 countries/regions) All ages	Time series regression Estimates are for the 99th vs 80th percentile of temperature distribution and for 99th vs 90th percentile Lag 0-21 days (heat and cold effects modelled)	Daily mean temperature	All-cause mortality (excluding external causes)	Trends over time, season, , day of week	All-cause mortality 99th vs 80th percentile: 5% (4.0,6.0) All-cause mortality 99th vs 90th percentile: 3% (3.0, 4.0)	Minimum mortality temperatures were estimated to be around the 75th percentile of the country-specific temperature distribution for all countries included in the study
De'Donato et al. 2015 [28]	1996-2002 and 2004-2010 London (study included data form 9 European cities)	Time series regression. Purpose of study was to compare risk of mortality before and after the heatwave of 2003 (in 2004 the HW plan was introduced). Estimates are for the 75th vs 99th percentile of temperature distribution	Daily mean temperature	All-cause mortality (excluding external causes) And deaths attributable to heat	Trends over time, season, humidity, wind speed, barometric pressure, NO2	1996-2002 All cause 2 %(1.6,2.5) 2004-2010 All cause 1.8% (1.12,1.23)	No significant difference in the estimated relative risk of mortality above the threshold temperature for the two time periods. Some cities in the study did have a reduced risk in the later time period (Athens, Rome, Paris)
Gasparrini et al 2015 [29]	1993-2006 10 governmental regions of England and Wales (study included data from 12 countries/regions) All ages	Time series regression (DLNM). Threshold (MMT) 90th percentile of temperature distribution. Location specific RR were pooled using multivariate meta-analysis. Attributable deaths and fraction of attributable deaths calculated from RR and contribution of days in the series above the MMT. Contribution of extreme heat also assessed (temperatures greater than the 97.5th percentile)	Daily mean temperature	Deaths attributable to heat	Trends over time, season, , day of week	All-cause mortality: Fraction of all deaths attributable to heat 0.30% (0.25,0.36)	MMT percentile ranges between 80th-90th percentiles of the temperature distribution for each region

Gasparrini et al. 2015 [30]	1993-1999 2000-2006 10 governmental regions of England and Wales (study included data from 12 countries/regions) All ages	Time series regression (DLNM). Threshold (MMT) 73rd percentile. RR at the 90th percentile vs 73rd percentile estimated Analyses restricted to summer period	Daily temperature	All-cause mortality	Trends over time, season, , day of week	RR at 90th vs 73rd percentile of temperature distribution 1993-2006 1.006 (0.993,1.019) 1993 1.005 (0.983,1.027) 2006 1.014 (0.995,1.032) RR at 99th vs 73rd percentile of temperature distribution 1993-2006 1.167 (1.108,1.230) 1993 1.158 (1.093,1.227) 2006 1.168 (1.111,1.229)	Difference in RR between the two time periods not significant for the UK (but a significant reduction in risk was seen for Japan, Spain and the US – p<0.001)

Table S2: Studies which examine the impact of heat on morbidity outcomes (health outcomes other than mortality) in the United Kingdom

Study	Study Population (time period, region, age)	Methods And where reported threshold (either absolute DC or percentile of temperature distribution) and lag period	Exposure	Outcome(s)	Time varying confounders included in model	Results: increase in morbidity outcome every 1 °C above threshold value (unless stated otherwise)	Comments
Kovats et al. 2004 [32]	1994-2000 Greater London All ages and by age category	Time series regression Modelled above a threshold – threshold varied by cause of hospital admission (12 °C for all-cause admissions) Lag 0-2 days	Daily mean temperature	Emergency hospital admissions – all cause and cause specific (cardiovascular, respiratory, cerebrovascular, renal – acute renal failure and kidney stones)	Long term trend, season, public holidays, day of week, relative humidity, pollution (ozone and PM10)	All cause -0.4% (-0.22, 0.13) Cardiovascular 1.71% (-2.70,6.33) Respiratory 5.44% (-1.55,-0.21) Renal 1.30% (0.27,2.35) Respiratory > 75 yrs 10.86% (4.44,17.67) During 1995 HW, small increase in hospital admissions – 2.6% (96% CI -2.2, 7.6)	Thresholds varied by cause of hospital admission (e.g. all cause – threshold at 12 °C, respiratory threshold was 23 °C). Risk of respiratory admission was increased with hot temperatures for all age categories.
Atherton et al. 2005 [34]	1998 Leicester (population admitted to Leicester Royal Infirmary) All ages and by age group (adult, paediatric)	Time series regression No information on threshold or lag	Maximum and minimum temperature	Total trauma admissions, adult and paediatric trauma admissions, adult neck of femur (NOF) admissions	Season, day of week, weekends and public holidays, month, school holidays	For each 5 °C rise in Max temperature Incidence Rate Ration (IRR): All trauma admissions 1.03 (0.99,1.07) Paediatric trauma admissions 1.11 (1.03,1.19). For each 5 °C rise in Min temperature IRR: Paediatric trauma admissions 1.24 (1.12,1.38).	
Lee et al. 2008 [39]	1988-2000 London All births on the	Time series regression Lag 0-6	Daily maximum temperature Exposure defined in relation to birth (i.e. temperature in 6 days preceding birth, rather than exposure in a given trimester or stage of pregnancy)	Preterm birth (occurring <37 weeks gestation)	Long term trend, season, public holidays, day of the week, PM_{10}, ozone	No evidence of an association between increased temperatures in the 6 days prior to birth and pre-term birth.	
Bhaskaran et al. 2010 [36]	2003-2006 15 conurbations in England and Wales	Time series regression Lag 0-1	Daily mean temperature	Myocardial infarction (MI) : all events with diagnosis of ST elevation and non-ST elevation MI on discharge or positive troponin	Long term trend, season holidays, day of week, influenza, respiratory syncytial viruses, PM_{10} , ozone	No evidence of an increased risk of myocardial infarction with heat	
Parsons et	1996-2006	Time series regression	Daily	Total adult and	Season, day of	For each 5 °C rise in Max temperature	No confidence intervals or

al. 2010 [35]	England and Wales All ages and by age group (adult and paediatric)	No information on threshold or lag	minimum and maximum temperature	paediatric trauma admissions	week, public and school holidays, year,	and increase in adult trauma admissions of 1.8% and of paediatric admissions of 10%.	significance reported
Thornes et al. 2014 [38]	2007-2011 Birmingham All ages	Compares daily temperature with ambulance call out data, but not as a full time series regression analysis (looks at correlation only without adjustment for other time varying factors).	Daily minimum, mean and maximum temperatures	Ambulance call outs and response times (categorised as total number of 999 calls for one day, total category A calls (life threatening) % of category A calls responded to within 8 mins, average travel time to arrive at incidences	None	Observed reduction in % of category A responses within 8 minutes at increasing temperatures (not quantified). During the 2003 heatwave there was a linear (positive) relationship between increasing maximum temperature and 999 calls.	Daily ambulance calls can be affected by the number of ambulances and staff on duty, business of A and E departments, road conditions, call volume and distance to the event which precipitated the call out
Bhaskaran et al. 2014 [37]	2003-2009 11 conurbations in England and Wales	Time-stratified case crossover Threshold 20°C 0-6 hours	Hourly temperature	Myocardial infarction (MI) : all events with diagnosis of ST elevation and non-ST elevation MI on discharge or positive troponin	Nitrogen dioxide, relative humidity, public holidays, day of the week, seasonality	Odds ration (OR) for MI at 1-6 hours: 1.019 (1.005,1.033)	Effect at 0-6 hours but not seen at longer lags is likely due to short term displacement. No significant effect modification seen by individual level factors such as whether patients had previous heart disease, were taking aspirin or had previous hypertension.

Appendix 2 - Supplementary material for Chapter 5

Table S1a: Features of Studies Examining Changes in Heat and Cold Susceptibility over Time

Study	Time period analysed	Population details: Location Age	Exposure(s) assessed and metric	Health outcome(s) Measure	Modelling approach for baseline estimates	Time varying factors &Lag periods	Sensitivity analyses
Bobb et al., 2014 [37]	1987-2005	105 US cities All ages Stratified by age group (<65yrs 65-74 yrs., >75 yrs.)	Heat only (only summer months) Metric: average daily temperature	Daily all-cause mortality (excluding external causes) Mortality by cause: Cardiovascular and Respiratory Expressed as heat related excess deaths per 1000 deaths	Time series regression (daily series) - 2 stage model: 1)city specific coefficients estimated 2) estimated excess heat related deaths for each year: i.e. each year allowed a different co-efficient on daily temperature (results compared for 1987 and 2005) City estimates combined to give overall average	Day of week and seasonal variation Long term trends (natural cubic spline 2df/3months) Air pollution not in main model (sensitivity analysis) Lag 0	Explored the relationship over time constraining it to be linear and without linear constraints Sensitivity analysis controlling for ozone and fine particular matter presented in supplementary materials. Note: with control for fine PM and ozone, there remained a significant reduction in heat related deaths in the flexible model, but not in the linear model when controlling for fine PM
Petkova et al., 2014 [36]	1900-1948 and 1973-2006	New York (US) All ages Stratified by age group (>15 yrs., 15-44 yrs. 45-64 yrs. >65 yrs.)	Heat only (only summer months) Metric: average daily temperature	Daily all-cause mortality Expressed as RR of mortality at 29 °C vs 22 °C	Time series regression (daily series) a) used distributed lag non-linear model to characterise temperature-mortality relationship over the two time periods b) modelled risk of mortality at 29°C vs 22°C for each decade	Day of week and seasonal variation (quadratic spline - 4 degrees of freedom (d.f.) Long term trends (natural spline 2 d.f.) Seasonal variation (natural spline with 4 d.f.) Air pollution not in model Lag of 5 days selected.	Tested models with both quadratic and natural cubic splines found quadratic splines gave better model fit. Varied d.f. for quadratic splines. within-summer Lags between 3-10 days considered.
Astrom et al., 2013 [39]	1901-2009	Stockholm, Sweden All ages Stratified by sex and age group (0–14yrs, 15–65yrs 65–79yrs 80+yrs)	Heat and cold 'extremes' Temperature extremes defined in main model (model 1) as above/below the 98th percentile for the entire period	Daily mortality Expressed as RR of mortality at 98th percentiles of temperature compared to mortality at average temperatures	Time series regression (daily series) Thresholds used as defined Modelled risk at extremes compared to bassline temperatures for heat and cold	Day of the week and public holidays long term trend (4 d.f. per year) binary variable for flu pandemics binary variable for when data are (in) complete (before/after 1947) Air pollution not in model	Sensitivity analysis: model 2 presented where extremes were defined as being above/below the decadal threshold rather than the 98th percentile for the whole time frame Sensitivity analyses of the estimated heat and cold coefficients using 300, 350, 450, and 500 d.f. for the smoothing parameter.
Ha et al., 2013 [38]	1993-2009 (exception of 1994 due to extreme heatwave)	Seoul, south Korea All ages Stratified by age: analysed data for >65 yrs. Used direct standardisation to standardise age/sex	Heat only Metric: average daily temperature Also assessed the effect of hot temperatures in early vs late summer	Daily all-cause mortality (excluding accidental deaths) Mortality by cause: cardiovascular mortality	Time series regression (daily series) a)used linear threshold model to analyse quantitative effects – threshold determined by data b)used natural cubic spline (NCS) function to assess the temperature–mortality relationship Model included indicator terms for each year Used a common threshold temperature value during the study period.	Day-of-week and holiday Seasonal variation (natural cubic spline function with 3 d.f.) Long-term trends (15df for 16 yrs.) Average daily humidity on the current and previous day (0–1 day lag) Air pollution not in model Lag 0	N/A

		with the Seoul 2009 population					
Matzarakis et al., 2011 [40]	1970-2007	Vienna, Austria All ages	Heat only Metric: Physiological equivalent temperatures (PET)	All-cause mortality	Time series analysis (daily series) Daily excess mortalities compared to baseline mortality /deviations from the average annual mortality: used baseline for average annual deaths calculated for each year to account for changing Life expectancy, etc.	Baseline used: average annual death rates No explicit control for other time varying short-term factors (e.g. air pollution, day of week etc.)	N/A
Christidis et al., 2010 [41]	1976-2005	England and wales All ages	Heat and cold Metric: Central England Temperature	All-cause mortality per million of population	Daily excess heat/cold related mortalities obtained by comparing to the average mortality within a 3 °C 'comfort zone' Used optimal detection to also examine contribution of warming climate and anthropogenic emissions under 3 different models : a) ALL - modelled weather data (HadGEM1) with anthropological & other forcing b) anthro - only anthropological forcing in modelled data c) actual data	No explicit control for other time varying short-term factors (e.g. air pollution, day of week etc.)	Sensitivity analyses carried out to check whether year choice affects results
Ekamper, 2009 [42]	1855-2006	Zeeland, Holland All ages Stratified by age: 1-4 yes, 20-49 yrs., 50-74 yrs., > 75yrs	Heat and cold Mean daily temperature	All-cause mortality	Times series analysis (negative binomial distribution) using daily mortality and daily temperature Thresholds used and allowed to vary for each 25 year time period analysed	Long term trend (using cubic smoothing spline, 7 d.f. per year) seasonal pattern (using sine and cosine functions) Excluded years of exceptionally high mortality: e.g. world war 2, 1918 flu epidemic etc. Results for lags 1-2.3-6, 7-14 and 15-30 days given.	Results from models of each lag period presented.
Barnett, 2007 [43]	1987-2000	107 US cities 'Elderly' (age range not given)	Increases in temperature in both summer and winter (i.e. examining effects of heat & cold) Temperature metric not given	Daily Cardiovascular mortality	Case-crossover design Time stratified	Day of week Humidity No influenza/air pollution	N/A
Carson et al., 2006 [44]	1900-1996	London (UK) All ages	Heat and cold. Metric: Mean weekly temperature Health Outcome:	Weekly all-cause mortality Mortality y cause: cardiovascular and respiratory mortality	Time series regression Linear hockey stick model using a threshold of 15 °C	Secular trends and seasonality: 7df per year for natural cubic splines excluded years of war and influenza pandemic For later period also included air pollution (PM10)	Controlling for air pollution and influenza For 1992–1996, % increase in mortality per °C below cold threshold was 1.27 (0.86, 1.68) without adjustment for air pollution or influenza, 1.27 (95 percent CI: 0.86, 1.69) controlling for weekly meanPM10, and 1.32 (0.90, 1.75) with additional adjustment for influenza A. In 1954–1964, the figures were 1.64 (1.10, 2.19) without adjustment for pollution,

							1.85 (95 percent CI: 1.30, 2.40) with adjustment for particulate pollution measured by the Owen's Smoke Filter, and 1.91 (95 percent CI: 1.30, 2.52) with pollution adjustment and omission of years with high influenza counts.
Davies et al., 2003 [46]	1964-1998	28 major US cities (Metropolitan Standardised Areas) Age standardised population	Heat only Metric: Apparent temperature (AT)	Daily all-cause mortality expressed as excess heat related mortality	Time series analysis: Analysed daily fluctuations in excess mortality with variation in temperature: converted daily mortality data (age standardised) to daily mortality anomalies by subtracting from each days mortality count the median mortality count for any given month Threshold for analysis was determined as the AT at which mortality rates were significantly higher than baseline rate. Threshold was allowed to vary between decades. For each city, excess death rates for all cities above threshold were summed by decade then averaged to give the city specific decadal mean	Monthly fluctuations in death rate captured by using monthly mean as baseline No explicit control for other time varying short-term factors (e.g. air pollution, day of week etc.)	N/A
Donaldson et al., 2003 [45]	1971-1997	North Carolina (NC) SE England (SEE) South Finland (SF) Age: over 55 years Models reported as adjusted for age/sex	Heat only Metric: daily mean temperature	Daily all-cause mortality expressed as heat related deaths	Time series analysis 3 °C minimum mortality threshold band determined Excess heat related mortality calculated as: mortalities at daily temperatures which exceeded the 3 °C threshold band, minus the daily mortality in that 3 °C band for the given month. Summed to give annual heat related mortality	Monthly fluctuations in death rate captured by using monthly mean as baseline No explicit control for other time varying short-term factors (e.g. air pollution, day of week etc.)	With and without controlling for age and sex changes between time periods.

Table S1b: Results of studies examining the change in heat/cold susceptibility over time

Study	Methods used to assess change in vulnerability over time	Temperature changes over time (°C)	Health outcomes (all CI/PIs and significance are reported for 95% level unless stated otherwise)	Explanatory factors where offered for changes in vulnerability
Bobb et al., 2014 [37]	Compared yearly excess heat related mortality over time period: Each year allowed a separate coefficient for daily temperature but constrained over time to be linear (sensitivity analysis included where no linear constraint)	Not reported	Heat related deaths per 1000 deaths: Combined results from all cities 1987 51 (95% PI:42,61) compared to 19 (95% PI: 12,27) in 2005 Overall reduction (all cities): 32 (18,45): significant at 95% level 74 of 105 cities displayed reduction in heat related mortality: one area Southern California the risk increased but not significant. In 18/105 cities temporal decline in mortality was statistically significant Nationally: excess heat related mortality declined for all age groups (<65,65-75, >_75) but for <65s non-significant Decline significant for excess heat related respiratory & cardiovascular mortality. Cities with cooler climates having larger temporal declines though these cities also had larger risks at the beginning of study period. Temporal trend slowed after year 2000	The % of homes with AC increased over all 79 cities – by around 1% per year Cities with larger increases in AC had larger decreases in mortality but association not significant Using excess deaths as an outcome means daily temperature changes/fluctuations in a given year contribute to magnitude of results so the changes in risk alone are difficult to assess. However, given that temperatures are unlikely to have decreased, this would be expected to increase excess deaths rather than lead to a declining trend The decrease in cardiovascular/respiratory heat related deaths may in part reflect decreasing risk factors for cardio-respiratory diseases in the population and better care (that are not picked up in the overall trend term included in the model)
Petkova et al., 2014 [36]	Compared RR at 29°C vs 22°C over time using decadal averages of the RR Random effects meta-regression, including a linear term for decade	Mean annual temperature(°C) 1900s 11.9 1910s 11.7 1920s 11.8 1930s 12.5 1940s 12.3 1970s 12.6 1980s 12.9 1990s 13.2 2000s 13	Results of random effects meta-regression showed a decrease in RR at 29°C vs 22°C (all ages) of 4.6% (2.4,6.7) per decade Reported more pronounced heat effects on mortality in first part of the century > 65 yrs.: highest initial risk and experienced most decline over time Harvesting effect: more prevalent in early part of population	Found a change in lag structure over time - harvesting effect more prevalent in the early part of the century - paper concludes because most vulnerable no form of protection in the earlier part of the century. Factors hypothesised for decrease in RR: Improvement in housing conditions, especially through the first part of the century, innovations such as refrigeration, and air conditioning: in 1970, 39% of surveyed households in New York had air conditioning and by 2003 this was 84% households
Astrom et al., 2013 [39]	Examined trend in RR of mortality at 98th percentiles of temperature compared to mortality at average temperatures. Sensitivity analysis – model 1 vs model 2 (model 1 – temperature extremes defined relative to whole baseline period,	Mean summer temp (°C) 1900s 15.1 1940s 16.6 1980s 16.2 2000s 17.5 Mean winter temp(°C) 1900s —2.2 1940s 3.5 1980s 0.3	Trends similar for men & women Significant declining trend in temperature related mortality risk for 0-14s for hot and cold Significant declining trend in risk for elderly and combined age categories for heat but non-significant for cold extremes In last decades, an upward trend in the heat risk for the 15-64 age group was observed	Death records around 46% incomplete until 1946 but authors expect variation in day to day deaths the same Life expectancy in Stockholm over the study period has increased from 56 years to 81 years No formal/quantitative attribution of declines in heat related mortality to given factors. However, potential explanations include improvements in health sector, urban design and population adaptation

	model 2 extremes defined relative to decade)	2000s 1.7	Models 1 & 2: model 1: generally reports higher estimates of risk than model 2 in the earlier parts of the century. Model 2 reports higher risks in the later part of the century. Potentially due to higher temperatures over time.	Regarding model 1 and model 2: Model 2 implicitly includes some aspect of 'adaptation' to increasing temperatures and accounts for increased temperatures over time
Ha et al., 2013 [38]	Divided the time series into two periods (1993 and 1995–2000, and 2001–2009) and included an interaction term for each study period Used a common threshold temperature value during the study period.	Average daily mean temperatures over 17 year study period: 24.4, 23.1, and 25.7 °C for summer, early summer, and late summer No increasing or decreasing trends in daily mean temperature reported.	Regarding 'high' temperatures (above threshold) the % increase in all-cause mortality per 1 °C increase in temperature above threshold: All-cause mortality 1990s 4.73 % (all ages) 2000s 6.05% (all ages) and 6.78 % (over 65s) 1990ss 6.78 % (over 65s) 200s 7.89 % (over 65s) Change not significant at the 95% confidence level CVD mortality 1990s 8.69 % (all ages) and 2000s (all ages) 5.27 % 1990s 10.47% (over 65s) and 7.29 %(over 65s) Change not significant at the 95% confidence level For all summers combined: associations with higher temperatures are stronger for the > 65 years and for CVD related mortality than for all-cause-related mortality (all ages).	Proportion of houses with air-conditioning in Seoul increased from 15 % to 71 % between 1994 and 2009 Total health expenditures were also associated related to the observed decline in temperature-related mortality Declines in temperature-related mortality were particularly noteworthy for late summer: possibility this represents intra-seasonal acclimation improving over time.
Matzarakis et al., 2011 [40]	linear regressions fitted to the mortality rates per 10 000 to assess % change per decade from 1970 to 2007 in relative mortality for given ranges of PET t test for the slope of the regression line and non-parametric Mann-Kendall test	Not reported	only the change in relative mortality as a % per decade reported in paper % change per decade from 1970 to 2007 in relative mortality for each PET range: <29°C - 0.15%: (CI not given: reported not significant) 29-35°C -0.83% (-0.68,-0.97) 35-41°C -0.96% (-0.77,-1.16) >=41°C -1.32 % (CI not given: reported not significant - low numbers)	Baseline mortality for the year may take into account some of the expected life expectancy /age structure but likely to have some residual confounding No age categories, therefore given that age above 60 years decreased from 1970-1990 as a proportion of the population and then increased after that, difficult to remove this effect No qualitative explanations for why sensitivity might be decreasing given
Christidis et al., 2010 [41]	2 comparisons given in paper: Compared the regression slopes (yearly) obtained from analysis over the time period for relationship between daily mortality per million population and daily temperature:	Data showed an average of 0.47°C warming per decade	slope of regression line for heat related mortality risk (SE in brackets) 1976 5.380 (0.574) 1996 2.616 (1.145) 2005 0.866 (0.970) Slope of regression line for cold related mortality risk (SE in brackets) 1976 -3.437 (0.243) 1996 -2.085 (0.158) 2005 -1.489 (0.112)	Sensitivity analyses carried out to check whether year choice affects results Lack of control for common time varying factors may have led to an over or underestimation of effects

	each year from 1976-2005 Change in heat/cold related deaths. Compare actual deaths from latest year with those that would have been obtained using regression slope from earlier years to act as a proxy for 'adaptation'.		Cold related mortality (CRM) decreased by 85 deaths per million per year from 1976-2005. In scenario with adaptation (2005 linear slope used) CRM reduction would have been more moderate: 47 deaths/million/year. Heat related mortality (HRM) increased by 0.7 deaths per million per year using the 2005 slope but under no adaptation scenario (1976 slope) HRM would have increased by 1.6 deaths per million per year. no appreciable change in MMT but done as a 3°C band	
Ekamper et al., 2009 [42]	Compare regression co-efficient from model between 25 year periods Compare MMT value in each 25 year time period analysed.	Daily mean Temperature (°C) 1855-79 9.9 1880-1904 10 1905-29 10.1 1930-1954 10.1 1955-1979 9.9 1980-2006 10.7 Number days with max temp > 25°C 1855-79 9 1905-29 7.2 1955-1979 7.7 1980-2006 15.8	Regression coefficients for heat related mortality Reported as decreasing over time – no test for significance: pattern apparent at lag 0 Pattern unclear (for a decreasing trend in regression co-efficient) for cold Decrease in heat related mortality reported to be start to disappear after 1930 Found shift in MMT to higher temperatures in later time periods analysed: MMT slightly below 15 °C for 1855-1897 and around 17°C for 1905-1929 and 1930-1954	Strongest temperature mortality relationships were for unskilled workers
Barnett, 2007 [43]	Compare the % increase in of cardiovascular deaths per 10 °F increase in temperature within a given season and across the time period 1987-2000	Not reported	% increase in risk per 10 °F rise in temperature summer 1987 4.7% (3.0, 6.5%) 2000 -0.4% (-3.2,2.5) Winter 1987 -4.2 (-5.1,-3.2) 1987 -4.9 (-6.8,-3.1) Change in deaths by geographical region: biggest declines in NW, NE, Industrial Midwest and Southern California: also the regions with highest summer mortality in 1987 Winter - little change over time in all regions except in Industrial Midwest where mortality risk with cold got worse, and in Southern California where it improved	Summer time- increase in temp associated with significantly smaller increase in mortality over the time period - hypothesised due to air conditioning or changes in health care. Winter time - little change in temperature and death relationship - hypothesised that improvements in standard of living were either not useful in decreasing deaths or not sufficient Effect of not controlling for influenza in winter time deaths in CVD mortality is unclear. There is some evidence that influenza vaccine is associated with a decreased risk of acute cardiovascular events but not conclusive (Warren-Gash et al. 2009)
Carson et al., 2006	Compared	Annual mean temperature(°C)	RR (CI) for heat related mortality and % attributable deaths	As using weekly data for analysis results for heat may have been attenuated, especially over the last half of the century when heat related

[44]	a) decadal RR and heat and cold related mortality over the time period and b)proportion of deaths attributable to heat/cold over the time period Threshold fixed at 15 °C for whole time period.	1900-1910 10 1927-1937 10.4 1954-1964 9.6 1986-1996 10.8 1900-1910 10 1927-1937 10.4 1954-1964 9.6 1986-1996 10.8	1900-1910 1.02(-0.16,.21) 0.4% (-0.06,0.86) 1927-1937 1.53(0.152.93) 0.89%(0.09,1.69) 1954-1964 0.29(-1.95,2.59) 0.06% (-0.39,0.5) 1986-1996 -1.34(-1.94,-0.75) -0.9%(-1.31,-0.5) RR (CI) for cold related mortality and % attributable deaths 1900-1910 2.52 (2, 3.03) 12.5%(10.1,14.9) 1927-1937 2.34 (1.72,2.96) 11.2%(8.4,14.0) 1954-1964 1.64 (1.10,2.19) 8.74%(5.93,11.5) 1986-1996 1.17(0.88, 1.45) 5.42% (4.13,6.69) Threshold fixed at 15 °C for whole time period. This was best fit with the data for the first 3 decades but for the 19 °C was a better fit	deaths may have been less due to GI/bacterial causes. Likely less relevant for cold as less prone to harvesting Found decreasing vulnerability to heat/cold despite increasing elderly population. Epidemiological transition For all causes of heat related death and for Cardiovascular/respiratory the general pattern is that the RR is lowers in the last decade: 1986-1996 but highest in the period 1927-1937. However for non-cardio-respiratory deaths there is a more convincing pattern of decline – possibly because at the beginning of the century more heat related deaths were due to GI/diarrheal causes.
Davies et al., 2003 [46]	Compared excess heat related mortality across decades Threshold above which heat effects were calculated was allowed to vary between decades.	Summertime trends in Apparent Temperature between 1964-1998: Significant increase in 9/28 cities (mostly in the Southern United States). In 19 other cities there was a trend of increasing AT but it was not significant.	Excess heat related deaths (+/- SE) in standard population of 1 million 1964-1966 & 1973-1979 41.0 (4.8) 1980-89 17.3(2.7) 1990-1998 10.5 (2.0) By 1980s, mortality rates declined in 41% of the cities that had elevated mortality a decade earlier Cities in the Northeast and Great Lakes had remaining excess deaths in 1990s but some decline Cities in West Coast - Seattle, Washington - actually increased excess deaths in the latest decades compared to the 1960s 12 cities showed no evidence of threshold AT above which heat related mortality begins to appear, in the 1990s. These were mostly in the South and SE.	Likely to be residual confounding from incomplete inclusion of time varying factors in model (mean monthly mortality used as baseline). Air conditioning prevalence for all regions except one increased during 80s-90s. Excluding the one region without air conditioning statistics- excess heat related mortality decreased by 1.14 deaths/year (per standard million population) for every one % increase in home air conditioning Some areas in the Us have reached 100% air con saturation Hypothesised (qualitative) reasoning given by authors for decreasing mortality: Improved urban planning and architecture, biological acclimatisation air conditioning
Donaldson et al., 2003 [45]	Analysed 2 factors: Change in temperature at which minimum mortality occurs Change in excess heat related mortality per 10^6 between 1971 and 1997 Regression analysis undertaken with the year as an explanatory variable	Changes in mean summer temperature between 1971-1997 (°C) (in brackets 95% CI for change): Northern California +1°C (0,2) South Finland 0°C (-1.5, 1,5) SE England +2.1°C (0.3,4.0)	Changes in Minimum Mortality Temperature over time: MMT : 1971 t then change between 1971 and 1996 first without control for age/gender second with control Northern California: MMT 25.3 °C in 1971, increased by 3.6 °C (significant at 5% level) South Finland 15.2°C increased by 1.3 °C (not significant) South East England 18.0°C increased by 2.7 °C (significant at 5% level) Changes in Excess heat related deaths per 10^6 unadjusted& adjusted for changes in age/sex: NC in 1971: 228 (140,317) decreased to 16 (-74,104) in 1996 representing a: decrease of 212 (59,365). Adjusted for age/sex decrease of 552 (significant at 95% level) SF in 1971 382 (257-507) decreased to 99 (-26,225) in 1996 representing a change of 282 (66-500). Adjusted for age/sex change of 414 (significant at 95% level)	Likely to be some residual confounding as taking monthly mean deaths as the baseline unlikely to have controlled for all other time varying factors other than temperature)

			SEE In 1971: 111(41,180) decreased to 108 (41,176) in 1996 representing a decrease of 2.1 (-119, 114). When adjusted for age/sex the decrease was 53 (significant at the 95% level)	

Appendix 3 - Supplementary material for Chapter 6

Table S1: Heat and cold related mortality risk by age category

Conurbation and Time Period	Threshold value	RR of Mortality (95% CI)	Mortality burden (AF) for temperature related Mortality within each age category (% of overall mortality)	RR of Mortality (95% CI)	Mortality burden (AF) for temperature related Mortality within each age category (% of overall mortality)	RR of Mortality	Mortality burden (AF) for temperature related Mortality within each age category (% of overall mortality)
Greater London: heat risk		0-65 years		65-74 years		Over 75 years	
Total	18.9	1.022 (1.014, 1.030)	0.299	1.024 (1.016, 1.032)	0.312	1.049 (1.044, 1.054)	0.612
Male		1.025 (1.016, 1.035)	0.341	1.020 (1.008, 1.030)	0.249	1.035 (1.028, 1.043)	0.444
Female		1.017 (1.005, 1.030)	0.231	1.031 (1.018, 1.044)	0.401	1.058 (1.052, 1.065)	0.733
Greater London: cold risk		0-65 years		65-74 years		Over 75 years	
Total	9	1.019 (1.011, 1.027)	2.006	1.027 (1.018, 1.035)	2.893	1.034 (1.028, 1.037)	3.775
Male		1.016 (1.006, 1.026)	1.678	1.025 (1.014, 1.036)	2.718	1.032 (1.025, 1.039)	3.588
Female		1.024 (1.011, 1.037)	2.530	1.029 (1.016, 1.042)	3.130	1.034 (1.028, 1.039)	3.840
Greater Manchester: heat risk		0-65 years		65-74 years		Over 75 years	
Total	16.8	1.008 (1.000, 1.021)	0.114	1.018 (1.005, 1.032)	0.237	1.025 (1.018, 1.033)	0.322
Male		1.009 (0.993, 1.026)	0.127	1.021 (1.004, 1.039)	0.274	1.019 (1.007, 1.031)	0.246
Female		1.006 (0 .986, 1.028)	0.087	1.015 (0.995, 1.035)	0.193	1.030 (1.020, 1.040)	0.372
Greater Manchester: cold risk		0-65 years		65-74 years		Over 75 years	
Total	7.9	1.022 (1.008, 1.037)	2.158	1.010 (0.994, 1.023)	0.899	1.032 (1.024, 1.040)	3.385
Male		1.029 (1.010, 1.047)	2.789	1.014 (0.995 1.033)	1.485	1.030 (1.017, 1.042)	3.118
Female		1.010 (0.987, 1.034)	1.018	1.001 (0 .980, 1.023)	0.141	1.034 (1.023, 1.044)	3.572
West Midlands: heat risk		0-65 years		65-74 years		Over 75 years	
Total	17.6	1.023 (1.009, 1.038)	0.304	1.015 (1.000, 1.029)	0.185	1.029 (1.020, 1.037)	0.343
Male		1.032 (1.014, 1.050)	0.416	1.014 (1.000, 1.033)	0.179	1.034 (1.021, 1.046)	0.400
Female		1.008 (0.985, 1.032)	0.110	1.015 (0 .995, 1.038)	0.191	1.025 (0.014, 1.036)	0.295
West Midlands: cold risk		0-65 years		65-74 years		Over 75 years	
Total	8.2	1.029 (1.015, 1.043)	3.106	1.029 (1.015, 1.044)	3.245	1.031 (1.024, 1.039)	3.677
Male		1.025 (1.007, 1.043)	2.692	1.031 (1.014,1.050)	3.476	1.026 (1.015, 1.038)	3.065
Female		1.035 (1.012, 1.058)	3.747	1.025 (1.004, 1.048)	2.878	1.036 (1.025, 1.046)	4.167

Table S2: Changes in heat and cold related YLL and mortality over time, cold and heat thresholds set at the 35th and 91st centiles of each time periods temperature distribution

Conurbation	Time Period	Mean Temp mean (median)	Threshold value (°C)	Total number of days above/below threshold over 4 year period (and average number per year)	RR of Mortality (95% CI)	Percentage of total mortality attributable to heat or cold	RR of YLL (95% CI)	Percentage of total YLL attributable to heat or cold
Greater London: heat risk	1996-1999	11.58 (11.5)	18.8	131 (33)	1.025 (1.016, 1.034)	0.311	1.015 (1.004, 1.026)	0.19
	2000-2003	11.60 (11.4)	18.9	126 (32)	1.059 (1.053, 1.066)	0.87	1.045 (1.037, 1.054)	0.677
	2004-2007	11.94 (11.3)	19.3	125 (31)	1.033 (1.025, 1.042)	0.449	1.025 (1.014, 1.036)	0.341
	2008-2011	11.35 (11.8)	18.7	123 (31)	1.033 (1.022, 1.044)	0.313	1.029 (1.014, 1.043)	0.28
Greater London: cold risk	1996-1999		9	508 (127)	1.016 (1.007,1.026)	1.768	1.012 (1.000, 1.025)	1.295
	2000-2003		9.1	502 (126)	1.036 (1.029, 1.043)	3.542	1.028 (1.018, 1.039)	2.733
	2004-2007		9.3	507 (127)	1.034 (1.025, 1.042)	3.603	1.032 (1.020, 1.043)	3.316
	2008-2011		9.1	502 (126)	1.034 (1.027, 1.040)	4.51	1.026 (1.017, 1.035)	3.344
Greater Manchester: heat risk	1996-1999	10.21 (10.2)	16.7	126 (32)	1.013 (0.999,1.026)	0.153	1.009 (0.992, 1.026)	0.116
	1999-2003	10.27 (10.2)	17	128 (32)	1.025 (1.013, 1.038)	0.307	1.030 (1.013, 1.047)	0.365
	2004-2007	10.68 (10.6)	17.1	131 (33)	1.023 (1.011, 1.035)	0.355	1.016 (1.000, 1.032)	0.254
	2008-2011	10.21 (10.2)	16.5	131 (33)	1.026 (1.010, 1.042)	0.259	1.013 (0.991, 1.035)	0.131
Greater Manchester: cold risk	1996-1999		7.9	511 (128)	1.026 (1.007, 1.046)	2.45	1.022 (0.996, 1.048)	1.969
	1999-2003		7.9	509 (128)	1.031 (1.018, 1.044)	2.953	1.021 (1.004, 1.039)	2.013
	2004-2007		8.3	501 (125)	1.041 (1.026, 1.057)	3.923	1.044 (1.023, 1.065)	4.024
	2008-2011		8	504 (126)	1.032 (1.018, 1.046)	4.164	1.027 (1.011, 1.043)	3.445
West Midlands: heat risk	1996-1999	10.54 (10.5)	17.4	127 (33)	1.029 (1.015, 1.044)	0.358	1.029 (1.011, 1.047)	0.364
	2000-2003	10.58 (10.3)	17.7	129 (32)	1.019 (1.005, 1.032)	0.237	1.012 (0.994, 1.029)	0.154
	2004-2007	10.93 (10.9)	17.8	130 (31)	1.030 (1.017, 1.042)	0.441	1.028 (1.011, 1.045)	0.426
	2008-2011	10.27 (10.6)	17.4	127 (31)	1.022 (1.006, 1.039)	0.212	1.025 (1.003, 1.048)	0.25
West Midlands: cold risk	1996-1999		8.1	504 (126)	1.010 (0.992, 1.028)	1.021	1.003 (0.981, 1.026)	0.34
	1999-2003		8.1	508 (127)	1.037 (1.024, 1.050)	3.643	1.024 (1.007, 1.041)	2.331
	2004-2007		8.4	510 (128)	1.045 (1.030, 1.060)	4.53	1.044 (1.024, 1.065)	4.348
	2008-2011		8.2	508 (127)	1.032 (1.022, 1.043)	4.397	1.042 (1.027,1.057)	5.363

Table S3: Four yearly heat and cold risks, using fixed thresholds for each conurbation

Conurbation	Time Period	Threshold value (°C)	Total number of days above/below threshold over 4 year period	RR of Mortality (95% CI)	Percentage (%) of total mortality attributable to heat or cold	RR of YLL (95% CI)	Percentage (%) of total mortality attributable to heat or cold
Greater London: heat risk	1996-1999	18.9	124	1.026 (1.017, 1.035)	0.304	1.016 (1.004, 1.027)	0.186
	2000-2003	18.9	126	1.059 (1.053, 1.066)	0.87	1.045 (1.037, 1.054)	0.677
	2004-2007	18.9	158	1.030 (1.023, 1.038)	0.507	1.022 (1.012, 1.032)	0.378
	2008-2011	18.9	109	1.035 (1.023, 1.046)	0.287	1.031 (1.015, 1.046)	0.258
Greater London: cold risk	1996-1999	9	508	1.016 (1.007,1.026)	1.768	1.012 (1.000, 1.025)	1.295
	2000-2003	9	496	1.037 (1.029, 1.044)	3.44	1.029 (1.018, 1.039)	2.657
	2004-2007	9	480	1.035 (1.027, 1.043)	3.361	1.033 (1.021, 1.045)	3.094
	2008-2011	9	492	1.034 (1.027, 1.041)	4.423	1.026 (1.017, 1.035)	3.376
Greater Manchester: heat risk	1996-1999	16.8	118	1.013 (1.000, 1.027)	0.15	1.009 (0.992, 1.027)	0.113
	2000-2003	16.8	144	1.024 (1.012, 1.036)	0.333	1.028 (1.012, 1.045)	0.397
	2004-2007	16.8	149	1.021 (1.010, 1.033)	0.381	1.015 (1.000, 1.030)	0.271
	2008-2011	16.8	111	1.026 (1.009, 1.042)	0.226	1.014 (1.000, 1.036)	0.125
Greater Manchester: cold risk	1996-1999	7.9	511	1.026 (1.007, 1.046)	2.45	1.022 (0 .996, 1.048)	1.969
	2000-2003	7.9	509	1.031 (1.018, 1.044)	2.954	1.021 (1.004, 1.039)	2.013
	2004-2007	7.9	463	1.044 (1.028, 1.061)	3.536	1.047 (1.025, 1.070)	3.62
	2008-2011	7.9	494	1.033 (1.021, 1.044)	4.08	1.027 (1.011, 1.044)	3.382
West Midlands: heat risk	1996-1999	17.6	124	1.031 (1.017, 1.046)	0.341	1.031 (1.013, 1.050)	0.35
	2000-2003	17.6	145	1.018 (1.005, 1.031)	0.247	1.011 (0 .995, 1.028)	0.16
	2004-2007	17.6	141	1.028 (1.017, 1.040)	0.469	1.026 (1.010, 1.042)	0.448
	2008-2011	17.6	121	1.024 (1.006, 1.041)	0.194	1.027 (1.003, 1.052)	0.228
West Midlands: cold risk	1996-1999	8	497	1.010 (0.992, 1.029)	1.024	1.003 (0.981, 1.026)	0.351
	2000-2003	8	500	1.038 (1.025,1.051)	3.533	1.024 (1.006, 1.042)	2.27
	2004-2007	8	475	1.048 (1.032, 1.064)	4.099	1.046 (1.025, 1.068)	3.972
	2008-2011	8	493	1.033 (1.022, 1.044)	4.227	1.042 (1.027,1.057)	5.065

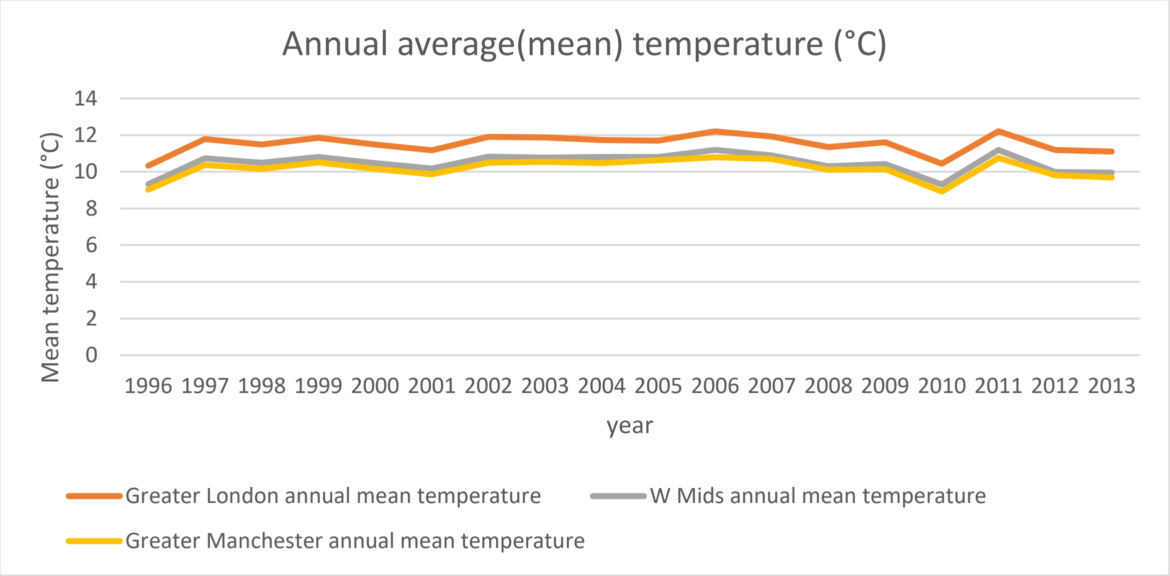


Figure S1: Average (mean) annual temperature over the time period analysed

Figure S2a: Yearly changes in risk of heat related mortality and YLL over time

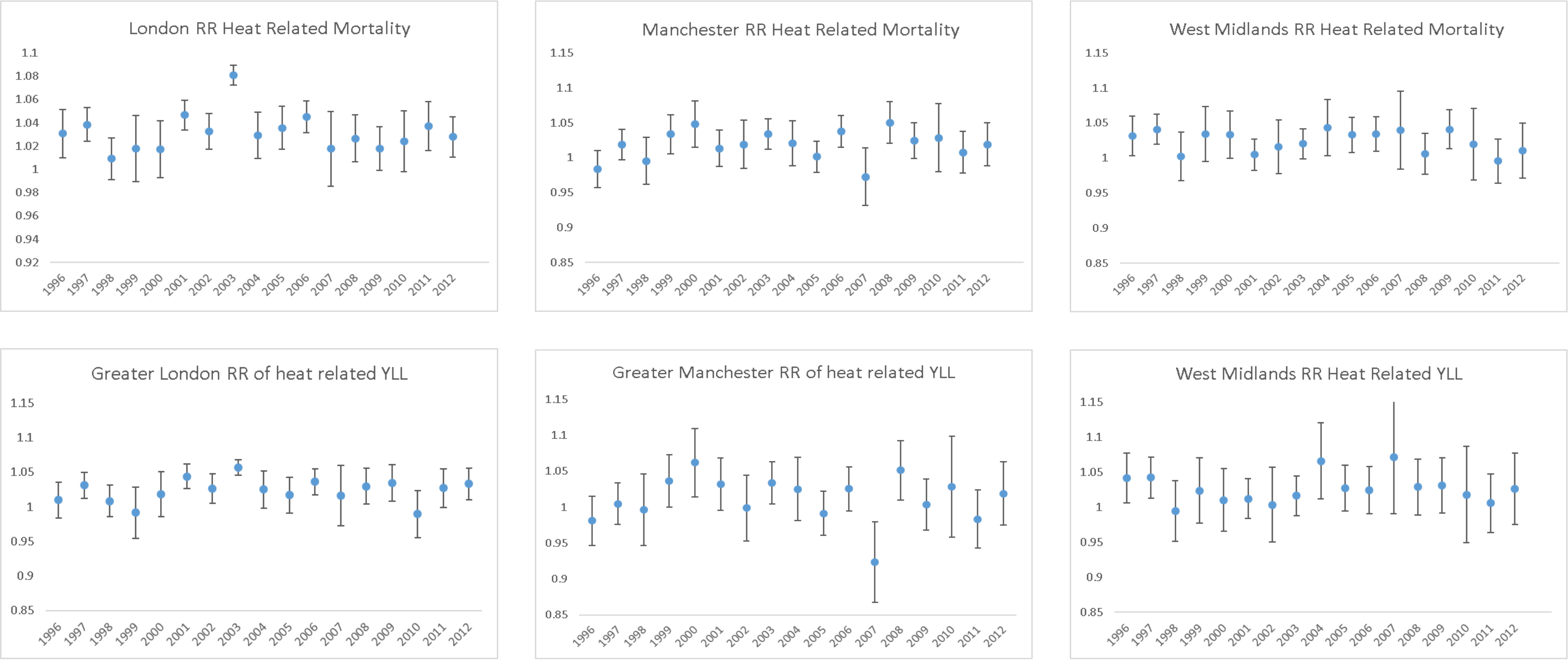


Figure S2b: Yearly Changes in risk of cold related mortality and YLL over time

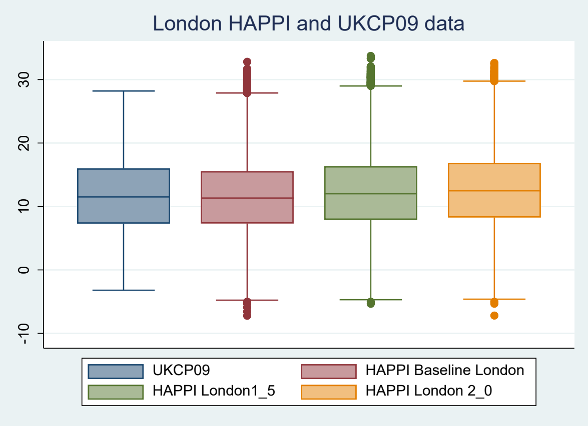
Appendix 4 - Supplementary material for Chapter 7

Supplementary Material S1

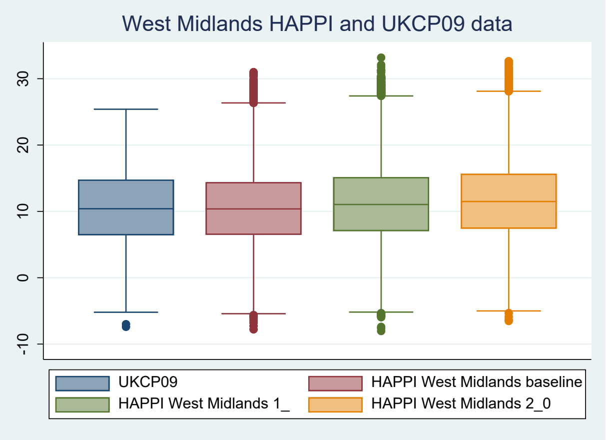
Year Round Summary data for UKCP09 and HAPPI data

G London	Mean Tmean Year round	P50 Year round	SD Year round	Mean Tmean Summer only	P50 Summer only	SD Summer only
UKCP09 gridded data 1995-2013	11.52	11.5	5.61	16.52	16.50	3.25
HAPPI historical data	11.39	11.33	5.54	16.14	16.02	3.51
HAPPI 1.5 degree data	12.13	12.00	5.64	16.98	16.82	3.61
HAPPI 2.0 degree data	12.59	12.47	5.68	17.50	17.37	3.64
West Midlands						
UKCP09 gridded data 1995-2013	10.46	10.40	5.45	15.32	15.3	3.14
HAPPI historical data	10.37	10.37	5.37	14.94	14.83	3.39
HAPPI 1.5 degree data	11.08	11.04	5.49	15.76	15.61	3.51
HAPPI 2.0 degree data	11.54	11.49	5.51	16.26	16.13	3.52
G Manchester						
UKCP09 gridded data 1995-2013	10.18	10.20	5.18	14.76	14.70	3.01
HAPPI historical data	10.08	10.09	5.08	14.35	14.22	3.24
HAPPI 1.5 degree data	10.75	10.73	5.16	15.09	14.91	3.34
HAPPI 2.0 degree data	11.18	11.14	5.17	15.54	15.37	3.35

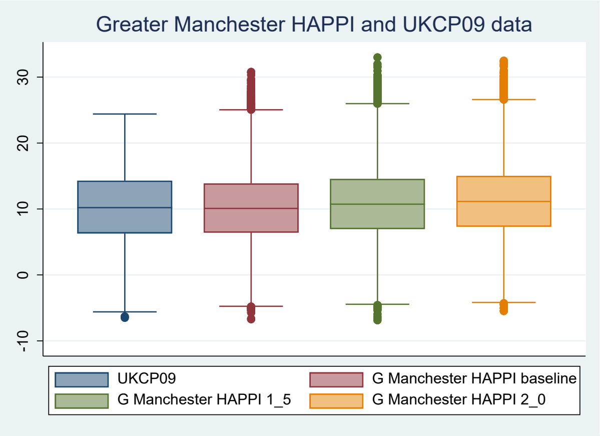
Greater London



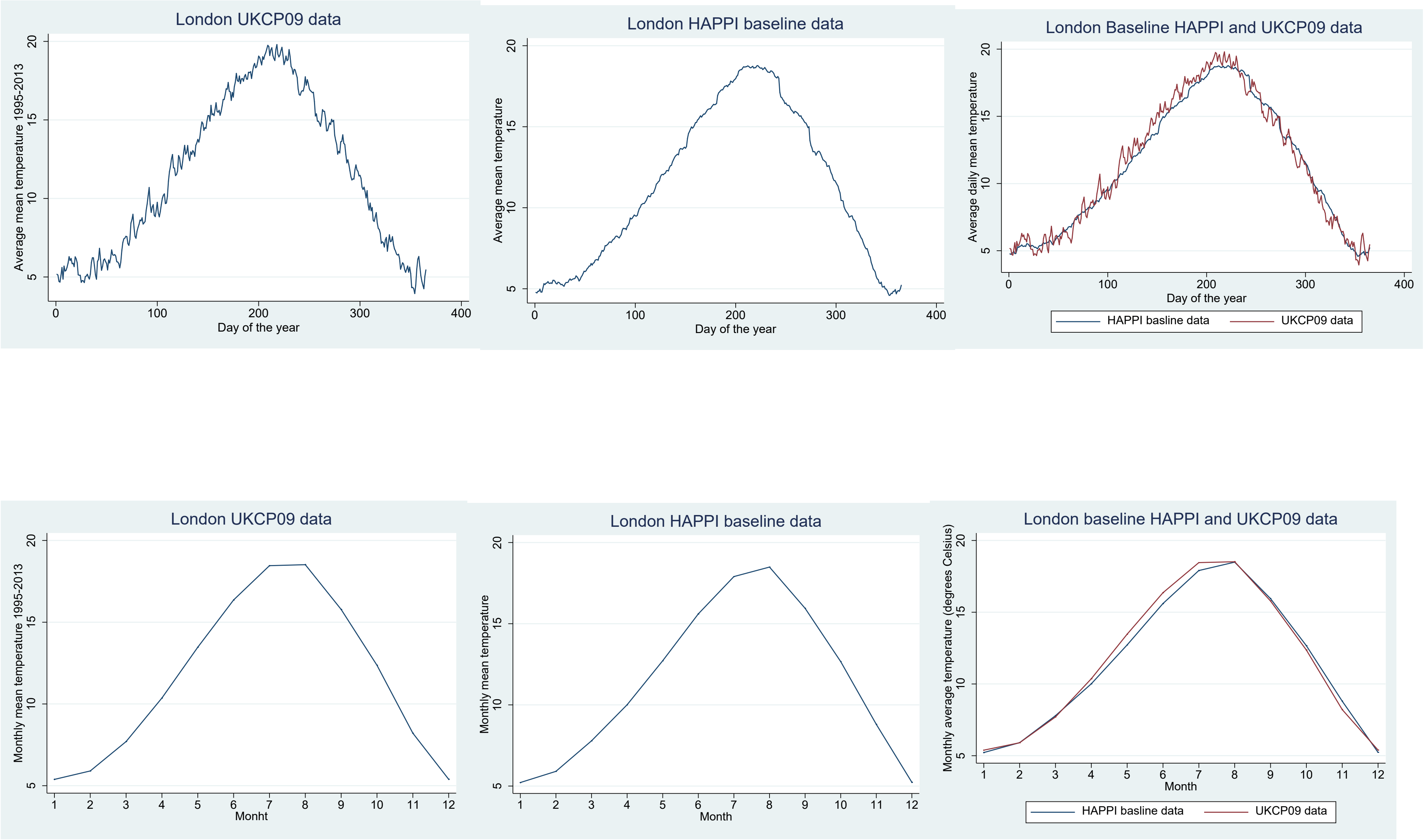
West Midlands

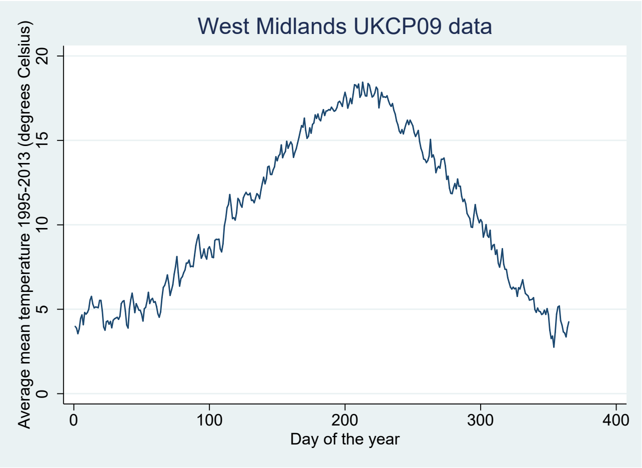


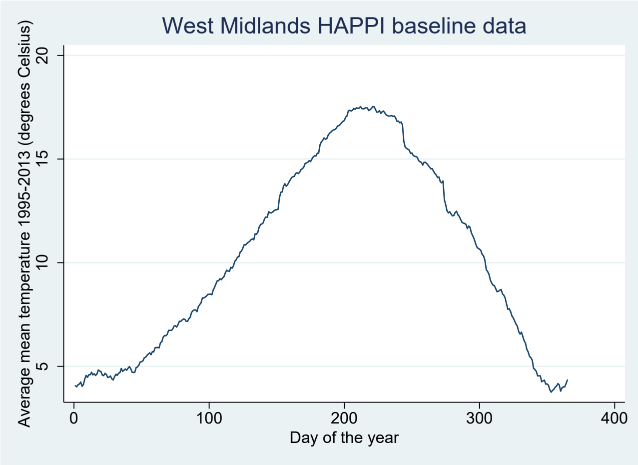
Greater Manchester



Supplementary materials – figure S2: Year round baseline series (HAPPI baseline runs bias corrected to UKCP09 data)




West Midlands UKCP09 data
Average mean temperature 1995-2013 (degrees Celsius)
0
5
10
15
20
0
100
200
300
400
Day of the year


West Midlands HAPPI baseline data
Average mean temperature 1995-2013 (degrees Celsius)
5
10
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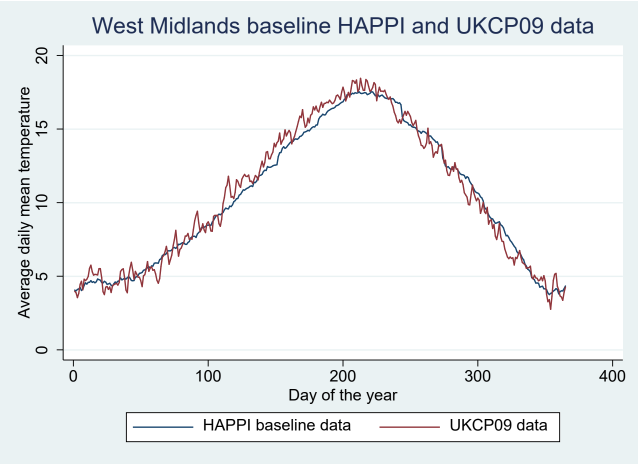
100
200
300
400
Day of the year


West Midlands baseline HAPPI and UKCP09 data
Average daily mean temperature
0
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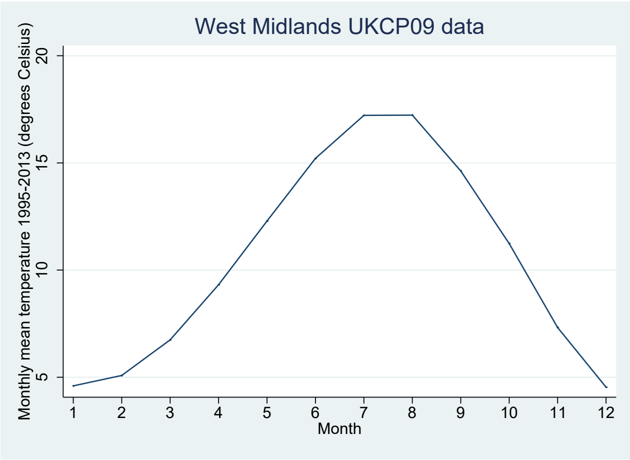
10
15
20
0
100
200
300
400
Day of the year
HAPPI baseline data
UKCP09 data


West Midlands UKCP09 data
Monthly mean temperature 1995-2013 (degrees Celsius)
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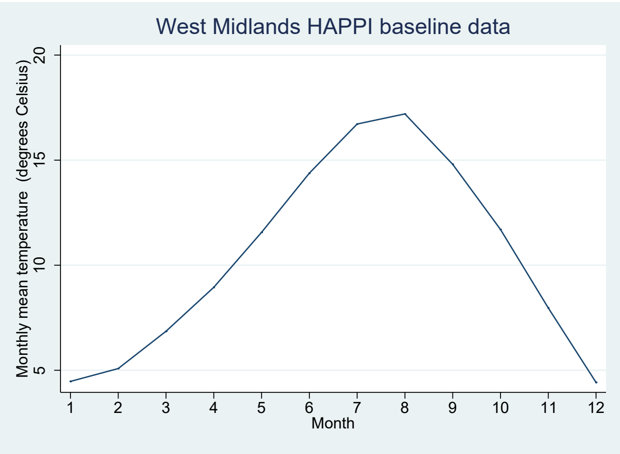
Month


West Midlands HAPPI baseline data
Monthly mean temperature (degrees Celsius)
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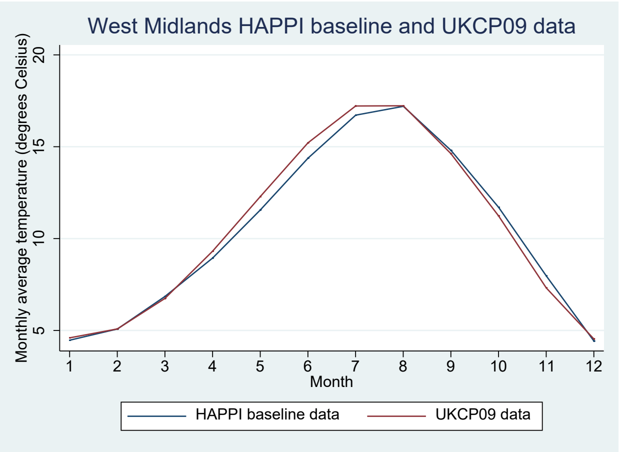
Month


West Midlands HAPPI baseline and UKCP09 data
Monthly average temperature (degrees Celsius)
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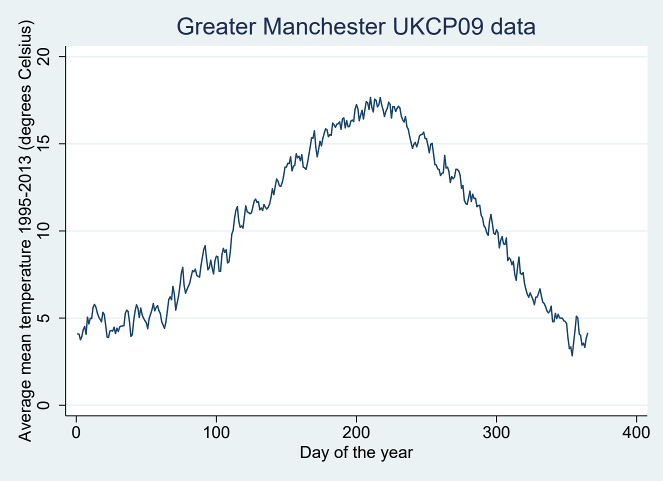
Month
HAPPI baseline data
UKCP09 data


Greater Manchester UKCP09 data
Average mean temperature 1995-2013 (degrees Celsius)
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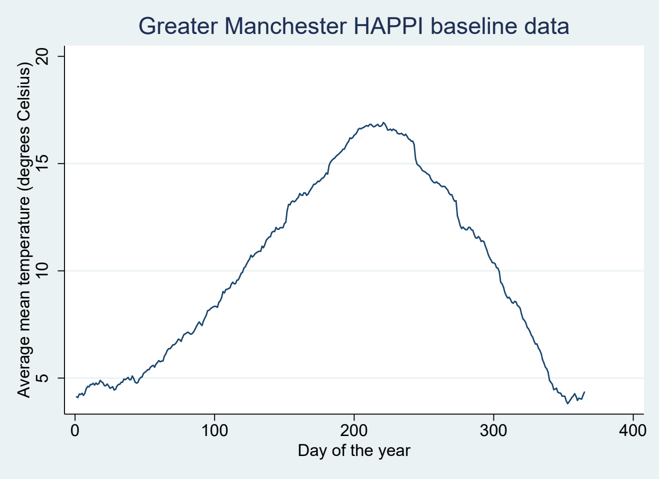
400
Day of the year


Greater Manchester HAPPI baseline data
Average mean temperature (degrees Celsius)
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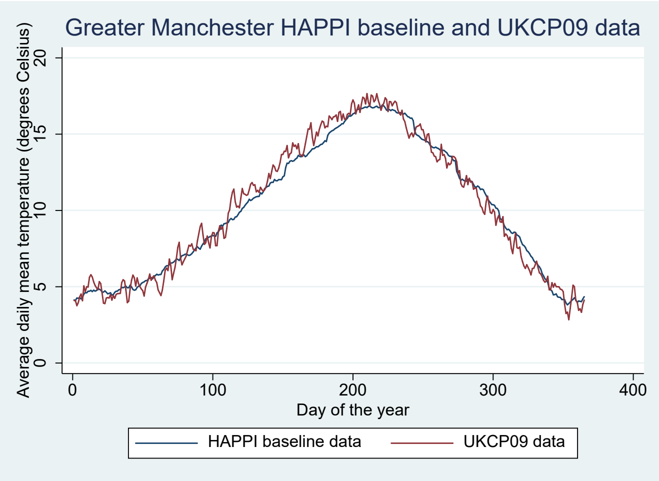
400
Day of the year


Greater Manchester HAPPI baseline and UKCP09 data
Average daily mean temperature (degrees Celsius)
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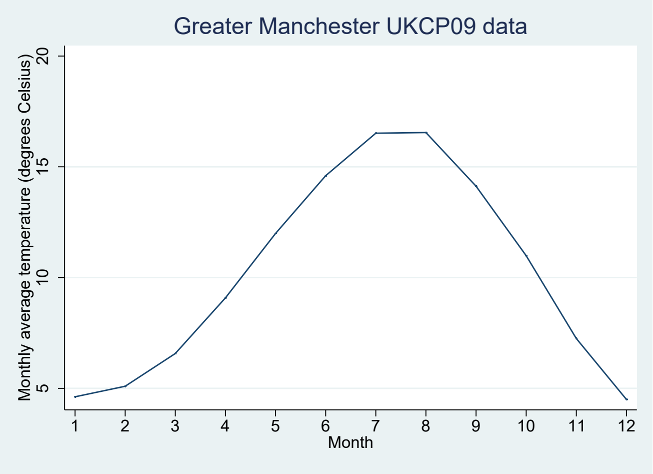
Day of the year
HAPPI baseline data
UKCP09 data


Greater Manchester UKCP09 data
Monthly average temperature (degrees Celsius)
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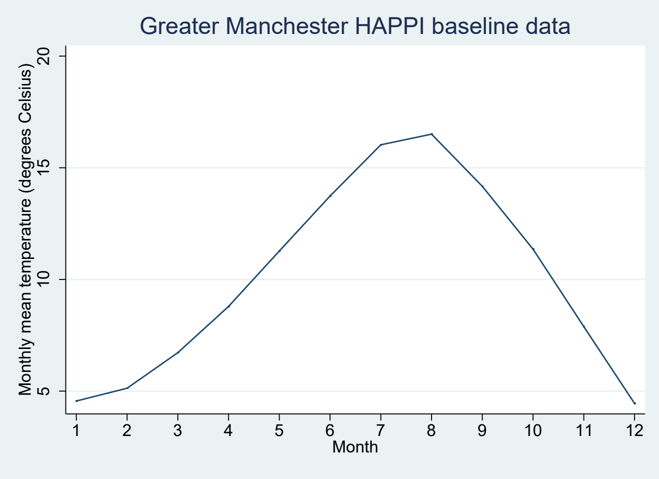
Month


Greater Manchester HAPPI baseline data
Monthly mean temperature (degrees Celsius)
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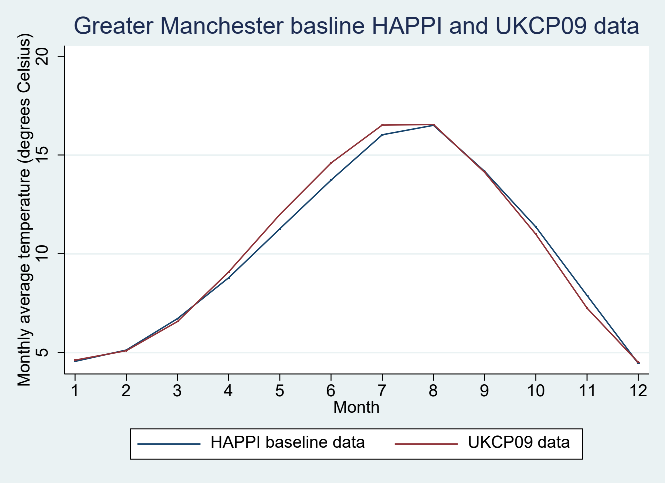
Month


Greater Manchester basline HAPPI and UKCP09 data
Monthly average temperature (degrees Celsius)
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Month
HAPPI baseline data
UKCP09 data

Supplementary Materials

Supplementary materials Table S3

Conurbation	Heat wave definition for conurbation (3 days > 99th percentile of the UKCP09 year round temperature distribution)	RR per degree above threshold (95% CI)	Additional mortality risk on heat wave days (compared to non-heat wave days) (95% CI) P value
Greater London	3 days > 22.9	1.041 (1.036, 1.046)	1.089 (1.046, 1.134) $p < 0.001$
West Midlands	3 days > 21.7	1.032 (1.021, 1.043)	1.024 (0.953, 1.101) $p = 0.432$
Greater Manchester	3 days > 20.9	1.020 (1.012, 1.029)	1.097 (1.008, 1.195) $P= 0.033$

Supplementary materials Table S4: Frequency of rare heatwave events under each HAPPI scenario

Conurbation and Duration of event	Historical HAPPI series : frequency of event across all simulations (nearest half year)	HAPPI 1.5 degrees: frequency of event across all simulations (nearest half year)	How many times more likely for 1.5 degrees compared to baseline	HAPPI 2 degrees: frequency of event across all simulations (nearest half year)	How many times more likely for 2 degrees compared to baseline
Greater London					
1 day > 29.5	1 in 20 years	1 in 6 years	3.33	1 in 4 years	5.00
1 day > 29.7	1 in 25 years	1 in 7 years	3.57	1 in 4.5	5.56
1 day > 31.0	1 in 50 years	1 in 25 years	2.00	1 in 16 years	3.13
1 day > 31.4	1 in 100 years	1 in 37 years	2.70	1 in 26 years	3.85
1 day > 31.6	1 in 150 years	1 in 50 years	3.00	1 in 32 years	4.69
3 days > 27.2	1 in 20 years	1 in 10 years	2.00	1 in 6 years	3.33
3 days > 27.6	1 in 25 years	1 in 12.5 years	2.00	1 in 8 years	3.13
3 days > 28.1	1 in 50 years	1 in 20 years	2.50	1 in 12 years	4.17
3days > 28.6	1 in 100 years	1 in 30 years	3.33	1 in 18 years	5.56
3days > 28.9	1 in 150 years	1 in 34 years	4.41	1 in 20 years	7.50
West Midlands					
1 day > 28.4	1 in 20 years	1 in 6 years	3.33	1 in 4 years	5.00
1 day > 28.7	1 in 25 years	1 in 7 years	3.57	1 in 5 years	5.00
1 day > 29.4	1 in 50 years	1 in 12.5 years	4.00	1 in 8 years	6.25
1 day > 30.5	1 in 100 years	1 in 56 years	1.79	1 in 20 years	5.00
1 day > 30.7	1 in 150 years	1 in 56 years	2.68	1 in 24 years	6.25
3 days > 25.9	1 in 20 years	1 in 10 years	2.00	1 in 6 years	3.33
3 days > 26.2	1 in 25 years	1 in 12.5	2.00	1 in 8 years	3.13
3 days > 27.1	1 in 50 years	1 in 17 years	2.94	1 in 13 years	3.85
3 days > 27.4	1 in 100 years	1 in 22 years	3.41	1 in 15 years	5.00
3 days > 27.6	1 in 150 years	1 in 28 years	3.57	1 in 18 years	5.56
Greater Manchester					
1 day > 27.7	1 in 20 years	1 in 6.5 years	3.08	1 in 4 years	5.00
1 day > 28.0	1 in 25 years	1 in 8years	3.13	1 in 5 years	5.00
1 day > 29.0	1 in 50 years	1 in 22.5 years	2.22	1 in 11.25 years	4.55
1 day > 29.6	1 in 100 years	1 in 34.5 years	2.90	1 in 19 years	5.26
1 day > 29.8	1 in 150 years	1 in 50 years	3.00	1 in 21.5 years	7.14
3 days > 25.2	1 in 20 years	1 in 12.5 years	1.60	1 in 7.5 years	2.67
3 days > 25.4	1 in 25 years	1 in 13.5 years	1.85	1 in 8.5 years	2.91
3 days > 26.1	1 in 50 years	1 in 21.5 years	2.33	1 in 13.5 years	3.68
3 days > 26.5	1 in 100 years	1 in 28 years	3.57	1 in 18 years	5.56
3 days > 26.8	1 in 150 years	1 in 32 years	4.69	1 in 20.5 years	7.32

Supplementary materials: table S1

Supplementary materials Table S5: Projected hear related mortality using epidemiological models with a heat wave term

	HAPPI baseline	HAPPI 1.5	HAPPI 2.0
Greater London			
Annual/summer Heat deaths only	261.6 (230.0, 292.6)	427.1 (375.8, 477.6)	541.2 (511.1, 697.8)
Additional Wave effect	28.2 (15.23, 40.6)	51.2 (27.7, 73.8)	64.4 (34.8, 92.8)
Total including HW	289.7 (245.2, 333.2)	478.3 (403.5, 551.3)	605.6 (511.1, 697.8)
HW effect as a % of the heat only related mortality for the given scenario	10.8	12.0	11.9
HW effect as a % of the HAPPI baseline scenario	10.8%	19.6%	24.6%
West Midlands			
Annual/summer Heat deaths only	62.9 (42.8, 82.3)	105.5 (71.8, 137.9)	131.9 (89.8, 172.2)
Additional Wave effect	2.5 (-5.3, 9.8)	4.9 (-10.2, 18.9)	6.0 (-12.6, 23.4)
Total including HW	65.44 (37.5, 92.1)	110.4 (61.74, 156.79)	137.9 (77.2, 195.7)
HW effect as a % of the heat only related mortality for the given scenario	4.0%	4.6%	4.6%
HW effect as a % of the HAPPI baseline scenario	4.0%	7.7%	9.55%
Greater Manchester			
Annual/summer Heat deaths only	44.3 (26.56, 61.5)	71.0 (42.6, 98.5)	87.2 (52.4, 121.0)
Additional Wave effect	10.5 (0.91, 19.4)	20.0 (1.7, 36.8)	24.3 (2.1, 44.7)
Total including jHW	54.8 (27.5, 81.0)	91.0 (44.4, 135.3)	111.5 (54.5, 165.7)
HW effect as a % of the heat only related mortality for the given scenario	23.9%	28.1%	27.8%
HW effect as a % of the HAPPI baseline scenario	23.9%	45%	55%