Environmental Health Nexus: Designing Predictive Models for Improving Public Health Interventions

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Dedication

This dissertation is dedicated to my unstoppable mother, Dongjing Yang.

Vision

- **Environmental Health Nexus** is the nexus of environmental health sciences as a complete domain. It highlights the fact that it is not only capturing the link between two discrete yet separate components (i.e., "environment" and "health"). Instead, it is capturing all connections and all core concepts among all networks that are relevant to environmental health sciences.

- **Designing Models** involves the analysis, construction, validation, application, and communication of a theoretical and/or computational model. This approach emphasizes that models are more than just abstractions of the reality - they could be customized and tailored for specific research questions and/or policy needs.

The environment embodies all surroundings of humans, including natural (e.g., climate, rivers, and animals) and built (e.g., roads and buildings) components. The environment is closely related to population health both directly and indirectly. Ambient temperature exposure and air pollution, for example, can directly affect population health through its direct impacts on human cardiovascular and respiratory functions [1–3]. Rainfall, on the other hand, can indirectly affect population health through its impacts on disease-transmitting vectors, such as mosquitoes [4]. The U.S. Global Change Research Group and the Intergovernmental Panel on Climate Change both highlight the importance of the environment on population health [5, 6].

Environmental health is a challenging research topic for a variety of reasons. First, it is difficult to select the appropriate environmental indicators. Thanks to technological advancements in instrument precision, remote sensing, and many other fields, there is now an unprecedented amount of environmental information available to researchers. Although data availability issues still exist, the bigger question now is how to select information that is most relevant and appropriate to answer research questions. For example, when studying the epidemiological link between ambient temperature and population health, the most fundamental task is to select the appropriate indicator for ambient temperature. Because there are over 60 potential indicators that are all designed to approximate temperature perceived by the human body, this task can be a challenge.

Second, along with the wide range of indicators comes a large volume of environmental data that is now available. Some ambient environmental indicators, such as air temperature, are available on a three-hour basis globally with high resolution since the

1980s (e.g., in [7]). Technologies such as geographic information systems (GIS) have empowered public health to access this information. However, extracting this information for public health purpose is not always easy and may involve specialized technical expertise. Furthermore, incorporating this high-granularity data with traditionally scarcer public health data also entails technical difficulties.

Last but not least, from a computational standpoint, it is challenging to work with high-dimensional data, especially given different research objectives. Environmental health issues do not usually deal with only a pair of exposure and response factors because no environmental factor exists independently. When studying dengue fever, for example, the link between temperature and disease occurrences is not two-dimensional because climate (e.g., rainfall), environmental (e.g., river network, non-human primates), and societal factors (e.g., human mobility network) are also involved [4, 8, 9]. Reducing high-dimensional data to the essentials in order to meet research objectives is easier said than done. It involves sophisticated quantitative methods such as complexity science [10]. It also largely depends on the specific research questions, e.g., if the model used to study the environmental health issue is for risk assessment, risk comparison, or disease forecast.

Despite the technical challenges, environmental information has tremendous potential in terms of ecosystem service for population health research. Existing research has already generated many valuable outcomes with great real-life implications. However, the uptake rates of such knowledge among public health policy- and decision-makers remain low. An important underlying reason is that current knowledge contains little necessary details needed to influence policies and decisions. Moreover, policy- and decision-makers often lack the technical expertise to translate the results from research articles into valuable information to their specific context. The relationship between research and policy is predominantly driven by the research, i.e., the supply-side of epidemiological knowledge. Such supply-driven model has already been proven to be suboptimal in terms of maximizing the impact of research [11].

Targeting the challenges discussed above, this dissertation focuses on designing quantitative predictive models for improving environmental health policy and decisions. More specifically, it generates evidence-based science to improve policies and decisions with respect to risk communication, impact assessment, and intervention planning. Although the end-users of specific studies included are environmental health managers and practitioners, the knowledge generated is also valuable to environmental health and methods researchers.

Within the overarching theme, two projects were completed over the course of this dissertation. The first project used environmental information to forecast infectious disease outbreaks. Infectious diseases that rely on vector-borne, water-borne, air-borne, and zoonotic transmissions are all considered environmentally sensitive infectious diseases. Two studies were completed for influenza outbreaks in the U.S. [12, 13] and dengue fever outbreaks in San Juan, Puerto Rico and Iquitos, Peru [14]. The research objective was to design statistical models that maximize forecast accuracy in terms of future outbreak timing and magnitude. Meteorological factors such as temperature, humidity, and precipitation were considered. The end-users in these projects were the U.S. Centers for Disease Control and Prevention, the National Oceanic and Atmospheric Administration, and local public health agencies. The end-goal was to reduce disease burden through preventative intervention planning.

The forecasting methods used in these disease forecast models were uniquely designed for environmentally sensitive infectious diseases. Based on the nature of the transmission mechanisms involved, the models considered substantial temporal delays between the environmental exposure and population health responses. Traditionally, researchers have relied on measurements such as auto-correlation and partial auto-correlation coefficients to assess these temporal delays. However, these coefficients are constrained by linear assumptions. In this project, mutual information (a concept in information theory) was adapted as an alternative measure that quantifies the delayed relationship between environmental exposure and health response [15].

The second component was to design evidence-based and policy-oriented models for managing population health risks associated with ambient temperature exposure. This component was a collaborative effort with the Minnesota Department of Health and the U.S. Centers for Disease Control and Prevention. The study site is the Minneapolis-St. Paul Twin Cities Metropolitan Area. The environmental indicator to measure ambient temperature exposure was selected using a data-driven approach. The risk assessment models aim at improving the quality of public health policy and decision-making.

This project expands on the existing risk assessment methods [16] by developing various modifications and extensions to meet the needs of risk communication [17], impact assessment [18], and intervention planning [19]. **In this dissertation, three studies from this second project (ambient temperature) are presented.**

The work described above has important epidemiological, methodological, and policy implications. It also contributes to a bigger picture, which is to design decision support tools for environmental health management. An ideal decision support tool should combine general and universal patterns in epidemiology with the local public health context to optimize policies and decisions under uncertain scenarios. This type of tool has been developed for ecosystem management (e.g., wetland restoration [20]) and for chronic care [21, 22]. However, for environmental health issues, this type of tool does not yet exist. Currently, environmental health management still largely relies on past experiences of policy and decision makers. Essential knowledge needed for creating such decision support tools is not yet fully available. This dissertation provides some of the missing answers, with the ultimate goal of rationalizing and optimizing public health policies and decisions regarding environmental health intervention.

Contents

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List of Abbreviations

Acronym	Meaning
AC	Attributable Cases
AF	Attributable Fraction
AP	Air Pollutant
AT	Air Temperature
BRACE	Building Resilience Against Climate Effects
CCR	Cost-to-Charge Ratio
CDC	Centers for Disease Control and Prevention
CV	Cross Validation
CVD	Cardiovascular Disease
Diab	Diabetes
DLNM	Distributed Lag Nonlinear Model
DPV	Daily Production Value
eCI	Empirical Confidence Interval

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Acronym	Meaning
EDV	Emergency Department Visits in Chapter 2 and 4; Emergency Department Visits followed by discharge in Chapter 3
EDHSP	Emergency Department Visits followed by hospitalization in Chapter 3
EPA	Environmental Protection Agency
ERC	Emergency Risk Communication
ERF	Exposure-Response Function
HI	Heat Index
HPD	Health Policy Division at the Minnesota Department of Health
ICD	International Classification of Disease
MDH	Minnesota Department of Health
MET	Minimum Effect Temperature
MMP	Minimum Morbidity Percentile
MMT	Minimum Mortality Temperature
MORT	Mortality in Chapter 3
MORB	Morbidity in Chapter 3
MT	Mortality in Chapter 2
MB	Morbidity in Chapter 2
NWS	National Weather Service
PFR	Professional Fee Ratio

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Acronym	Meaning
qAIC	quasi-Akaike Information Criterion
RMSE	Root Mean Squared Error
RND	Renal Disease
RPD	Respiratory Disease
RR	Relative Risk
TCMA	Minneapolis – St. Paul Twin Cities Metropolitan Area
USD	U.S. Dollar
VSL	Value of Statistical Life
WBGT	Wet Bulb Globe Temperature
WHO	World Health Organization
yo	Years Old

Chapter 1

An Introduction to Ambient Temperature and Human Health

This dissertation focuses on designing quantitative predictive models for improving public health policies and decisions that manage risks associated with ambient temperature. In the context of this dissertation, ambient temperature is a synonym for outdoor temperature. Health risks, on the other hand, are estimated using population health outcomes such as mortality and morbidity. The earliest research on the epidemiological link between ambient temperature and human health dates back to the 1930s, when a group of researchers in Cincinnati discovered an association between winter temperature and acute coronary thrombosis [23]. In recent years, there have been rapid developments in temperature and health research.

Ambient temperature exposure is a concerning environmental health risk for two reasons. First, there is a large global health burden. Using data from 350 locations in 14 countries, [24] estimated that 7.71% of all mortality can be attributed to non-optimal ambient temperature exposure. The nature of this exposure is non-exclusive, which means a large majority of the population is exposed to certain degrees, regardless of age, sex, occupation, or socioeconomic status. The exposure is also relevant to a wide range of diseases. Hypothermia and hyperthermia are examples of diseases directly related to ambient temperature. Additionally, certain chronic conditions, such as cardiovascular, respiratory, renal diseases and diabetes, can also be exacerbated by ambient temperature [25–27]. This exposure may indirectly affect population health through agriculture and food security [6]. Second, environmental health risks from ambient temperature are likely going to become more complex given the context of global climate change [28, 29]. The overall warming trend only reflects one aspect of ambient temperature changes. The occurrences of extreme temperature exposure and the shift of overall daily temperature distributions also need to be considered [5, 30, 31]. As a part of climate change adaptation policies, there is great potential to reduce health risks incurred by ambient temperature. Examples of useful interventions that have been implemented are community cooling centers, urban green spaces, and community outreach [32].

It is a challenging task to design quantitative models appropriate for informing public health policies that manage risks associated with ambient temperature. For example, there is little consensus on indicator selection for both exposure and health response. Ambient temperature can be directly measured by air temperature. However, there are also compound temperature metrics such as heat index, wind chill index, wet bulb globe temperature, physical equivalence temperature, and universal thermal climate index. The advantage of these compound temperature metrics is that they are designed to approximate temperature perceived by the human body. They also incorporate other meteorological factors such as humidity, wind speed, sun angle, solar radiation, and precipitation. As for health response, available indicators include but are not limited to deaths, emergency department visits, emergency hospitalizations, hospital admissions, ambulance dispatches, and emergency calls.

There is another important challenge that also regards research methods. In the case of ambient temperature and human health, there is often a significant temporal delay between exposure and response [33–35]. For cold exposure in particular, health risks may remain significantly increased for weeks after the original point of exposure. In the rest of this dissertation, this temporal delay will be referred to as lag. As a result of lag effects, the data collected for population health outcomes reflect a complex reality - the health response on day t is the sum of the effects of days prior to that day; the exposure on day t has effects for days after that day. A quantitative method that can tease out the effects of ambient temperature from such complexity is essential. Recent developments in time-series statistics (e.g. the distributed lag non-linear model [16]) have provided new opportunities for researchers to investigate exposure-response functions with significant temporal delays.

Despite high interest from research and the policy communities, there is still a considerable barrier between knowledge and practice considering ambient temperature exposure and population health. In other words, the uptake rates of knowledge regarding the epidemiological link between ambient temperature and human health remain low among public health policy/decision makers. The fundamental reason for this is that current research efforts are largely driven by the supply-side - the research communities. Many existing studies on temperature and health topics lack the necessary scope to link them to a specific aspect of public health practice or intervention. However, an effective mechanism to maximize research impact should reflect inputs from both the supply- and the demand-sides [11].

The three studies included in this dissertation address the challenges and barriers discussed above and focus on designing quantitative models for informing public health policies that manage risks associated with ambient temperature.

Chapter 2 shows how quantitative models can be used to improve emergency risk communication (ERC) [17]. ERC programs such as heat and extreme cold warnings are some of the most important tools used by the U.S. Environmental Protection Agency (EPA), the National Weather Service (NWS), and the Minnesota Department of Health (MDH) to manage the health risks associated with extreme temperature. ERC programs are activated when the temperature is expected to cross a given threshold in the following 24-72 hours [36]. Although there is substantial evidence that extreme temperature can exacerbate certain chronic health conditions (e.g., cardiovascular, respiratory, renal diseases, and diabetes) [25–27], current ERC messaging does not contain this information. Chapter 2, therefore, explores whether ERC messaging can be tailored to protect individuals with these chronic conditions.

After investigating six extreme temperature thresholds as potential activation criteria, Chapter 2 discovers that extreme cold thresholds can be used to target cardiovascular and respiratory diseases, whereas extreme heat thresholds can be used to target renal diseases. Some chronic diseases show higher increased relative risks at moderately low temperatures instead of extremely low temperatures. ERC may not be the optimal option in these cases. Other risk communication options should be explored.

Chapter 3 shows how quantitative models can be used for impact assessment [18]. The objective is to summarize the overall impact of ambient temperature exposure in terms of health-related economic costs. This approach is particularly relevant for public health issues such as ambient temperature exposure when multiple population health endpoints (e.g., mortality and emergency department visits) need to be considered [37]. Impact assessment provides the ability to compare across different public health issues and prioritize resource allocation during intervention planning.

Chapter 3 finds that, in the Minneapolis St. Paul Twin Cities Metropolitan Area (TCMA), the annual health-related economic cost of non-optimal ambient temperature exposure is $2.70 billion [95%eCI: 1.91 billion, 3.48 billion] (2016$) considering only extreme temperature exposure and is $9.4 billion [95%eCI: 6.05 billion, 12.57 billion] (2016$) considering both moderate and extreme temperature exposure. While older adults (65+ years old) are the largest contributors to the overall health-related economic costs, children and adolescents (0-19 years old) contribute the largest number of individuals being affected by ambient temperature.

Chapter 4 shows how quantitative models can be used for guiding intervention [19]. Existing research on temperature and health has shown that youth are a high-risk group considering ambient temperature exposure [28, 38]. However, few studies have provided the necessary details that could guide interventions on this topic. They have not investigated the heterogeneity in risk among children and therefore do not provide any information on the individuals to be prioritized when it comes to intervention. This chapter is dedicated to bridging this research gap. It adopts an early-life developmental approach widely used in environmental contaminants research and identifies age ranges among children that experience higher morbidity risks compared to children overall.

Chapter 4 develops a new approach to compare exposure response functions across different age groups by considering both the pair-wise risk estimates and the overall attributable risks. This study finds that individuals 3-11 years old experience higher morbidity risks than children overall when exposed to low temperatures. Conversely, children 3-5 and 12-14 years old experience higher morbidity risks than children overall when exposed to high temperatures. Newborns, infants, and toddlers (0-2 years old) are sensitive to moderate temperature exposure instead of extreme temperature exposure. Intervention programs should prioritize these groups.

Chapter 5 summarizes the studies included and articulates potential directions for future research. It also discusses the implication of the current research in the context of the bigger picture - using environmental information to inform public health policy and decision making.

Chapter 2

Designing Models for Risk Communication

Liu, Y., Hoppe, B. O., & Convertino, M. (2018). Threshold Evaluation of Emergency Risk Communication for Health Risks Related to Hazardous Ambient Temperature. Risk Analysis. doi: https://doi.org/10.1111/risa.12998

Key Findings

- Emergency risk communications can be tailored for targeting cardiovascular and respiratory diseases given extreme cold exposure and renal diseases given extreme heat exposure.
- For ambient temperature related risk assessment, it is crucial to consider multiple type of exposure (i.e., cold, heat) and multiple public health endpoints (i.e., mortality and morbidity).
- For some specific diseases, there are contrasting patterns in the exposure-response functions corresponding to mortality and morbidity outcomes.

Summary

Emergency risk communication (ERC) programs that activate when the ambient temperature is expected to cross certain extreme thresholds are widely used to manage relevant public health risks. In practice, however, the effectiveness of these thresholds has rarely been examined. The goal of this study is to test if the activation criteria based on extreme temperature thresholds, both cold and heat, capture elevated health risks for all-cause and cause-specific mortality and morbidity in the Minneapolis – St. Paul Metropolitan Area.

A distributed lag nonlinear model combined with a quasi-Poisson generalized linear model is used to derive the exposure-response functions between daily maximum heat index and mortality (1998-2014) and morbidity (emergency department visits; 2007-2014). Specific causes considered include cardiovascular, respiratory, renal diseases, and diabetes. Six extreme temperature thresholds, corresponding to 1st-3rd and 97th-99th percentiles of local exposure history, are examined.

All six extreme temperature thresholds capture significantly increased relative risks for all-cause mortality and morbidity. However, the cause-specific analyses reveal heterogeneity. Extreme cold thresholds capture increased mortality and morbidity risks for cardiovascular and respiratory diseases and extreme heat thresholds for renal disease.

Percentile-based extreme temperature thresholds are appropriate for initiating ERC targeting the general population. Tailoring ERC by specific causes may protect some but not all individuals with health conditions exacerbated by hazardous ambient temperature exposure.

2.1 Introduction

Public health risks associated with hazardous ambient temperature have been widely documented over the past decades. Research and policy communities are interested in this particular exposure due to its serious social and economic consequences [6, 39]. A recent multi-country observational study estimated that 7.71% of total mortality can be attributed to hazardous temperature exposures [24]. In 2006, a single two-week heat wave in California led to 5.40 billion USD healthcare costs [37]. Under the context of global climate change, the relevance and complexity of this health issue will likely increase [6, 39]. Annual mean temperatures are projected to rise, and extreme heat events will become more frequent and intense [30, 40, 41]. Meanwhile, the rate of adaptation to climate change remains highly uncertain [42]. This study contributes to the understanding and managing of public health risks related to hazardous ambient temperature.

Emergency risk communication (ERC) programs that warn the public when certain extreme temperature thresholds are crossed are common interventions in managing public health risks related to extreme temperature exposure (National Weather Service, 2012). The primary objective of this study is to test if different extreme temperature thresholds can capture elevated relative risks in population health. In practice, these thresholds are often pre-determined absolute (e.g., 95 or 100°F) [43] or percentile values (e.g., 98^{th} or 99^{th} percentile of historical temperature distribution) [44, 45]. The latter is favored as it allows localized extreme temperature definitions [46]. However, few studies have empirically examined how well these thresholds in ERC programs correlate with increased public health risks. Moreover, current ERC programs predominantly target the general population. Yet, numerous studies show that certain chronic health conditions, such as cardiovascular diseases (CVD) [47–50], respiratory diseases

(RPD) [25, 47, 50–53], renal diseases (RND) [26, 47, 48, 53–55], and diabetes (Diab) [27, 47, 48, 53], may increase an individuals vulnerability to hazardous temperature exposure. This study investigates whether ERC programs can be tailored to protecting such individuals, as a means of reducing total health burden. For example, an ERC program may be tailored for CVD by including information specific to this health condition if extreme temperature thresholds can capture elevated risks for CVD mortality and morbidity.

To achieve this primary objective, this study will assess the relationships between ambient temperature exposure and population health while considering different types of temperature exposure (i.e., cold and heat) and population health outcomes (i.e. mortality and morbidity). By far, many temperature and health studies focus on the relationship between heat and mortality [47, 49, 56] or between heat and morbidity [26, 27, 54, 55]. An increasing number of studies have investigated the impacts of both cold and heat on mortality [24, 33, 57] while some others extend the research focus to the impacts of heat on both mortality and morbidity [37, 58–60]. Only a small number of studies have investigated the impacts of cold exposure on mortality [49, 61] or morbidity [3, 62]. This study is among the first to address the impacts of both heat and cold exposures on both mortality and morbidity using the same study population. As a secondary objective, this study will also highlight the burden of health underestimated when some key exposure or population health outcome types are not considered.

2.2 Materials and Methods

The analyses in this study are based on data from the Minneapolis – St. Paul Twin Cities Metropolitan Area (TCMA), which has a continental climate [63]. The TCMA is comprised of seven counties (Anoka, Carver, Dakota, Hennepin, Scott, Ramsey, and Washington) in east central Minnesota (Appenxis A.1). Although the TCMA has a reputation as the coldest major metropolitan area in the United States, with harsh and long winters (Nov.-Apr.), its summer months (May-Sep.) can be extremely hot and humid.

2.2.1 Environmental and Public Health Data

This study defines ambient temperature exposure using daily maximum Heat Index ($\mathrm{HI}_{\mathrm{max}}$). It is estimated by averaging $\mathrm{HI}_{\mathrm{max}}$ from seven weather stations across the TCMA. $\mathrm{HI}_{\mathrm{max}}$ is selected after considering three temperature metrics (air temperature, wind chill index, heat index) and three statistical features (daily minimum, mean, and maximum), totaling nine variables. The specific procedure of temperature variable selection can be found in Appendix A.2. The Heat Index is an apparent temperature measurement designed to approximate temperature perceived by the human body during summer [64, 65]. It considers both air temperature and relative humidity. $\mathrm{HI}_{\mathrm{max}}$ is currently used in the activation criteria of ERC in the TCMA when hazardous heat is expected [43]. Outside of summer months, daily $\mathrm{HI}_{\mathrm{max}}$ is comparable to daily maximum air temperature (Appendix A.3) [65].

Population mortality and morbidity are defined as total daily counts of deaths and emergency department visits (EDV), respectively. The mortality data (1998-2014) of the TCMA is provided by the Office of Vital Records at the Minnesota Department of Health (MDH). The EDV data (2005-2014) is obtained through MDH's Health Policy Division (HPD) from the Minnesota Hospital Association. The morbidity data before Jan. 1st 2007 was excluded in further analysis to preserve consistent coding standards for specific disease causes.

After reviewing disease definitions in the existing literature [27, 54, 58, 66–68], this study adopts the broadest definitions in terms of International Classification of Disease (ICD) codes: CVD (ICD-9: 390-459, ICD-10:I00-I99), RPD (ICD-9: 460-519, ICD-10: J00-J99), RND (ICD-9:580-599, ICD10:N00-N39) and Diab (ICD-9: 250, ICD-10: E10-E14). A patient belongs to a specific cause group if one or more of the primary cause and potential contributor codes belong to the ICD range of that cause. Consequently, one patient may be counted in multiple causes.

2.2.2 Statistical Analyses

A distributed lag non-linear model (DLNM) [16] is used to derive the exposure-response functions. This approach allows us to simultaneously study the exposure-response relationships and the lag-response relationships without assuming linearity. In this study, a lag term l is used to describe the temporal delay between exposure and response. The exposure-response relationship describes relative risk (RR) as a function of temperature at a given l. The lag-response relationship describes RR as a function of lag lengths at a given temperature x. The core assumption of DLNM is that the mortality or morbidity at time t (Y_t) is the combined effect of the exposure-response and the lag-response relationships. The concepts behind DLNM have also been applied to hydrology and physics, with the purpose of identifying the best lag time linking independent and dependent variables [69, 70]. The lag-response relationship in DLNM also makes it possible to easily investigate harvesting effects of cold and heat exposures. Harvesting refers to a temporary increase in mortality and morbidity that does not lead to an overall increase in health burden [71]. It implies that a hazardous temperature exposure may shift some mortality and morbidity cases that would have happened over the following days earlier. Therefore, harvesting effect is often associated with overestimated risks when not considered.

This study assumes the exposure-response relationship to be a natural cubic spline function with three knots at 10^{th}, 75^{th}, and 90^{th} percentiles of temperature observations, and the lag-response relationship to be a natural cubic spline with three knots equally spaced across the natural logarithm of the total lag range. The maximum lag time considered is 28 days. The exposure-response and lag-response relationships are together expressed as a *cross-basis* (*cb*) function, which is then applied to a quasi-Poisson generalized linear model (GLM):

$$\log(E(Y_t)) = \beta_0 + cb + ns(Date, df) + \beta_1 \cdot dow + \underbrace{\beta_2 \cdot holidays}_{\text{Morbidity Model Only}} \tag{2.1}$$

where Y_t is mortality or EDV counts observed at time t. $Date$ accounts for the long-term trend, assuming a natural cubic spline function with 8 and 7 degrees of freedom (df) given to each year in the mortality and morbidity models, respectively. The weekday effect is captured by the dow. The term $holidays$ is a dummy variable indicating federal holidays and is only included in the morbidity model based on the results of likelihood ratio tests.

Model specification is based on diagnostics from testing various combinations of parameters. We vary the number (between three and five) and locations (e.g. 10^{th}, 50^{th}, and 90^{th} percentiles) of knots on the natural cubic spline function assumed for the exposure-response relationship, the degrees of freedom given to each year on the long-term trend line (from six to nine), and the maximum lag times (from 14 to 35 days with seven-day increments). Only large maximum lags are considered because the adverse health effects of cold exposure may persist in the population for longer than two weeks [33–35]. Specific model diagnostics are standardized quasi-Akaikes Information Criterion (qAIC) and mean squared error from 10-fold cross-validation. Ozone (O_3) and particulate matter with a diameter smaller than 2.5 μm ($PM_{2.5}$) were considered as potential confounders and did not significantly affect the ERF estimates. More information about this process can be found in Appendix A.4. The final parameter sets selected for all-cause mortality and morbidity models are carried over to cause-specific analyses.

Minimum Effect Temperature (MET) is the exposure level that corresponds to the minimum risk estimate (RR=1). It is the baseline for all other RR calculations and is cause- and health outcome-specific. In mortality-only studies, MET is also referred to as minimum mortality temperature (MMT). In practice, it is common for researchers to pick a MET a priori [27, 58].Pre-selected METs frequently fall into the 60-85°F range, corresponding to approximately 70^{th}-80^{th} percentiles of local temperature distribution. This study relaxes these assumptions by estimating MET from data. Point estimates are the lowest points of exposure-response functions. Uncertainty around these point estimates is calculated using a re-sampling (n=10,000) technique developed by [72]. This study then plugs the MET uncertainty ranges back into the statistical models to test the robustness of the RR estimations. With the final models, risk estimates corresponding to the 1^{st}-3^{rd} and 97^{th}-99^{th} percentiles of observed temperature history are extracted for further investigation.

Population health burden, in terms of fraction (AF) and cases (AC) attributable to hazardous temperature exposure, is calculated using a method from [73]:

$$\mathrm{AF}_{x,t} = 1 - \exp(\sum_{l=0}^{L} \beta_{x_{t-l},l}) \tag{2.2}$$

$$\mathrm{AC}_{x,t} = AF_{x,t} \cdot Y_t \tag{2.3}$$

In equation (2.2), $\mathrm{AF}_{x,t}$ is the AF at time t when the exposure level is x; $\beta_{x_(t-l),l}$ is the contribution to total risks at time t by exposure level at t-l (i.e., x_{t-l}), after l days have elapsed; L is maximum lag considered. In equation (2.3), $\mathrm{AC}_{x,t}$ is the AC at time t when the exposure level is x; Y_t is the total mortality or EDV counts observed at time t. This setup implies a backward perspective, i.e., the population health outcomes observed at time t is the sum of the responses from exposures at $t - L...t$. The uncertainty of AF and AC are assessed through Monte Carlo simulations (n=5000) [73] and are expressed as 95% empirical confidence intervals (eCI) since analytical confidence intervals cannot be easily derived [74].

All analyses in this study were performed using R (v 3.2.4) (R Foundation for Statistical Computing, Vienna, Austria) [75]. Packages **dlnm** [76] and **boot** [77] and functions **attrdl** [73] and **findmin** [78] are useful to the analyses.

2.3 Results

In the TCMA, there were 301198 cases of mortality and 6.64 million cases of EDV during their respective study periods, averaging to 49 deaths and 2273 EDVs per day. More details on the descriptive analytics can be found in Appendix A.5 and A.6. The mortality sample is predominately elderly whereas the age of the morbidity sample is near normally distributed centering on 37 years old. Between 1998 and 2014, HI_{max} ranged from -12°F to 114°F. The overall distribution is bi-modal, peaking at 36°F and 82°F (Appendix A.7).

This study first explores the general seasonal patterns observed in daily all-cause mortality (All_{MT}) and morbidity (All_{MB}) compared to HI_{max}. Shown in Figure 2.1(a), there is slightly higher average daily mortality during winter than summer, by roughly 5-10 cases. Moreover, there is a visible inverse association between All_{MT} and HI_{max}, i.e. the time that All_{MT} peaks each year coincides with when HI_{max} reaches its annual low. Such associations are not observed between All_{MB} and HI_{max}. All_{MB} is slightly higher than average between late December and early January, during the holiday seasons.

The first step of the statistical analysis was to establish the exposure-response functions between HI_{max} and all-cause population health outcomes (All_{MT} and All_{MB}). In Figure 2.2(a), the ERF shows a classic U-shape, indicating that All_{MT} RR increases as HI_{max} moves towards both cold and heat extremes. The MET is 84°F with a 95% eCI of [64°F, 84°F]. There is a significantly increased RR for All_{MT} when HI_{max} is above 89°F or below 44°F. The maximum RRs due to heat (1.62 [CI: 1.21, 2.16]) and cold (1.47 [CI: 1.22, 1.77]) are reached at historical highest and lowest HI_{max}. The ERF between HI_{max} and All_{MB} is also roughly U-shape, shown in Figure 2.2(b). With a MET of 74°F [eCI: 69°F, 81°F], the ERF indicates significantly increased RR over a broader range of HI_{max}, above 81°F or below 69°F. The maximum All_{MB} RR for heat (1.16 [CI: 1.03, 1.30]) and cold (1.21 [CI: 1.12, 1.31]) correspond to HI_{max} of 100°F and -12°F, respectively.

The ERFs between HI_{max} and cause-specific population health outcomes tell a different story. In Figure 2.3(a), CVD_{MT} RR is only significantly increased when HI_{max} is extremely low (<12°F). CVD_{MB} RR is significantly greater than 1 over a low to moderately low (4-60°F) as well as a high to extremely high exposure range (90-104°F). RRs for both RPD_{MT} and RPD_{MB} increase substantially as HI_{max} drops in winter (Figure 2.3(b)). Regarding heat exposure, RR is significantly greater than 1 only for RPD_{MT}, not RPD_{MB}. In Figure 2.3(c), RRs for RND_{MT} and RND_{MB} both increase significantly over high-temperature ranges. In winter, RR is significantly greater than 1 only for RND_{MB}, not RND_{MT}. Among all causes examined, RND has the largest discrepancy between the MET point estimates of mortality and morbidity. The MET for RND_{MT} is 84°F [eCI: 28°F, 86°F] and that for RND_{MB} is 65°F [eCI: 59°F, 72°F]. $Diab_{MT}$ does not show significant association with HI_{max} at any exposure level and is therefore omitted from Figure 2.3(d). $Diab_{MB}$ RR is significantly higher than baseline over a low to moderately low exposure range (10-52°F). Cause-specific METs used for the above analyses can be found in Appendix A.8. Sensitivity analyses that vary METs along their respective eCIs do not significantly change the exposure ranges that correspond to significantly increased RRs. Furthermore, this paper did not identify any harvesting effects.

Specific RRs corresponding to six extreme temperature thresholds (defined by 1^{st}-3^{rd} and 97^{th}-99^{th} percentiles historical observations) are extracted for further examination. Multiple extreme temperature thresholds are selected because health departments and weather agencies often need to communicate risks at different magnitudes and urgencies. This study assumes that a given threshold is effective for capturing population health risks if that threshold and any thresholds more extreme to it all capture significant increased RRs. For example, if the increased RR is significant at the 97^{th} percentile but not at the 98^{th} or 99^{th} percentiles, then 97^{th} percentile is not an effective temperature threshold for initiating extreme heat ERC programs. Moreover, ERC can be tailored to specific causes only when a threshold is effective for both mortality and morbidity outcomes.

The first two rows of Table 2.1 indicate that all six extreme exposure thresholds are effective for capturing all-cause mortality or morbidity. However, the effectiveness of these thresholds differs substantially considering different disease causes. All three extreme cold thresholds (1^{st}-3^{rd} percentiles) can be used in tailoring ERC for CVD and RPD. The highest two heat thresholds (98^{th}-99^{th} percentiles) can be used in tailoring ERC for RND. For RND patients exposed to extreme cold and CVD and RPD patients exposed to extreme heat, effective thresholds are found for only one of the mortality or morbidity outcomes. The RR estimates for $\mathrm{Diab_{MB}}$ stands out, as there is only statistical significance at a less extreme cold exposure threshold, i.e. 3^{rd} percentile $\mathrm{HI_{max}}$. A threshold-based approach cannot effectively target Diab because the riskiest temperature range is moderate cold (4^{th}-30^{th} percentiles), as opposed to extremely cold exposures (1^{st}-3^{rd} percentiles). Upon further examination, the ERFs of $\mathrm{CVD_{MB}}$ and $\mathrm{RND_{MB}}$ also show similar patterns. This result does not conflict with our previous conclusion: extreme temperature thresholds can effectively capture elevated risks for CVD and RPD. However, they may not be capturing the riskiest exposures.

ERFs are further used to calculate the attributable cases (AC) and attributable fractions (AF) as representations of population health burden. Results are shown in Table 2.2 and 2.3. Health burden is calculated for two temperature ranges: the cold range, defined by the lowest recorded $\mathrm{HI_{max}}$ (-12°F) and the MET; and the heat range, defined by the MET and the highest recorded $\mathrm{HI_{max}}$ (114°F). These ranges include both extreme and moderate levels of exposure. Overall, 7.01% [eCI: 1.24%, 12.27%] of All_{MT} and 5.53% [eCI: 3.91%, 7.09%] of All_{MB} in the TCMA are associated with hazardous ambient temperature exposures. Both cold and heat ranges have led to significant health burden, although the majority of the burden is due to cold exposures: 6.54% [eCI: 1.11%, 11.51%] of All_{MT} and 5.20% [eCI: 4.00%, 6.37%] of All_{MB} are associated with exposures to temperature in the cold ranges. Based on cause-specific analyses, there is significant RPD_{MT} burden given exposure to the heat range and of RND_{MT} burden given exposure to the cold range. Regarding morbidity, the cold ranges have led to significant health burden in all disease causes considered.

2.4 Discussion

Using data from the TCMA, this study investigates the association between ambient temperature exposure and a range of all-cause and cause-specific population health outcomes (mortality and morbidity) in the context of ERC. The ERFs for All_{MT} and All_{MB} show classic U-shape patterns, with RRs that increase as HI_{max} moves toward the extremes. These results are consistent with the existing literature [24, 53, 58, 79, 80].

Through cause-specific analyses, this study shows that RRs for both CVD_{MT} and CVD_{MB} increase as temperature decreases during the cold seasons, confirming some existing findings [49, 61, 81]. When it comes to heat, there is little consensus in the existing literature regarding its impacts on CVD. [47], [66], and [2] discovered significant associations between high temperature and CVD_{MT} whereas [81] reported null results regarding these associations. The link between CVD_{MB} and heat exposure has also been identified [50, 82] and discounted [25, 48]. Our result shows that there is a slight increase in RR for only CVD_{MB} when HI_{max} is high. The association between RPD and cold exposures are more consistent in literature for both mortality [52, 61] and morbidity [62, 83]. The effects of cold exposure on RPD are expected based on factors that uniquely exist in winter due to low ambient temperatures, such as cross-infections from indoor crowding, suppression of human immunity to respiratory infections, and suitable environments for bacterial survival [3, 84]. This study confirms the strong association between RPD_{MT} and heat, which has already been described in [52, 56, 85]. But the link between RPD_{MB} and heat has been both identified [25, 50, 51] and discounted [48, 86]. This study supports the latter. The strong association between heat and RND observed in the TCMA agrees with the existing literature [48, 54, 55, 58, 87]. However, this study is one of the first to report an increased RR for RND_{MB} related to moderately low temperature. To the best of our knowledge, this pair of exposure-response function has not been investigated before on the population level. $Diab_{MT}$ is the only health outcome that does not show any response to HI_{max}. The morbidity ERF, on the other hand, shows that Diab is only impacted by extremely low temperatures, confirming the discovery of [27].

When interpreting the all-cause and cause-specific ERFs, it is important to keep in mind the factors that may affect the statistical power of the patterns observed. For example, CVD_{MT} is only associated with extreme cold lower than 12°F and RPD_{MB} is only associated with extreme heat greater than 94°F. Although there is existing literature that supports these findings, we acknowledge that these temperature ranges, given that they are located at the ends of the temperature distribution, are based on low data density. Therefore, the interpretation of these seemingly significant relationships requires caution. Future research may solve this issue via cause-specific multi-country or multi-city meta-analysis. Another factor that may affect the interpretability and statistical power of this study is the sample size. For example, our study did not find any association between Diab_{MT} and ambient temperature exposure and thus have omitted Diab_{MT} from much of the discussion. However, it is possible that this result is a statistical artifact due to low sample size. In order to provide context for interpreting the results of this study, we provide the daily case counts of specific causes and population health outcomes in Appendix A.9 and A.10.

A number of factors could have led to the heterogeneous results between the ERFs derived in this study and those in the existing literature. [58] described how disease causes can be defined differently between studies, which highlights the importance of keeping the response definition in mind when drawing comparisons between different studies. For example, this and many studies identify CVD cases using the most inclusive criteria: ICD-9: 390-459 or ICD-10: I00-I99 [47, 52, 66, 88]. [58] did not include any cerebrovascular diseases (ICD-9: 430-459) in their CVD group (Kingsley et al., 2016). [83] only included ICD9: 390-403, 410-416, 420-429, and 785. Heterogeneity could also result from different criteria that determine if a patient belongs to a certain cause group. Each emergency room record or death certificate has one primary diagnostic or cause of death code and 1 to 25 secondary contributor codes. It is common to consider only the primary diagnostic or cause-of-death codes, as did [27]. However, some studies had a deeper look at the health records. For instance, [53] scanned for the first nine secondary contributor codes. This study scanned all available information. Last but not the least, morbidity can represent various population health outcomes, such as hospitalization, EDV, outpatient visits, and emergency medical service dispatches (e.g. ambulance). When comparing morbidity results to existing literature, it is crucial to differentiate by these outcomes.

Risk estimates at different ERC thresholds defined by percentiles are extracted from their respective ERFs. For the general population, all six thresholds correspond to significantly increased RRs for all-cause mortality and morbidity. Therefore, all extreme temperature thresholds considered in this study are appropriate for initiating ERC that broadly targets the general population. For specific health conditions, the results suggest that ERC programs can be effectively tailored for CVD and RPD given extreme cold exposures and RND given extreme heat exposures. Including information related to these health conditions in the ERC may reduce health burden associated with extreme temperature exposure. Some effective temperature thresholds cannot be used to tailor ERC programs, such as the extreme cold thresholds for RND, and extreme heat thresholds for CVD and RPD. The reason is that increased RRs exist only for one of mortality and morbidity, not both. There is no consistent evidence that these disease groups are sensitive to extreme temperature exposures. Thus, ERC programs cannot be tailored for these subgroups in the TCMA.

Contrasting patterns between cause-specific mortality and morbidity analyses have been briefly mentioned before by [25] and [86]. However, these studies could not confirm the validity of the observations as they are drawing information from different study designs, study populations, and study periods. This study fills in the research gap by showing that such contrasting patterns exist even after controlling for these factors. However, it is not within the scope of this study to investigate the underlying mechanisms. The contrasting patterns may indicate that some biological mechanisms are more fatal than debilitating. They may also be statistical artifacts stemming from low data density or small sample sizes. Future research should focus on testing the universality and finding the potential explanations of these patterns.

The AF and AC corresponding to each ERF are calculated. Compared to ERFs, AF and AC estimates are not as impacted by low data density because they weight the ERFs by the numbers of occurrences at different temperature levels. At extreme temperature levels, risk estimates are weighted less as they are derived using fewer data points. Considering cold exposure, the results of CVD, RND, and Diab stand out. There was significant health burden of these causes associated with cold exposure. However, CVD was the only health condition that can be effectively targeted by thresholds-based ERC. On the ERFs, it is evident that the cold-related health risks do not peak at cold extremes in these cause-specific analyses. Instead, they peak at moderately cold exposures. To better manage cold-related health risks for CVD, RND, and Diab, other channels of risk communication or management need to be explored, such as patient engagement during primary care because ERC may not be the most appropriate intervention.

We acknowledge that the implementation of ERC should consider other factors beyond those explored in this study. Temperature thresholds that capture increased RR for certain population health outcomes are merely a premise to successful intervention. For example, the magnitude of the increased RR can also be highly relevant for ERC planning. CVD_{MT} and CVD_{MB} have increased RR at all extreme cold thresholds. However, the risk estimates are both lower than 1.20, and the lower bounds of their corresponding CIs are hardly greater than 1.00. Thus, using extreme cold thresholds to initiate ERC for managing CVD risks during extremely cold days may have limited impacts. Furthermore, public health practitioners grapple with alert fatigue when designing ERC programs [89]. Overly frequent use of ERC may be counterproductive, leading to desensitization of the population and reducing the rate of behavioral changes [89].

Our study is among the first that considers the entire ambient temperature spectrum for both types of population health outcomes (i.e. mortality and morbidity). Besides the implications for ERC programs, the AF and AC calculated during all-cause and cause-specific analyses can provide further insights on the missing pieces of studies that fail to consider all relevant perspectives. Our models show that a total of 47,094 individuals each year experiencing adverse health impacts due to hazardous temperature exposure in the TCMA. Only 9.08% of the impacts can be attributed to heat, and 2.64% of the individuals died. Thus, existing studies on temperature and health that focus only on heat and mortality may be underestimating the true population health burden. In the TCMA, such underestimation is substantial. Further, only considering mortality outcomes may lead to the conclusion that certain health conditions, such as CVD and Diab, are not associated with ambient temperature exposure. This conclusion would be inaccurate as indicated by their significantly positive AF and AC for cold-related morbidity.

An important limitation of this study is the underlying assumption that the exposure-response functions in the TCMA remain constant throughout the study period. This assumption may be challenged in two ways. First, the exposure-response functions may change over the study periods due to local mitigation and adaptation efforts or changes in demographics or socioeconomic statuses. [90] detailed the significant changes in population resilience to heat from the beginning of the 20th century (1900-1948) to more recent decades (1973-2006). [91] showed that the risk of $\mathrm{CVD}_{\mathrm{MT}}$ declined between 1987 and 2000. Assuming that exposure-response functions remain constant, as does this study, can be problematic. Second, exposure-response functions may also vary by time of year. For example, [92] suggest a reduction in heat-related mortality risks as summer progresses. Using one set of exposure-response functions throughout the year may overlook some important seasonal dynamics. Future studies should investigate and integrate these dynamics to explore how they may affect the ERFs and the burden of health estimates. Another limitation is that the temperature exposure in this study is approximated by averaging weather station measurements and may differ from actual individual-level exposure. Future studies should consider using more granular information to approximate individual-level exposures. This direction will likely provide useful information on high-risk groups (defined by potential risk factors such as age and occupation) for managing temperature-related adverse health impacts.

This study validates the most important premise of effective ERC: the extent to which the threshold-based activation criteria are related to all-cause and cause-specific health risks. Future research should evaluate the effectiveness of ERC programs in terms of risk reduction. The methods applied in this study can be repeated in other locations as data become available with the goal of uncovering the universality of exposure-response functions, particularly regarding the contrasting patterns between cause-specific mortality and morbidity.

2.5 Conclusion

This study finds that extreme temperature thresholds can capture significantly increased risks for population-level health outcomes. Thus, extreme temperature thresholds are appropriate activation criteria for ERC that broadly target the general population. Cause-specific analyses suggest that ERC can be tailored to protect cardiovascular and respiratory disease risks given extreme cold exposures, and renal disease risks given extreme heat exposures. Considering different exposure and health outcome types are crucial to understanding the adverse health impacts associated with hazardous ambient temperature exposure. Failing to consider any of these components may lead to an underestimation of the corresponding health burden.

Tables

Table 2.1: Relative Risks Results at Extreme Temperature Thresholds

		Extreme Cold			Extreme Heat		
		1^{st} %ile	2^{nd} %ile	3^{rd} %ile	97^{th} %ile	98^{th}h %ile	99^{th} %ile
Disease Category	Population Health Outcome	5°F	9°F	12°F	93\dg F	95°F	98°F
All-cause	Mortality	**1.29**	**1.26**	**1.23**	**1.06**	**1.08**	**1.14**
		[1.15, 1.46]	**[1.13, 1.40]**	**[1.11, 1.37]**	**[1.02, 1.10]**	**[1.03, 1.14]**	**[1.05, 1.23]**
	Morbidity	**1.20**	**1.20**	**1.19**	**1.04**	**1.05**	**1.07**
		[1.15, 1.26]	**[1.15, 1.25]**	**[1.15, 1.24]**	**[1.02, 1.07]**	**[1.02, 1.08]**	**[1.03, 1.10]**
CVD	Mortality	**1.2**	**1.18**	**1.17**	1.02	1.04	1.07
		[1.01, 1.43]	**[1.00, 1.39]**	**[1.00, 1.36]**	[0.97, 1.09]	[0.97, 1.13]	[0.96, 1.21]
	Morbidity	**1.07**	**1.08**	**1.09**	**1.04**	**1.05**	**1.06**
		[1.00, 1.15]	**[1.02, 1.15]**	**[1.03, 1.16]**	**[1.00, 1.07]**	**[1.01, 1.09]**	**[1.01, 1.12]**
RPD	Mortality	**1.66**	**1.56**	**1.49**	1.08	1.11	**1.09**
		[1.29, 2.15]	**[1.23, 1.97]**	**[1.19, 1.87]**	[0.99, 1.16]	[0.99, 1.24]	**[1.01, 1.42]**
	Morbidity	**2.3**	**2.2**	**2.14**	1.01	1.02	1.04
		[2.06, 2.56]	**[2.00, 2.42]**	**[1.96, 2.36]**	[0.98, 1.04]	[0.98, 1.07]	[0.97, 1.12]
RND	Mortality	1.2	1.17	1.16	1.1	**1.16**	**1.27**
		[0.85, 1.70]	[0.85, 1.61]	[0.85, 1.57]	[0.99, 1.23]	**[1.00, 1.34]**	**[1.02, 1.59]**
	Morbidity	**1.09**	**1.09**	**1.08**	**1.08**	**1.08**	**1.09**
		[1.00, 1.18]	**[1.01, 1.17]**	**[1.01, 1.16]**	**[1.01, 1.13]**	**[1.02, 1.14]**	**[1.02, 1.17]**
Diab	Mortality	1.52	1.46	1.42	1.01	1.01	1.01
		[0.60, 3.83]	[0.58, 3.68]	[0.56, 3.59]	[0.45, 2.28]	[0.46, 2.17]	[0.51, 1.98]
	Morbidity	1.07	1.08	**1.09**	1.02	1.03	1.04
		[0.96, 1.18]	[0.97, 1.18]	**[1.00, 1.18]**	[0.98, 1.06]	[0.98, 1.08]	[0.87, 1.11]

Specific disease groups investigated include (a) all-cause, (b) cardiovascular disease (CVD), (c) respiratory disease (RPD), (d) renal disease (RND), and (e) diabetes (Diab). White and shaded boxes are extreme temperature thresholds that can and cannot be used to effectively tailor emergency risk communication programs.

Table 2.2: Health Burden, Mortality (1998-2014)

Cause	Cold[a] AF (%) [95%eCI]	Cold[a] AC [95%eCI]	Heat[a] AF (%) [95%eCI]	Heat[a] AC [95%eCI]
All	6.54 [1.10, 11.51]	19719 [3622, 34467]	0.46 [0.14, 0.76]	1390 [441, 2316]
CVD	5.58 [-2.93, 13.17]	7975 [-3621, 18741]	0.25 [-0.17, 0.65]	351 [-259, 930]
RPD	12.12 [0.13, 22.40]	8382 [64, 15402]	0.55 [-0.04, 1.10]	381 [-26, 751]
RND	7.02 [-9.58, 19.98]	2501 [-3324, 7165]	0.85 [0.00, 2.51]	304 [-3, 586][b]
Diab	NA	NA	NA	NA

CVD = cardiovascular disease; RPD = respiratory disease; RND = renal disease; Diab = Diabetes; AF = attributable fraction; AC = attributable cases; eCI = empirical confidence interval; NA = not applicable.

[a] Health burden related to cold is defined as population health responses to HImax between recorded lowest HImax and minimum effect temperature; that related to heat is defined as population health responses to HImax between minimum effect temperature and recorded highest HImax. [b] When testing the statistical significance of AC for renal disease, the p-value is 0.051. This result is considered significant in this study.

Table 2.3: Health Burden, Morbidity (2007-2014)

Cause	Cold[a]		Heat[a]	
	AF (%) [95%eCI]	AC [95%eCI]	AF (%) [95%eCI]	AC [95%eCI]
All	5.2 [4.00, 6.37]	345358 [267205,421343]	0.48 [0.9, 0.87]	32076 [6588, 57086]
CVD	3.78 [1.91, 5.52]	56928 [29474, 83611]	0.43 [-0.11, 0.96]	6483 [-1810, 14762]
RPD	22.5 [18.95, 25.83]	298295 [254129, 343313]	0.12 [-0.10, 0.33]	1598 [-1172, 4360]
RND	2.24 [0.46, 3.96]	15624 [3814, 27244]	1.21 [-0.03, 0.72]	8431 [-567, 17104]
Diab	3.86 [0.76, 6.68]	22201 [5135, 38903]	0.21 [-0.02, 0.72]	1219 [-1778, 4112]

CVD = cardiovascular disease; RPD = respiratory disease; RND = renal disease; Diab = Diabetes; AF = attributable fraction; AC = attributable cases; eCI = empirical confidence interval; NA = not applicable.

[a] Health burden related to cold is defined as population health responses to HImax between recorded lowest HImax and minimum effect temperature; that related to heat is defined as population health responses to HImax between minimum effect temperature and recorded highest HImax.

Figures

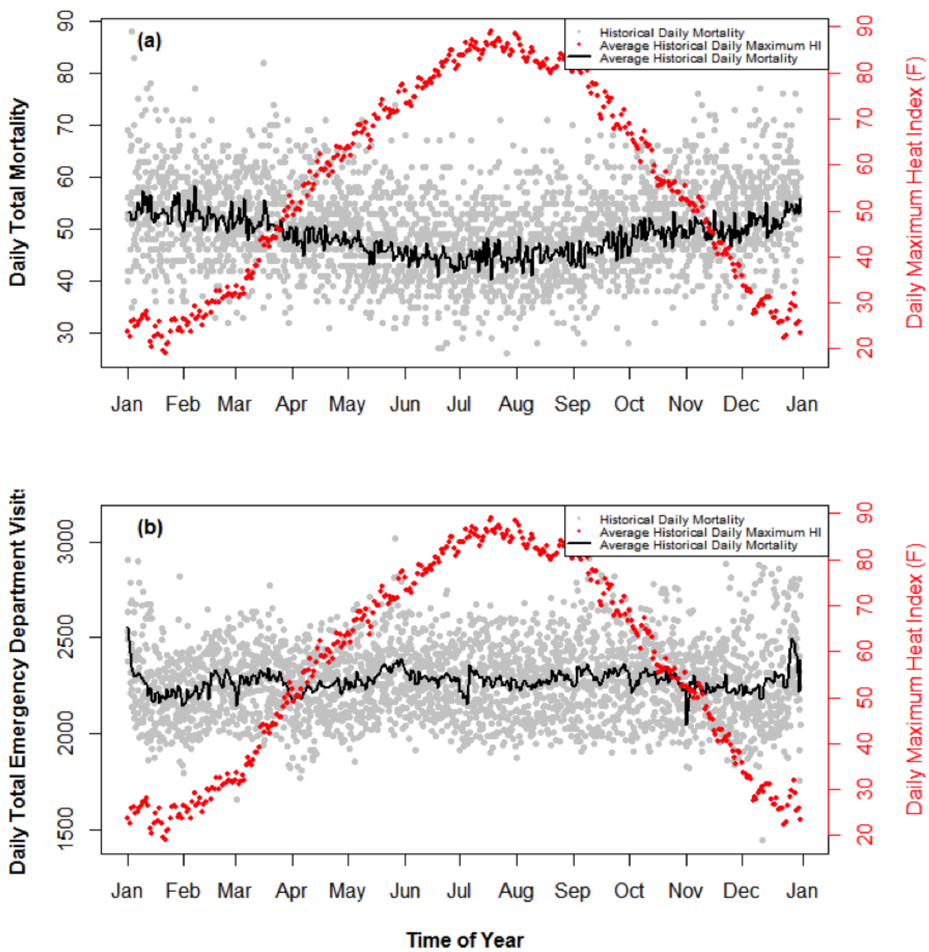

Figure 2.1: Seasonality of HI_{max} and All-Cause Population Health Outcomes in the Minneapolis – St. Paul Twin Cities Metropolitan Area

The black solid lines represent historical average (a) daily mortality (1998-2014) and (b) daily morbidity (emergency department visits, 2007-2014). The gray points are historical HI_{max} by the day of year. The red line indicates the historical average HI_{max} by the day of year (1998-2014).

Red solid lines in (a) represent the ERF and its 95% CI in terms of mortality.

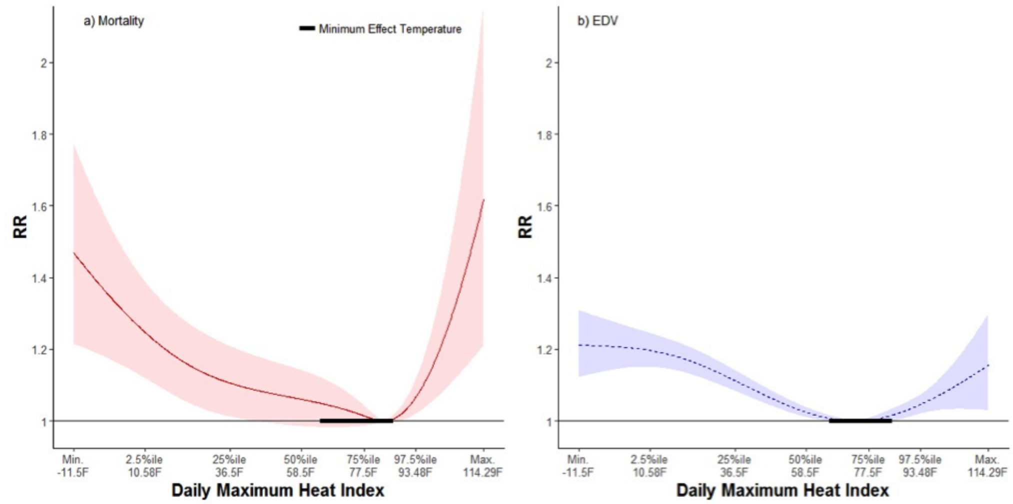

Figure 2.2: Exposure-Response Function (ERF) between Ambient Temperature and All-Cause Mortality (1998-2014) and Morbidity (Emergency Department Visits, 2007-2014) in the Minneapolis – St. Paul Twin Cities Metropolitan Area

The association is modeled using quasi-Poisson generalized linear model, adjusted for a natural cubic spline for HI_{max} (degrees of freedom = 3, knots = 10^{th}, 75^{th}, 90^{th} percentiles, maximum lag considered = 28 days), day of week, and a natural cubic spline for long-term trend (8 degrees of freedom/year). Blue and dashed lines in (b) represent the ERF and its 95% CI in terms of EDV. The association is modeled using a natural cubic spline for HI_{max} (degrees of freedom = 3, knots = 10^{th}, 75^{th}, 90^{th} percentiles, maximum lag considered = 28 days), day of week, a natural cubic spline for long-term trend (7 degrees of freedom/ year), and federal holidays. Black solid lines show the 95% eCI of MET obtained through bootstrapping.

Specific causes investigated include (a) cardiovascular disease (CVD), (b) respiratory disease (RPD), (c) renal disease (RND), and (d) diabetes (Diab). Model specifications are carried over from the all-cause mortality and morbidity analyses. Red and solid lines represent the ERF and its 95% CI in terms of mortality. Blue and dashed lines represent the ERF and its 95% CI in terms of EDV. $Diab_{MT}$ is not included, as it shows

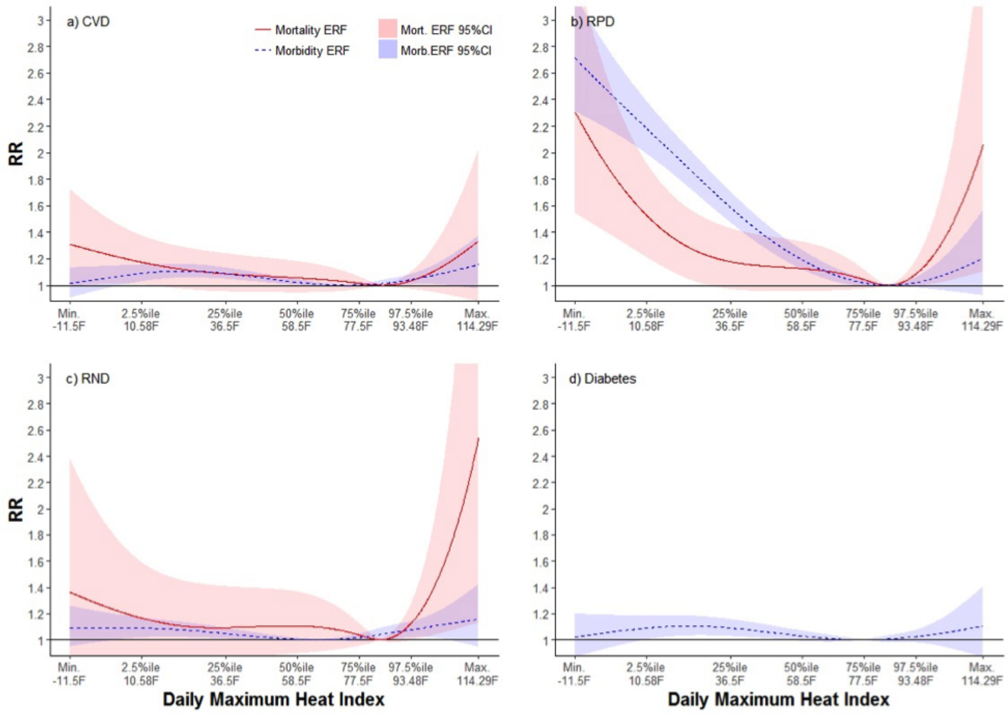

Figure 2.3: Exposure-Response Function (ERF) between Ambient Temperature and Cause-specific Mortality (1998-2014) and Morbidity (Emergency Department Visits, 2007-2014) in the Minneapolis – St. Paul Twin Cities Metropolitan Area

no association with HI_{max} at any temperature level.

Chapter 3

Designing Models for Impact Assessment

Liu, Y., Saha, S., Hoppe, B. O., & Convertino, M. Degrees and Dollars - Health Costs Associated with Non-optimum Ambient Temperature Exposure. In agency review.

Key Findings

- Extreme temperatures (defined as the bottom and top 5 percentiles) lead to $2.70 billion [95%eCI: $1.91 billion, $3.48 billion] ($2016) health related costs in the Twin Cities area each year.

- Moderate to extreme temperatures (defined as the bottom and top 30 percentiles) lead to $9.40 billion [95%eCI: $6.05 billion, $12.57 billion] ($2016) health related costs in the Twin Cities area each year.

- Mortality burden among the elderly is the greatest contributor to health related costs associated with suboptimal ambient temperature exposure.

Summary

Non-optimum ambient temperature exposure is a concerning public health threat that can affect a variety of health conditions. Previous studies have primarily focused on risk assessment, with few having examined the relevant health outcomes from an economic perspective. In order to support climate-related health decision-making, this study estimates the economic burden from adverse public health outcomes associated with ambient temperature exposures in the Minneapolis – St. Paul Twin Cities Metropolitan Area.

A distributed lag nonlinear model is used to derive the exposure-response functions and to assess the public health outcomes. The analysis is stratified by health outcome (mortality and morbidity) and age group (youth, non-senior adult, and senior). Multiple cost types (medical costs and productivity loss) are considered when estimating the total economic burden.

Results show that exposure to extreme low and high temperatures (defined as the lowest and highest 5 percentiles) lead to $2.70 billion [95%eCI: $1.91 billion, $3.48 billion] ($2016) in economic costs annually. Including moderately low and high-temperature exposures (defined as lowest and highest 30 percentiles) raises the estimate up to $9.40 billion [95%eCI: $6.05 billion, $12.57 billion] ($2016).

The majority of the economic costs can be attributed to cold exposures rather than heat, and to mortality costs rather than morbidity. The youth and the senior age groups are more vulnerable compared to non-senior adults, indicating potential benefits in strategically targeting them in public health practices. The findings of this study can also be integrated with future cost-benefit analyses of interventions.

3.1 Introduction

Ambient temperature exposures can be linked to substantial adverse health impacts, involving a wide range of health conditions [61, 81, 93, 94]. Within the context of global climate change, such health risks are particularly concerning [6]. Estimates from 2006-2010 show that 1300 and 670 premature deaths are related to extreme cold and heat exposure in the U.S. each year [95]. However, based on issues of reporting and surveillance, such estimates are likely much smaller than the true burden [6]. Besides more accurate risk assessment, decision makers tasked with protecting communities from non-optimum temperature exposures also require a comprehensive understanding of the relevant economic burden to the population in order to prioritize initiatives, allocate resources, and justify budgets for public health planning [96].

Even though many researchers have studied the relationship between ambient temperature and population health, relatively few have assessed adverse health outcomes in terms of associated economic burdens. [37], [67], and [97] are among the few that have provided such economic estimates. Nevertheless, the characterization of exposure and/or health response in these studies makes the integration of the results into health intervention planning difficult. For instance, in [37], only a specific two-week long heat wave in California during summer 2006 is analyzed, whereas temperature-related adverse health impacts occur throughout the year with considerable seasonal variability [24, 92]. [67] and [97] only consider hospitalization as the health response. Nevertheless, existing research shows that temperature affects a range of health outcomes, such as mortality [24], hospitalizations [82], and emergency department visits [80, 98]. Failing to account for multiple outcomes lead to underestimation of the corresponding economic burdens.

Targeting these research gaps, this study introduces a comprehensive approach that converts adverse health outcomes to cost estimates that capture the economic burden of non-optimum ambient temperature exposure. Adverse health outcomes, in the context of this study, include mortality, emergency department visits, and emergency hospitalizations. The relationship between exposure and response is modeled using a distributed lag non-linear model (DLNM) [16]. Costs criteria considered include both medical costs and productivity loss. The study site is the Minneapolis – St. Paul Twin Cities Metropolitan Area (TCMA). The results of this study provide evidence to support future cost-benefit analysis for potential interventions.

3.2 Materials and Methods

3.2.1 Public Health Data

The TCMA includes seven counties in southeast Minnesota: Anoka, Carver, Dakota, Hennepin, Ramsey, Scott, and Washington. Mortality (MORT) data (1998-2014) for the region were obtained from the Office of Vital Records, Minnesota Department of Health (MDH). Morbidity data (2005-2014) were collected from 142 emergency rooms within the local healthcare network and were provided by the Health Economics Program of MDH. The morbidity dataset further breaks into emergency department visits followed by discharge (EDV) and emergency department visits followed by hospitalization (EDHSP), i.e., emergency hospitalization. This study assumes that patients do not stay for treatment in an emergency department for longer than 3 days. Thus, emergency department visits that did not end in hospitalization but lasted longer than three days were removed. Consequently, 11138 EDV records (approximately 0.17% of total morbidity records) were removed. The datasets are further broken down by age: youth (0-19 years old (yo)), adult (20-64 yo), and senior (65+ yo).

3.2.2 Cost-related Parameters

The total health-related costs of MORT rely on the Value of a Statistical Life (VSL). It is the societal willingness to pay for mortality risk reductions [99]. By definition, it is free of any health, demographic, or socioeconomic characteristics. In this study, we will use the VSL value derived by the U.S. Environmental Protection Agency (EPA) for cost-benefit analyses of the Clean Air Act [100]. More recent estimates are also considered for sensitivity analysis [101].

Total medical care costs of morbidity depend on the total billed charges reported on hospital records adjusted by the Cost-to-Charge Ratios (CCR) and Professional Fee Ratios (PFR). CCR converts the total amount that a patient pays to an amount that approximates what the medical facility receives for providing service to that individual [102]. For this study, CCR is calculated based on when and where service occurred. PFR further includes costs that are non-facility based, such as salaries for physicians and other healthcare professionals. This study uses the PFR value for EDV among commercially insured individuals, 1.286, estimated by [103]. Notably, PFR estimates for EDHSP or for Medicaid visits do not vary substantially for other insurance types, based on the same study.

Daily Productivity Value (DPV) is used to estimate the productivity loss due to EDV and EDHSP, drawn from [104]. DPV reflects a combination of factors such as average daily working hours, usual hourly compensation, daily market compensation and more. [104] provided the DPV estimations for 5-year age groups starting from 15-19 yo. In the context of this study, [104]s results indicate that the youth (0-19 yo) and the senior (65+ yo) age groups generally do not work more than 2 hours/day on average for formal market compensation. The 20-64 yo age group tends to work 3-5 hours/day. Consequently, the average DVP weighted by age distribution in Minneapolis [105] is $8.74/day ($2007) for the youth, $175.78/day ($2007) for the adults, and $57.12/day ($2007) for the senior population. More details on how these values are calculated can be found in Supplemental Information Appendix B.1 From here on, all costs in this study are estimated in terms of 2016 dollar unless otherwise noted.

3.2.3 Environmental Data

Historical meteorological data for the TCMA were extracted for seven weather stations within the regional boundaries. Ambient temperature exposure in this study is represented by daily maximum heat index (HI_{max}), which is calculated using air temperature (°F) and relative humidity (%). HI is a useful indicator of approximate temperature experienced by the human body during summer. Although there are a variety of ways to calculate HI [51], this study adopted the method established by [65] for consistency with National Weather Service (NWS) standards. Currently, the NWS uses HI_{max} thresholds to initiate heat-related emergency response plans (e.g., heat alerts). Outside of summer months during which HI_{max} is primarily used, the values of HI_{max} are comparable to daily maximum air temperature in the TCMA. All individuals within the TCMA are assumed to be exposed to the same ambient temperature, an average of HI_{max} from the seven weather stations, during a given time in history.

Although not selected for the final model, air pollution was considered during the model selection phase. Data on ozone (O_3) and particulates with a diameters equal or smaller than 2.5 μm ($PM_{2.5}$) were obtained from the Minnesota Pollution Control Agency for the years 2000 to 2013. More details on the exploratory analysis using air pollution as a potential confounder can be found in Appendix B.2.

We used a distributed lag nonlinear model (DLNM) to derive the exposure-response function (ERF) between observed temperature and population health outcomes [16]. This method is appropriate because there are distinct temporal delays (lag l) between the exposures and responses considered in this study. The model is set up as a quasi-Poisson generalized linear model:

$$\log(E(Y_t)) = \beta_0 + cb + ns(Date, df) + \beta_1 \cdot dow + \underbrace{\beta_2 \cdot holidays}_{\text{Morbidity Model Only}} \tag{3.1}$$

where Y_t is the daily counts of public health outcomes; cb is a cross-basis function that captures both the exposure-response relationship (i.e., how different exposure levels affect human health at a given time) and the lag-response relationship (i.e., how a given exposure level affects human health at different time lags). This model further adjusts for day of week (dow), a long term trend ($Date$), holiday effects ($holidays$, only for morbidity model). All risk estimates using this model are calculated relative to the reference temperature that minimizes relative risk (RR) instead of to a pre-selected reference temperature [72]. This baseline is referred to as the minimum effect temperature (MET) in this study. Although a synonym to minimum mortality temperature (MMT), MET is used here to show that such reference temperature is relevant for studying both mortality and morbidity outcomes. Additional details regarding the specifications of risk models can be found in the Appendix B.3.

3.2.4 Attributable Fraction and Attributable Cases

While ERF shows that the risks increased associated with non-optimum ambient temperature exposures, attributable fractions (AF) and attributable cases (AC) capture the specific health burden given local temperature history. In other words, AF is the percentage of and AC is the number of cases among public health outcomes associated with non-optimum ambient temperature exposures. In order to calculate the AF and AC, this study uses a method developed by [106]. The underlying assumption is a backward temporal perspective – the health response at a given time t is a result of many exposure events that led up to it. AF and AC are therefore defined as:

$$\mathrm{AF}_{x,t} = 1 - \exp(\sum_{l=0}^{L} \beta_{x_{t-l},l}) \tag{3.2}$$

$$\mathrm{AC}_{x,t} = AF_{x,t} \cdot Y_t \tag{3.3}$$

where x is the ambient temperature exposure level at time t; $\beta_{x_{t-l},l}$ is the natural logarithm of RR given exposure at time $t - l$ (i.e., x_{t-l}) after l days have elapsed; Y_t is daily counts of population health outcomes at time t. For the purpose of interpretation, we examined two temperature ranges for attributable risks: moderate to extreme exposures, defined by the bottom and top 30 percentiles of the historical temperature record (40 and 76°F, respectively); and extreme exposures, defined by the bottom and top 5 percentiles of the historical temperature records (18 and 89°F, respectively). The goal is to compare the health outcomes and relevant economic burdens attributable to different levels of cold and heat exposures. Both AF and AC are examined to identify the most vulnerable and the most affected age groups.

When it comes to uncertainty assessment, it is challenging to obtain an analytical solution using this approach [74, 106]. Therefore, Monte Carlo simulations (n = 5,000) are used. Uncertainty, therefore, is expressed as 95% empirical confidence intervals (eCI).

3.2.5 Year-to-Year Variations for Cost Estimation

Various parameters that estimate costs, such as Cost-to-Charge Ratios (CCR), differ drastically from year to year. Consequently, there is a need to explore the year-to-year variability in AC. This study proposes an incremental approach for this purpose:

$$AC(y)_p = \begin{cases} \sum_{i=1}^{m_y} AC_{x,t_i} & \text{if } y = 1 \\ \sum_{i=1}^{m_y} AC_{x,t_i} - \sum_{i=1}^{m_{y-1}} AC_{x,t_i}, & \text{if } y > 1 \end{cases} \tag{3.4}$$

where $AC(y_p$ denotes the point estimation of AC during year y; my is the number of observations in the first y years of the time series. The uncertainty around $AC(y)_p$ is assumed to depend on that of $AC(y)_{p.tot}$. In other words, for each simulation result of total attributable cases ($AC_{tot.sim}$), there is an annual attributable cases (AC_{sim}) defined as:

$$AC(y)_{sim} = \frac{AC(y)_p}{AC_{tot.p}} \cdot AC_{tot.sim} \tag{3.5}$$

The results of this intermediate step are shown in Appendix B.4.

3.2.6 Overall Cost Function

In this study, three public health outcomes (MORT, EDV, EDHSP) are examined to calculate the annual costs associated with non-optimum ambient temperature exposure in the TCMA. The loss due to MORT is the product of total lives lost and VSL.

The mean VSL estimation based on a meta-analysis conducted in 1997 is \$4.8 million (\$1990), equivalent to \$10.11 million in 2014 [100] after adjusting for income growth and inflation. Procedures used to convert 1990 estimations to other years can be found in Appendix B.5.1.1 to B.5.1.3. Moreover, we also considered several updated VSL estimates [101]. These studies and their corresponding estimate, ranging from \$5.56 to \$13.90 million are shown in SI Section B.5.1.4. This approach is currently employed by the United States Environmental Protection Agency (e.g. Environmental Benefit Mapping and Analysis Program) [107, 108], Food and Drugs Administration [109], and the Department of Transportation [101] to assess the costs of premature deaths in impact assessment.

The two cost elements for EDV and EDHSP include medical care costs and productivity loss. Medical care cost is the product of attributable EDV or EDHSP and the total cost of care. The total cost of care is determined by three factors: total billed charges reflected on emergency department records or discharge forms, cost-to-charge ratios (CCR), and the professional fee ratio (PFR):

$$\begin{aligned}\text{Morbidity Loss} &= \text{Medical Costs} + \text{Productivity Loss}\\ &= \text{Attributable EDV/EDHSP}\times\\ &(\text{Total Bill Charges} \times \text{CCR} \times \text{PFR}+\\ &+ \text{Length of Stay} \times \text{DPV})\end{aligned} \tag{3.6}$$

In this study, the first two elements are both drawn from hospital records. PFR, on the other hand, is drawn from [103]. As for productivity loss, only two parameters are involved. Expected lengths of stay are obtained through hospital records. The daily productivity loss (DPV) this study used is drawn from [104] and is weighted based on the population age distribution in the TCMA. For details, see Appendix B.1.1.

3.3 Results

Descriptive statistics of the study population are shown in Table 3.1. Between 1998 and 2014, there were 301198 deaths in the TCMA, with 2.63%, 22.76% and 74.91% of the sample corresponding to each of the 0-19, 20-64, and 65+ yo age groups. The morbidity dataset contained 8,117,358 emergency department visits, of which 11138 were removed due to possible clerical errors. Of the rest, 17.86% (1447793) were EDHSPs. EDVs on average stayed in the emergency room for 1.05 days and were predominantly adults (20-64 yo). EDHSP individuals on average stayed in the emergency room and then the hospital combined for 4.42 days.

Figure 3.1 shows the exposure-response functions (ERF) for total and age group-specific daily mortality and morbidity. These functions characterize the level of risks associated with each temperature exposure level relative to the reference level (i.e., MET), at which RR corresponds to 1. For the total population, MET is 84°F for MORT (marked in red) and 71°F for EDV and EDHSP (marked in blue and green, respectively) as indicated in Figure 3.1(a). (For other MET estimates in Figure 3.1(b-d), please refer to Appendix B.6). Relative to these METs, the ERFs show classic U- or J- shapes. As expected, moderate exposure levels correspond to non-significant or mild health risks. Temperatures greater than 95°F (98^{th} percentile) are associated with increased RR for MORT and EDV but not for EDHSP. Cold exposures below 44°F are consistently associated with increased RR across all population health outcomes considered. Age-specific analyses reveal three additional pieces of information that are important for understanding the relationship between temperature and population health. First, the oldest age group (65+ yo) is the only group that shows a statistically significant association between MORT and ambient temperature exposure. RR increases at both ends of the temperature range as shown in Figure 3.1(d). The MORT of the two younger age groups do not respond significantly to any temperature exposure levels based on our results; thus, it does not make sense to calculate the relevant MORT burden for these groups. Such result confirms the findings in existing literature, such as [110, 111]. Second, based on measures of morbidity, heat exposures only significantly affect youth (0-19 yo) as shown in Figure 3.1(b). No significant increase in RR for adults or seniors is observed in terms of morbidity. Regarding this particular aspect, outcomes from comparable studies are highly diverse, ranging from little to none association across age groups [60, 112] to significant associations in two or more age groups [58, 113]. Third, cold significantly affects all age groups in terms of both population health outcomes at both extreme and moderate to extreme levels, consistent with existing literature [80, 114].

Figure 3.2 and Figure 3.3 compare the results of AF and AC across different exposure types (cold and heat) and magnitudes (moderate to extreme exposures and extreme exposures only) by age group. MORT results, marked as red, are only calculated for seniors. Between 1998 and 2014, 13,991 (6.19%) deaths of individuals 65 or above were related to moderate to extreme cold exposures, and 3,444 (1.53%) occurred during or following extreme exposures. Moderate to extreme heat exposures were associated with 2,016 (0.89%) senior deaths, and 1,144 (0.51%) senior deaths occurred during or following extreme heat exposures.

EDV and EDHSP results, marked as blue and green respectively, were analyzed in the same way. The youngest age group (0-19 yo) was the only age group with statistically significant health burden associated with heat exposures. There were 23478 [8751, 37860] (1.2% [0.44%, 1.92%]) cases of EDV and 1089 [194, 1929] (0.78% [0.14%, 1.39%]) cases of EDHSP linked to moderate to extreme heat exposures. Among them, 12079 [7512, 16420] (0.62% [0.39%, 0.84%]) EDV cases and 657 [102, 1189] (0.47% [0.07%, 0.85%]) EDHSP cases were associated with extreme heat exposures. Heat was not linked to a significant health burden among adults (20-64 yo) or seniors (65+ yo) in this study population. Regarding cold, there are statistically significant AF and AC for both health outcomes and for all age groups considering moderate to extreme exposures. Given EDV, youth has the highest AF as well as AC (7.03% [5.89%, 8.10%], 137622 [115749, 157331], respectively). However, the EDHSP-specific analysis shows that although youth has the highest AF (6.63% [2.48%, 10.27%]), seniors have the highest AC (24252 [15750, 32327]). The underlying reason is that there are much more total senior EDHSPs than youth EDHSPs. When narrowing exposures down to only extreme cold, all estimates become smaller than before as expected. The statistical significance of AF and AC among senior EDVs disappear. All other patterns described above remain valid. The attributable EDHSP for youth, adult, and senior are 2488 [1225, 3680], 4372 [1992, 6732], and 4445 [2319, 6509] their differences become smaller than that considering moderate to extreme cold exposures. Overall, 0-19 yo is the most vulnerable but not always the most affected age group. Based on attributable EDHSP, seniors and adults are both more affected than youth. Numbers used to generate Figure 3.2 and 3.3 can be found in Appendix B.7.

Our final analysis focused on cost estimation. This study calculated the total health-related costs for both moderate to extreme exposures and extreme exposures only in order to provide perspectives given different public health policy objectives (Table 3.2

and 3.3). The first component of the total economic costs is mortality costs, which largely relies on the VSL. After taking into consideration inflation and income growth, based on total AC in the 65+ yo age group and the VSL estimated by [100], the mortality costs related to moderate to extreme cold and heat exposures are $8119.33 million [eCI: $4158.15 million, $11862.49 million] and $1167.50 million [eCI: $478.11 million, $1839.77 million] per year, respectively based on VSL estimate of 10.11 million in 2014 and the mortality burden estimate in Table 3.2. The mortality costs related to extreme cold and heat are $2005.67 million [eCI: $1152.52 million, $2809.77 million] and $665.06 million [eCI: $276.35 million, $1.051.53 million] dollars per year, respectively based on the same VSL estimate and the mortality burden estimate in Table 3. Updated VSL values identified by [101] does not lead to substantial changes in estimation (Appendix B.5.1.5).

Morbidity costs involve two criteria, EDV and EDHSP, and two sub-criteria, medical costs (MC) and productivity loss (PL). After taking into consideration inflation, the overall results show that the medical costs for EDHSP are much higher than that of EDV due to the duration of stay. Additionally, the medical costs due to cold exposures are much higher than that of heat due to higher health burden. Among EDV cases, the largest contributor to annual medical costs was the 0-19 yo age group under cold exposure. This age group accounted for $8.15 million [eCI: $7.78 million, $8.50 million] in medical expenses associated with moderate to extreme cold exposures and $2.21 million [eCI: $2.11 million, $2.32 million] associated with only extreme cold exposures. Among EDHSP cases, the largest contributor to annual medical costs was the 65+ yo age group under cold exposure, which accounted for $37.25 million [eCI: $33.60 million, $40.92 million] in medical expenses associated with moderate to extreme cold exposures and $6.85 million [eCI: $5.81 million, $7.90 million] associated with only extreme cold exposures.

Productivity loss is the product of total lengths of stay in the emergency room or hospital and daily production value (DPV). After taking into consideration inflation, results show that the productivity loss is predominantly associated with the adult age group (20-64 yo) for both EDV and EDHSP cases under cold exposures. Considering moderate to extreme cold exposures among adults, the annual productivity loss was $1.63 million [eCI: $1.41 million, $1.84 million] due to EDV cases and $1.93 million [eCI: $1.64 million, $2.22 million] due to EDHSP cases. Considering extreme cold exposures only, the annual productivity loss was $0.29 million [eCI: $0.23 million, $0.35 million] due to EDV cases and $0.46 million [eCI: $0.38 million, $0.55 million] dollars due to EDHSP cases.

The final result shows that each year, the health burden associated with ambient temperature exposure leads to economic costs of approximately $9.40 billion [eCI: $6.05 billion, $12.57 billion] if we consider both moderate and extreme exposures and $2.70 billion [eCI: $1.91 billion, $3.48 billion] if we only consider extreme exposures in the TCMA. Morbidity loss makes up roughly 0.12-2.48% of the total costs depending exposure magnitude and age group.

3.4 Discussion

This study calculated the health-related economic costs due to ambient temperature exposures for the TCMA approximately $9.40 billion [eCI: $6.05 billion, $12.57 billion] dollars annually when both extreme and moderate exposures are considered. This comprehensive estimate relies on multiple criteria, capturing different population health outcomes. The World Health Organization (WHO) recommends the use of such multi-criteria approaches for estimating health-related costs associated with climate change as a means of internalizing an array of external costs, enabling comparison across different outcomes, providing explicit rules for balancing a range of information [115]. Our method provides valuable information about the magnitude of economic costs from particular sources in the TCMA, demonstrating certain methodological strengths that recommend its application for other jurisdictions.

Our findings highlight that temperature-related costs vary strongly by age. Seniors are the only age group for which mortality is significantly associated with extreme and moderate temperature conditions for both cold and heat. These results are broadly consistent with those of [116], which demonstrated that mortality attributable to ambient temperature exposure is greater for persons 65+ yo compared to younger age groups. Consequently, the overall mortality costs were essentially just mortality costs for seniors. Factors that make seniors more vulnerable to ambient temperature exposures include social isolation [117], poverty [118], a high prevalence of chronic health conditions [116], and reduced ability to take preventive actions to mitigate exposures [119]. Regarding morbidity outcomes, i.e., EDV and EDHSP, the relative risks for youth increase more rapidly than other age groups as temperature move to the extremes of both cold and heat. This age group also has the highest morbidity AF associated with cold exposures and is the only age group whose morbidity AF associated with heat is statistically significant. However, there were many more senior EDHSP cases than youth cases. Seniors hospitalized after emergency department visits likely require more intensive and extensive medical services due to co-morbidities and reduced physiological capacity [116, 119]. Therefore, it is understandable that seniors contribute more to medical costs even though youth are associated with higher risks of EDHSP given non-optimum temperature exposure.

Results suggest that studies that limit their analysis to seniors *a priori*, under the assumption that other age groups are not as severely impacted by ambient temperatures, may be under-reporting the true number of individuals affected, leading to substantial under-estimation of total population health burden. Consequently, the total economic burden calculated using such health burden may also suffer from under-estimations, although to a much smaller degree than does total population health burden. The reason is that the total economic burden is predominantly driven by MORT, and only the senior age group shows a significant response to temperature in terms of MORT. With regard to public health services, strategically focusing on both the youngest and the oldest individuals appears necessary. Specific examples of potential interventions are risk communication and education targeting local schools and health care providers regarding preventive measurements. Strategic prioritization among age groups will depend on the objective of the decision maker. For instance, targeting youth is justifiable when the goal is to protect the most vulnerable individuals. Targeting seniors or adults, especially for cold, may more significantly reduce economic costs.

This study examines the entire temperature range experienced by the TCMA throughout a typical year instead of constraining exposure to a particular range. There are three underlying reasons for this design. First, given the continental climate of the TCMA, the region experiences both extreme cold and extreme heat. The local population is more accustomed to severe winter weather than to the increasingly hot summers. Second, both low and high-temperature exposures can pose health risks to the population. Although there are numerous studies that focus on health risks from extreme heat, recent findings indicate that moderate heat and cold exposures may be more dangerous [24]. Finally, preventing adverse health outcomes from ambient temperatures, either low or high, can rely on similar interventions, such as risk communication (e.g., weather alerts), exposure management (e.g., cooling or warming shelters), and community engagement (e.g., education programs or planning guidance). In a typical cost-benefit analysis in the context of temperature risk management, when interventions simultaneously affect cold and heat exposures, health outcome evaluation that also summarizes cold and heat effects are more applicable when using decision support tools such as multi-criteria decision analysis [120].

Our study results show that cold exposures are responsible for the majority of the total health-related economic costs for the TCMA. This holds true regardless of health outcome or age category. Harsh winters and freezing temperatures pose serious health risks even for a well-acclimatized population. One potential explanation for the larger cost burden related to cold is the considerable inflow of immigrants and refugees to the TCMA from warmer climates, who may not be accustomed to or prepared for cold weather exposures. Minnesota ranks among the top U.S. states for refugee resettlement [121]. The majority of new foreign-born residents arrive from Somalia, Burma, and Iraq, countries where the coldest annual temperatures rarely drop below 65°F [122]. However, comparing cities with different levels of immigrant influx may provide answers to this hypothesis in the future.

The health burden related to low ambient temperature might contain overestimation due to residual confounding. Such bias may arise due to the exclusion of respiratory infections as a confounder. Some previous studies, such as [59], investigated weekly influenza variation as a confounder while studying the relationship between temperature and winter hospital admissions and found statistically significant results. This study, however, does not adopt the same assumption since we believe the evidence of a causal relationship between temperature and respiratory infections has not yet been established. Studies like [123] suggests the possibility for respiratory infections to be considered a mediator instead of a confounder in studying the link between winter temperature and population health. Overestimation in our results will exist if new evidence emerges that confirms respiratory infections as a confounder in the causal pathway.

An existing study adopted a multi-criteria cost estimation approach similar to the one used in this study to estimate the economic burden related to a two-week extreme heat event in California [37]. In their study, a given public health outcome (premature death or emergency room visits) corresponded to one medical cost estimation. Our study takes this approach a step further by integrating productivity loss. For instance, an emergency room visit will incur both medical costs and productivity loss. One of the biggest strengths of this approach is transparency. Although different public health outcomes are eventually summed to obtain the total economic costs, it is easy to backtrack to the itemized cost criterion that contributes the most (or the least) to the overall economic burden. For instance, in our study, 98% of the total economic burden can be traced back to mortality although the remaining 2% affects a much larger number of individuals (Appendix B.8). The theoretical framework of this study is flexible. When new parameter estimates become available, updated total costs can be easily produced.

A potential limitation of this study lies in the cost function, which consists of two components: mortality costs and morbidity costs. As mentioned above, VSL is a measure of societal willingness-to-pay for reducing mortality risks. In practice, there are two study designs that are used to obtain VSL estimations: stated preferences studies and hedonic wage studies [108]. The former is based on surveys with questions regarding hypothetical scenarios, which can introduce certain bias [124]. The latter is generally believed to provide more accurate estimates, although estimations are based on employed adults [108]. Using such VSL estimates on youth and seniors, the two age groups that are most vulnerable to ambient temperature exposures yet less likely to be employed, could be problematic. Further, there is currently little consensus on how VSL varies by age [108]. The most intuitive speculation is younger workers have a higher VSL since they have more years loss as a result of premature deaths. However, some evidence has shown an inverted U-shape relationship [125, 126]. Our study assumed VSL to be insensitive to age. It is also important to point out that when adding mortality costs and morbidity costs, we are adding theoretical costs (i.e., willingness-to-pay) to transactions that have actually occurred (i.e., medical bills). To compensate for this limitation, we provide itemized costs as well as overall costs of public health burden associated with non-optimum ambient temperature exposures.

There are additional health-related costs attributable to the ambient temperature that this study did not include, such as visits to outpatient clinics or physicians offices. It is possible individuals affected by ambient temperature use such medical services when their conditions are mild. This study also did not consider any medical costs incurred after discharge, such as prescription drug costs. Unfortunately, we did not find high-quality data on these variables.

3.5 Conclusion

This study describes an approach for assessing economic costs incurred by the health burden associated with ambient temperatures. This information can help develop effective public health interventions, targeting specific at-risk populations, and allocating scarce resources, particularly with the threat of shifting temperature patterns due to climate change. We find that the use of multiple criteria aggregated to different age categories can lead to a useful composite indicator of costs while also providing insight into age-dependent differences across cost criteria that may be useful for targeting interventions and bolstering adaptation planning.

Tables

Table 3.1: Descriptive Statistics of the Study Population

Age Category	Mortality (1998-2014)			Morbidity (2005-2014)					
	MORT			EDV			EDHSP		
	tot	μ	σ	tot	μ	σ	tot	μ	σ
0-19	7034	1	1	1957692	536	84	139318	38	9
20-64	68550	11	3	3980639	1090	127	721132	197	22
65+	225,614	36	7	720096	197	40	587343	161	18
All	301198	48	8	6658427	1823	210	1447793	396	36

Table 1 describes the study population in the Minneapolis-St. Paul Metropolitan Area. Three population health outcomes are Mortality; EDV - Emergency Department Visits; EDHSP - Emergency Department Visits followed by hospital admission. tot sums the total number of cases for each population health outcomes over the course of 17 years for mortality and 10 years for morbidity. μ - daily mean case counts; σ - daily variability measured by standard deviation.

Table 2 summarizes the cost estimation of each criterion of the annual total health cost (US$2016) attributable to moderate to extreme ambient temperature exposure. MM = million.

Table 3.2: Health-related Economic Costs Associated with Moderate to Extreme Exposure Ranges

Health Outcome	Cost Criteria	Age Group	Moderate-Extreme Cold Exposure $HI_{max} <30^{th}$%ile (unit=$MM) Expected Value [95% eCI]	Moderate-Extreme Heat Exposure $HI_{max}>70^{th}$%ile (unit=$MM) Expected Value [95% eCI]
MORT	-	0-19	-	-
		20-64	-	-
		65+	8119.33 [4158.15, 11862.49]	1167.50 [478.11, 1839.77]
EDV	Medical Costs	0-19	8.18 [7.82, 8.54]	1.4 [1.15, 1.65]
		20-64	7.17 [6.25, 8.11]	-
		65+	2.54 [2.01, 3.06]	-
	Productivity Loss	0-19	0.16 [0.15, 0.16]	0.03 [0.02, 0.03]
		20-64	1.64 [1.43, 1.85]	-
		65+	0.12 [0.10, 0.15]	-
EDHSP	Medical Costs	0-19	12.81 [10.63, 14.98]	1.51 [1.11, 1.94]
		20-64	27.69 [23.53, 31.81]	-
		65+	37.2 [33.48, 40.85]	-
	Productivity Loss	0-19	0.04 [0.03, 0.05]	0.005 [0.004, 0.006]
		20-64	1.93 [1.63, 2.21]	-
		65+	0.78 [0.71, 0.86]	-
Total	-	-	8215.18 [4908.92, 11357.45]	1,171.47 [614.26, 1749.07]

Table 3 summarizes the cost estimation of each criterion of the annual total health cost (US$2016) attributable to extreme ambient temperature exposure. MM = million.

Table 3.3: Health related Economic Costs Associated with Extreme Exposure Ranges

Health Outcome	Cost Criteria	Age Group	Extreme Cold Exposure HI_{max} <5^{th}%ile (unit=$MM) Expected Value [95% eCI]	Extreme Heat Exposure HI_{max} >95^{th}%ile (unit=$MM) Expected Value [95% eCI]
MORT	-	0-19	-	-
		20-64	-	-
		65+	2005.67 [1152.52, 2809.77]	665.06 [276.35, 1041.53]
EDV	Medical Costs	0-19	2.21 [2.11, 2.32]	0.73 [0.65, 0.81]
		20-64	1.27 [1.00, 1.54]	-
		65+	-	-
	Productivity Loss	0-19	0.04 [0.04, 0.04]	0.01 [0.01, 0.02]
		20-64	0.29 [0.23, 0.35]	-
		65+	-	-
EDHSP	Medical Costs	0-19	3.49 [2.87, 4.13]	0.91 [0.63, 1.22]
		20-64	6.57 [5.39, 7.77]	-
		65+	6.85 [5.81, 7.90]	-
	Productivity Loss	0-19	0.01 [0.01, 0.01]	0.003 [0.002, 0.004]
		20-64	0.46 [0.38, 0.55]	-
		65+	0.15 [0.12, 0.16]	-
Total	-	-	2033.24 [1318.64, 2725.38]	667.61 [343.46, 993.11]

Figures

Figure 1 shows the exposure-response functions (ERF) derived using a distributed lag non-linear model. Three population health outcomes, [mortality (MORT, red), Emergency Department Visits (EDV, blue), and Emergency Department Visit followed by hospital admission (EDHSP, green) are considered for a) total population, b) 0-19 year-olds, c) 20-64 year-olds, and d) 65+ year-olds. Solid lines indicate relative risks (compared to minimum effect temperature) significantly greater than 1 and dotted lines indicate non-statistically significant results.

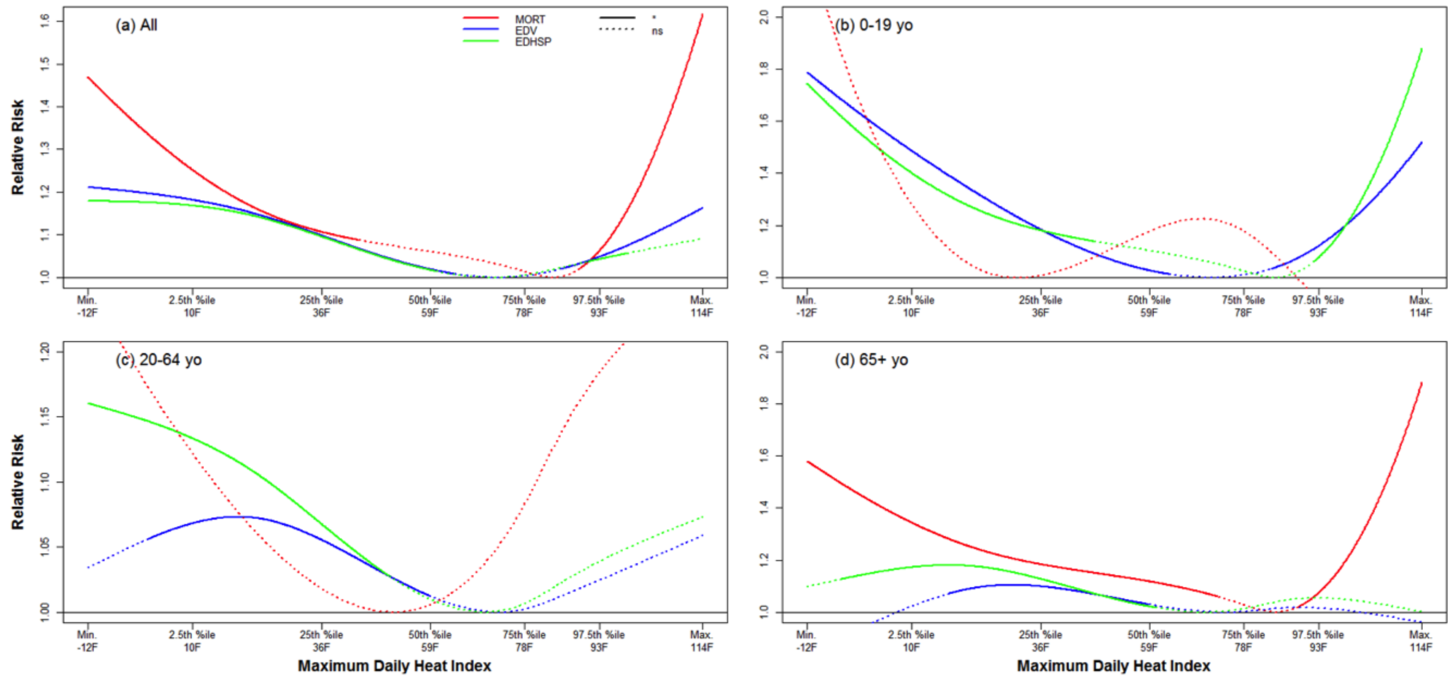

Figure 3.1: Exposure-Response Functions by Age Group and by Health Outcome

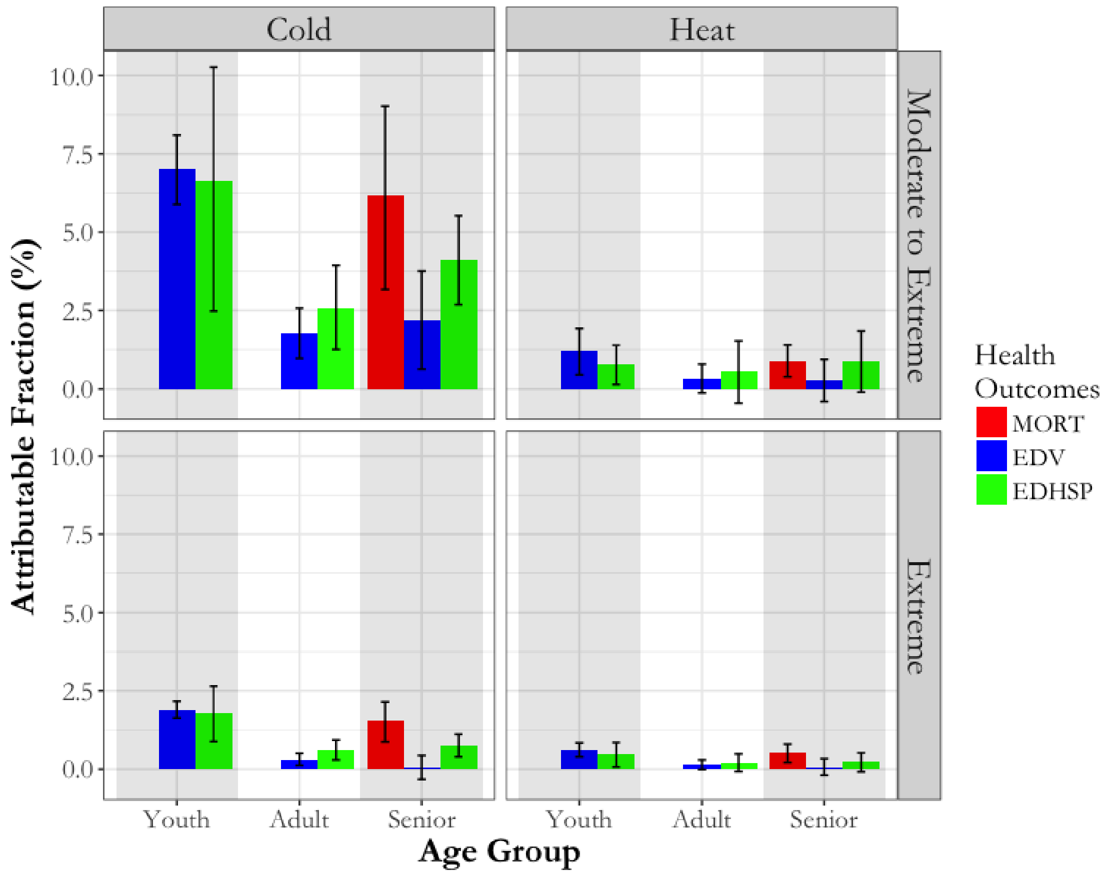

Figure 3.2: Attributable Fractions by Age Group and by Health Outcome

Figure 2 shows the attributable fraction (AF, %) of mortality (MORT, red), Emergency Department Visits (EDV, blue), and Emergency Department Visits followed by hospital admission (EDHSP, green) due to moderate to extreme levels or extreme levels only of cold and heat exposures. The uncertainty range is defined by 95% empirical confidence intervals obtained by Monte Carlo simulations (n=5000). Figure 2 does not include mortality results regarding 0-19 year olds or 20-64 year olds because there is no increased relative risk of mortality at any exposure level for these age groups.

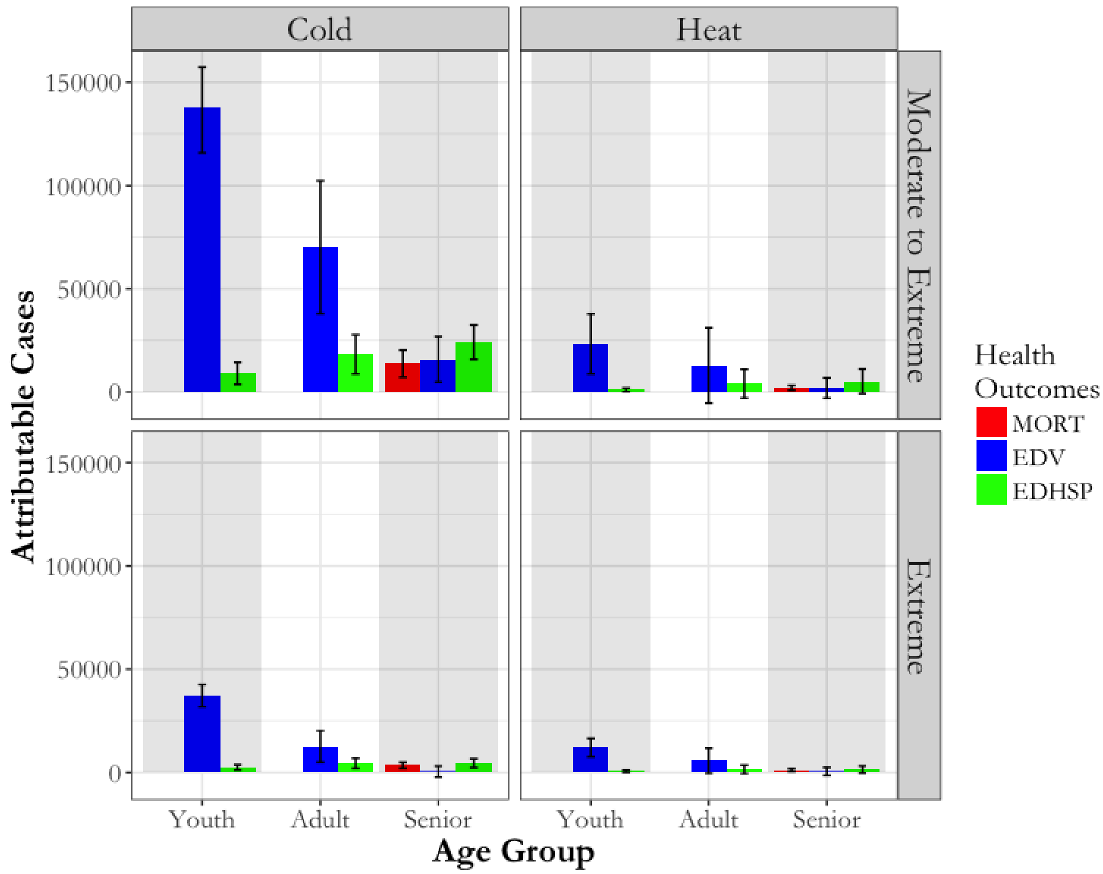

Figure 3.3: Attributable Cases by Age Group and by Health Outcome

Figure 3 shows the attributable cases (AC) of mortality (MORT, red), Emergency Department Visits (EDV, blue), and Emergency Department Visits followed by hospital admission (EDHSP, green) due to moderate to extreme levels or extreme levels only of cold and heat exposures. The uncertainty range is defined by 95% empirical confidence interval obtained by Monte Carlo simulations (n=5000). Figure 2 does not include mortality results regarding 0-19 year olds or 20-64 year olds because there is no increased relative risk of mortality at any exposure level for these age groups.

Chapter 4

Designing Models for Intervention Planning

Liu, Y., Saha, S., Hoppe, B. O., & Convertino, M. Improving Risk Assessment by Increasing Age Granularity among Children Exposed to Suboptimal Ambient Temperature. *In preparation.*

Key Findings

- Among all children (0-18 years old), 3-11 year-olds experience higher health risks when exposed to low temperatures; 3-5 and 12-14 year-olds experience higher health risks when exposed to high temperatures.
- Newborns, infants, and toddlers (0-2 years old) are more sensitive to moderate to extreme temperature exposures (bottom and top 30 percentiles) than to extreme temperature exposures (bottom and top 5 percentiles).
- Cause-specific health risks differentiate by age groups in some but not all cases.

Summary

Suboptimal ambient temperature exposure is a concerning environmental health risk with a serious public health burden. Although it is well established that children experience higher health risks when exposed to suboptimal ambient temperature compared to adults, there is little understanding of how these health risks differentiate within this group by age. In order to improve public health intervention, this study seeks to identify vulnerable individuals among children (0-18 years old) by increasing age granularity.

A distributed lag nonlinear model is used to derive the exposure-response functions and to assess the public health burden for five distinct age groups among children (0-18 years old). Public health outcome is measured by emergency department visits in the Minneapolis-St. Paul Twin Cities Metropolitan area between 2005 and 2014. The analysis is further stratified by disease causes.

Results show that 5-11 year-olds experience higher health risks compared to children overall when exposed to suboptimal low temperatures; 3-5 and 12-14 year olds experience higher health risks compared to children. Some disease groups (e.g., respiratory diseases) affect children across all five age groups while others (e.g., skin diseases) affect some age groups more than the others.

This study shows that health responses to suboptimal ambient temperature exposure among children differ by age groups. The findings of this study are useful for public health agencies to develop targeted intervention strategies based on vulnerability when managing relevant health risks.

4.1 Introduction

Recent literature indicates that suboptimal ambient temperature exposures are associated with serious mortality and morbidity burden [28, 127]. A recent meta-analysis using 350 locations around the world estimates that 7.71% mortality is associated with suboptimal ambient temperature exposure [24]. Additionally, there is evidence that children experience higher health risks than adults when exposed to risky ambient temperature [28, 38, 128]. During a 2006 heat wave in California, higher all-cause morbidity risks were observed among children compared to adults [53, 59]. There are three mechanisms that could explain this vulnerability: physiological [129, 130], metabolic [28, 131], and behavioral [28, 132, 133]. (Sarofim et al. 2016; Sheffield and Landrigan 2011; U.S. Environmental Protection Agency 2005).

Not only are children at higher risks than adults, they also have higher within-group heterogeneity by age in terms of exposure levels (both duration and magnitude) and health response capacity [38, 134]. For example, high schoolers have high health response capacities and also high exposure levels [134]. Newborns, infants, and toddlers have low health response capacities and also low exposure levels [133]. Therefore, general statements such as children are experiencing higher health risks than adults when exposed to suboptimal temperature provides little useful information for public health practitioners seeking to develop evidence-based intervention strategies targeting the most vulnerable individuals.

Nevertheless, no epidemiology study has yet investigated the risk heterogeneity by age among children exposed to suboptimal ambient temperature exposure. Existing studies that conduct risk assessments for children tend to use only one stratum to include all young individuals [49, 135–139]. Targeting this knowledge gap, the primary research objective of this study is to identify age groups among children (0-18 years old) [140] that experience higher all-cause morbidity risks than others when exposed to suboptimal ambient temperature.

Additionally, a secondary research objective to further investigates if there is cause-specific morbidity risk differentiation among children by age group. Although respiratory [59, 141, 142], gastrointestinal [143, 144], and infectious diseases [145–147] have been the primary interests of the existing literature, all major disease groups are considered in this study.

The study population is the emergency department visits (EDV) by children within the Minneapolis – St. Paul Twin Cities Metropolitan Area (TCMA). The results from the primary research objective are useful for public health agencies and practitioners to develop intervention strategies that most effectively target vulnerable individuals. The results from the secondary research objectives are useful for pediatric environmental health researchers to uncover underlying causal mechanisms between ambient temperature and childrens health.

4.2 Materials and Methods

4.2.1 Public Health Data

Data on EDV were collected through the Minnesota Hospital Association and made available by the Health Economics Program at the Minnesota Department of Health.

For all-cause analysis, the study period is Jan 1^{st}, 2005 Dec 31^{st}, 2014 (3562 days). EDVs longer than 3 days without hospitalization were assumed clerical errors because it is uncommon for emergency departments to accommodate extended stays. For cause-specific analysis, disease causes are based on International Classification of Disease (ICD) codes, Version 9 and 10. This study begins with exploring 17 general categories of diseases. Specific disease causes and their corresponding ICD codes used are in the Appendix C.1. In 2005, the hospital systems in the TCMA underwent changes regarding the coding standards of major health conditions. Therefore, the study period of cause-specific analysis is truncated to Jan 1^{st}, 2007 Dec 31^{st}, 2014 (2922 days) to avoid bias.

In order to identify the high-risk individuals by age, the EDV dataset is aggregated into five age groups defined by 3-6 year ranges: newborn, infants, and toddlers (0-2 years old); pre-school children (3-5 years old); school age children (6-11 years old); young teens (12-14 years old); and teenagers (15-18 years old). These age groups are selected a priori based on existing literature [49, 135–139], the definitions used by the National Center on Birth Defects and Developmental Disabilities [148], and the definitions used by the AAPs Committee on Environmental Health [140]. Some studies only focus on newborn and infants (0 years old) [47, 149]. This study compares this group with 1-2 and 0-2 years olds to explore if such differentiation is necessary in the study population.

4.2.2 Environmental Data

The TCMA consists of seven counties in central-east Minnesota, a mid-west state in the United States. Temperature data was provided by the National Weather Service (Twin Cities/Chanhassen, MN) and is calculated by averaging the observations from seven weather stations within the TCMA. This study considers two temperature metrics: air temperature and heat index (HI). Heat index is a compound metric of temperature and humidity that approximates temperature perceived by the human body [51, 65]. This study further examined three statistical features for each temperature metric: daily minimum, mean, and maximum.

Air pollution is investigated as a potential confounder. Data on particulate matter with a diameter smaller than 2.5 μm ($PM_{2.5}$) and ozone (O3) are available for Jan 1^{st}, 2000 Dec 31^{st}, 2013. Ozone was not measured during summers prior to 2006. Therefore, the sensitivity analysis on the potential confounding effect is truncated to Jan 1^{st}, 2006 Dec 31^{st}, 2013 to avoid missing data issues.

4.2.3 Statistical Analysis

This study uses a distributed lag linear model (DLNM) [16] combined with a generalized linear model assuming quasi-Poisson distribution to derive the exposure-response functions (ERFs) between ambient temperature exposure and childrens EDV. This method accounts for temporal delays between exposure and response i.e., the lag effects. In the case of ambient temperature exposure, such temporal delays can range from several days to several weeks [51]. This method also relaxes the assumption of linearity, which allows the model to better approximate real ERFs [150].

A DLNM framework allows for high flexibility in terms of model design as it simultaneously estimates the exposure-response relationship and a lag-response relationship. An exposure-response relationship describes the health response using different temperature at a given time t. This study assumes that the exposure-response relationship can be captured by a natural cubic spline with three knots at 10^{th}, 50^{th}, and 90^{th} percentile temperature distribution. A lag-response relationship describes the health response of at a given temperature for different time steps, e.g., t, $t-1$ ... $t-l$ where l is the maximum temporal delay (i.e. lag days) considered. This study assumes that the lag-response relationship can be captured by a natural cubic spline with three equally spaced knots across the natural logarithmic log range. The maximum lag considered is 28 days. The general form of the ERF can be expressed as the following:

$$\begin{aligned} \ln(E(Y_t)) &= \beta_0 + cb + ns(Date, df) + \beta_1 \cdot dow \\ &+ \beta_2 \cdot holidays + \beta_3 \cdot summer \end{aligned} \tag{4.1}$$

where cb is the cross-basis function that represents the pair of splines described above, capturing the assumptions for both exposure-response and lag-response relationship, Y_t represents the daily counts of EDV for different age groups among children, and $\beta_{(0-3)}$ are coefficients. This model also adjusts for weekday effect using the day of week (i.e. *dow*) as a categorical variable, for long-term trend using a natural spline function derived using Date and 7 degrees of freedom (df)/year, and for holiday effects using a binary variable *holiday* (i.e. federal holidays and 2 days following). For children above 6, this model further adjusts for summer school breaks using a binary variable *summer*.

This study uses a data-driven approach to determine model parameters. Quasi-Akaike Information Criterion (qAIC) and results from cross-validation (CV) are equally weighted when evaluating combinations of model parameters. With Y_t representing the daily counts of total EDV among all children (0-18 years old), the model development process tests 180 different combinations of model parameters in predictors included in the final model. Examples are the maximum lag and the number of knots on spline functions. The optimal combination of parameters is carried over to further analysis specific to age and to disease groups.

The outputs of DLNM are relative risk (RR) estimates, which rely on their respective reference baselines, in this case, the minimum morbidity percentile (MMP). MMP is the temperature corresponding to the lowest morbidity risk and is specific to age and disease group. [72] discovered that in cases where daily counts (Y_t) are low, biases during spline estimation could generate an MMP at temperature extremes (i.e. 0th or 100th percentiles). From a biological standpoint, it is unlikely for temperature extremes to be the optimal conditions for human health [150]. To mitigate such biases, they introduced a spline re-sampling process that can be used to simulate a sample of MMPs as the uncertainty range. In this study, for a given age and disease group, the median of the simulated sample (n=5000) is considered the MMP when the lowest point estimate of ERF falls on temperature extremes. This approach does not assume ERF to be U- or J- shaped. Linear relationships can still be captured.

EDV risks among different age groups are compared using two approaches. First, we compare the probability density functions of point estimates at different exposure ranges. Extreme temperatures (defined as bottom and top 5 percentiles, $\leq$ 7°F and $\geq$ 77°F) and moderate to extreme temperatures (defined as bottom and top 30 percentiles, $\leq$ 33°F and $\geq$ 54°F) are both considered. We then use one- and two-tailed weighted pairwise Wilcoxon rank-sum tests to compare each age group to children as a whole (0-18 years old) at different exposure ranges. In other words, pairs of RR point estimates are weighted by the data density of the corresponding temperature level. For example, the difference between $\mathrm{RR}_{0-2,32^{\circ}\mathrm{F}}$ and $\mathrm{RR}_{0-18,32^{\circ}\mathrm{F}}$ is weighted by the frequency of temperature observations around 32°F. This first approach directly compares the shape of ERFs by effect estimates only; it does not take into consideration the uncertainty (i.e., confidence interval) surrounding the point effect estimates. Second, attributable fractions (AF) of EDV associated with suboptimal ambient temperature are compared using one- or two-tailed $t-tests$. AF describes the proportion of total EDVs during the study period that is associated with ambient temperature and is considered the measure of health burden in this study. In a DLNM framework, methods used to calculate AF have been described in [73]. This approach considers uncertainty (i.e., confidence interval) yet overlooks the specific shapes of ERFs. ERFs with different shapes may have similar AFs. Therefore, the two approaches described above complement each other in determining if certain age groups are experiencing higher EDV risks than the others. Statistical significance is defined by type I error rate smaller than 0.05.

The secondary research objective of this study is to explore if morbidity risks related to specific disease groups differentiate by age. Here, comparing the shape of ERFs is less of interest. Thus, only AFs are calculated. Since this study examines all 17 major disease groups, it is likely that the small sample sizes in some strata may make it difficult to generate meaningful and interpretable results. This study uses two criteria to decide if a disease group can be included in the further analysis: (1) if the seven-year total case count is large enough (>1000 cases); (2) if the number of days with zero-counts is small enough (<500 days).

We performed the analyses in this study using R (v 3.3.2) (R Foundation for Statistical Computing, Vienna, Austria). We used packages dlnm [76] and boot [151] and functions attrdl [73] and findmin [72].

4.3 Results

4.3.1 Descriptive and Exploratory Analysis

There are a total of 1979275 cases of EDV in the TCMA between 2005 and 2014 of children (0-18 years old) after removing 769 clerical errors (Table 4.1). The mean (SD) of the total daily EDV counts is 542 (85). Among the five age groups, the largest group is 0-2 year-olds, representing 35.58% of the total study population. The mean (SD) of daily counts within this group is 193 (42). The smallest group is 12-14 year-olds, representing 10.43% of the total study population. Seasonal variations by age group are plotted in Appendix C.2. Overall, higher than normal EDV counts are observed for periods around federal holidays. EDV counts among 0-2 year-olds are generally lower in summer than in winter. Among individuals 6 years old or above, EDV counts are lower during summer vacations at school compared to school years.

The EDV counts by age group and by disease causes can be found in the Appendix C.3 and C.4. Nine specific causes are included in the statistical analysis based on their sufficient sample sizes: (1) endocrine, nutritional and metabolic diseases, and immunity disorders (short as metabolic disease from here on); (2) diseases of the nervous system and sense organs (short as nervous system diseases); (3) diseases of respiratory system (short as respiratory diseases); (4) diseases of digestive system (short as digestive diseases); (5) diseases of the genitourinary system (short as genitourinary diseases); (6) diseases of the skin and subcutaneous tissue (short as skin diseases); (7) diseases of the musculoskeletal system and connective tissue (short as musculoskeletal disease); (8) symptoms, signs, and ill-defined conditions (short as ill-defined conditions); and (9) injury and poisoning.

The environmental variable selection process shows that daily mean and maximum air temperature and HI lead to similar model performances. This study uses daily mean air temperature ($TMean$) to measure ambient temperature exposure. In the TCMA, $TMean$ has a bimodal distribution with two peaks at 33°F and at 70°F. During 2005-2014, mean (SD) of $TMean$ is 47°F (22°F).

4.3.2 Identifying Vulnerability by Age Group

Figure 4.1 shows the ERFs for all children and for each age group. Comparing ERF of all children (0-18 years old, Figure 4.1, top left) to the ERF of the total population (children, adults, and elderly, Appendix C.5) confirms that overall childrens health is more sensitive to suboptimal temperature. That is, the EDV RR increases more steeply for children than the total population when temperature moves from MMP towards the temperature extremes. Moreover, the MMP of children is slightly higher than that of adults (Appendix C.6, $p<0.05$).

In the risk assessment models, air pollution ($PM_{2.5}$ or O_3) does not significantly affect the effect estimates and therefore is not included in the final model (Appendix C.7). A one-at-a-time exclusion exercise on the final models reveals that predictors contributing the most to reducing the root mean squared errors is *dow* and *Date* (Appendix C.8). This is not surprising because they represent the baseline EDV among children while this study seeks to estimate the excessive EDV. In other words, there are EDVs that will occur regardless of ambient temperature exposure due to weekly- or seasonally-varying factors that are not explicitly accounted for. By including *dow* and *Date*, the model adjusts for such residual confounding and is capable of teasing out the accurate effect sizes of temperature (captured by *cb*).

All five age groups among children are affected by cold exposure (Figure 4.1). Children above 6 years old are minimally affected by heat exposure. Children above 12 have relatively wide uncertainty ranges in terms of MMP (20-75°F and 22-65°F, respectively), meaning that only exposures towards the ends of the temperature spectrum affect them. Children 0-11 years old, on the contrary, have very narrow uncertainty ranges in terms of MMP. Age group specific MMPs and their corresponding temperature values are in Appendix C.9. The comparison among 0, 1-2, and 0-2 year-olds does not reveal significant differences. Therefore, in the TCMA, it is not necessary to study newborns (0 years old) separately from similarly young individuals (Appendix C.10), as did in some existing literature [47, 149].

The distributions of RR point estimates by age group and by exposure range are shown in Figure 4.2. Considering extreme cold exposures (bottom 5 percentile $TMean$ distribution), 3-5 and 6-11 year-olds have higher RRs than the baseline established by 0-18 year-olds (Figure 4.2, top left panel). Taking moderate cold exposures into consideration (bottom 30 percentile TMean distribution) revealed that 0-2 year-olds also experienced higher RRs than the baseline (Figure 2, bottom left panel). This differentiation is not evident in the bottom left panel of Figure 4.2 because the boxplots cannot capture differences in data density, which inform weighted estimates (Appendix C.11). Considering extreme heat exposures (top 5 percentile TMean distribution), 3-5 and12-14 year-olds have higher RRs than the baseline established by 0-18 year-olds (Figure 4.2, top right panel). Taking moderate heat exposures into consideration (top 30 percentile TMean distribution) revealed that 0-2 year-olds also experienced higher RRs than the baseline (Figure 4.2, bottom right panel).

The distributions of the health burdens (i.e., AF of EDV) by age group and by exposure range are shown in Figure 4.3. The results are broadly consistent with the analyses that rely on RR, described above. The differentiation between 0-2 year-olds and the baseline established by 0-18 year-olds is now more evident. Considering only extreme temperatures (both cold and heat), 0-2 year-olds have lower health burden than the baseline. However, when moderate exposures are included (both cold and heat), 0-2 year-olds have higher health burden than the baseline. Kernel density plots of RRs and AFs by age group and by exposure range are plotted in Appendix C.12 and C.13.

4.3.3 Identifying Health Burden by Cause

Cause-specific analyses are repeated for each age group. The corresponding health burdens (i.e. AF of EDV) are presented in Table 2 and 3. Baseline MMPs specific to age and disease groups are in Appendix C.14. The 95% empirical confidence intervals of the AF are provided in Appendix C.15 and C.16.

Overall, there are four disease groups that consistently lead to health burden associated with cold and heat exposures across different age groups and exposure ranges: nervous system diseases, respiratory diseases, ill-defined conditions, and injury and poisoning. Other disease groups show less consistent results. Both cold and heat exposures lead to significant health burden among children younger than 6, regardless of exposure ranges. Considering metabolic diseases, only cold exposures (both extreme and moderate to extreme) lead to significant health burden and such effects only exist among children younger than 15. Considering skin diseases, only heat exposures (both extreme and moderate to extreme) lead to significant health burden. The effects are valid only for 3-5 and 12-18 year-olds.

Not having significant cause-specific health burdens (i.e. AF of EDV) for all children (0-18 years old) does not necessarily mean there is no significant cause-specific burden for every age group among children (Table 4.2 and 4.3). For example, the results based on 0-18 year-olds indicate that there is no significant genitourinary health burden associated with suboptimal ambient temperature. However, risk assessment with greater age granularity shows that there is significant AF of EDV among children 3-5 years old, regardless of exposure range, and among children 12-14 years old when exposed to moderate to extreme heat. Similarly, the results based on 0-18 year-olds indicate that there is no significant musculoskeletal health burden associated with suboptimal ambient temperature. However, risk assessment with greater age granularity shows that there is significant AF of EDV associated with cold exposure (both extreme and moderate to extreme) among children 12-14 years old.

There are some inconsistencies comparing the cause-specific health burden between extreme and moderate to extreme temperature exposures. For example, with regard to musculoskeletal diseases, considering only extreme temperatures leads to the conclusion that there is significant health burden associated with extreme cold among children above 12 years old (Table 4.2). Considering both moderate and extreme temperatures show that cold exposure leads to significant health burden among 0-2 and 12-14 year-olds, and heat exposure leads to significant health burden among 15-18 year-olds (Table 4.3).

4.4 Discussion

This study provides evidence on the age-related heterogeneity of morbidity risks among children (0-18 years-old) exposed to suboptimal ambient temperature using five distinct age groups. This study not only identifies specific early life stages when health risks are particularly high, but demonstrates that the common practice of grouping youth into a single broad age category, particularly in temperature risk studies, obscures variations in vulnerability that are invaluable for informing targeted risk reduction strategies.

Considering cold exposure (both extreme and moderate to extreme), 3-11 year-olds experience higher morbidity risks (measured by EDV RR and AF) than the all children age 0-18. Considering heat exposure, 3-5 and 12-14 year-olds experience higher morbidity risks (measured by EDV RR and AF) than the all children age 0-18. Potential explanation for the consistently higher-than-baseline mortality risks among 3-5 year-olds include the increased time this age group spends outdoors and their low physiological/ metabolic capacity to respond to suboptimal ambient temperature [133, 152].

Results from this study underscore the importance of considering both extreme and moderate to extreme temperature exposure ranges when planning public health interventions for children. Considering extreme exposures only (both cold and heat), individuals 0-2 years old show lower or similar EDV RRs and AFs compared to all children age 0-18. However, considering moderate to extreme exposures (both cold and heat), individuals between 0 and 2 years old show higher EDV RRs and AFs compared to all children age 0-18. This suggests that studies that only focus on extreme temperature exposures may miss the morbidity risks experienced by newborns, infants, and toddlers (0-2 year-olds), who appear more vulnerable to moderate temperature exposures.

To the best of our knowledge, this is the first study that presents evidence on the age-related heterogeneity among children considering health response to suboptimal ambient temperature. The majority of related studies represented in existing literature mainly rely on one broad age group to represent children [49, 135–139]. The results of this study fill an important research gap identified before [38, 133]. The age groups used in this study are selected in order to capture the key differences among children in terms of physiological/ metabolic capacities and behavior. In addition, these age groupings are meaningful for designing targeted public health interventions. For example, having identified 3-5 year-olds as a particularly vulnerable group, a reasonable point of intervention would be at the local preschools and kindergartens.

Variations of exposure-response functions by age among children has been a long-standing area of concern for risk assessment efforts aimed at environmental contaminants (e.g. carcinogens) [153]. Both the U.S. Environmental Protection Agency and the International Life Science Institute have recognized the importance of life-stage analysis for childrens health [133, 154]. This study argues that the same approach should be applied to assessing the risks of ambient temperature on childrens health. Adopting life-stage analysis and integrating more granular age groups can improve the interpretability of the epidemiological evidence, refine the understanding of differential exposures, and provide more specific insights for intervention planning.

This study also discovered disease causes with cause-specific exposure response functions that differ by age group. Suboptimal temperature exposures (both cold and heat) are significantly associated with increased risks of nervous system diseases, respiratory diseases, ill-defined conditions and injury and poison in all age group. Among them, respiratory diseases are particularly of interest in temperature and health research [38, 141, 145, 155]. Regarding respiratory disease burden associated with suboptimal ambient temperature, our study finds that although low temperature affects all age groups similarly, heat exposure affects 6-14 year-olds significantly more than the others. To the best of our knowledge, the links between ambient temperature and nervous system diseases, ill-defined conditions, and injury and poison have not been studied before based on ICD codes. Ill-defined conditions are described by a small range of ICD codes (ICD-9: 780:799) for symptoms with no known cause (e.g. diarrhea and fever with no known causes), or abnormal findings, rendering this endpoint and its relationship to childrens health difficult to interpret in a policy context.

Other disease groups have less consistent results. For example, only cold is associated with significant metabolic morbidity burden among children. Only heat is associated with significant skin morbidity burden among children. Additionally, extreme heat lead to significant skin morbidity burden among 3-5 and 12-18 year olds while moderate to extreme heat lead to significant skin morbidity burden only among 3-5 year olds. Before this study, only one study has related an increase in ambient temperature has been associated with to a decreased severity of eczema based on a 9 year-old study population [156]. Suboptimal temperature exposure (both cold and heat) is also associated with increased digestive and genitourinary health burden among 0-5 and 12-14 year-olds but not the others. The evidence regarding digestive diseases have been previously identified based on 0-6 and 0-15 year-old study populations [143, 146]. Risk estimates for musculoskeletal diseases are changes substantially when comparing extreme exposures versus moderate to extreme exposures to both cold and heat.

It is important to note that the cause-specific analysis involves two-part stratification (i.e. by age and disease groups) from the original study population. The strength of this design is that it generates more refined risk assessments. In other words, this study is able to maximize the value of the information available and investigates a wide range of disease causes. However, a weakness of this approach is that the sizes of some strata become relatively small. Therefore, caution should be taken in the interpretation of cause-specific effect estimates, despite statistical significance. Moreover, the cause-specific analysis in this study is designed to understand the variation of disease risks by age group. It is not within the scope of this study to uncover potential mechanisms that have led to the observed impacts. Further research using other study designs (e.g. prospective cohort studies, case-crossover studies) should be employed to explain the health risks observed in this study and investigate the underlying physiological, metabolic, or behavior mechanisms.

There are some limitations to this study. First, some disease groups were excluded from cause-specific analyses because the sample sizes are not large enough for this particular study design. Infectious disease is among the disease groups that have been most frequently linked to hazardous ambient temperature exposure among children [137, 147]. However, there is insufficient data to draw any conclusions regarding this topic in the TCMA. Second, the health outcome of children is measured by EDV in this study. Mortality is not considered because the daily counts among children are extremely low in the study population. There are many other health outcome measures that are not considered here, such as hospitalizations and ambulance transports. Existing studies have shown that there may be contrasting patterns depending on specific public health endpoints [17, 59]. Future research should include multi-endpoint analysis when adequate data become available. Finally, this study only uses data from the TCMA.

Similar analyses would need to be repeated at other locations with similar or different socioeconomic characteristics, climate types, and demographics (as did [24]) to assess the generalizability of our results patterns.

This study is relevant to a pressing climate and health issue. Global temperature is expected to increase by 2°C by the end of the century compared to pre-industrial times (IPCC 2014)., driving changes in the frequency of extreme temperature events [30] and shifts in daily temperature distributions [31]. Studies such as this one will provide essential information for public health adaptations that prioritize vulnerable individuals prevent some of the diverse health threats inherent to a rapidly changing climate.

4.5 Conclusion

This study improves risk assessment by increasing age granularity for children exposed to suboptimal ambient temperature. Among all children (0-18 years old), 3-11 year-olds experience higher health risks when exposed to low temperatures; 3-5 and 12-14 year-olds experience higher health risks when exposed to high temperatures. Cause-specific health risks differentiate by age groups in some but all cases. This study provides useful information for informing public health intervention targeting vulnerable individuals.

Tables

Table 4.1: Descriptive Statistics of the Study Population by Age Group (Emergency Department Visits, 2005-2014)

Age Group	Daily Mean	Daily S.D.	Proportion (%)	Total Counts
0-18 years old	542	85	100	1,979,275
0-2 years old	193	42	35.58	704,249
3-5 years old	90	21	16.63	329,065
6-11 years old	99	23	18.29	389,315
12-14 years old	57	12	10.43	186,119
15-18 years old	80	12	14.85	370,527

Table 4.2: Health Burden (i.e., Attributable Fraction, %) Associated with Extreme Temperature Exposures by Age Group

Disease Cause	Age Group (Years Old) Exposure Range Attributable Fraction (%)											
	0-18		0-2		3-5		6-11		12-14		15-18	
	Cold	Heat	Cold	Heat	Cold	Heat	Cold	Heat	Cold	Heat	Cold	Heat
Metabolic	4.2	0.37	3.99	0.27	6.14	0.93	4.32	0.93	3.57	1.06	2.06	0.24
Nervous	2.00	0.25	1.21	0.12	3.41	0.93	3.11	2.47	1.10	3.41	2.85	0.35
Respiratory	4.94	0.60	3.01	-0.05	5.64	0.50	7.03	1.91	6.1	2.82	4.52	0.47
Digestive	1.39	0.56	1.78	0.65	3.54	-0.47	-0.25	1.35	0.21	1.75	0.41	0.85
Genitourinary	0.30	0.45	0.11	0.31	3.74	2.26	-1.95	0.64	1.05	3.09	0.04	0.97
Skin	-0.20	1.25	-1.22	0.33	0.85	2.48	1.85	2.11	-0.36	3.89	0.68	3.03
Musculoskeletal	0.76	0.05	-0.34	1.29	-0.23	-0.76	0.77	1.12	2.81	1.07	1.60	0.45
Ill-defined	3.29	0.57	2.21	0.31	5.04	0.7	4.54	1.64	3.12	1.4	2.56	0.18
Injury & Poison	0.62	1.79	-0.24	1.62	-0.28	2.3	0.47	3.1	2.32	2.44	1.83	1.14

Extreme cold and heat exposures are defined as the bottom and top 5 percentiles daily mean temperature ($<7^{\circ}$F, $>77^{\circ}$F). Statistically significant (defined as when the lower bound of the 95% empirical confidence interval greater than 0) health burdens related to moderate to extreme cold and heat are represented by blue and orange boxes.

Table 4.3: Health Burden (i.e., Attributable Fraction, %) Associated with Moderate to Extreme Temperature Exposures by Age Group

Disease Cause	Age Group (Years Old) Exposure Range Attributable Fraction (%)											
	0-18		0-2		3-5		6-11		12-14		15-18	
Disease Cause	Cold	Heat	Cold	Heat	Cold	Heat	Cold	Heat	Cold	Heat	Cold	Heat
Metabolic	17.16	0.58	16.08	0.47	27.33	1.49	22.99	1.63	15.91	1.63	4.23	0.47
Nervous	9.81	1.16	7.52	0.2	18.01	1.56	1.53	8.13	1.53	8.13	0.91	0.55
Respiratory	20.28	0.81	14.11	0.15	22.74	0.82	21.66	5.46	21.66	5.46	16.25	0.90
Digestive	6.68	1.00	7.61	1.62	17.99	0.79	0.59	3.11	5.78	3.11	1.13	1.64
Genitourinary	1.67	0.69	1.13	0.51	15.67	3.6	1.97	10.91	1.97	10.91	0.96	4.84
Skin	1.34	3.18	-0.68	0.86	6.05	8.37	0.03	9.33	0.30	9.33	1.06	8.77
Musculoskeletal	2.20	0.40	4.10	8.46	5.12	-0.62	4.00	4.27	4.00	4.27	5.78	0.77
Ill-defined	14.01	0.95	10.60	0.65	21.18	1.14	9.48	2.64	9.49	2.64	8.11	0.42
Injury & Poison	1.22	10.11	0.41	7.96	0.98	12.72	2.6	12.68	2.60	12.68	2.19	6.72

Moderate to extreme cold and heat exposures are defined as the bottom and top 30 percentiles daily mean temperature (<33°F, >64°F). Statistically significant (defined as when the lower bound of the 95% empirical confidence interval greater than 0) health burdens related to moderate to extreme cold and heat are represented by blue and orange boxes.

Figures

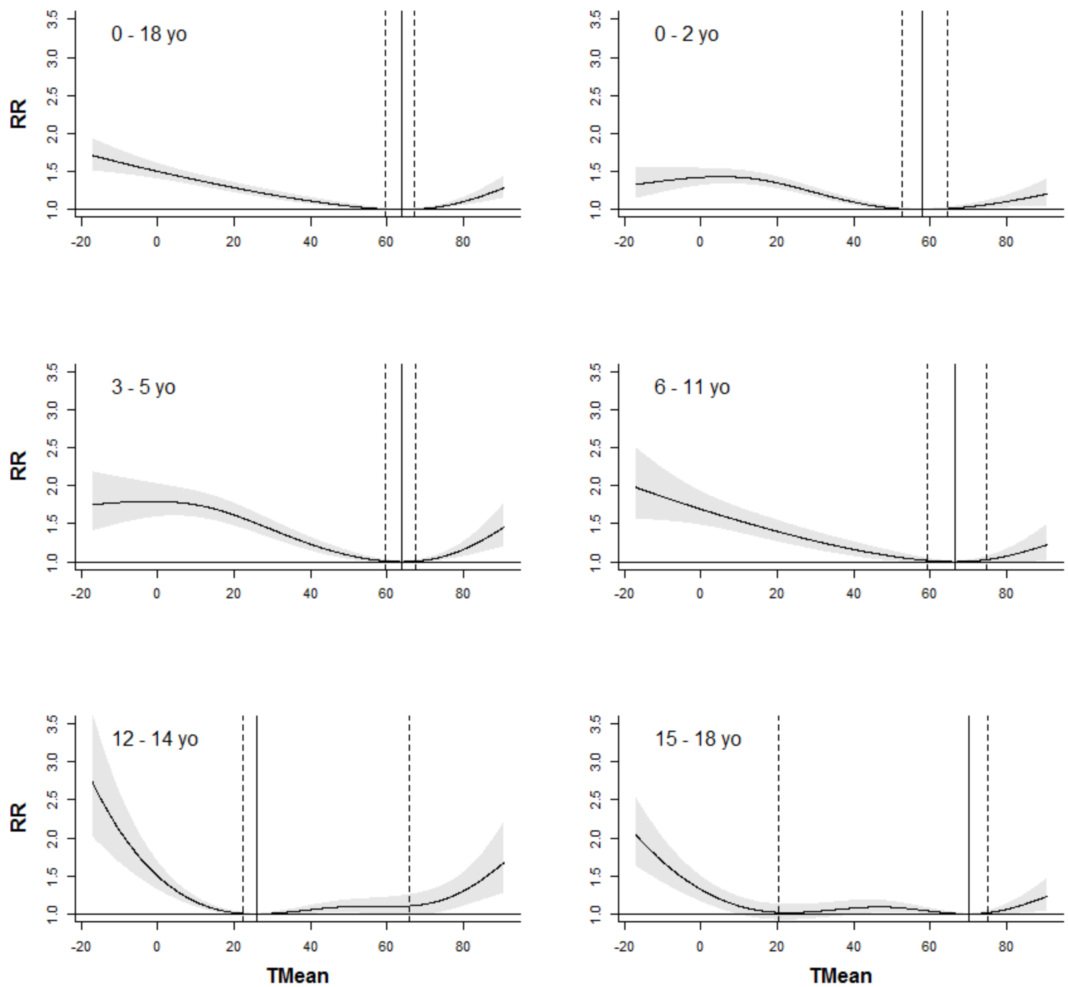

Figure 4.1: Exposure-Response Functions by Age Group among Children

Solid line indicates minimum morbidity temperature. Dashed lines shows the 95% empirical confidence interval of the minimum morbidity temperature. $TMean$ represents Daily mean temperature; RR represents relative risk.

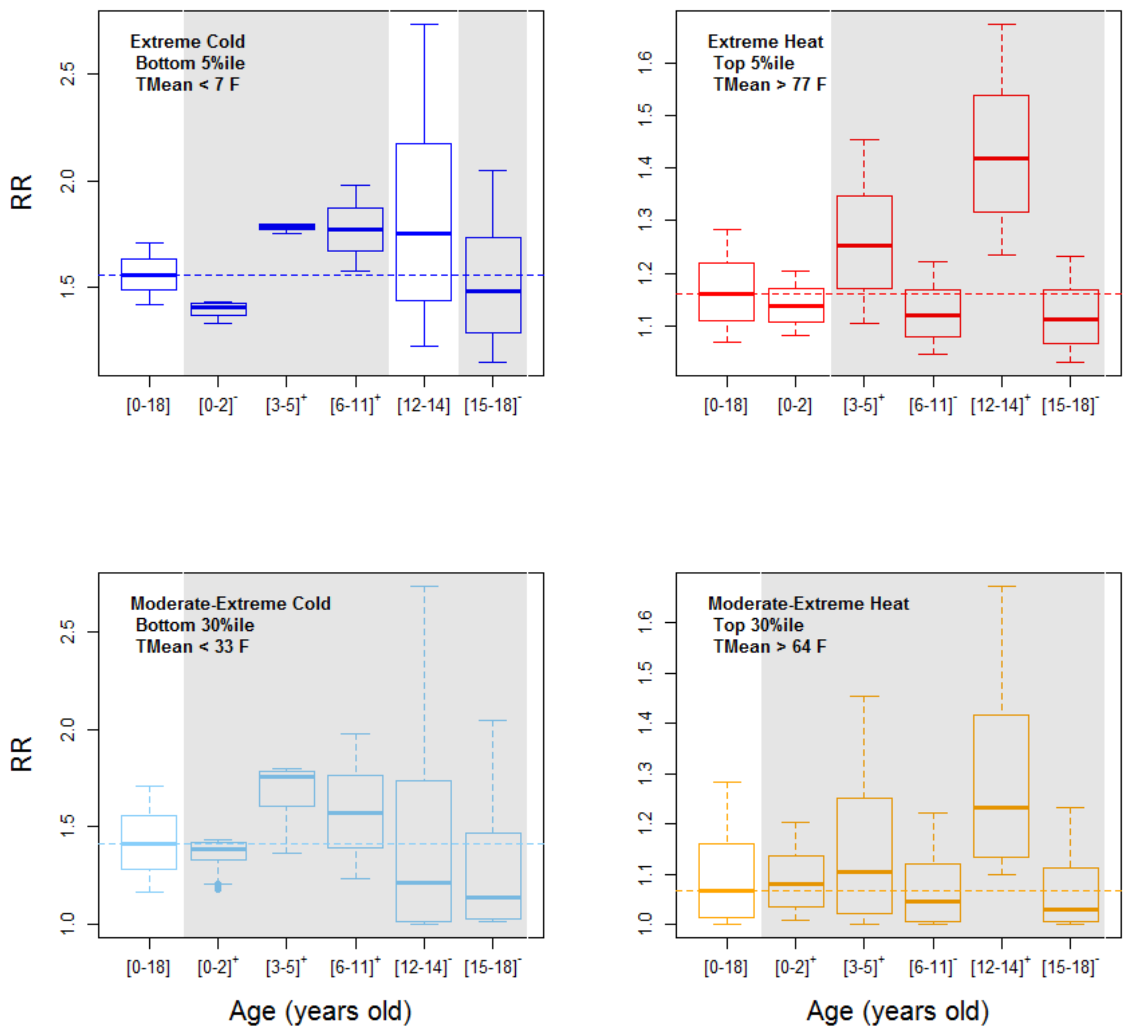

Figure 4.2: All-Cause Relative Risk Estimates by Age Group

Shaded areas are specific age groups with relative risks significantly different from the all-children average (0-18 years old). The superscript "+"/"-" indicate statistically significant greater than/ less than children overall (0-18 years old).

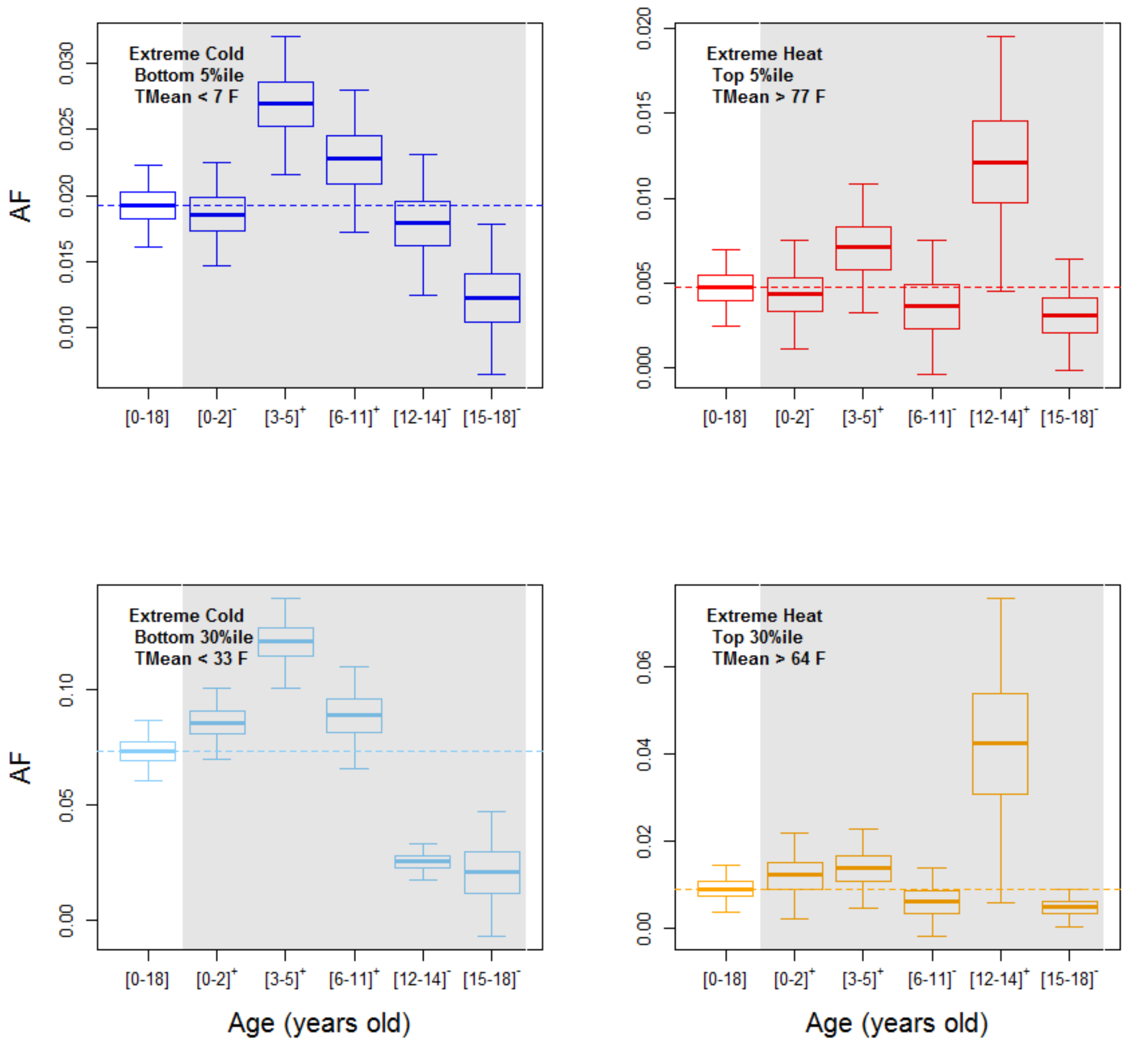

Figure 4.3: All-Cause Attributable Fractions Estimates by Age Group

Shaded areas are specific age groups with attributable fractions significantly different from the all-children average (0-18 years old). The superscript "+"/"-" indicate statistically significant greater than/ less than children overall (0-18 years old).

Chapter 5

Contribution and Future Directions

This dissertation demonstrates ways that quantitative models can be designed to inform different aspects of public health policies targeting risks associated with ambient temperature exposure. The results presented in this dissertation have immediate and practical values for public health agencies. Chapter 2 finds evidence to support tailoring emergency risk communication messages to protect individuals with chronic diseases exacerbated by extreme temperature exposures [17]. Chapter 3 develops a compound indicator using a multi-criteria approach to capture the overall economic impact of ambient temperature exposures [18]. And Chapter 4 sets up an age grouping selection framework for public health intervention among children exposed to ambient temperature exposure [19]. Besides these policy implications, this dissertation has also contributed to both environmental epidemiology and to developing quantitative methods.

5.1 Contributions to Environmental Epidemiology

The objective of Chapter 2 is to use quantitative research methods to inform risk communication [17]. This study is also the first to provide risk assessment for both mortality and morbidity under both cold and heat exposures. Existing literature tends to only focus on mortality or on heat exposure. This study is also the first to provide empirical evidence on the contrasting patterns between mortality- and morbidity-based exposure-response functions for specific chronic conditions. Such patterns have been previously speculated. However, without controlling for the study population and analytical methods, no conclusions could be drawn prior to this study.

The objective of Chapter 3 is using a quantitative modeling approach to support impact assessment [18]. This study is the first to provide a single compound indicator to capture the general impact of ambient temperature as a continuous exposure. Previous studies with economic estimates only investigate extreme temperature exposures as independent and acute weather events. The cost function developed in Chapter 3 adopts a multi-criteria approach. When new parameters of this function become available, this cost function can be updated easily.

The objective of Chapter 4 is to use a quantitative modeling approach to guide intervention [19]. This study is the first to adopt an early-life developmental approach to study ambient exposures such as temperature. This approach has traditionally been seen in environmental contaminants (e.g., carcinogen) research [133]. It is also the first to investigate the heterogeneity among children exposed to non-optimum ambient temperature. The cause-specific analysis generates hypotheses for further research on the underlying mechanisms that explain childrens vulnerability.

5.2 Contributions to Methodological Improvements

In Chapter 2-4, we have made innovative use of the distributed lag-nonlinear model (DLNM) [16] as an appropriate method for risk assessment regarding ambient temperature and human health. However, there is currently little consensus on determining the specifications of this model. Some existing studies that utilize DLNM do not provide justifications for their model specifications, while others borrow model specifications from other studies with different study populations and settings [114, 146]. This dissertation formalizes an approach to determining model specifications by equally weighting quasi-Akaike Information Criterion (q-AIC) and mean square error (MSE) from cross-validation. This approach should continue to be validated in the future by applying it to a broad range of environmental scenarios.

The cost function developed in Chapter 3 requires estimates of health burden (i.e., attributable cases) on an annual basis [18]. The original method for calculating attributable cases only provides one total estimate for the entire period under consideration [73]. Chapter 3 provides a modification to this original method that allows researchers to generate annual attributable cases. The results are only used to calculate overall health-related costs in this dissertation. However, the modification can be applied to further study the relationship between health burden and temperature occurrences or to develop a seasonal level early-warning system for potentially high-risk years for health outcomes associated with ambient temperature.

Chapter 4 is designed to guide public health interventions targeting children exposed to hazardous ambient temperature [19]. This objective requires pair-wise comparisons between exposure-response functions of different age groups. However, such comparison has historically been a challenge in temperature and health research. Since the results from this type of analysis are exposure-response functions, it is difficult to directly compare curves without selecting one unique indicator. A number of existing studies have selected attributable fraction as the indicator for this purpose. However, exposure-response functions with different shapes may lead to the same attributable functions. Chapter 4 solves this problem by also including a pair-wise comparison of the risk estimates. This comparison is achieved by using the Wilcoxon rank-sum test.

5.3 Future Directions for Temperature and Health Research

The purpose of the studies included in this dissertation is to inform public health policies and decisions regarding ambient temperature and human health. The ultimate goal for this line of research is policy and decision optimization. Such optimization will take into consideration the overall risk assessment (e.g., exposure-response functions), potential future projections (e.g., climate projections), specific local context (e.g., population resilience), features of potential intervention options (both cost and effectiveness), and resource constraints (e.g., budget). A good example is [20]. The result of the optimization process will yield an optimal set of actions that maximize benefits and minimize losses. Policy and decision optimization is a significant improvement from current practices, which largely depend on policy and decision makers past experiences.

This type of optimization model exists in health services research and has been used to manage chronic diseases, such as cancer [22] and HIV[21]. However, in the case of ambient temperature exposure, there are still many missing pieces beyond the existing literature and beyond the scope of this dissertation. For example, although current climate change adaptation policies have included a wide range of options that may help to reduce the health burden from hazardous ambient temperature [32], there is little information regarding their cost and effectiveness. Future research on temperature and health should focus on these areas.

Additionally, it is not within the scope of these studies to investigate the potential mechanisms of which ambient temperature is affecting human health. For example, among children, the potential mechanisms can be summarized as behavioral, metabolic, and physiological [38]. Knowing which mechanisms are driving increased health risks can provide unique insights for designing intervention programs. Future research and different study designs than the ones used in this dissertation should contribute to seeking these answers.

5.4 Future Directions for Policy-oriented Environmental Health

Despite the challenges described in this dissertation, the epidemiological link between ambient temperature and human health is relatively straightforward compared to many other environmental health issues. Most of the outcomes of ambient temperature exposure are not of an infectious nature. The health response data is highly reliable. The primary environmental information used here is temperature, although a few others (e.g., humidity, air pollution) have been considered during model development phases.

An example of an environmental health issue that is much more complex is dengue fever, a mosquito-borne disease. Dengue fever is an environmentally sensitive infectious disease because both natural (e.g., rainfall, temperature, still water sources) and built (e.g., residential areas) environment can affect mosquito activities[4, 8, 9]. Due to the infectious nature of the disease, it is essential to consider human mobility and contact network when studying the transmission dynamics of dengue fever [8]. The data on health response is sometimes questionable because in a clinical setting, dengue fever can be confused with chikungunya, another infectious disease borne by the same mosquito vector [157]. There are non-human stakeholders, such as wild primates [158]. Developing risk assessment models for environmental health issues such as dengue fever will be challenging due to high-dimensional environmental information.

Additionally, the causal links between high-dimensional environmental information and disease outcomes are also more complex in the case of environmental health issues like dengue fever. For example, it is reasonable to assume that higher rainfall is associated with mosquito activities because higher rainfall is associated with likelihood of still water accumulation on the ground, which creates an ideal environment for mosquitoes to lay eggs. However, it is also reasonable to assume that lower rainfall is associated with mosquito activities because during dry spells people tend to fill up their water containers. This environmental condition is preferred by one of the primary mosquito vectors of concern, *Aedes aegypti*, to lay eggs. Such complex and most likely non-linear relationships between rainfall and dengue fever suitability need to be untangled by more sophisticated methods. Additionally, efforts are also needed to understand the relationships among environmental factors such as temperature, rainfall, river networks, human mobility, and flood risk. Advanced quantitative research methods (e.g., information theory, network science, and machine learning) will contribute to the risk assessment research for these environmental health issues. Policy-oriented risk assessment will then follow to maximize the impacts of said research.

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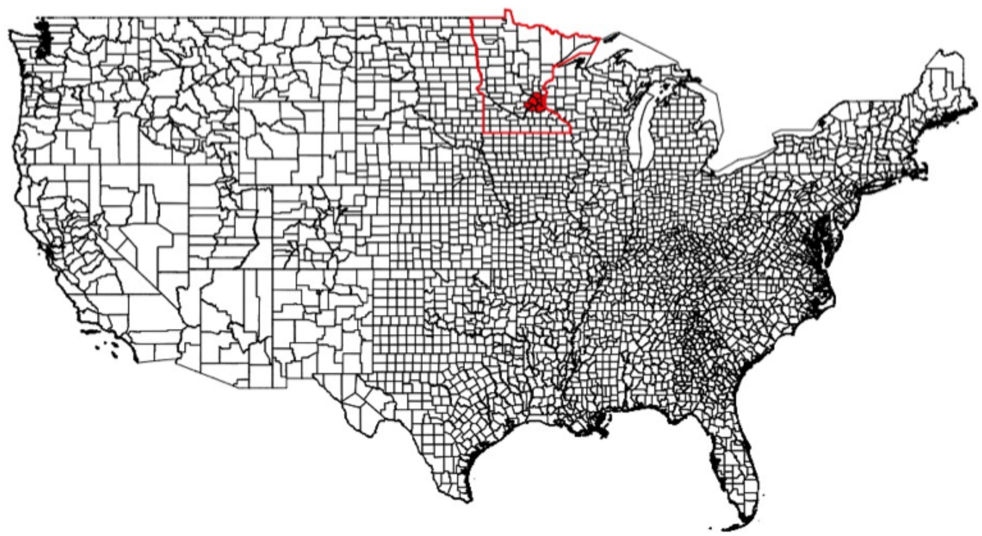
Appendix A

Chapter 2 Supplemental Information

A.1 The Location of the TCMA in the Continental United States (Map)



The state of Minnesota is marked by the red polygon. The Twin Cities Metropolitan Area is marked by the red area.

A.2 Selection of Temperature Variable

Step 1: Obtain environmental data on 3 temperature metrics: air temperature (AT), heat index (HI), wind chill index (WCI). Among them, AT is directly measured with equipment. HI(F) is calculated using the equation stated in a technical attachment of the National Weather Service (NWS)(Rothfusz, 1990):

$$\begin{aligned} HI = -42.379 + 2.04901523T + 10.14333127RH - .22475541TRH - \\ .00683783T^2 - .05481717RH^2 + .00122874T^2RH + \\ .00085282TRH^2 - .00000199T^2RH^2 \end{aligned} \tag{A.1}$$

where T is air temperature (°F) and R is the relative humidity (%).

The WCI is calculated using an equation drawn from NWSs official website [159]:

$$WCI = 35.72 + 0.6215T - 35.75V^{0.16} + 0.4275TV^{0.16} \tag{A.2}$$

where T is air temperature (°F) and V is wind speed (mph).

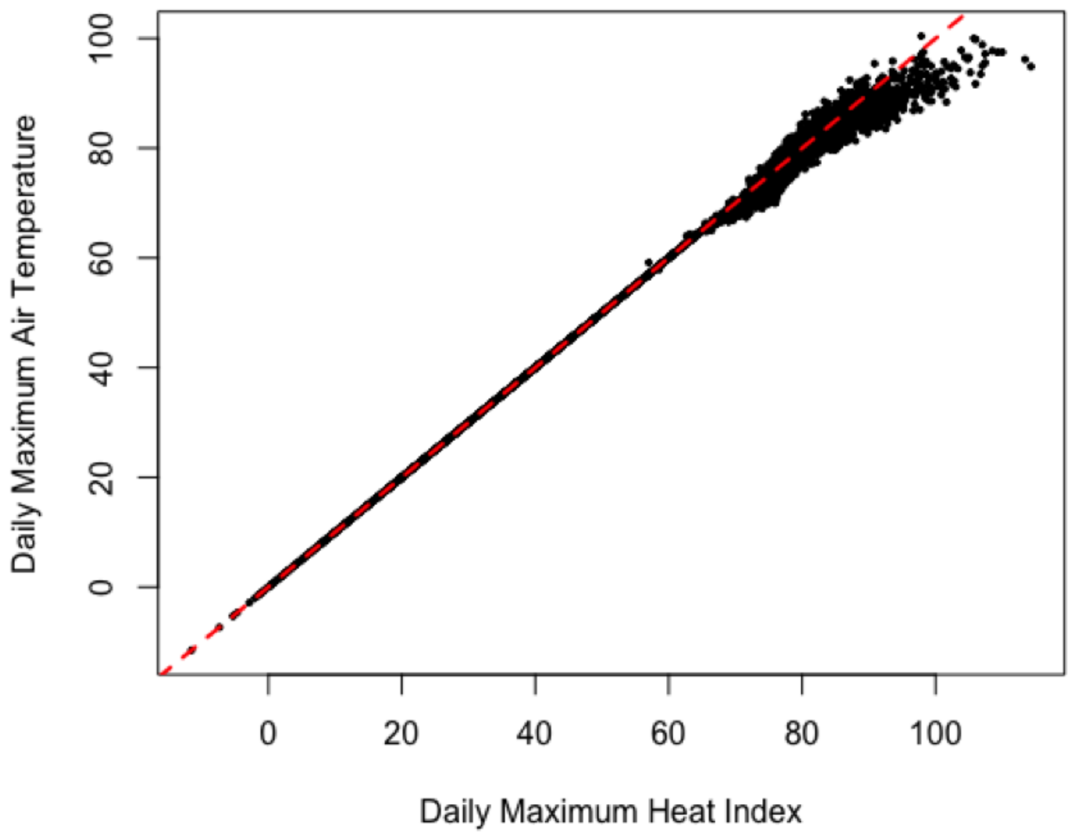
Step 2: Calculate the statistical features for each temperature metric: minimum, mean, maximum. This procedure leads to 9 candidate temperature variables: $\mathrm{AT}_{\mathrm{min}}$, $\mathrm{AT}_{\mathrm{mean}}$, $\mathrm{AT}_{\mathrm{max}}$, $\mathrm{HI}_{\mathrm{min}}$, $\mathrm{HI}_{\mathrm{mean}}$, $\mathrm{HI}_{\mathrm{max}}$, $\mathrm{WCI}_{\mathrm{min}}$, $\mathrm{WCI}_{\mathrm{mean}}$, and $\mathrm{WCI}_{\mathrm{max}}$.

Step 3: Use different temperature variables to derive the exposure-response function (ERF) between temperature and all-cause mortality. More specifically, the ERF is modeled using quasi-Poisson generalized linear model, adjusted for a natural cubic spline for temperature (degrees of freedom = 3, knots = 10th, 75th, 90th percentiles, maximum lag considered = 28 days), day of week, and a natural cubic spline for long-term trend (8 degrees of freedom/year).

Step 4: Compare models based on diagnostics: R-squared, rooted mean squared error, partial auto-correlation coefficients of model residuals, and the Quasi-Akaike's Information Criterion (qAIC).

Step 5: The final temperature variable selected for the temperature and all-cause mortality is HI_{max}. It then extends to studying other population health outcomes.

A.3 Daily Maximum Heat Index vs. Daily Maximum Air Temperature



Heat Index is one of apparent temperature measurements that approximate temperature exposures perceived by the human body during summer. Outside of summer months, or more precisely when HI_{max} is smaller than 57°F, there is no difference between maximum daily air temperature measurements and HI_{max}.

A.4 Potential Confounding

We did not investigate the potential confounding effect of humidity since by definition Heat Index already capture the variations in temperature as well as humidity. This study has only looked at potential confounding from air pollutants: Ozone (O_3) and fine particles with a diameter smaller than 2.5 μm ($PM_{2.5}$). Existing studies have not agreed on whether or not to include air pollutants while studying the ties between temperature and population health. None of [47, 51, 85, 118] found interactions between ambient temperature and Ozone. However, some others either found O_3 to significantly affect the relationship between HI_{max} and population health outcomes [160, 161] or include it in their analyses a priori [50, 58, 162]. Evidence on the confounding effect of PM2.5 is more consistent and is unlikely to exist [47, 48, 51].

In this study, we tested both air pollutants using the all-cause mortality and all-cause morbidity models as a baseline. Results are shown in Appendix A.11, A.12 and A.13. The only case that an additional pollutant to the baseline model returns a positive p-value is $PM_{2.5}$ in terms of emergency department visits. However, the exposure-response function between temperature and morbidity is not changed at all by including $PM_{2.5}$. This result is consistent with existing literature [47, 51, 118]. Consequently, the main models in the paper do not include any air pollutants as confounders.

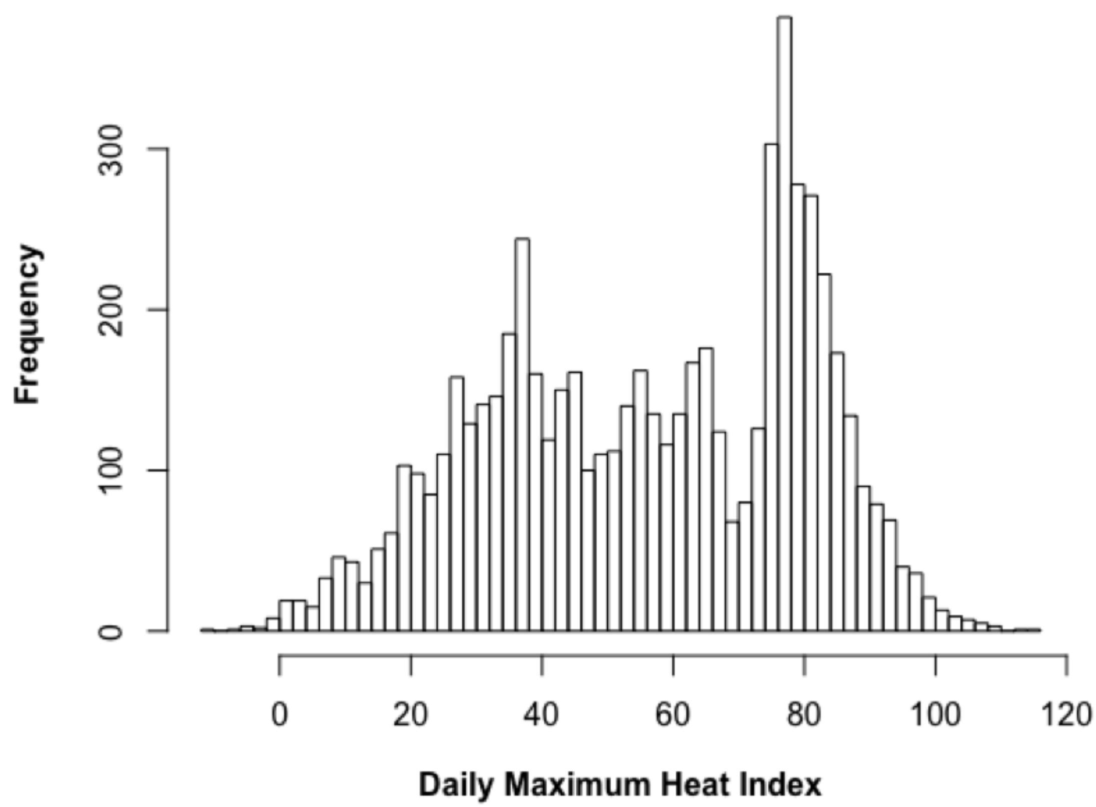
A.5 Descriptive Statistics of Study Population, Mortality (1998-2014)

Categorized by	Levels	Counts	Proportion (%)
Sex	Female	144269	47.9
	Male	156923	52.1
Age	<18	6371	2.12
	>=18 & <65	69213	22.98
	>=65	225614	74.91
Residence	Anoka	23371	7.76
	Carver	6099	2.02
	Dakota	23687	7.86
	Hennepin	148618	49.34
	Ramsey	75173	24.96
	Scott	8210	2.73
	Washington	16040	5.33
Race	White	278103	92.33
	Black	13626	4.52
	American Indian	2299	0.76
	Asian	5986	1.99
Ethnicity	Hispanic	4358	1.45
Total		301198	100

A.6 Descriptive Statistics of the Study Population, Morbidity (Emergency Department Visits) (2007-2014)

Categorized by	Levels	Counts	Proportion (%)
Sex	Female	3635854	54.74
	Male	3006129	45.26
Age	<18	1605614	24.17
	>=18 & <65	4000371	60.23
	>=65	1035998	15.6
Residence	Anoka	747390	11.25
	Carver	144799	2.18
	Dakota	744525	11.21
	Hennepin	2910597	43.82
	Ramsey	1386675	20.88
	Scott	266349	4.01
	Washington	441648	6.65
Total		6641983	100

A.7 Histogram of Daily Maximum Heat Index in the Minneapolis – St. Paul Twin Cities Metropolitan Area



A.8 Minimum Effect Temperatures

Short Names	Long Names	MET-Mortality[a]	MET-Morbidity[a]
CVD	Cardiovascular Disease	85 [61, 89]	74 [70, 81]
RPD	Respiratory Disease	85 [78, 87]	85 [82, 89]
RND	Renal Disease	84 [28, 86]	65 [59, 72]
Diab	Diabetes	NA	77 [71, 86]
All	All Cause	84 [64, 86]	74 [69, 81]

[a] The minimum effect temperature is the temperature that corresponds to the lowest relative risk on the exposure-response function. The 95% empirical confidence interval is generated using a re-sampling method developed in [72].

A.9 Cause-specific Descriptive Statistics of the Study Population Mortality (1998-2014)

Short Names	Long Names	Proportion[a] (%)	Average Daily Count	Standard Deviation of Daily Counts
CVD	Cardiovascular Disease	47.45	23.02	5.42
RPD	Respiratory Disease	22.95	11.13	3.87
RND	Renal Disease	11.83	5.74	2.69
Diab	Diabetes	9.6	4.66	2.27
All	All-cause	100	48.51	8.24

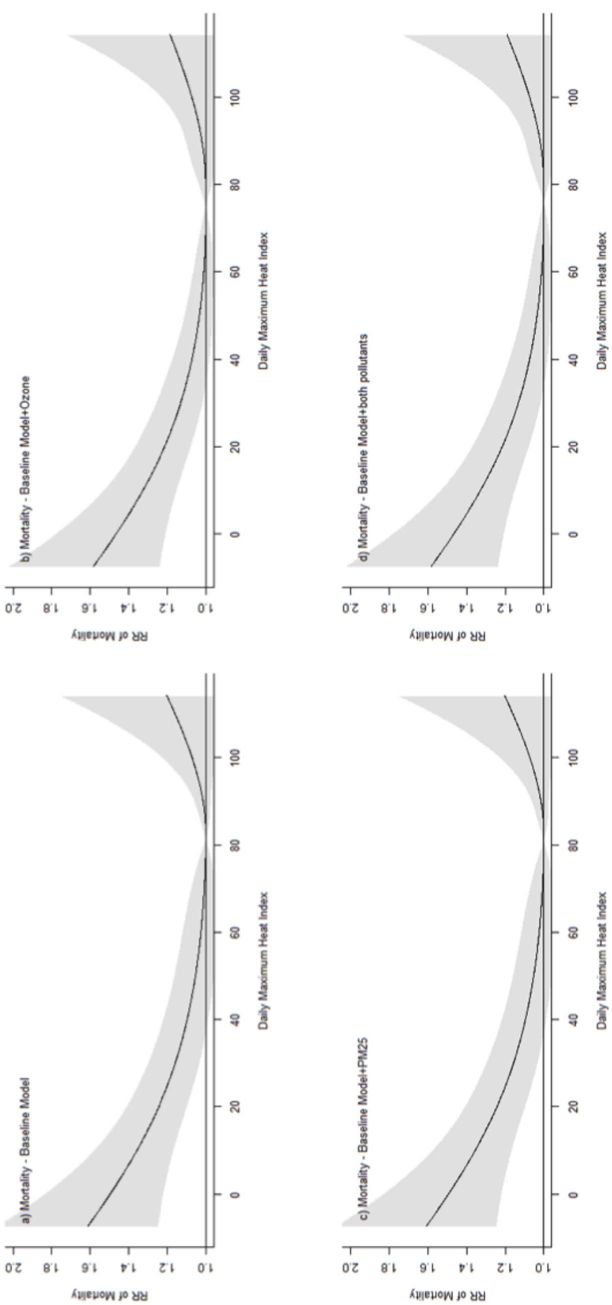
[a] Proportion is calculated by cause-specific count or cause- and age-specific count divided All count (301198).

A.10 Cause-specific Descriptive Statistics of the Study Population Morbidity (2007-2014)

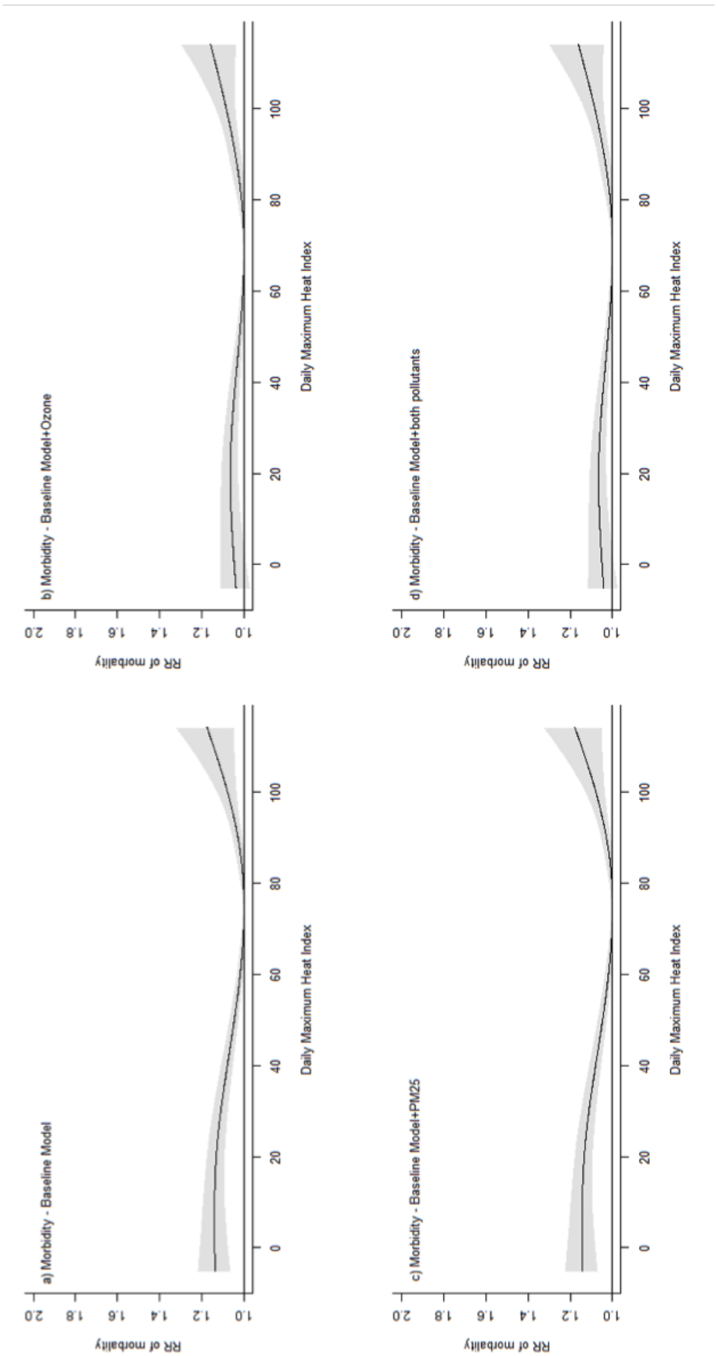
Short Names	Long Names	Proportion[a] (%)	Average Daily Count	Standard Deviation of Daily Counts
CVD	Cardiovascular Disease	22.69	515.77	62.94
RPD	Respiratory Disease	19.96	453.63	97.32
RND	Renal Disease	10.48	238.2	32.79
Diab	Diabetes	8.65	196.69	28.39
All	All-cause	100	2273.1	195.01

[a] Proportion is calculated cause- and age-specific count divided All count (6641983).

A.11 Air Pollutants as Confounder, Mortality Models



A.12 Air Pollutants as Confounder, Morbidity Models



A.13 Potential Confounding by Air Pollutants

Model	Variable[a]	p-value Mort-ERF	p-value in Morb-ERF
Baseline + O3	ns(O3, 3) 1	0.844304	0.102873
	ns(O3, 3) 2	0.392036	0.114562
	ns(O3, 3) 3	0.382376	0.240568
Baseline + PM2.5	ns(PM2.5, 3) 1	0.881938	0.000672*
	ns(PM2.5, 3) 2	0.258019	0.007188*
	ns(PM2.5, 3) 3	0.531497	0.534935
Baseline + both pollutants	ns(O3, 3) 1	0.697665	0.656427
	ns(O3, 3) 2	0.156157	0.582836
	ns(O3, 3) 3	0.38865	0.24692
	ns(PM2.5, 3) 1	0.64531	0.000021*
	ns(PM2.5, 3) 2	0.274274	0.000759*
	ns(PM2.5, 3) 3	0.420149	0.35454

[a] Same-day pollution levels are included in the baseline model as a natural spline function with 3 degrees of freedom. Therefore, ns(O_3, 3) 1 indicates the first polynomial segment of the natural cubic spline function of O_3 given 3 degrees of freedom.

* p-value smaller than 0.05

Appendix B

Chapter 3 Supplemental Information

B.1 Age-based & Year-Specific Daily Production Value

B.1.1 Methods

The daily production value is based on Economic Productivity by Age and Sex 2007 *Estimates for the United States* [104]. In their study, DPV is the sum of daily market compensation (from working at a job) and household service daily value (e.g. household management). Here, we convert DPV for other years using the following equation:

$$\begin{aligned} DPV_{year}(\$2016) &= DPV_{2007}(\$2007) \times \frac{CPI_{year}}{CPI_{2007}} \times \frac{CPI_{2016}}{CPI_{year}} \\ &= DPV_{2007}(\$2007) \times \frac{CPI_{2016}}{CPI_{2007}} \end{aligned}$$

This section continues to use the CPI values identified above from the U.S. Bureau of Labor Statistics [163].

B.1.2 DPV by Age Groups

Age	Proportion of Total Population	DPV ($2007)	Weighted DPV ($2007)
0-4	7.3	0	8.74
5-0	5.4	0	
10-14	4.9	0	
15-19	7	30.73	
20-24	9.7	90.19	175.78
25-29	9.1	152.69	
30-34	9.1	190.86	
35-39	7.95	209.24	
40-44	7.95	212.71	
45-49	7.05	211.71	
50-54	7.05	205.86	
55-59	5.4	175.8	
60-64	3.7	142.82	
65-69	1.95	79.39	57.12
70-74	1.95	63.89	
75-79	1.5	50.83	
80-84	1.5	41.91	
85+	1.6	41.91	

The Weighted DPV ($2007) is calculated as the following:

$$DPV_{ag} = \sum_{i \in ag} \frac{p_i}{p_{ag}} \times DPV_i \tag{B.1}$$

where DPV_{ag} is the weighted DPV of a given age group (ag), i is a 5-year age range that belongs to ag, p_i is the proportion of age range i in the total population, p_{ag} is the proportion of ag in the total population, and DPV_i is the DPV of age range i.

B.2 Air Pollution as Potential Confounder

B.2.1 Materials and Methods

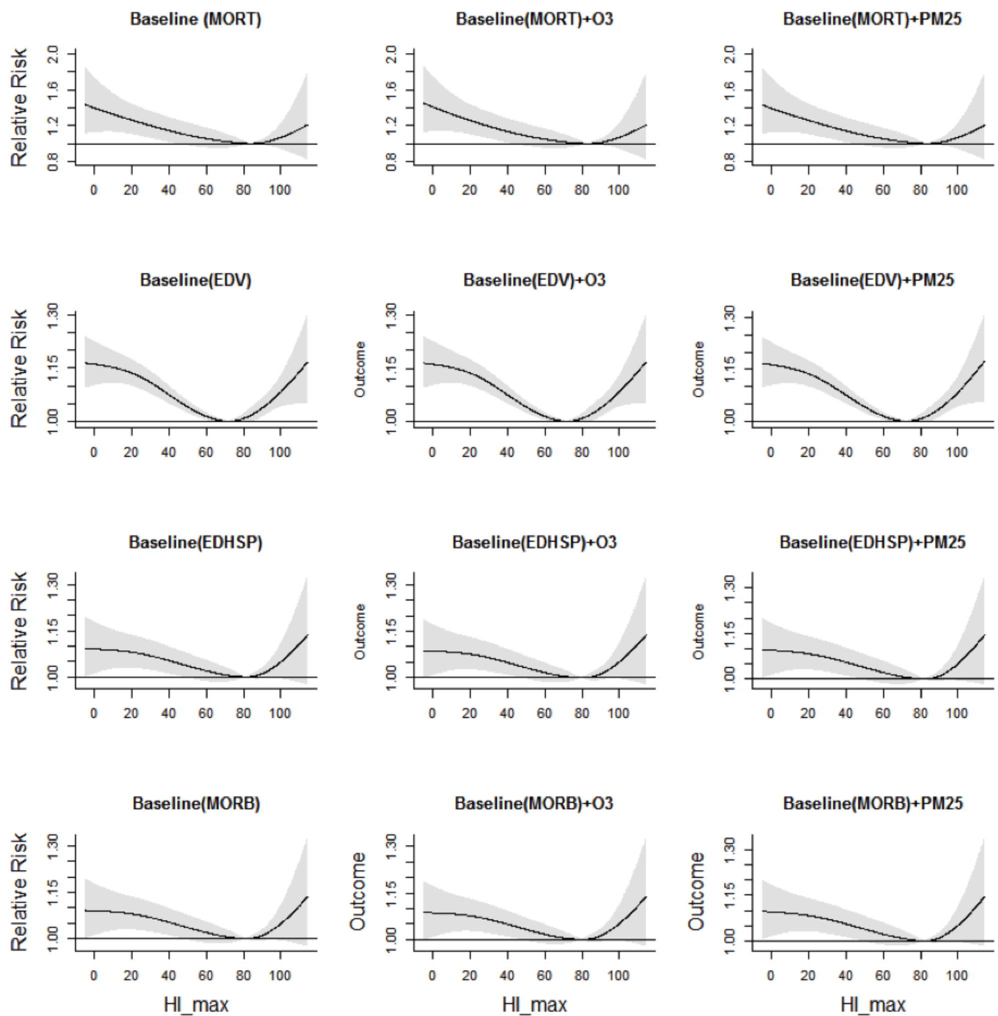
This study investigates Ozone (O_3) and Particulate Matter with radius smaller or equal than 2.5 μm ($PM_{2.5}$) for potential confounding effects by air pollutants (AP) in the risk assessment model of temperature and population health. Current literature has not fully agreed on the statistical significance of such effects. Therefore, this study conducts sensitivity analysis to see how the inclusion of AP data may affect the results. [50] and [164] included air pollutants in their analyses as air pollutants theoretically qualify as confounders. O_3 and $PM_{2.5}$ are risk factors for mortality and morbidity, are associated with temperature, and are not in the causal pathway between temperature and population health. The risk assessment model in [160] considers O_3 but not $PM_{2.5}$ as a confounder based on model diagnostics. [165] and [25] did not include O_3 since it did not lead to substantial changes in risk assessment results.

In this study, the AP related sensitivity analysis is restricted to a nine-year period between 2005 and 2013 due to data availability. The historical records of AP was originally available for 2000-2013. However, O_3 was measured only during summer months prior to 2005, leading to severe issue of missing data between 2000 and 2004. In the remaining O_3 time series, 2006 and 2009 did not have records for October. As O_3 is highly seasonal, we randomly sampled October O_3 from October of other years during which data is available. The time series of $PM_{2.5}$ has less than three missing data points that are not close to each other. This study assumes the $PM_{2.5}$ level on these days are identical to that on their previous days, respectively. The public health data used in the sensitivity analysis was truncated for the time horizon established by the air pollutants data. Age-stratification is not considered in this sensitivity analysis. Models that adjust for same day (lag=0) O_3 and $PM_{2.5}$ using a natural cubic spline given 3 degrees of freedom are compared to the baseline model, the final model used in the main text of this study. Three criteria are subsequently used to evaluate the comparison: (1) the shape and confidence interval of exposure-response function (by observation); (2) the p-value of O_3 and $PM_{2.5}$ variables in the regression models; and (3) the corresponding attributable risk point estimations.

The following sections show the results regarding the three criteria stated above. Our results suggest that it is justifiable to exclude AP from the risk assessment model in this study as doing so does not lead to substantial changes in health burden estimates.

B.2.2 Results

B.2.2.1 The Exposure Response Functions



MORT mortality; EDV emergency department visits; EDHSP emergency hospitalizations; MORB emergency department visits and emergency hospitalizations. This plot compares the exposure response function when adjust for AP to their respective baseline models. There is no significant change in their shapes or ranges of non-optimum (i.e., statistically significant) temperature exposure levels.

B.2.2.2 Model Diagnostics

Health Outcome	Model	p-value		
		ns(AP, 3) 1	ns(AP, 3) 2	ns(AP, 3) 3
MORT	Baseline	-	-	-
	O_3	0.99	0.16	0.75
	$PM_{2.5}$	0.93	0.56	0.87
EDV	Baseline	-	-	-
	O_3	0.53	0.83	0.81
	$PM_{2.5}$	<0.01	0.01	0.64
EDHSP	Baseline	-	-	-
	O_3	<0.01	0.18	0.64
	$PM_{2.5}$	<0.01	0.2	0.76
MORB	Baseline	-	-	-
	O_3	0.11	0.79	0.97
	$PM_{2.5}$	<0.01	0.01	0.67

MORT mortality; EDV emergency department visits; EDHSP emergency hospitalizations; MORB emergency department visits and emergency hospitalizations. This table shows the p-value of the air pollutants when included in the baseline model. $PM_{2.5}$ is significant for all morbidity outcomes (EDV, EDHSP, MORB). O_3 is only significant for EDHSP.

B.2.2.3 Attributable Risk Comparison

Health Outcome	Model	Attributable Fraction (AF)	Attributable Cases (AC, %)
Mort	Baseline	13478	8.34
	O_3	12846	7.95
	$PM_{2.5}$	13249	8.2
EDV	Baseline	267248	4.53
	O_3	267561	4.54
	$PM_{2.5}$	267206	4.53
EDHSP	Baseline	40446	3.09
	O_3	37736	2.89
	$PM_{2.5}$	42710	3.27
Morb	Baseline	302441	4.2
	O_3	302957	4.19
	$PM_{2.5}$	303280	4.21

MORT represents mortality; EDV represents emergency department visits; EDHSP represents emergency hospitalizations; MORB represents emergency department visits and emergency hospitalizations. This table shows the attributable fractions (AF) and attributable cases (AC) as a result of including AP in the baseline model. Mort indicates mortality. Relatively larger changes are observed for EDHSP although the percentage changes are still smaller than 10%.

B.3 Deriving the Exposure Response Function Model Specifications

In this study, the risk assessment model (i.e. the model use to derive the exposure response function) assumes the exposure response relationship to be a natural cubic spline with three internal knots at 10^{th}, 75^{th}, 90^{th} percentiles of the $\mathrm{HI}_{\mathrm{max}}$ distribution. The lag-response relationship is also assumed to be a natural cubic spline function. Three internal knots are equally spaced through the logarithmic lag range. The maximum lag considered is 28 days. Long-term trend is assumed to be a natural cubic spline function with 8 and 7 degrees of freedom given to each year for the mortality and morbidity models, respectively. Holiday effect is only significant for morbidity outcomes and is adjusted for by including a binary variable that equals 1 on federal holidays and 3 following days and 0 on other days.

Originally, a large number of parameter combinations were tested by switching the center knots of the exposure response relationship to 50th and 25th percentiles; the maximum lag considered to 14, 21, and 35 days; the degree of freedom given to the long-term trend during each year to 6-10; and by including air pollution (O_3 and $PM_{2.5}$). The combination of parameter with that optimizes q-AIC (quasi-Akaikes Information Criterion) and residual partial autocorrelation was selected.

B.4 Annual Attributable Cases Estimation

	Mort	EDV			EDHSP		
	Senior	Youth	Adult	Senior	Youth	Adult	Senior
1998	1188	-	-	-	-	-	-
1999	1,536	-	-	-	-	-	-
2000	1,445	-	-	-	-	-	-
2001	1,525	-	-	-	-	-	-
2002	1,507	-	-	-	-	-	-
2003	1,389	-	-	-	-	-	-
2004	1,359	-	-	-	-	-	-
2005	1416	15640	8515	1915	1392	2322	3221
2006	1327	17352	9929	2472	1578	2549	3579
2007	1346	18894	8932	2159	1677	2699	3681
2008	1527	20197	10793	2648	1707	3015	4096
2009	1444	19099	10350	2546	1672	2775	3621
2010	1445	17817	9983	2388	1451	2691	3516
2011	1654	21783	12137	3026	1567	2982	3909
2012	1353	16110	9807	2924	1245	2247	3174
2013	1729	22230	13074	3614	1554	3079	4142
2014	1721	23033	13641	3436	1605	3027	3972
Total	24,911	192155	107161	27128	15,448	27,386	36,911

This table shows the results of the Year-to-Year Variations for Cost Estimation under the Data and Methods Section. Year-to-year variations are assessed because many cost estimation parameters changes on an annual basis.

B.5 Cost Estimation Parameters

B.5.1 Adjusting Value of Statistical Life

B.5.1.1 Methods

In a U.S. Department of Transportation Memorandum titled Guidance on Treatment of the Economic Value of a Statistical Life (VSL) in the U.S. Department of Transportation Analyses - 2015 Adjustment, the following equation was used to approximate VSL values in years other than when it was originally estimated [101]:

$$VSL_{year} = VSL_{base} \times \frac{CPI_{year}}{CPI_{base}} \times (\frac{RI_{year}}{RI_{base}})^{\eta} \tag{B.2}$$

where CPI is the Consumer Price Index, RI is Real Income, which refers to individual income after adjusting for inflation, and η is the income elasticity based on which societal Willingness to Pay (WTP) increase with Real Income. VSL_{base} in the main analysis is from an EPA meta-analysis [100] although various other, updated VSL estimates are also used to check the results. It is not yet certain how VSL changes by age groups [166]. The VSL for elderly, for instance, have been shown to be both lower and higher than population average [125, 126, 167, 168]. In this study, VSL does not vary by age. The BenMAP (Environmental benefits Mapping and Analysis Program - Community Edition) uses an η with central estimate of 0.4 for Premature Mortality [107]. This value is adopted by our study since we believe a Statistical Life is a normal good - an increase in income will lead to a rise in demand. However, we are also aware that some recent studies have provided drastic different estimations for η. For instance, [169] has shown income elasticity ranging from 2.24 at low incomes to 1.23 at high incomes. With values greater than 1, studies like this have shown that statistical life could be considered a luxury good.

Using the parameters discussed, the following sections estimate the VSL in the context of this study, and then provide the mortality costs estimates based on EPA as well as updated VSL values.

B.5.1.2 Consumer Price Index

Year	CPI
1990	127
1991	130.4
1992	135
1993	139.2
1994	143.6
1995	147
1996	151.9
1997	155.4
1998	158.3
1999	163.3
2000	170.1
2001	176.5
2002	179.6
2003	182.7
2004	187.9
2005	193.1
2006	196.2
2007	201.247
2008	208.958
2009	207.889
2010	211.728
2011	219.339
2012	224.459
2013	228.811
2014	232.013
2015	230.567
2016	234.145

The Consumer Price Index (CPI) for all urban consumers is used in this study to capture inflation. Data is obtained through the U.S. Department of Labor, Bureau of Labor Statistics [163]. This data is specific to the Minneapolis – St. Paul MN-WI Combined Statistical Area for all items. The reference period (during which CPI = 100) is 1982-84.

B.5.1.3 Income-Based Willing to Pay Adjustments

Year	Low	Center	High
1997	1.009685	1.049381	1.128201
1998	1.012248	1.062778	1.1647
1999	1.01501	1.077372	1.205346
2000	1.017342	1.089828	1.240791
2001	1.017327	1.089745	1.240554
2002	1.018005	1.09339	1.251059
2003	1.01954	1.101673	1.275164
2004	1.021781	1.113866	1.311246
2005	1.023681	1.124291	1.342672
2006	1.025017	1.131672	1.36525
2007	1.025666	1.135277	1.376378
2008	1.024676	1.129785	1.359452
2009	1.021716	1.113508	1.310176
2010	1.023051	1.120826	1.332167
2011	1.023712	1.124463	1.343195
2012	1.024862	1.130815	1.362613
2013	1.025588	1.134841	1.375031
2014	1.026868	1.141967	1.397211

The Income-Based Willingness to Pay (WTP) Adjustments is obtained from the Environmental Benefits Mapping and Analysis Program - Community Edition users manual (p.113) [107]. The values in this table is calculated as the following:

$$(\frac{RI_{year}}{RI_{1990}})^{\eta} \tag{B.3}$$

where Real Income (RI) essentially is income after taking into consideration inflation on purchasing power. The reference period (when Income-based WTP adjustments = 1) is 1990. The low, center, high estimations are a result of different income elasticity (η) approximations of 0.08, 0.4, 1 although in this study we fix η at 0.4.

B.5.1.4 VSL Results

Year	VSL Estimates (million $2016)										
	[100]	[170]	[171]	[172]	[173]	[174]	[175]	[169]	[176]	[177]	[177]
1998	9.41	7.17	7.23	12.89	9.89	9.91	8.41	9.77	8.04	5.18	12.94
1999	9.53	7.27	7.33	13.06	10.03	10.05	8.52	9.9	8.15	5.25	13.12
2000	9.64	7.35	7.42	13.21	10.14	10.16	8.62	10.02	8.25	5.31	13.27
2001	9.64	7.35	7.42	13.21	10.14	10.16	8.62	10.02	8.25	5.31	13.27
2002	9.68	7.38	7.44	13.26	10.18	10.2	8.65	10.05	8.27	5.32	13.31
2003	9.75	7.43	7.5	13.36	10.26	10.27	8.71	10.13	8.34	5.36	13.41
2004	9.86	7.52	7.58	13.51	10.37	10.39	8.81	10.24	8.43	5.42	13.56
2005	9.95	7.59	7.65	13.63	10.47	10.48	8.89	10.33	8.51	5.47	13.69
2006	10.01	7.64	7.7	13.72	10.53	10.55	8.95	10.4	8.56	5.51	13.78
2007	10.05	7.66	7.73	13.77	10.57	10.59	8.98	10.43	8.59	5.53	13.82
2008	10	7.62	7.69	13.7	10.52	10.53	8.94	10.38	8.55	5.5	13.75
2009	9.85	7.51	7.58	13.5	10.37	10.38	8.81	10.23	8.43	5.42	13.56
2010	9.92	7.56	7.63	13.59	10.43	10.45	8.87	10.3	8.48	5.46	13.64
2011	9.95	7.59	7.65	13.63	10.47	10.49	8.9	10.33	8.51	5.48	13.69
2012	10.01	7.63	7.7	13.71	10.53	10.54	8.95	10.39	8.56	5.51	13.77
2013	10.04	7.66	7.72	13.76	10.56	10.58	8.98	10.43	8.59	5.53	13.81
2014	10.11	7.71	7.77	13.85	10.63	10.65	9.03	10.5	8.64	5.56	13.9

B.5.1.5 Total Mortality Cost Estimates (Sensitivity Analysis)

Exposure Type	[100]	[170]	[171]	[172]	[173]	[174]	[175]	[169]	[176]	[177]	[177]
Extreme Cold Only	**2.01**	1.53	1.54	2.75	2.11	2.11	1.8	2.09	1.71	1.1	2.76
Moderate to Extreme Cold	**8.11**	6.19	6.24	11.12	8.54	8.56	7.26	8.43	6.94	4.47	11.17
Extreme Heat Only	**0.67**	0.51	0.51	0.91	0.7	0.7	0.59	0.69	0.57	0.37	0.91
Moderate to Extreme Heat	**1.17**	0.89	0.9	1.6	1.23	1.23	1.04	1.21	1	0.64	1.61

Total mortality costs estimates discussed in the main text are marked by bold fonts.

B.6 Minimum Effect Temperatures by Age Groups and Health Outcomes

Age Group	MET		
	MORT	EDV	EDHSP
	°F (%ile)	°F (%ile)	°F (%ile)
0-19	-	71 (62.46)	84 (89.13)
20-64	-	73 (63.75)	70 (61.99)
65+	85 (90.39)	75 (66.98)	70 (61.99)
All	84 (89.13)	72 (63.09)	71 (62.46)

MET is the most comfortable temperature for human body regarding different population health outcomes (MORT, EDV, EDHSP) and different age strata (0-19 yo, 20-64 yo, 65+ yo, and all). Specific to MORT, MET is commonly seen in literature as minimum mortality temperature (MMT). This study uses MET to indicate that such most comfortable temperatures are relevant for both mortality and morbidity outcomes.

B.7 Estimates Used to Generate Figure 3.2 and 3.3 in Main Text

B.7.1 Moderate to Extreme Exposures

Health Outcome	Age Group	Moderate-Extreme Cold Exposure $HI_{max}<30^{th}$%ile		Moderate-Extreme Heat Exposure $HI_{max}>70^{th}$%ile	
		AF [95% eCI]	AC [95% eCI]	AF [95% eCI]	AC [95% eCI]
MORT	0-19				
	20-64				
	65+	6.19 [3.17, 9.02]	13991 [7197, 20158]	0.89 [0.38, 1.40]	2016 [863, 3193]
EDV	0-19	7.03 [5.89, 8.10]	137622 [115749, 157331]	1.2 [0.44, 1.92]	23478 [8751, 37860]
	20-64	1.77 [0.97, 2.57]	70464 [37961, 102260]	0.32 [-0.14, 0.79]	12733 [-5,415, 31057]
	65+	2.21 [0.62, 3.76]	15921 [4741, 26936]	0.27 [-0.41, 0.94]	1943 [-3075, 6827]
EDHSP	0-19	6.63 [2.48, 10.27]	9242 [3666, 14339]	0.78 [0.14, 1.39]	1089 [194, 1929]
	20-64	2.57 [1.25, 3.94]	18504 [8727, 27641]	0.56 [-0.46, 1.53]	4,026 [-3036, 10829]
	65+	4.13 [2.68, 5.52]	24252 [15750, 32327]	0.87 [-0.11, 1.84]	5091 [-802, 10993]

AF and AC for MORT is calculated based on 1998-2014; for EDV and EDHSP is calculated based on 2005-2014.

B.7.2 Extreme Exposures

Health Outcome	Age Group	Extreme Cold Exposure HI_max <5%ile		Extreme Heat Exposure HI_max >95%ile	
		AF [95% eCI]	AC [95% eCI]	AF [95% eCI]	AC [95% eCI]
MORT	0-19				
	20-64				
	65+	1.53 [0.89, 2.12]	3444 [2040, 4792]	0.51 [0.20, 0.79]	1,144 [466, 1812]
EDV	0-19	1.9 [1.63, 2.17]	37208 [31734, 42494]	0.62 [0.39, 0.84]	12,079 [7512, 16420]
	20-64	0.31 [0.12, 0.50]	12376 [4895, 20169]	0.14 [-0.01, 0.29]	5,602 [-496, 11759]
	65+	0.06 [-0.33, 0.43]	426 [-2354, 3075]	0.06 [-0.2, 0.33]	440 [-1553, 2414]
EDHSP	0-19	1.79 [0.88, 2.64]	2488 [1225, 3680]	0.47 [0.07, 0.85]	657 [102, 1189]
	20-64	0.61 [0.29, 0.93]	4372 [1992, 6732]	0.21 [-0.07, 0.48]	1,495 [-653, 3478]
	65+	0.76 [0.39, 1.11]	4445 [2319, 6509]	0.23 [-0.08, 0.52]	1402 [-353, 3128]

AF and AC for MORT is calculated based on 1998-2014; for EDV and EDHSP is calculated based on 2005-2014.

B.8 Proportions of Morbidity Costs in Total Costs

Statistical Features	Morbidity Costs Proportion (%)		
	Cold Exposure	Heat Exposure	All Exposure
Mean	1.03	0.37	1.13
Minimum	0.56	0.16	0.65
Maximum	2.42	1	2.35

Costs proportion is calculated by dividing the costs attributable to morbidity outcomes by the costs attributable to both mortality and morbidity outcomes. Cold exposure is defined as the temperature range between the minimum daily maximum heat index (HI_{max}) and the minimum effect temperature (MET, specific to health outcome and age group); heat exposure is defined as the temperature range between the MET and the maximum HI_{max}. All temperature exposure includes the entire temperature range.

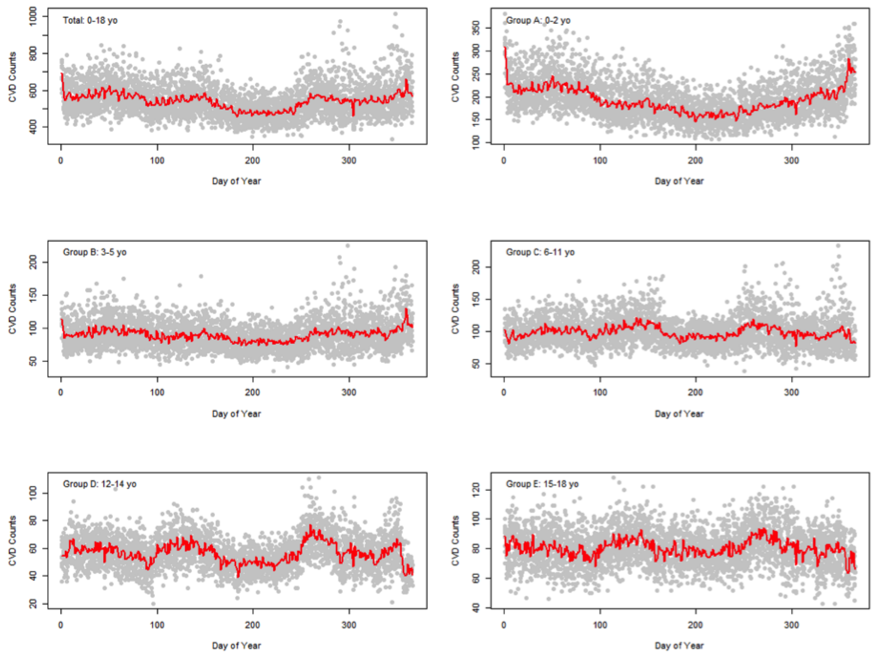
Appendix C

Chapter 4 Supplemental Information

C.1 International Classification of Disease (ICD) Codes Used For Specific Disease Groups

Disease Group #	Disease Group Name (Long)	Disease Group Name (Short)	ICD-9	ICD-10
1	Infectious and parasitic diseases		1-139	A00-B99
2	Neoplasms		140-239	C00-D48
3	Endocrine, nutritional and metabolic disease, and immunity disorders	Metabolic diseases	240-279	D50-D89
4	Diseases of blood and blood-forming organs		280-289	E00-E99
5	Mental disorders		290-319	F00-F99
6	Diseases of nervous system and sense organs	Nervous system diseases	320-389	G00-G99
7	Diseases of the circulatory system		390-459	I00-I99
8	Diseases of the respiratory system	Respiratory Diseases	460-519	J00-J99
9	Diseases of the digestive system	Digestive diseases	520-579	K00-K93
10	Diseases of the genitourinary system	Genitourinary diseases	580-629	N00-N99
11	Complications of pregnancy, children birth, and the puerperium		630-679	O00-O99
12	Diseases of skin and subcutaneous tissue	Skin diseases	680-709	L00-L99
13	Diseases of the musculoskeletal system and connective tissue	Musculoskeletal diseases	710-739	M00-M99
14	Congenital anomalies		740-759	Q00-Q99
15	Certain conditions originating in the perinatal period		760-779	P00-P96
16	Symptoms, signs, and ill-defined conditions	Ill-defined conditions	780-799	R00-R99
17	Injury and poisoning	Injury and poisoning	800-999	S00-T98

C.2 Seasonality Plots by Age Group



Grey points historical observation. Red line historical average observation.

C.3 Total Daily Case Counts by Age and Disease Groups (2007-2014)

Disease Group #	0-18 yo	0-2 yo	3-5 yo	6-11 yo	12-14 yo	15-18 yo
1	22380	13298	2964	2876	853	2389
2	18442	14560	1046	1285	525	1026
3	88550	40586	11006	12970	7048	16940
4	38398	21112	3784	4889	2584	6029
5	115601	15363	3183	13148	19530	64377
6	234836	125358	41269	35003	11438	21768
7	27046	16321	1249	1984	1653	5839
8	445126	2122218	83356	79516	24899	45137
9	149882	65892	20023	27274	11163	25530
10	75110	24304	7579	9524	5813	27890
11	23714	13301	1	1	256	10155
12	99935	49610	14021	16333	6549	13422
13	120045	22401	10231	23865	20832	42716
14	30736	22108	2501	2932	1165	2030
15	31853	30576	249	314	284	430
16	720995	299928	116469	127732	51496	125370
17	436955	100522	71318	101089	62293	101033

Shaded boxes are disease groups that do not meet inclusion criteria for further analysis.

yo years old.

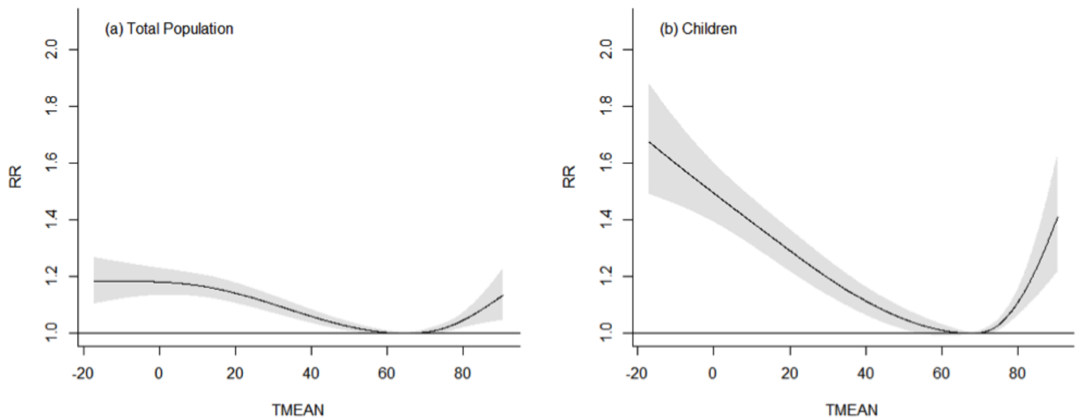
C.4 Total Zero-count Days by Age and Disease Groups (2007-2014)

Disease Group #	0-18 yo	0-2 yo	3-5 yo	6-11 yo	12-14 yo	15-18 yo
1	4	52	1079	1154	2186	1299
2	8	26	2048	1901	2463	2071
3	0	0	87	52	296	9
4	0	7	835	609	1251	362
5	0	19	1054	50	19	0
6	0	0	0	0	74	2
7	1	16	1918	1499	1695	443
8	0	0	0	0	7	0
9	0	0	3	2	70	1
10	0	2	246	127	409	0
11	3	42	2921	2921	2685	120
12	0	0	38	23	349	28
13	0	1	129	3	5	0
14	1	3	1283	1147	1968	1469
15	0	0	2685	2625	2650	2525
16	0	0	0	0	0	0
17	0	0	0	0	0	0

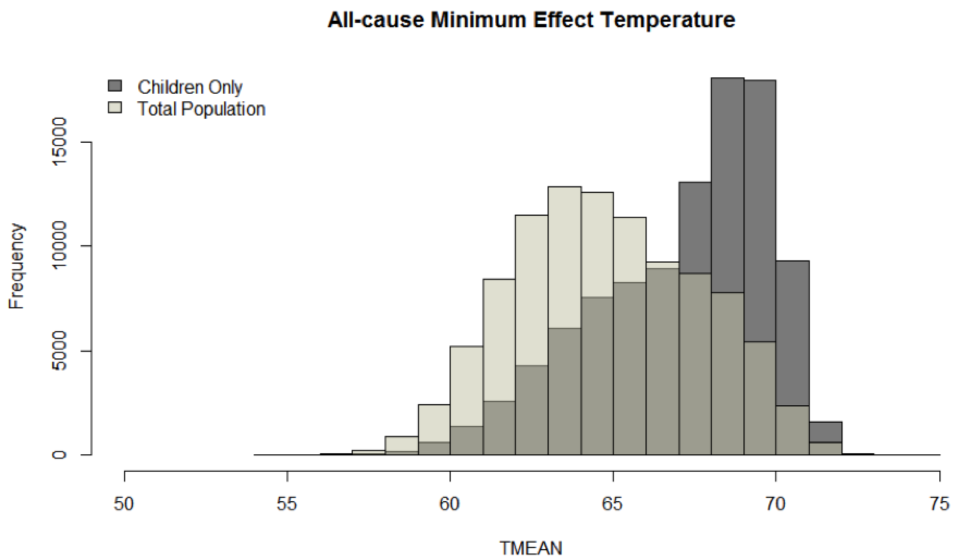
Shaded boxes are disease groups that do not meet inclusion criteria for further analysis.

yo years old.

C.5 Exposure-Response Functions of Children and the Overall Population



C.6 Seasonality Plots by Age Group



Notes:

Random sampling n = 100,000

Total Population, Minimum Morbidity Temperature: 65°F [95%eCI: 60°F, 70°F]

Children, Minimum Morbidity Temperature: 67°F [95%eCI: 61°F, 71°F]

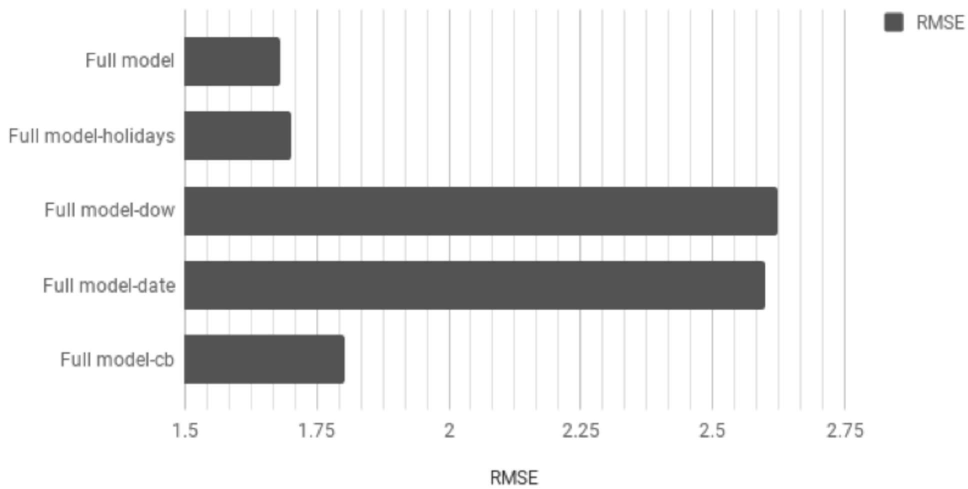
The optimal temperature for children is statistically significantly higher than that of the general population (p <0.05).

C.7 Air pollution as A Potential Confounder

Tests	Attributable Fraction Associated All-range Temperature (%)
Final Model	9.022769
Final Model + O_3	9.149385
Final Model + $PM_{2.5}$	9.072148

Final model includes the cross-basis functions (temperature), *Date* (long-term trend), *dow* (day of week, week day effect), *holidays* (holiday effects), and *summer* (summer break at local school districts).

C.8 One-at-a-time Exclusion Exercise on Final Regression Models

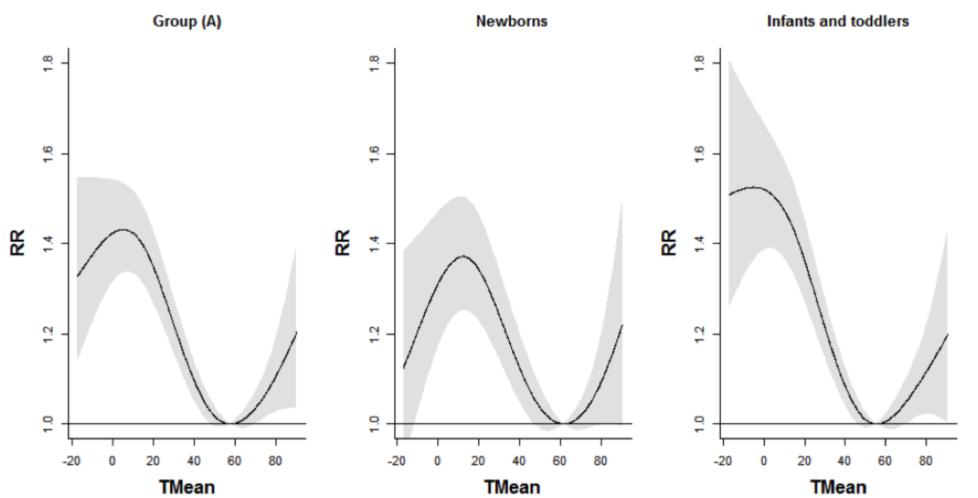


C.9 Minimum Morbidity Temperature and Minimum Morbidity Percentile by Age Group

Age Group	Minimum Morbidity Temperature (°F)		Minimum Morbidity Percentile (%)	
	Point Estimate	CI	Point Estimate	CI
0-18 yo	63	[60, 67]	70.18	[64.07, 75.85]
0-2 yo	58	[53, 65]	61.5	[55.20, 71.19]
3-5 yo	64	[60, 68]	70.18	[63.19, 76.86]
6-11 yo	66	[59, 75]	74.75	[63.55, 92.33]
12-15 yo	26	[22, 66]	20.81	[16.92, 73.85]
(16-18 yo	70	[20, 75]	81.87	[15.33, 61.76]

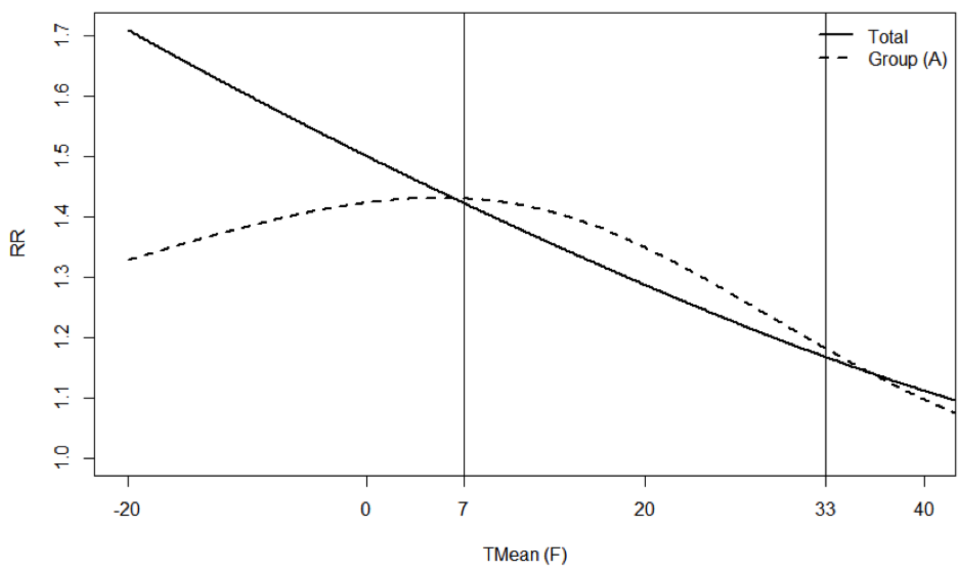
yo - years old.

C.10 Exposure-Response Comparisons among Young Children (0-2 years old)



Notes: Group (A): 0-2 years old; Newborns : 0 years old; Infants and Toddlers: 1-2 years old

C.11 Exposure-Response Comparisons between Young Children (0-2 years old) and All Children (0-18 years) by Cold Exposure Ranges

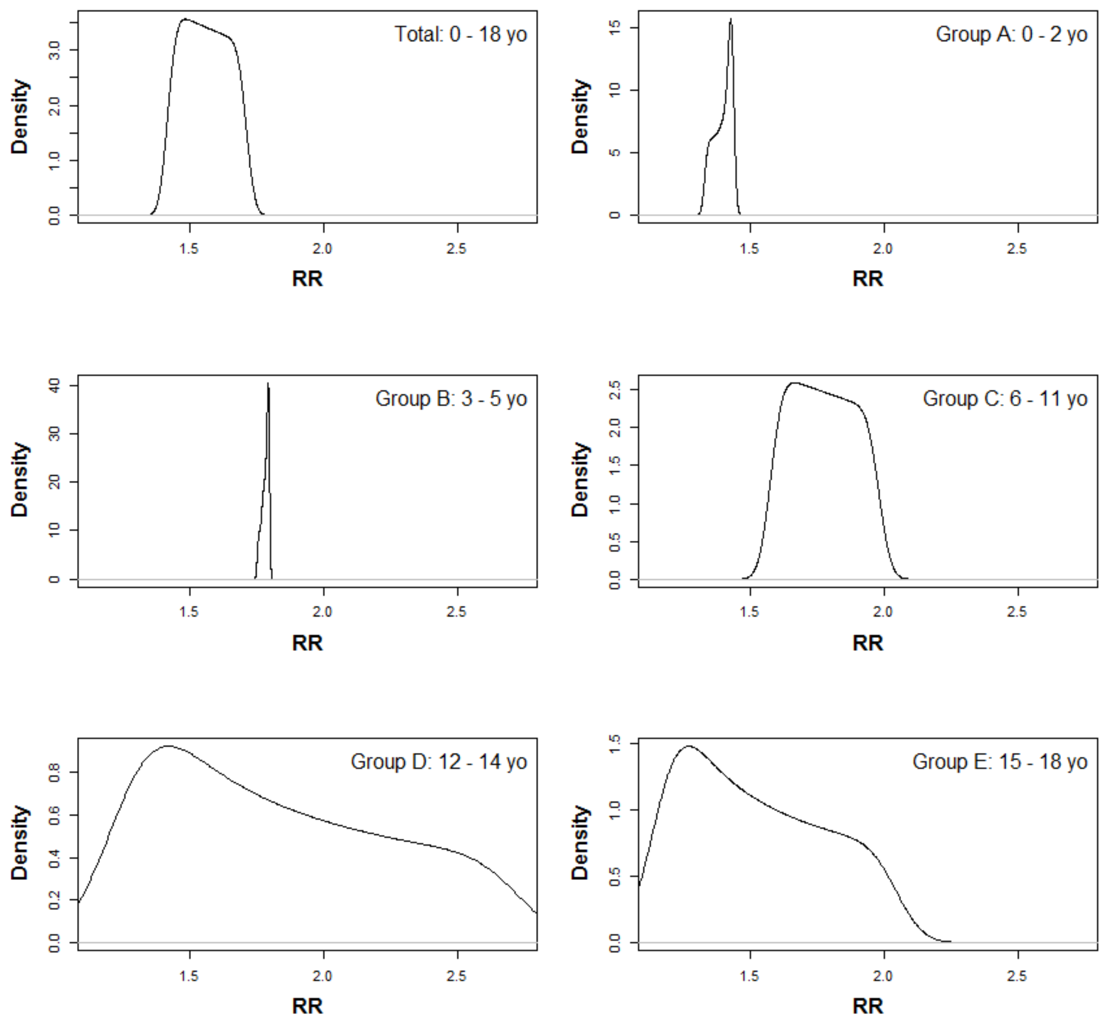


Group (A) represents 0-2 year old newborns, infants, and toddlers.

In this study, extreme cold exposure is defined at the bottom 5-percentile $TMean$ observations. The threshold is 7°F. During 2005-2014, there are 171 days that fall into this category. Moderate to extreme cold is defined as the bottom 30-percentile TMean observations. The threshold is 33°F. During 2005-2014, there are 1097 days that fall into this category. In the Wilcoxon weighted rank-sum test, the RR estimate between 7°F and 33°F is weighted more than five times the RR estimates below 7°F. Therefore, in the bottom left panel in Figure 4.2 (main text), although it is not evident from the boxplots that group A is different from the total childrens estimate, the superscript indicates statistically significant difference.

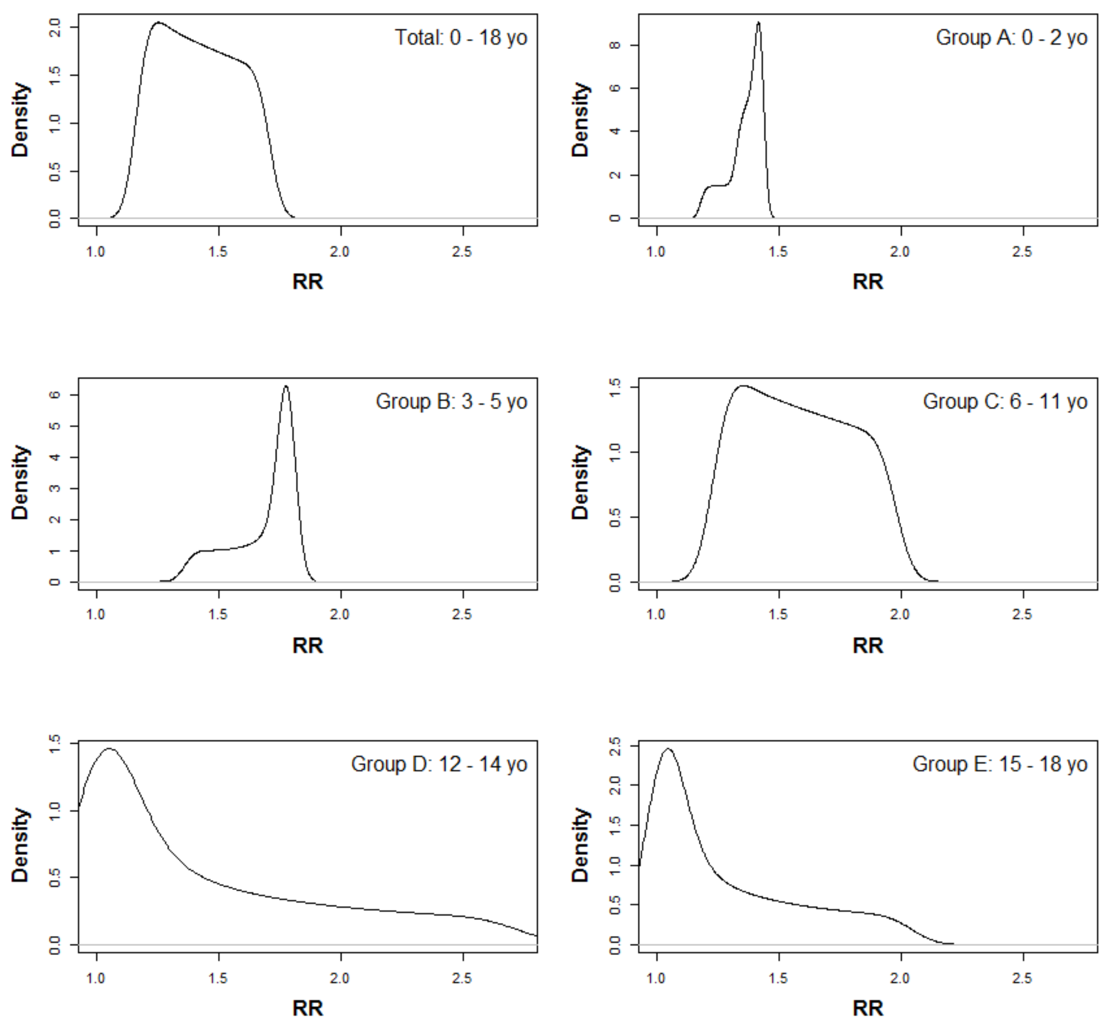
C.12 Probability density function of Relative Risks by Age Group

C.12.1 Extreme Cold Exposures



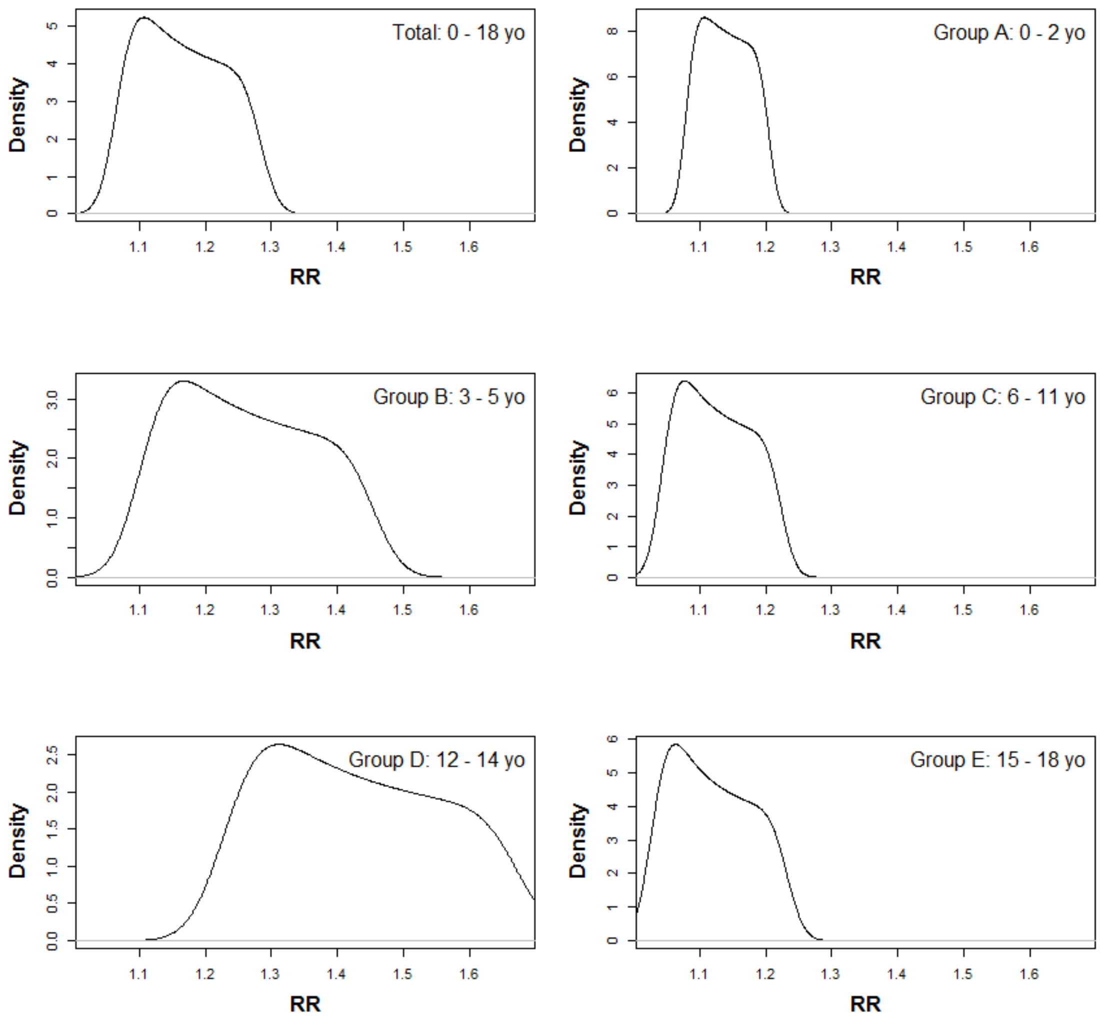
Notes: Extreme cold exposure is defined as the bottom 5 percentiles $TMean$.

C.12.2 Moderate to Extreme Cold Exposures



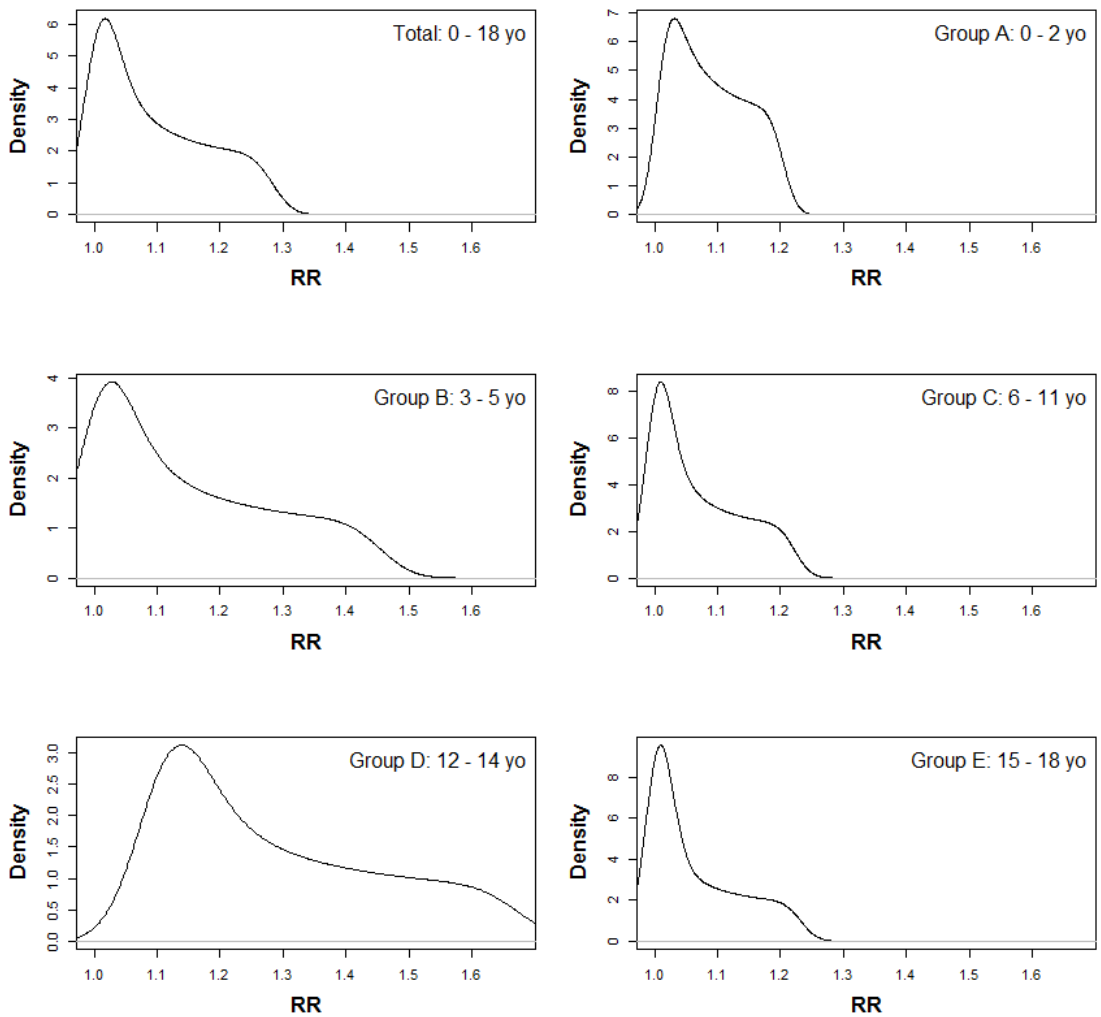
Notes: Extreme cold exposure is defined as the bottom 30 percentiles $TMean$.

C.12.3 Extreme Heat Exposures



Notes: Extreme cold exposure is defined as the top 5 percentiles $TMean$.

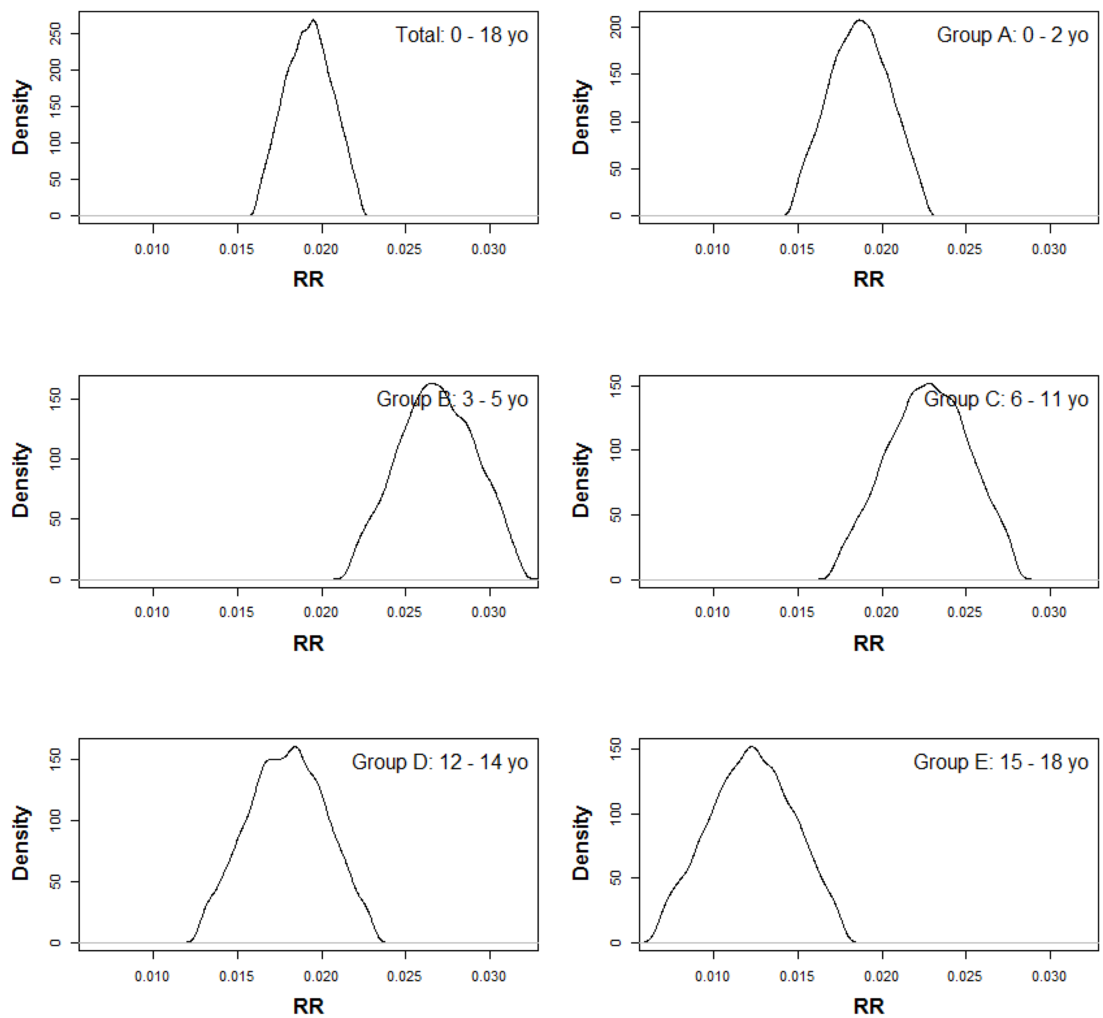
C.12.4 Extreme Heat Exposures



Notes: Extreme cold exposure is defined as the top 30 percentiles $TMean$.

C.13 Probability density function of Attributable Fractions by Age Group

C.13.1 Extreme Cold Exposures



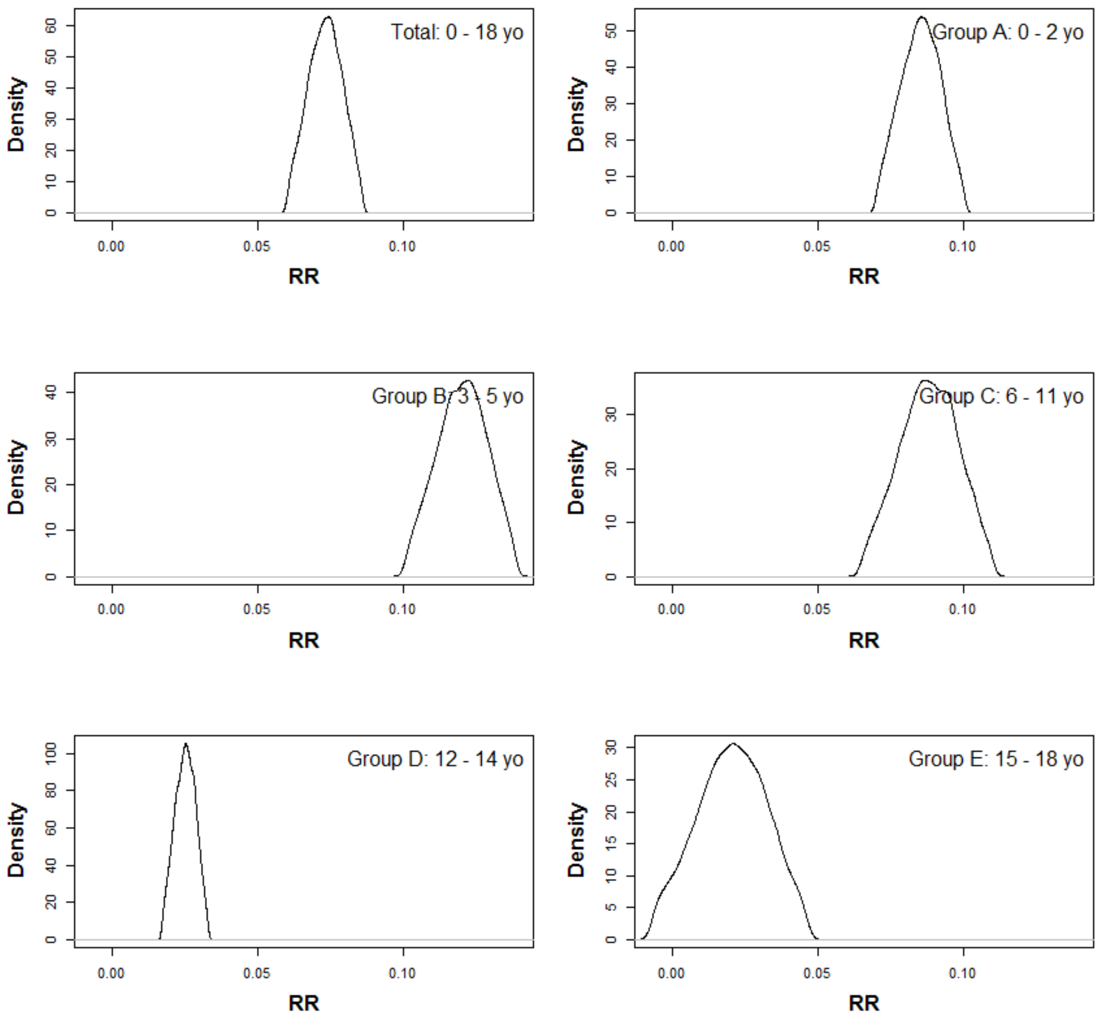
Notes: Extreme cold exposure is defined as the bottom 5 percentiles $TMean$.

C.14 Minimum Morbidity Percentile by Age and Disease Groups

Disease	Minimum Morbidity Percentile					
Group #	0-18 yo	0-2 yo	3-5 yo	6-11 yo	12-14 yo	15-18 yo
1	8.68	0.3	82.56	89.29	44.11	24.18
2	8.84	7.26	9.58	95.81	34.67	40.31
3	81.3	75.03	77.27	90.94	79.13	86.69
4	74.26	5.42	82.04	82.39	1.7	77.6
5	89.13	2.6	47.67	91.43	86.53	89.51
6	72.78	78.59	75.3	69.8	20.32	81.87
7	20.32	15.83	94.58	7.64	47.89	20.7
8	79.44	88.64	79.55	76.86	69.74	84.91
9	72.78	63.77	86.69	41.07	72.78	9.91
10	80.37	83.87	76.7	91.68	12.4	4.85
11	7.12	0.44	76.7	14.13	12.54	80.72
12	63.91	71.55	53.7	74.95	15.17	27.3
13	92.09	4.22	84.75	16.16	21.71	83.98
14	92.88	91.76	83.98	86.77	30.53	16.46
15	8.95	9.91	60.35	13.12	29.87	16.95
16	75.68	70.32	77.52	74.51	71.03	86.99
17	12.46	7.48	5.97	11.31	15.64	13.61

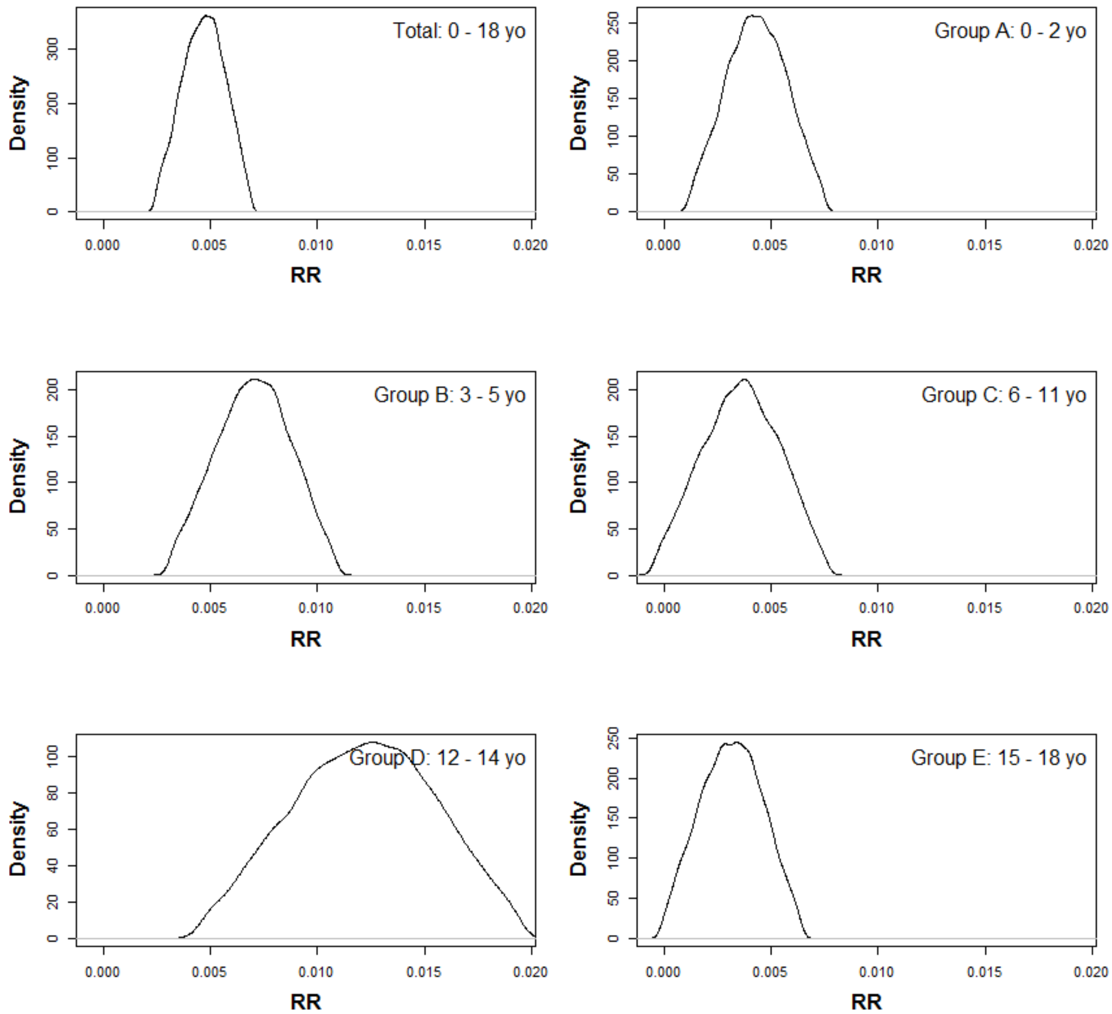
Notes: Shaded boxes are disease groups that do not meet inclusion criteria for further analysis. yo years old.

C.14.1 Moderate to Extreme Cold Exposures



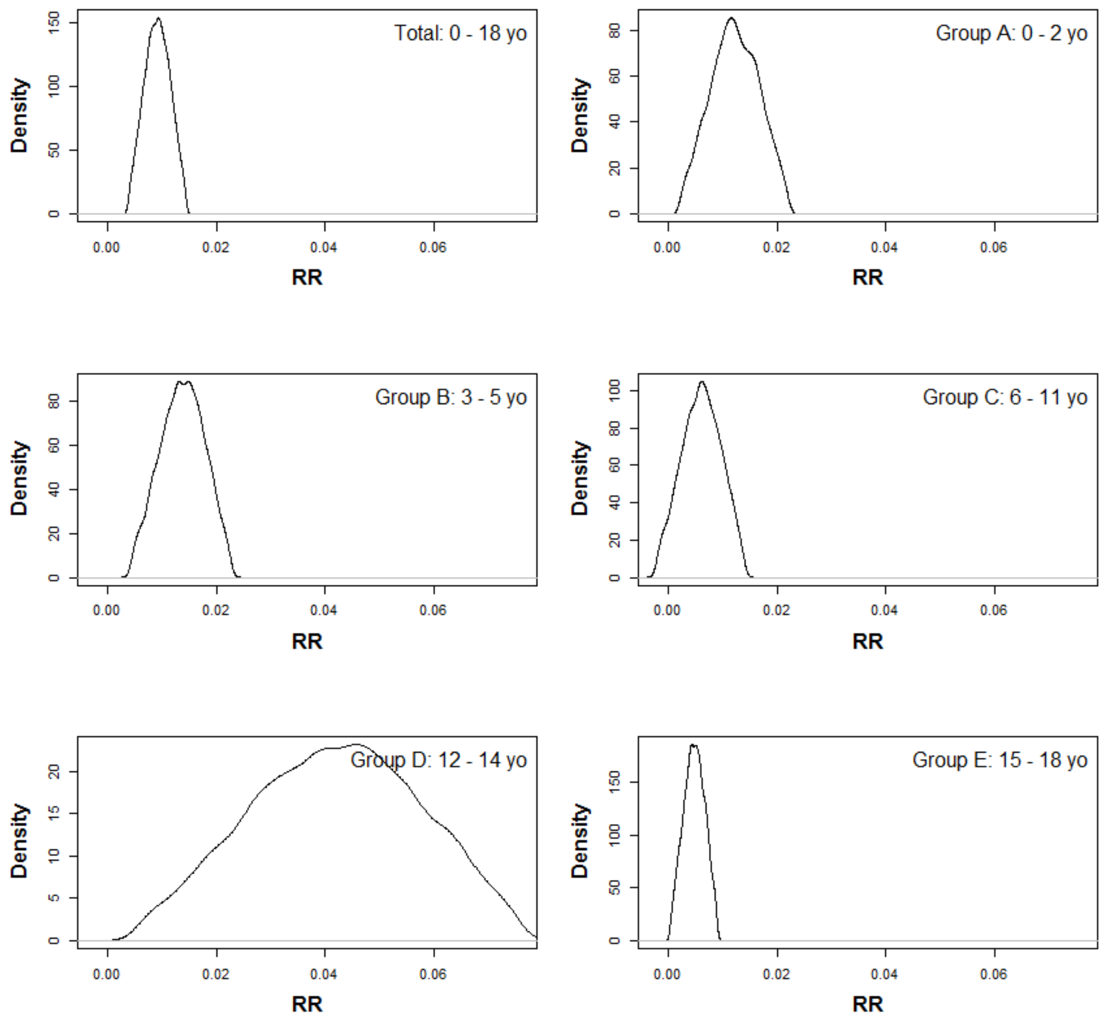
Notes: Extreme cold exposure is defined as the bottom 30 percentiles $TMean$.

C.14.2 Extreme Heat Exposures



Notes: Extreme cold exposure is defined as the top 5 percentiles $TMean$.

C.14.3 Extreme Heat Exposures



Notes: Extreme cold exposure is defined as the top 30 percentiles $TMean$.

C.15 Attributable Fractions of Extreme Temperature Exposures by Age and Disease Groups

C.15.1 Children (0-18 years old)

Disease Group Name (Short)	Disease Group #	Attributable Fraction (%)	
		Cold	Heat
Metabolic diseases	3	4.2 [3.19, 5.16]	0.37 [-0.11, 0.83]
Nervous system diseases	6	2 [1.22, 2.73]	0.65 [0.27, 1.02]
Respiratory diseases	8	4.94 [4.26, 5.57]	0.5 [0.2, 0.79]
Digestive diseases	9	1.39 [0.59, 2.16]	0.56 [0.12, 0.98]
Genitourinary diseases	10	0.3 [-0.84, 1.35]	0.45 [-0.15, 1]
Skin diseases	12	-0.2 [-1.1, 0.62]	1.25 [0.59, 1.86]
Musculoskeletal diseases	13	0.76 [-0.23, 1.66]	0.05 [-0.25, 0.36]
Ill-defined conditions	16	3.29 [2.82, 3.74]	0.57 [0.31, 0.82]
Injury and poison	17	0.62 [0.31, 0.91]	1.79 [1.16, 2.34]

C.15.2 Newborns, Infants, Toddlers (0-2 years old)

Disease Group Name (Short)	Disease Group #	Attributable Fraction (%)	
		Cold	Heat
Metabolic diseases	3	3.99 [2.39, 5.44]	0.27 [-0.45, 0.97]
Nervous system diseases	6	1.21 [0.11, 2.26]	0.12 [-0.32, 0.56]
Respiratory diseases	8	3.01 [1.96, 4.02]	-0.05 [-0.3, 0.19]
Digestive diseases	9	1.78 [0.72, 2.76]	0.65 [-0.08, 1.33]
Genitourinary diseases	10	0.11 [-2.08, 1.89]	0.31 [-0.61, 1.2]
Skin diseases	12	-1.22 [-2.71, 0.12]	0.33 [-0.57, 1.14]
Musculoskeletal diseases	13	-0.34 [-0.78, 0.09]	1.29 [-0.95, 3.22]
Ill-defined conditions	16	2.21 [1.57, 2.83]	0.31 [-0.04, 0.66]
Injury and poison	17	-0.24 [-0.68, 0.17]	1.62 [0.65, 2.54]

C.15.3 Preschool Children (3-5 years old)

Disease Group Name (Short)	Disease Group #	Attributable Fraction (%)	
		Cold	Heat
Metabolic diseases	3	6.14 [3.76, 8.12]	0.93 [-0.37, 2.07]
Nervous system diseases	6	3.41 [1.8, 4.82]	0.93 [0.23, 1.58]
Respiratory diseases	8	5.64 [4.56, 6.63]	0.5 [-0.04, 0.97]
Digestive diseases	9	3.54 [1.39, 0.37]	-0.47 [-0.47, 1.15]
Genitourinary diseases	10	3.74 [0.74, 6.16]	2.26 [0.38, 3.91]
Skin diseases	12	0.85 [-1.1, 2.47]	2.48 [0.5, 4.27]
Musculoskeletal diseases	13	-0.23 [-3.25, 2.13]	-0.76 [-2.41, 0.69]
Ill-defined conditions	16	5.04 [4.19, 5.86]	0.7 [0.2, 1.16]
Injury and poison	17	-0.28 [-0.69, 0.1]	2.3 [0.92, 3.61]

C.15.4 School-age Children (6-11 years old)

Disease Group Name (Short)	Disease Group #	Attributable Fraction (%)	
		Cold	Heat
Metabolic diseases	3	5.32 [2.95, 7.34]	0.16 [-0.71, 0.93]
Nervous system diseases	6	3.11 [1.6, 4.47]	1.54 [0.56, 2.47]
Respiratory diseases	8	7.03 [6.03, 7.93]	1.36 [0.78, 1.91]
Digestive diseases	9	-0.25 [-1.85, 1.22]	-0.03 [-1.56, 1.35]
Genitourinary diseases	10	-1.95 [-1.23, 4.57]	-0.36 [-1.41, 0.64]
Skin diseases	12	1.85 [-0.08, 3.53]	0.84 [-0.56, 2.11]
Musculoskeletal diseases	13	0.77 [-0.39, 1.83]	-0.83 [-3.1, 1.12]
Ill-defined conditions	16	4.54 [3.73, 5.32]	1.16 [0.64, 1.64]
Injury and poison	17	0.47 [-0.05, 0.96]	1.97 [0.79, 3.1]

C.15.5 Young Teens (12-14 years old)

Disease Group Name (Short)	Disease Group #	Attributable Fraction (%)	
		Cold	Heat
Metabolic diseases	3	3.57 [-0.09, 6.36]	1.06 [-0.77, 2.63]
Nervous system diseases	6	1.1 [-0.72, 2.67]	3.41 [0.87, 5.44]
Respiratory diseases	8	6.1 [4.78, 7.27]	2.82 [1.87, 3.68]
Digestive diseases	9	0.21 [-3, 2.73]	1.75 [0.21, 3.13]
Genitourinary diseases	10	1.05 [-1.21, 2.96]	3.09 [-0.44, 5.79]
Skin diseases	12	-0.36 [-2.78, 1.58]	3.89 [0.02, 6.87]
Musculoskeletal diseases	13	2.81 [1.53, 3.97]	1.07 [-0.8, 2.7]
Ill-defined conditions	16	3.12 [1.86, 4.29]	1.4 [0.65, 2.11]
Injury and poison	17	2.32 [1.59, 2.97]	2.44 [1.23, 3.54]

C.15.6 Teenagers (15-18 years old)

Disease Group Name (Short)	Disease Group #	Attributable Fraction (%)	
		Cold	Heat
Metabolic diseases	3	2.06 [-0.25, 4]	0.25 [-0.75, 1.18]
Nervous system diseases	6	2.85 [1.05, 4.4]	0.35 [-0.64, 1.32]
Respiratory diseases	8	4.52 [3.34, 5.6]	0.47 [-0.14, 1.05]
Digestive diseases	9	0.41 [-0.61, 1.33]	0.85 [-0.96, 2.42]
Genitourinary diseases	10	0.04 [-0.48, 0.52]	0.97 [-0.88, 2.6]
Skin diseases	12	0.68 [-0.98, 2.13]	3.03 [0.73, 5.07]
Musculoskeletal diseases	13	1.6 [0.13, 2.91]	0.45 [-0.24, 1.12]
Ill-defined conditions	16	2.56 [1.66, 3.37]	0.18 [-0.21, 0.56]
Injury and poison	17	1.31 [0.75, 1.83]	1.14 [0.13, 2.11]

C.16 Attributable Fractions of Moderate to Extreme Temperature Exposures by Age and Disease Groups

C.16.1 Children (0-18 years old)

Disease Group Name (Short)	Disease Group #	Attributable Fraction (%)	
		Cold	Heat
Metabolic diseases	3	17.16 [13.1, 20.63]	0.58 [-0.09, 1.24]
Nervous system diseases	6	9.81 [6.67, 12.64]	1.16 [0.31, 1.94]
Respiratory diseases	8	20.28 [17.89, 22.47]	0.81 [0.34, 1.26]
Digestive diseases	9	6.68 [3.18, 9.75]	1 [0, 1.96]
Genitourinary diseases	10	1.67 [-3.6, 6.32]	0.69 [-0.23, 1.54]
Skin diseases	12	1.34 [-2.34, 4.68]	3.18 [1.19, 5.05]
Musculoskeletal diseases	13	2.2 [-2.61, 6.33]	0.4 [-0.22, 1.03]
Ill-defined conditions	16	7.97 [-0.73, 14.72]	1.05 [-0.24, 2.23]
Injury and poison	17	0.36 [-0.79, 1.49]	4 [-5.05, 11.02]

C.16.2 Newborns, Infants, Toddlers (0-2 years old)

Disease Group Name (Short)	Disease Group #	Attributable Fraction (%)	
		Cold	Heat
Metabolic diseases	3	16.08 [9.4, 21.51]	0.47 [-1.03, 1.8]
Nervous system diseases	6	7.52 [2.733, 11.69]	0.2 [-0.55, 0.94]
Respiratory diseases	8	14.11 [9.92, 17.88]	0.15 [-0.03, 0.32]
Digestive diseases	9	7.61 [3.17, 11.53]	1.62 [-0.65, 3.71]
Genitourinary diseases	10	1.13 [-9.24, 9.36]	0.51 [-0.57, 15.2]
Skin diseases	12	-0.68 [-7.33, 5.04]	0.86 [-1.42, 2.98]
Musculoskeletal diseases	13	4.1 [0.97, 6.97]	8.46 [-2.42, 16.47]
Ill-defined conditions	16	7.86 [-2.24, 15.54]	0.69 [-0.31, 1.65]
Injury and poison	17	0.32 [-0.89, 1.43]	3.41 [-5.85, 10.75]

C.16.3 Preschool Children (3-5 years old)

Disease Group Name (Short)	Disease Group #	Attributable Fraction (%)	
		Cold	Heat
Metabolic diseases	3	27.33 [19.8, 32.87]	1.49 [-0.9, 3.48]
Nervous system diseases	6	18 [12.08, 22.95]	1.56 [0.16, 2.82]
Respiratory diseases	8	22.74 [19.19, 25.78]	0.82 [0.05, 1.54]
Digestive diseases	9	17.99 [10.19, 23.93]	0.79 [0.15, 1.37]
Genitourinary diseases	10	15.67 [4.16, 23.2]	3.6 [0.08, 6.53]
Skin diseases	12	6.05 [-0.39, 11.16]	8.37 [0.4, 14.71]
Musculoskeletal diseases	13	5.12 [-7.77, 13.87]	-0.62 [-2.1, 0.66]
Ill-defined conditions	16	16.55 [-14.39, 30.07]	-0.41 [-4.09, 2.41]
Injury and poison	17	29.93 [-68.61, 45.63]	7.94 [-3.43, 12.02]

C.16.4 School-age Children (6-11 years old)

Disease Group Name (Short)	Disease Group #	Attributable Fraction (%)	
		Cold	Heat
Metabolic diseases	3	22.99 [15.1, 29.02]	0.82 [-0.26, 1.8]
Nervous system diseases	6	11.36 [4.96, 16.42]	2.92 [0.57, 5]
Respiratory diseases	8	26.95 [24.2, 29.27]	2.25 [1.16, 3.26]
Digestive diseases	9	-0.57 [-5.39, 3.71]	-0.03 [-1.56, 1.35]
Genitourinary diseases	10	10.93 [-2.9, 19.62]	1.47 [-0.27, 3.05]
Skin diseases	12	6.76 [-1.93, 13.43]	1.4 [-1.48, 3.94]
Musculoskeletal diseases	13	1.19 [-0.3, 2.51]	-0.73 [-13.9, 9.15]
Ill-defined conditions	16	9.69 [-22.56, 25.59]	-0.49 [-2.63, 1.14]
Injury and poison	17	7.07 [-6.99, 13.92]	21.64 [-99.82, 37.36]

C.16.5 Young Teens (12-14 years old)

Disease Group Name (Short)	Disease Group #	Attributable Fraction (%)	
		Cold	Heat
Metabolic diseases	3	15.91 [1.69, 24.72]	1.63 [-1.53, 4.21]
Nervous system diseases	6	1.53 [-1.22, 3.88]	8.13 [-4.22, 16.88]
Respiratory diseases	8	21.66 [17.18, 25.29]	5.46 [3.09, 7.53]
Digestive diseases	9	5.78 [-7.07, 15.3]	3.11 [-0.19, 5.9]
Genitourinary diseases	10	1.97 [-0.8, 4.24]	10.91 [-5.87, 21.19]
Skin diseases	12	0.03 [-2.93, 2.37]	9.33 [-12, 22.1]
Musculoskeletal diseases	13	4 [2.03, 5.72]	4.27 [-6.15, 12.12]
Ill-defined conditions	16	-0.21 [-18.31, 10.49]	9.87 [-32.07, 26.4]
Injury and poison	17	5.59 [-31.28, 16.35]	26.25 [-72.98, 43.35]

C.16.6 Teenagers (15-18 years old)

Disease Group Name (Short)	Disease Group #	Attributable Fraction (%)	
		Cold	Heat
Metabolic diseases	3	4.23 [-7.88, 12.7]	0.47 [-0.36, 1.2]
Nervous system diseases	6	0.91 [0.8, 15.18]	0.55 [-0.85, 1.83]
Respiratory diseases	8	16.25 [11.68, 20.21]	0.9 [0.32, 1.43]
Digestive diseases	9	1.13 [-0.05, 2.28]	1.64 [-7.95, 9.02]
Genitourinary diseases	10	0.96 [-1.42, 3.1]	4.84 [-46.3, 12.54]
Skin diseases	12	1.06 [-2.24, 3.82]	8.77 [-2.61, 17.33]
Musculoskeletal diseases	13	5.78 [-0.76, 11.12]	0.77 [0.01, 1.51]
Ill-defined conditions	16	2.53 [-3.33, 6.54]	3.64 [-39.25, 22.52]
Injury and poison	17	4.67 [-14.42, 13.44]	8.83 [-141.1, 31.37]