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Research Report

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Impact of Climate Change on Health and Drug Demand

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About This Report

It is anticipated that extreme weather events due to climate change will increase the prevalence of a number of acute and chronic diseases. As a result, the demand for drugs to prevent or treat those conditions is likely to increase. If the anticipated increase in demand for these drugs is not planned for, already strained medical supply chains will be further strained, resulting in poor health outcomes among affected patient populations and additional costs to health systems.

In this study, we estimated how the anticipated effects of climate change on the prevalence of a sample of four chronic conditions will affect demand for drugs needed to treat them. To generate these estimates, we conducted an environmental scan of the peer-reviewed and grey literature and developed a medical condition–specific systems dynamics model.

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Summary

We conducted an environmental scan and found that extreme temperatures, precipitation, drought, and elevated levels of ground ozone and wildfire-associated air pollution adversely affect human health. Many medical conditions are affected by climate change: maternal-fetal health, cardiovascular disease, asthma, chronic obstructive pulmonary disease, water and food-borne infectious diseases, fungal infections, vector-borne illnesses, mental health, cancer, stroke, kidney disease, diabetes, and neurodegenerative diseases, such as Alzheimer's disease.

In this study, we designed a systems dynamics model to estimate the impact of climate change on human health and resultant drug demand, focusing on four conditions: cardiovascular disease, asthma, stage 5 chronic kidney disease (also known as end-stage renal disease), and Alzheimer's disease. When selecting conditions to model, we prioritized those that are among the most common chronic conditions in the United States and on the top ten list of the leading causes of death in the country in 2022.

For each of these conditions, we identified standard-of-care treatments to model future demand: metoprolol, albuterol, heparin, and donepezil. Metoprolol is an antihypertensive drug that is used as first-line treatment in many cardiovascular diseases. Albuterol is an inhaled bronchodilator that is first-line in the treatment of asthma. Heparin is an anticoagulant required for end-stage renal disease patients on hemodialysis. Lastly, donepezil belongs to the anti-cholinesterase class of drugs that are first-line in the treatment of mild to moderate Alzheimer's disease. With the exception of donepezil, these generic drugs have all experienced past or current shortages, hence may be more likely to be susceptible to future shortages.

The model estimates that climate change may lead to an increase in drug demand for three of the four medical conditions. These include asthma, end-stage renal disease, and Alzheimer's, all of which are expected to increase in prevalence due to climate change despite concomitant increases in disease related mortality due to climate change. However, demand for metoprolol to treat cardiovascular disease is expected to decrease as a result of higher cardiovascular disease mortality rates under severe climate change scenarios. These examples highlight the complexity of climate change's potential impacts on health and drug demand.

The model's estimations provide a preview of the potential future drug demand under varying climate conditions. This and future versions of the model can be used to inform policies and innovations for mitigating climate change's anticipated impact on demand by ensuring sufficient drug supply under various climate scenarios. More specifically, these findings can help inform development of proactive strategies for identifying supply chain risks and building supply chain resiliency—for example, through stockpiling and further diversification of both U.S.-based and non-U.S.-based supply chains for high-demand drugs.

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Chapter 1. Objective and Approach

Objective

Climate change is increasing the frequency and intensity of extreme weather events and related disasters. Past studies have linked extreme weather events—including extreme hot and cold weather—to poor health outcomes and increased demand for health services and drugs used to treat conditions that are predicted to become more prevalent with a changing climate (Salas et al., 2024). At the same time, drug shortages have been an ongoing public health concern for decades and could become more so with the increase in climate-related demand. The U.S. government and the private sector—including suppliers, manufacturers, distributors, wholesalers, and providers—need a better understanding of how climate change could affect disease burden and the demand for drugs. Such information can support advance planning to strengthen medical supply chain resiliency.

We attempted to shed light on these issues by (1) estimating the degree to which disease burden will increase in a sample of medical conditions likely to be affected by climate change and (2) modeling future demand for a sample of drugs used to treat the sampled conditions.

Overview of Approach

We started by conducting an environmental scan of peer-reviewed and grey literature focused on the following topics:

1. the conditions most likely to be affected by climate change and their prevalence
2. the most common drugs, biologics, and/or medical devices needed to treat those conditions and their baseline (i.e., current) demand
3. any supply chain shortages experienced by these commonly used drugs
4. models estimating future increases in disease prevalence as a result of climate change.

This scan helped determine the final sample of four conditions and drugs (one to treat each of these conditions). The information gleaned from the above steps served as inputs for a medical condition–specific systems dynamics model that we developed to predict demand for those drugs in the context of various climate change scenarios (described in Chapter 3). The model estimated demand for each drug under various assumptions for climate impact.

Organization of This Report

The remainder of this report consists of three chapters and four appendixes. In Chapter 2, we present the methods and results for the environmental scan. In Chapter 3, we outline the methods

and results for the systems dynamics model. In Chapter 4, we discuss the study findings and future directions. We provide further details of our methods and analysis in the appendixes.

Chapter 2. Environmental Scan

We conducted reviews of peer-reviewed and grey literature to gather information required for developing a condition-specific systems dynamics model to estimate domestic future drug demand under climate change assumptions. In addition to identifying the list of medical conditions most likely to be affected by climate change, we identified the types of drugs that are most commonly used to treat the medical conditions. We paired the list of conditions with drugs that are among first-line treatments for each condition.

Methods

Peer-Reviewed and Grey Literature Search Strategies

Our search strategies (outlined in Appendix A) were structured by key concepts and combined to meet the different informational needs of the scan. Initially, we grouped chronic and acute health condition search terms using the International Classification of Diseases (ICD) standard classification of health categories (World Health Organization [WHO], undated). The search focused on the following types of health conditions: respiratory, cardiovascular, nephrological, allergies, malignant neoplasms, heat stress disorders, dermatologic, eye conditions, reproductive and maternal health, neurologic, mental health and psychiatric, and infectious (including vector-borne diseases).

Then we compiled climate change search terms, including meteorological events and factors relating to climate change such as air pollution. We developed a separate search strategy to identify existing climate models. This search combined the previous health and climate change terms with epidemiologic and statistical terms to inform the model.

Finally, the drug and pharmaceutical supply and demand terms combined specific drugs, both brand name and generic, and terms relating to demand and utilization.

A professional librarian searched the following electronic databases in April 2024: PubMed, Web of Science Core Collection (which consists of Science Citation Index Expanded [SCI-EXPANDED], Social Sciences Citation Index [SSCI], and Emerging Sources Citation Index [ESCI]), ESC Atlas of Cardiology, the Derwent Patents Citation Index (Clarivate), Scopus (Elsevier), Academic Search Complete (EBSCOhost), Military Database (ProQuest), and IEEE Xplore. We restricted the search strategy for health impacts and climate change to U.S. studies published in English between 2014 and 2024. To enable a broader knowledge of the modeling literature, we expanded the search to include international studies from 2000 to 2024. Expanding modeling literature to include international studies was important because the number of models that predict future prevalence of medical conditions in the United States (especially under

climate scenarios) are limited. The librarian manually removed duplicates using EndNote's duplicate identification strategy.

We adapted the above search for the grey literature review, which included the document repositories of the WHO, the Centers for Disease Control and Prevention (CDC), the U.S. Department of Health and Human Services (HHS), and the U.S. Environmental Protection Agency (EPA).

Results

Peer-Reviewed and Grey Literature Search Results

Our peer-reviewed search strategies yielded a total of 1,523 unique articles from the combined database results. After the initial screening of titles and abstracts, 80 articles advanced to the second level of screening (full-text review). Of these, 67 articles were deemed relevant for report inclusion and further analysis. Our grey literature search strategies yielded a total of 122 unique articles. After the initial screening of titles and abstracts, 103 articles advanced to the second level of screening (full-text review). Of these, 41 articles were deemed relevant for report inclusion and further analysis. Among the studies that underwent full-article review, the research designs were primarily observational. These observational studies varied in the types of the methods used and included case-crossover, time series, health impact assessment, ecological, cross-sectional, surveillance, cohort, case control designs, review articles, and modeling studies.

Climate Threats and Health

Climate change presents significant health threats to human populations around the globe. Increasing atmospheric carbon dioxide and other greenhouse gases are driving an increase in the earth's temperature. These climatologic factors affect the prevalence of both acute illnesses, such as infectious diseases, and chronic diseases through the effects of temperature, humidity, and other weather-related phenomena on pathogens, vectors, animal hosts, land use, and migration (Edelson et al., 2023). Both hot and cold temperature extremes have been associated with increased morbidity and mortality (Gasparrini et al., 2015; Gronlund et al., 2018). Recent longer and more-severe heatwaves have proven to be especially fatal (DHHS, undated). Thunderstorm-related atmospheric changes can trigger acute respiratory illnesses and are anticipated to become more frequent as temperatures rise. Drought and high winds can circulate increased levels of particulate matter, such as PM2.5 (particles that are 2.5 microns or less in diameter that can travel deep into the respiratory tract), leading to respiratory illness and increased all-cause mortality (Abadi et al., 2022; Sun et al., 2015). Particulate matter, which can be a component of air pollution and wildfires, has been associated with higher atmospheric concentrations of carbon dioxide, which can lead to increased pollen production and a prolonged pollen season.

Climate change has been identified as a major contributor to the increasing frequency and size of wildfires, and it has also been shown to exacerbate flood risks in U.S. coastal regions that pose various risks to human health (National Oceanic and Atmospheric Administration, National Centers for Environmental Information [NOAA], 2023), such as exposure to waterborne pathogens (Levy, Smith, and Carlton, 2018). Furthermore, climate change has been associated with a rise in surface ozone levels that, in turn, have been associated with increased mortality (Sun et al., 2015; Alexeeff, Pfister, and Nychka, 2016).

The extent to which extreme weather risks affect human health may be determined by the nature of the physical hazards, such as heat and wind; the extent of a population's exposure to the hazard; the vulnerability of the population; and the resiliency of the affected community. Regardless of the type of weather event, all types of extreme weather can result in infrastructure and/or societal disruption. Furthermore, extreme weather events can result in extremely high economic costs to the United States. As of July 2024, the cost of weather-related disasters in the United States has already reached $37.9 billion in 2024 alone (NOAA, National Centers for Environmental Information, 2024).

Climate-Vulnerable Health Conditions in the United States

A number of health conditions are particularly vulnerable to the effects of climate change—although the mechanisms for these vulnerabilities are not always well understood. Climate change is expected to increase the prevalence of these conditions, and people with these conditions are more susceptible to climate change's adverse effects. Below, we discuss examples of those conditions for which there is evidence for negative impact from climate change as reported in U.S.-based studies. Given differences in population demographics and disease prevalence in other countries compared to the United States, we base the discussion of the effect of climate-vulnerable conditions in the United States exclusively on U.S.-based studies.

Cardiopulmonary Disease

Heat, wildfire smoke, air pollution, and elevated ozone levels can all exacerbate cardiopulmonary stress. Extreme temperatures have been associated with increased risk of various cardiovascular conditions, such as myocardial infarction (i.e., heart attacks) (Rowland et al., 2020), and increased risk of adverse outcomes for stroke and other cardiovascular diseases (CVDs) (Mazidi and Speakman, 2020). Several direct and indirect mechanisms are responsible for these effects. Higher temperatures lead to higher surface blood circulation and sweating, both of which contribute to higher levels of strain on the heart. Furthermore, high temperatures may lead to sleep disturbances and decreased physical activity, both of which increase the risk of CVD. Both high and low temperatures have been reported to increase risk of coagulopathy (i.e., clot formation), which can facilitate cardiovascular events (Levi, 2018).

Increased levels of air pollution are linked to higher risk of acute coronary syndrome, peripheral artery disease, cardiac arrhythmia, and heart failure (Rowland et al., 2019, Mazidi and

Speakman, 2020). Climate change also amplifies the adverse health effects of diabetes (a risk factor for CVD) (Al-Shihabi, Moore, and Chowdhury 2023). For example, a Commonwealth of Virginia–based study showed an association between cold weather and increased diabetes-related emergency department (ED) visits (Davis, Driskill, and Novicoff, 2022).

Wildfire smoke is associated with poor respiratory outcomes as well, such as decreased lung function among people with and without preexisting asthma (Wilgus and Merchant, 2024). Exposure to extreme heat and precipitation events is associated with increased asthma-related hospitalizations (Soneja et al., 2016). Furthermore, dust outbreaks that worsen particulate matter air pollution have been associated with chronic obstructive pulmonary disease (COPD) exacerbations (Gutierrez et al., 2020).

Kidney Disease

The prevalence of chronic kidney disease (CKD) has increased over the past two decades (Kovesdy, 2022), especially in areas with chronic heat stress and air pollution. Dehydration secondary to heat stress is one mechanism that can worsen poor kidney function. A study of 2 million U.S. veterans found that exposure to increased PM2.5 and gaseous pollutants, in addition to exacerbating many of the risk factors associated with kidney disease, such as hypertension and diabetes, led to the progression of CKD and renal failure (Rasking et al., 2022). One hypothesis to explain this effect is that particulate matter entering the bloodstream can result in pathological changes in the kidneys (Tavera Busso et al., 2018). Among patients with CKD, extreme heat has been associated with increased hospitalizations and mortality (Remigio et al., 2019).

Mental Health and Neurological Diseases

Climate-related events such as wildfires have been associated with increased risk for mental health conditions (Clayton, 2021), such as major depressive disorder, posttraumatic stress disorder, and generalized anxiety disorder (Wettstein and Vaidyanathan, 2024; Monsour et al., 2022).

Exposure to heat stress in an animal model study was associated with “misfolding” of brain proteins—a process by which the shape of a protein changes—causing protein aggregation. In the context of heat exposure, one can postulate that similar processes in humans may lead to increasing prevalence of Alzheimer’s disease (Bongioanni et al., 2021). Individuals with neurological disorders such as Alzheimer’s disease are also at increased risk of health complications due to extreme heat largely because of an inability to take steps to protect themselves from heat exposure. Furthermore, extreme heat can result in dehydration and increase the risk of infection and kidney disease in this population (Stella et al., 2023). Concerns have been raised for similar risks from heat waves among individuals with other neurodegenerative diseases, such as Parkinson’s disease and motor neuron diseases (Bongioanni et al., 2021).

Infectious Diseases

Lyme disease, a tick-borne disease and the most common vector-borne illness in the United States, has been found to have earlier annual disease onset (Monaghan et al., 2015), and warmer temperatures have been reported to contribute to the expanding habitat of the Lyme-carrying tick putting more people at risk. Past outbreaks of West Nile Virus, another vector-borne infectious disease, have been attributed to stagnant water reservoirs and elevated temperatures in the context of drought (Limaye et al., 2019).

Exposure to storm-related flooding has been associated with a rise in Shiga toxin-producing *Escherichia coli* (E. coli) infections and an increase in Legionnaires' disease and cases of cryptosporidiosis (Lynch and Shaman, 2023). Prior research has shown an association between extreme precipitation and waterborne diseases such as Salmonellosis (Morgado et al., 2021) and *Vibrio vulnificus* infections (Archer et al., 2023). One study demonstrated a potential association between climate-mediated flooding and *Clostridium difficile* infections (Lin, Wade, and Hilborn, 2015).

Fungal infections have also been reported to be on the rise as a result of climate change. For example, rising heat and moisture may be creating ideal conditions for the growth of the Coccidioides fungus—the organism responsible for Valley Fever—and contributing to an increased incidence of infections in previously unaffected regions (Gorris et al., 2019). Valley Fever outbreaks may be associated with severe dust storms that increase dust concentrations and disperse the fungus.

Maternal-Fetal Health

Heat exposure throughout pregnancy puts women at risk of heat illness and heat stroke (CDC, undated-b). Exposure to temperature extremes increases the risk of cardiovascular complications for pregnant women during labor and delivery (Ha et al., 2017). Extreme temperatures have also been associated with an increased risk of poor fetal growth (Sun et al., 2019) and stillbirths (Ha et al., 2017).

Cancer

Existing literature raises concerns about a potential link between a warming planet and increased incidence of skin cancer (Parker, 2021). Furthermore, wildfires have been reported to increase the concentration of hazardous air pollutants—chemicals that are known or suspected carcinogens (Rice et al., 2023; Tee Lewis et al., 2023).

Climate-Vulnerable Populations and Locations

The effects of climate-related weather events are widespread and certain populations and locations are particularly vulnerable to their impacts (Tee Lewis et al., 2023; Zhang et al., 2019). Children (Leffers, 2022), pregnant women (Ha et al., 2017), and older adults (Carnes, Staats, and Willcox, 2014) are particularly vulnerable to the health effects of climate change. Overall,

climate change disproportionately affects the health status of people of color because of socioeconomic inequities (Flores et al., 2020) and health care disparities (Berberian, Gonzalez, and Cushing, 2022; Guirguis et al., 2018). In the context of climate change, these vulnerable populations are at greater risk because of higher exposure to climate threats and lack of ability and/or resources to prepare, adapt, and recover from climate-related extreme weather events (Tee Lewis et al., 2023).

Depending on the specific geographic region in the United States, the nature and severity of climate threats vary. Furthermore, certain localities may be at higher risk. An important example is extreme heat in urban centers, which is a major environmental health stressor. Urban heat events are those above the 90th percentile of historical temperatures for a given location and are exacerbated by the "urban heat island" phenomenon (Howard, 2012; Debbage and Shepherd, 2015). The *urban heat island* refers to the strong correlation between urban environments and high temperatures stemming from impermeable urban surfaces, human activity, and the relative paucity of green environments (such as grass and trees) to mitigate rising temperatures. Furthermore, risk of extreme precipitation (for example, in the setting of hurricanes) is variable across the United States, with coastal areas being at highest risk (Federal Emergency Management Agency, undated).

Climate Effects on Demand for Health Services and Drugs

Severe weather events can also disrupt health systems and access to services—for example, through surges in patient volumes or impeded physical access to health facilities (Flores et al., 2020). Delayed access to health services and needed drugs can result in acute exacerbation of chronic conditions, such as asthma, diabetes, and congestive heart failure, leading to a need for ED services or hospitalization. A study of 42 large disasters in the United States found an increase in ED visits among Medicare beneficiaries in the week following the event in affected counties (Salas et al., 2024).

Climate Effects on Medical Supply Chains

Medical supply chains are sensitive to disruptions, such as those resulting from natural disasters. After a natural disaster, there is a surge in disease burden and demand for related drugs, making timely access to health care facilities and medical treatment critical. Furthermore, extreme weather-related events can interrupt manufacturing and/or delivery of medical supplies to end users. Increased demand for drugs and challenges with insufficient supplies in the context of extreme weather climate events can affect access to time-sensitive treatments.

According to the U.S. Food and Drug Administration (FDA), about a quarter of drug shortages in the United States in 2023 were due to increased drug demand (FDA, 2024). Other reasons for drug shortages in that year included delays in shipment, active ingredient shortages, and manufacturers not complying with practice standards. Currently, the FDA does not have the

authority to require manufacturers to report shortages that are likely due to increases in demand for drugs, making mitigating drug shortages more challenging.

Increased demand in the context of climate-related events can compound existing drug shortages (Kolbe and Beleche, 2024; NASEM, 2022). Such shortages may be exacerbated during, or even as a result of, public health emergencies (for example, during the coronavirus disease 2019 [COVID-19] pandemic and in the aftermath of Hurricane Maria). Extreme weather events may hinder production of drugs and/or the "last mile" delivery of the products to end users (Kolbe and Beleche, 2024; NASEM, undated; NASEM, 2022).

Chapter 3. Systems Dynamics Model

To understand how climate change might affect future demand for drugs, we developed a *systems dynamics framework* that can simulate and predict demand under various climate change scenarios (Homer and Hirsch, 2006). Through the simulation framework and scenario analysis, the model provides initial but valuable insights into the possible health impacts of climate change, and resultant changes in demand for drugs, which can help support informed decisionmaking for emergency preparedness and build supply chain resiliency. The model produces four key outcomes: (1) quantitative estimates of changes in prevalence of select medical conditions; (2) estimates of mortality due to specific climate change impacts; (3) identification of age groups most likely to be affected by climate change impacts; and (4) estimates of changes in demand for the sampled drugs used in treating the medical conditions under different climate change scenarios.

This chapter describes the sampling strategy for medical conditions and products that are the focus of the modeling effort, model design, inputs, assumptions, and limitations, and then presents the results of the analyses. Additional technical details about the model and data inputs are available in Appendixes B, C, and D.

Methods

Medical Condition and Drug Sampling Strategies

Our environmental scan yielded literature indicating that the following health conditions are climate-vulnerable: maternal-fetal health, CVD, asthma, COPD, water- and food-borne infectious diseases, fungal infections, vector-borne illnesses, mental health, cancer, stroke, Alzheimer's disease and other neurodegenerative diseases, kidney disease, and diabetes. From this list, we selected asthma, CVD, end-stage renal disease, and Alzheimer's, as described in more detail below. These are among the most common chronic diseases in the United States and among the top ten leading causes of death in the country. Furthermore, we prioritized conditions with related drugs that are first-line treatments and that had experienced past and/or current shortages according to the 2022 report *Essential Medicines Supply Chain and Manufacturing Resilience Assessment* (Next Foundry for American Biotechnology, Advanced Regenerative Manufacturing Institute, and Nexight Group, 2022), which was sponsored by the Administration for Strategic Preparedness and Response (formerly the Office of the Assistant Secretary for Preparedness and Response).

We used three criteria to sample the drugs used to treat the selected medical conditions. We prioritized drugs that are considered standard-of-care in the treatment of each medical condition,

those that have experienced past and/or current shortages, and those with existing data regarding their baseline annual utilization in the United States. We also worked to select drugs that are largely indicated for the selected conditions or family of conditions. With these criteria, we selected four drugs: albuterol, metoprolol, heparin, and donepezil. All the sampled drugs have experienced past and/or current shortages, except for donepezil (Next Foundry for American Biotechnology, Advanced Regenerative Manufacturing Institute, and Nexight Group, 2022).

Cardiovascular Disease and Metoprolol

CVD refers to diseases of the heart and blood vessels (American Heart Association, undated). The term CVD includes a number of diseases, including coronary artery disease, congestive heart failure, stroke, and arrhythmia, among others (Cleveland Clinic, undated). CVD is among the most common chronic diseases in the United States and is the leading cause of death in the nation (CDC, undated-a; CDC, undated-c). Approximately 5 percent of Americans 20 years of age and older suffer from one or more forms of CVD (Tsao et al., 2023).

Metoprolol belongs to the beta-blocker class of anti-hypertensive drugs (Harvard Medical School, undated). Hypertension, or elevated blood pressure, is a risk factor for coronary artery disease, stroke, congestive heart failure, and other CVDs (Fuchs and Whelton, 2020). Therefore, metoprolol is used in patients with hypertension and for heart rate control (for example, in patients with atrial fibrillation) and for the treatment of congestive heart failure. Metoprolol is administered in oral and intravenous formulations (Medical News Today, undated).

Asthma and Albuterol

Asthma is a chronic condition that affects lung airways. It is among the most common chronic diseases in the United States (CDC, undated-c). As of 2021, 7.7 percent of the U.S. population suffered from asthma (National Center for Health Statistics, 2024).

Albuterol is a short-acting inhaled beta-agonist and is first-line in the treatment of individuals with asthma diagnosis (National Center for Biotechnology Information, undated-a). Albuterol is most commonly administered in powder form using an inhaler or in liquid form through an oral nebulizer (Straight Nursing, undated).

End-Stage Renal Disease and Heparin

CKD results from damage to the kidneys over time that prohibits the kidneys from effectively filtering blood (NIDDK, undated-b). If a kidney transplant is not possible or available, renal replacement therapy (RRT) through hemodialysis or peritoneal dialysis is the preferred treatment for patients with stage 5 CKD—also referred to as end-stage renal disease (ESRD). In the United States, about every two in 1,000 people have ESRD (NIDDK, undated-a). Patients with ESRD on hemodialysis generally need three sessions per week to ensure normal electrolyte levels in the bloodstream (National Kidney Foundation, undated). The absence of

hemodialysis, or missed sessions, can lead to electrolyte imbalances that can result in cardiac arrhythmia and death (National Kidney Foundation, undated).

Hemodialysis requires unfractionated heparin to prevent clotting during the procedure (Cronin and Reilly, 2010; National Center for Biotechnology Information, undated-b). However, heparin is used in many other contexts to prevent clotting.

Alzheimer's Disease and Donepezil

Alzheimer's disease is a neurodegenerative disease and a type of dementia (Alzheimer's Association, undated). It is among the top ten leading causes of death in the United States (CDC, undated-c).

Donepezil belongs to the cholinesterase inhibitor class of drugs that are considered first-line in the treatment of mild to moderate Alzheimer's disease (National Institute on Aging, undated).

Model Overview

We developed estimates for future drug demand from 2024 projected to 2040 under different climate impact assumptions for the four drugs, each considered first-line in treating one of four sampled conditions likely to be affected by climate change. Our approach utilizes a systems dynamics framework based on ordinary differential equations (ODEs) to simulate and predict future drug demand on a daily time scale. This method emphasizes causal relationships, dynamic interactions, and feedback loops. Systems dynamics models are deterministic (as opposed to stochastic), simulate continuous time (as opposed to discrete time), and incorporate transition rates between simulated states (as opposed to transition probabilities) (Einzinger, Leskovar, and Wytrzens, 2012). Using information from our environmental scan, we estimated medical condition prevalence trends and related drug demand time trends. Historical data informed the ranges of values for each model parameter, and we estimated the impact of key variables, such as temperature, precipitation, and air quality on disease prevalence (please see the subsection on "Climate Impacts").

The core of our model consists of coupled ODEs that describe the rate of change in drug demand, accounting for climate change effects. To estimate demand changes specific to climate change effects, we developed a baseline model that assumes no change from current climate conditions but incorporates non-climate-related changes in disease prevalence and incidence rates, all-cause and disease-specific mortality rates, and population by age group. Details on the data sources and modeling approaches for each of these input variables is available in Appendix C. Given initial conditions, such as the initial prevalence of the disease and hazard rates for the risk of developing the disease across different age groups, the model integrates these dynamics to predict future prevalence, from which we can then derive the future demand for specific drugs.

To account for climate change scenarios and make comparisons relative to the baseline scenario, we adjusted the hazard rates for developing the diseases, all-other-cause mortality, and

disease-specific mortality based on specific factors related to climate change factors. This was done through a two-step approach:

1. First, using estimates from the literature, we linked temperature projections under five emissions scenarios to three key climate factors: days of extreme heat, number of hurricanes reaching the U.S. mainland, and wildfire-associated air quality changes (increases in PM2.5 and ozone levels).
2. Second, we used statistical estimates from the literature to link these four climate factors to associated changes in health outcomes, including all-cause mortality, disease-specific mortality, and incidence rates of the sampled medical conditions.

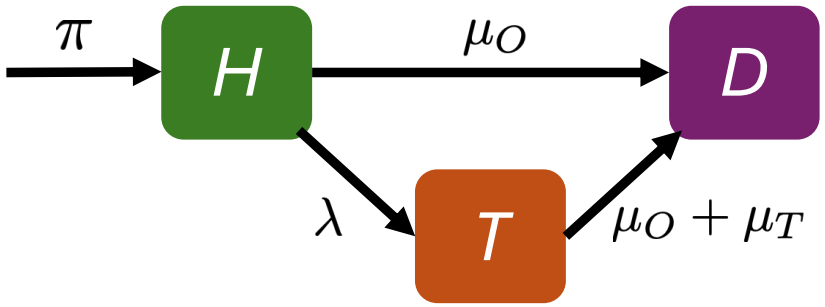
The model integrates the modified hazard rates, mortality rates, and incidence rates assumed under various climate change scenarios, and, to account for uncertainties, we sampled the parameter values within their estimated uncertainty ranges. We ran 100 different simulations for each climate change scenario (detailed under "Model Outputs," below) to generate a comprehensive set of possible outcomes and explore a wide range of potential future climate conditions.

Model Design

The model design applied to all four diseases is identical. However, the models for each disease are informed by different data sources and inputs that influence how the various factors affecting the prevalence of these diseases change with climate change. For more information on the specific data sources and inputs used for each medical condition, see Appendix C.

Our model operates on a daily time scale from 2024 to 2040. As shown in Figure 3.1, our model consists of three compartments representing different states and population groups: the presumed Healthy Population (*H*), which includes all individuals not diagnosed with the disease; the Diagnosed and Treated Population (*T*), which consists of individuals diagnosed with the disease and receiving treatment; and the Deceased Population (D), which includes individuals who have died from any cause, including deaths attributable to the disease of interest. The model predicts the number of individuals in each compartment over time, broken down by age group.

Figure 3.1. Illustration of Model Compartments and Relationships



NOTE: π is the rate at which individuals enter the healthy population through migration or birth. Individuals from the healthy population compartment (H) may die or receive a diagnosis for the medical condition and treatment and ultimately die. The rate at which individuals from the healthy population compartment die from any cause is represented by μ_O. The transition of individuals from the healthy compartment to the diagnosis and treated compartment is governed by age-specific hazard rates denoted by λ. The transition of individuals from the diagnosed and treated compartment (T) to the compartment of deceased population (D) is designated by μ_O plus μ_T where $\mu_O$is the rate at which individuals from the healthy population compartment die and $\mu_T$is the condition-specific mortality rate.

Climate Impacts

The model produces estimates of future disease prevalence across five climate scenarios, based on the Shared Socioeconomic Pathways (SSPs) developed in the Intergovernmental Panel for Climate Change's (IPCC's) Sixth Assessment Report (Masson-Delmotte et al., 2021). The SSPs are a set of five scenarios used by the IPCC to estimate future greenhouse gas (GHG) emissions under different levels of adoption of climate change mitigation and adaptation policies (Table 3.1). For the purposes of this study, these scenarios can be understood as being organized in order of least to highest severity of climate change.

Table 3.1. Climate Scenarios Used in the Model

Scenario Name	Scenario Description	Mean Global Temperature Change by 2040 (relative to 2024, degrees Celsius)
SSP 1–1.9	Very low GHG emissions: CO2 emissions reach net zero around 2050	0.228
SSP 1–2.6	Low GHG emissions: CO2 emissions reach net zero after 2050	0.297
SSP 2–4.5	Intermediate GHG emissions: CO2 emissions around current levels until 2050	0.379
SSP 3–7.0	High GHG emissions: CO2 emissions double by 2100	0.457
SSP 5–8.5	Very high GHG emissions: CO2 emissions double by 2050	0.556

SOURCE: Scenario descriptions from Arias et al. (2021); mean global temperature changes derived from EPA (undated-c) and Masson-Delmotte et al. (2021).

Our model focused on four climate change factors that could be linked to health outcomes: extreme heat days, hurricanes making landfall in the United States, and wildfire-associated changes in air quality (including PM2.5 and ozone) (Table 3.2). While these are not the only climate-related events that may affect our medical conditions of interest, these four indicators were chosen based on the availability of data and existing research examining their effect on human health. In order to translate global temperature changes under each climate change scenario (Table 3.1) to changes in our four climate factors of interest, we first modeled U.S. temperature change as a function of global temperature change. Then, using historical temperature and climate data, we modeled future frequency of extreme heat days, number of hurricanes making landfall in the United States, and wildfire extent (thus wildfire-associated air quality changes). Additional details on the data sources and methods used to develop these estimates are available in Appendix C.

Table 3.2. Indicators Used to Represent Exposure to Climate Threats

Climate Event	Indicator
Extreme heat	• Annual number of extreme heat days
Precipitation	• Annual number of hurricanes making landfall in the United States
Air quality	• Average annual concentration of wildfire-related PM2.5
	• Average annual concentration of wildfire-related ozone

Climate-Health Linkages

Estimates of the four climate threats above were then linked to disease-specific incidence and mortality using estimates from the literature. In some cases, the literature provided specific evidence for the relationship between event exposure and a health outcome (e.g., the relative risk of asthma mortality during a heat wave). In other cases, we had to use proxies such as condition-related hospitalizations due to a climate event to estimate our outcome variables. Full descriptions of each data source and linkage methodology used are available in Appendix C.

Model Outputs

To capture the relationships between temperature changes, extreme weather manifestations, and the outcomes of interest, we employ an experimental design incorporating a large sample of parameter values. Each relationship is characterized by estimates with uncertainty bounds. For our study, we generated 100 unique combinations of parameter values, each sampled within its specified uncertainty range. The 100 unique parameter combinations are sampled using the Latin Hypercube approach (Iman, Helton, and Campbell, 1981). This method efficiently explores the uncertainty space, ensuring a homogeneous sample consistent with the specified probability distribution functions for each input parameter. The model varied parameters linking climate effects to the manifestations of extreme weather events, and subsequently to disease-specific incidence and mortality rates, as well as all-cause mortality rates. The baseline scenario does not include variability since it assumes no climate change effects, keeping input parameters constant.

The model outputs include (1) the total population of healthy people, which includes individuals who have not been diagnosed with the disease, by age; (2) the prevalence of the disease, encompassing all individuals who have been diagnosed, categorized by age group; (3) the total aggregate number of deaths, accounting for both deaths caused by the disease and those from all other causes. Changes in prevalence estimates are considered equivalent to the future change in demand for the relevant medical products.

Assumptions and Limitations

Our systems dynamics model, like all models, approximates reality and has limitations due to strategic simplifications, often driven by the lack of precise data. These simplifications should be considered when interpreting the results and should be addressed in future model iterations. Future work could focus on modeling efforts that address these limitations through refinement and research.

First, there are limitations in our modeling approach that arise from using a systems dynamics model. Our model's dynamics are governed by a set of coupled ODEs that describe the population flows between compartments over time. This approach employs a deterministic framework, predicting the average population dynamics without accounting for random variations or individual differences within a given model compartment. Instead of tracking each individual separately, the model deals with population densities, focusing on the proportion or number of people in each compartment rather than following individual trajectories. The population is divided into compartments, each representing a specific state or condition (e.g., healthy, diagnosed). The model assumes that everyone within a compartment is identical in terms of health status and behavior, with transitions between compartments occurring according to predefined rates influenced by environmental factors and interventions. This does not take into account individual risk factors such as body mass index (BMI), differences in treatment adherence, disease exacerbation or natural progression, or health impacts on the undiagnosed population. The model also does not account for seasonal variation in disease incidence or

mortality. Similarly, the model assumes that new births and immigrants are healthy and do not have a pre-existing disease diagnosis. Each of these simplifications may lead to over- or underestimation of disease prevalence and therefore future drug demand.

The model is also limited by the availability and granularity of relevant climate and health data sources. For example, we were unable to incorporate subnational geographic variation in climate variables. These heterogeneities were averaged in our model, resulting in broad error bounds in parameter estimates. In addition, we focused on a limited set of climate factors based on data availability; however, these do not provide a comprehensive picture of potential health impacts of climate change. Future work might identify additional data sources to incorporate a wider range of climate factors into future models.

Similarly, the limited number of studies examining the impacts of climate-related events on disease-specific incidence and mortality necessitated some simplifications and assumptions. For some of the medical conditions, we were unable to find direct data linking the extreme weather event in question with the incidence of the relevant disease; in such cases, we used proxies such as hospitalizations, disease events, or disease exacerbations and assumed that the rate of increase in true incidence would be similar to the proxy (see Appendix C). This may result in overestimations of future prevalence because hospitalizations can occur multiple times, unlike the one-time event of disease diagnosis, and in the case of Alzheimer's disease, the extreme weather event may not lead to the development of the disease; rather it may cause adverse reactions that require the patient to seek medical attention.

The model builds on existing prevalence, incidence, and mortality data. While mortality data for each condition are available, incidence data are harder to obtain. Where incidence data were unavailable, we assumed stable prevalence based on historical data (see Appendix C). Self-reported prevalence data, as was used for CVD and estimates, may be less reliable than incidence or mortality data. Future work might explore additional data sources for these inputs to enhance robustness of the model.

Finally, the model focuses on future demand for one drug to treat each medical condition. Each of these medical conditions have other potential treatment options that are not accounted for in our model. The choice of drug used in the model is largely illustrative, as our model estimates demand as a function of disease prevalence. In reality, large increases in demand for specific drugs may result in shifts to alternative products. Future models might explore the more complex dynamics of how demand for all drugs treating a given medical condition might shift due to climate change impacts.

Results

The model produced estimates of disease prevalence, all-cause mortality, and drug demand for four diseases across five climate scenarios. Overall, the model estimated increases in prevalence relative to the baseline scenario for three of the four modeled diseases: asthma,

ESRD, and Alzheimer's. In contrast, the model estimated decreases in prevalence relative to the baseline scenario for CVD due to increased mortality in older age groups due to climate change factors. These modeled changes in disease prevalence translate into parallel changes in drug demand, with a decreased overall demand for metoprolol (CVD), but increased overall demand for albuterol (asthma), heparin (ESRD), and donepezil (Alzheimer's).

For each disease, we developed three key plots to illustrate our findings. The first plot (3.2a, 3.3a, 3.4a, 3.5a) shows the projected percentage change in disease prevalence from the initial year (2024) to the final year (2040) across all age groups. These plots show changes in prevalence relative to the baseline (no change in climate variables), highlighting those changes in future prevalence that can be attributed to the climate variables in the model. In these plots, we use a yellow and orange palette for the colored bands to illustrate the range of projected prevalence estimates under selected climate change scenarios. The concentration of orange in the fan indicates where the majority of these trajectories lie, representing the median, while the yellow areas depict the less likely trajectories. Appendix D shows the estimated absolute change in prevalence stratified by age group.

The second plot for each disease (3.2b, 3.3b, 3.4b, 3.5b) shows the projected percentage change in total aggregate deaths from the initial year (2024) to the final year (2040) across all age groups. This plot includes deaths due to the specific disease being modeled and other cause mortality. In these plots, we use a blue and violet palette for the colored bands to illustrate the range of projected total deaths under selected climate change scenarios. The concentration of violet in the fan indicates where the majority of these trajectories lie, representing the median, while the blue areas depict the less likely trajectories. Appendix D shows the estimated percentage change in total aggregate deaths stratified by age group.

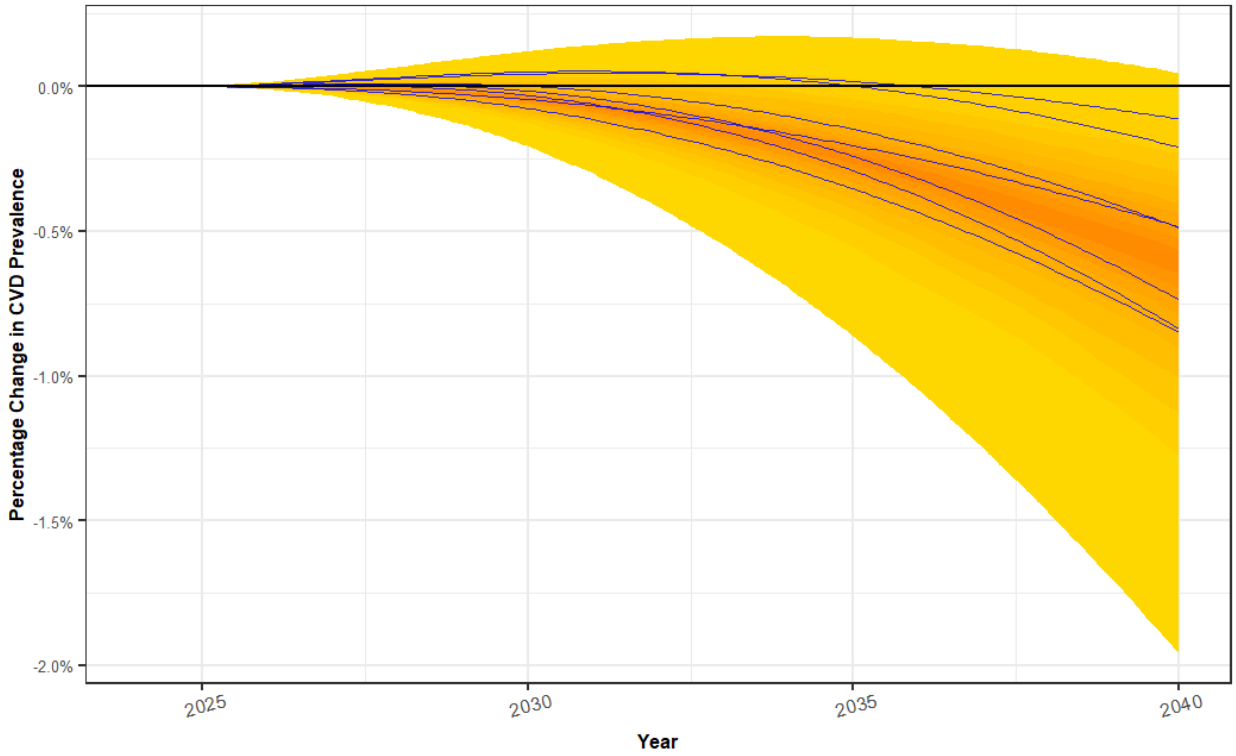
In each of these two sets of figures (Figures 3.2a, 3.2b, 3.3a, 3.3b, 3.4a, 3.4b, 3.5a, and 3.5b), the lines represent seven specific case runs of the model dynamics. We made the choice to select seven case runs at random. The seven lines are not indicative of climate scenarios but rather serve as illustrative examples of individual trajectories. The close agreement between the lines and the bands is a feature of the deterministic model used, though this is not always the case.

The third plot (3.2c, 3.3c, 3.4c, 3.5c) is a box plot showing the percentage change in demand for the specific drug associated with each disease in the final year (2040) relative to the baseline (2024) scenario demand across all age groups. Each boxplot shows the distribution of demand estimates generated across the 100 model runs for each climate scenario.

Climate Change and Demand for Metoprolol

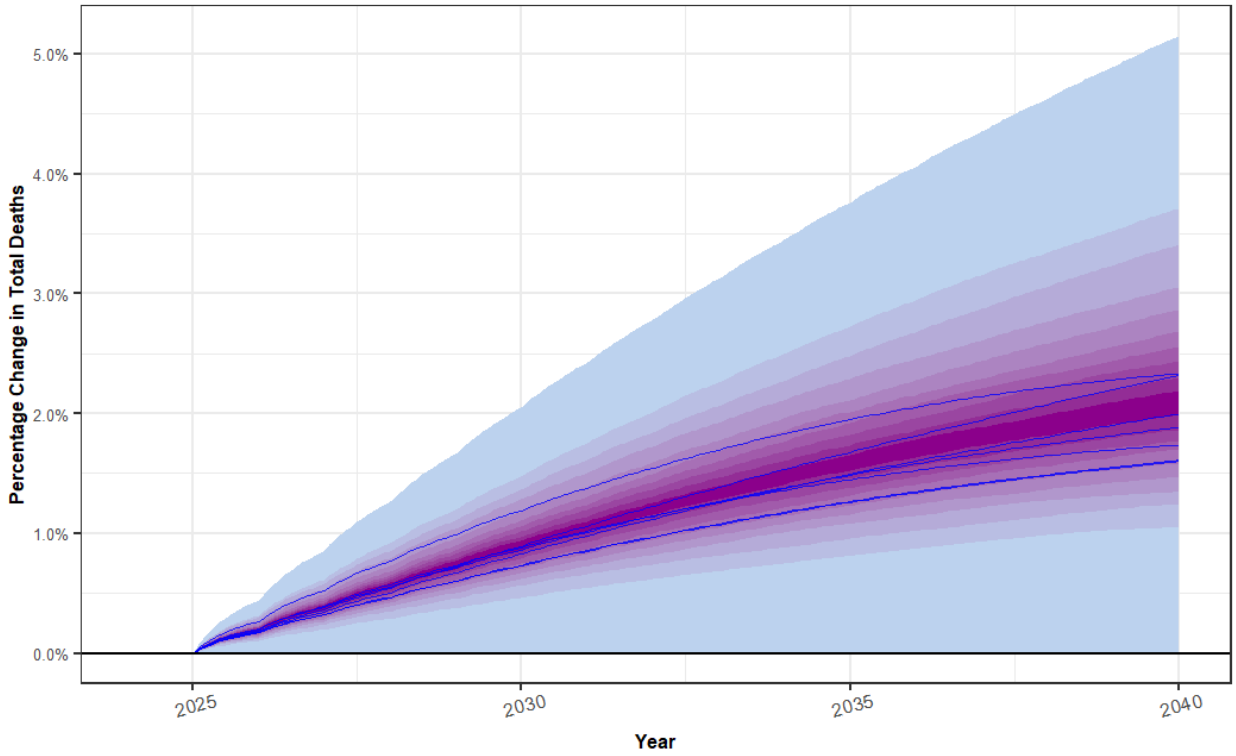
Figures 3.2a–3.2c present the results of the CVD/metoprolol model. Aggregated across all age groups (Figure 3.2a), overall prevalence is estimated to be slightly lower than in the baseline scenario. This is driven by increased disease-specific and general mortality under climate change scenarios, as shown in Figure 3.2b. Overall, these changes in prevalence and mortality result in an estimated decrease in demand for metoprolol by 0.4 percent to 0.9 percent (Figure 3.2c).

Figure 3.2a. Results of Cardiovascular Disease/Metoprolol Model: Projected Percentage Change in CVD Prevalence Compared to Baseline Under All Climate Change Scenarios and All Age Groups, 2024–2040



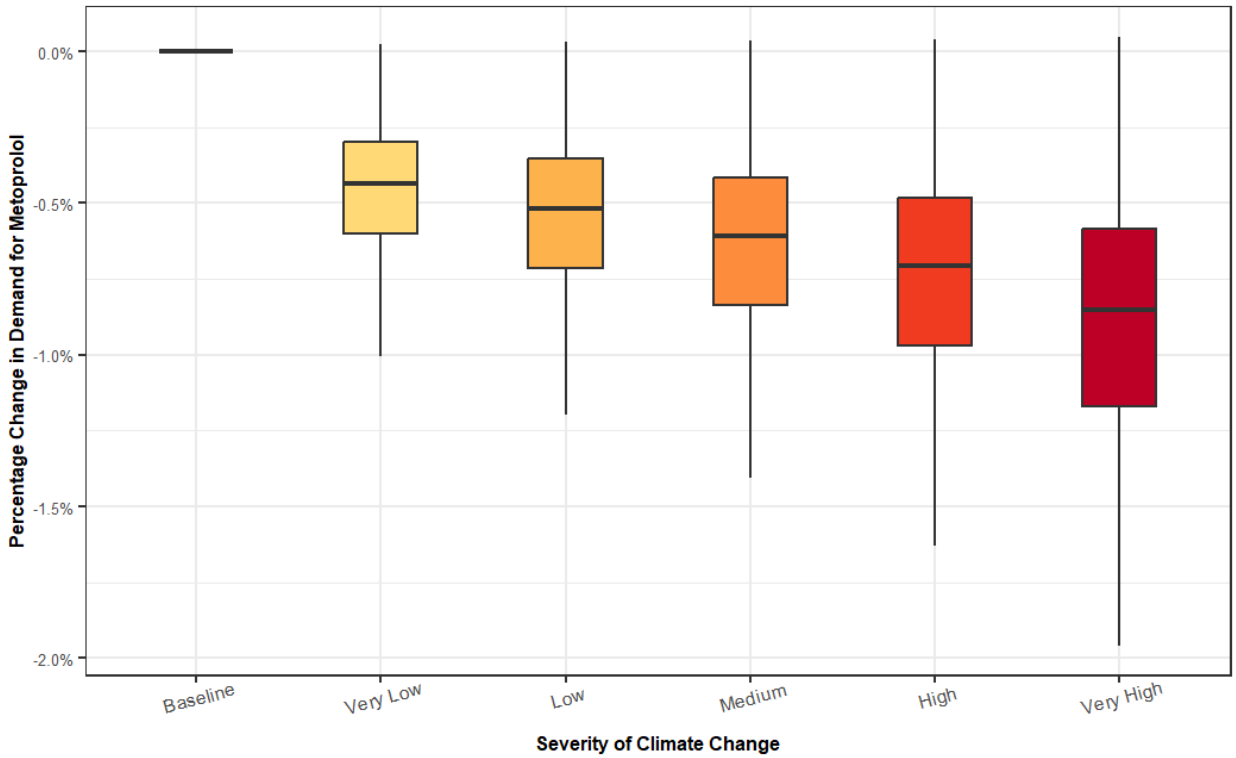
NOTE: Yellow and orange areas = range of projected prevalence estimates under selected climate scenarios; orange = more likely trajectory, yellow = less likely trajectory. Blue lines = randomly selected model runs.

Figure 3.2b. Results of Cardiovascular Disease/Metoprolol Model: Projected Percentage Change in Total Deaths Compared to Baseline Under All Climate Change Scenarios and All Age Groups, 2024–2040



NOTE: Blue and violet areas = range of projected total deaths under selected climate scenarios; violet = more likely trajectory, blue = less likely trajectory. Blue lines = randomly selected model runs.

Figure 3.2c. Results of Cardiovascular Disease/Metoprolol Model: Predicted Percentage Change in Demand for Metoprolol (2040)



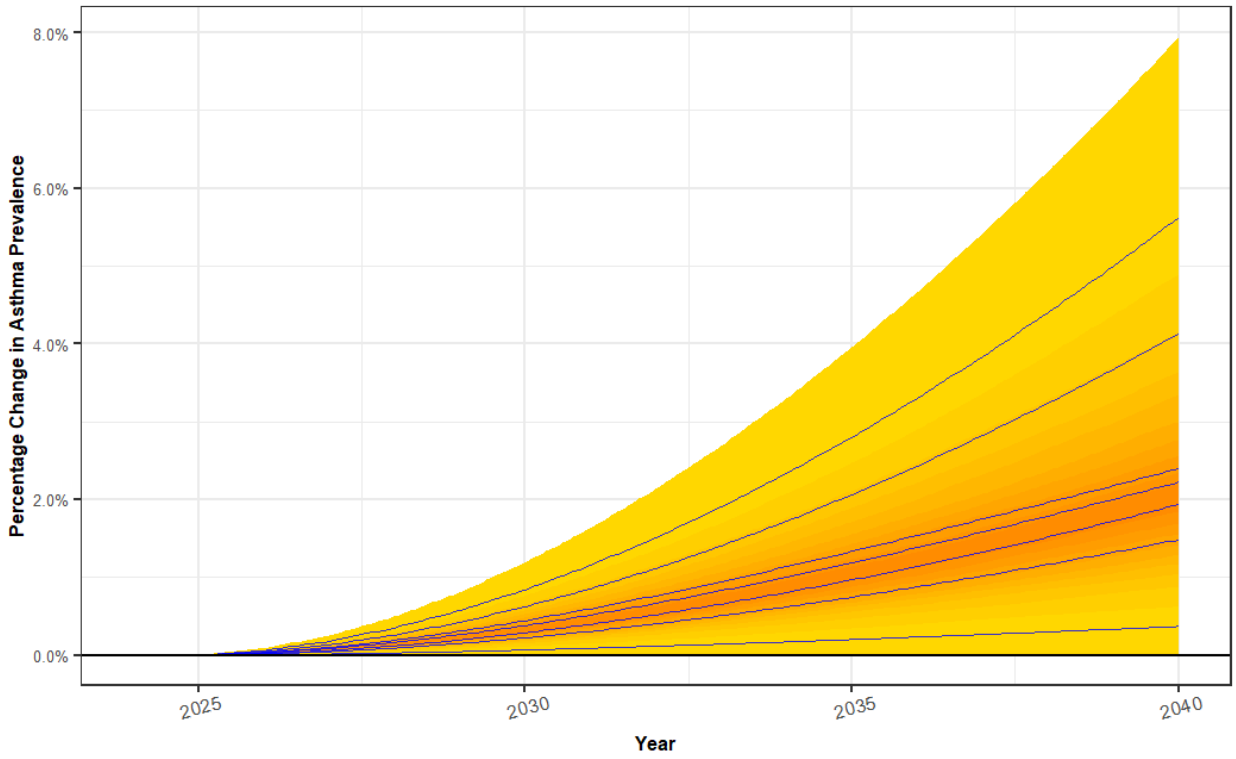
Analyzing the CVD model by age group results reveals nuanced impacts across different age groups under various climate change scenarios (Appendix D). Under the baseline scenario, CVD prevalence is projected to moderately increase for the three younger age groups (ages 20–64 years), with the trend stabilizing around 2035. In climate change scenarios, this increase becomes slightly more pronounced, as extreme weather events affect incidence rates more than mortality rates. For the three older age groups (ages 65 and above), baseline projections indicate a significantly greater increase in CVD prevalence, likely due to the aging population. Initially, under climate change scenarios, the rise in incidence rates is counterbalanced by higher mortality rates. However, in the oldest age group (85+), the increase in mortality rates eventually outweighs the rise in incidence rates. Changes in estimated demand for metoprolol by age group would be expected to mirror the changes in prevalence.

Climate Change and Demand for Albuterol

Figures 3.3a–3.3c present the results of the asthma/albuterol model. Aggregated across all age groups (Figure 3.3a), overall asthma prevalence is estimated to increase relative to the baseline scenario. Similarly, aggregate deaths from asthma and other causes are expected to rise under all climate change scenarios, driven by increased disease-specific and general mortality

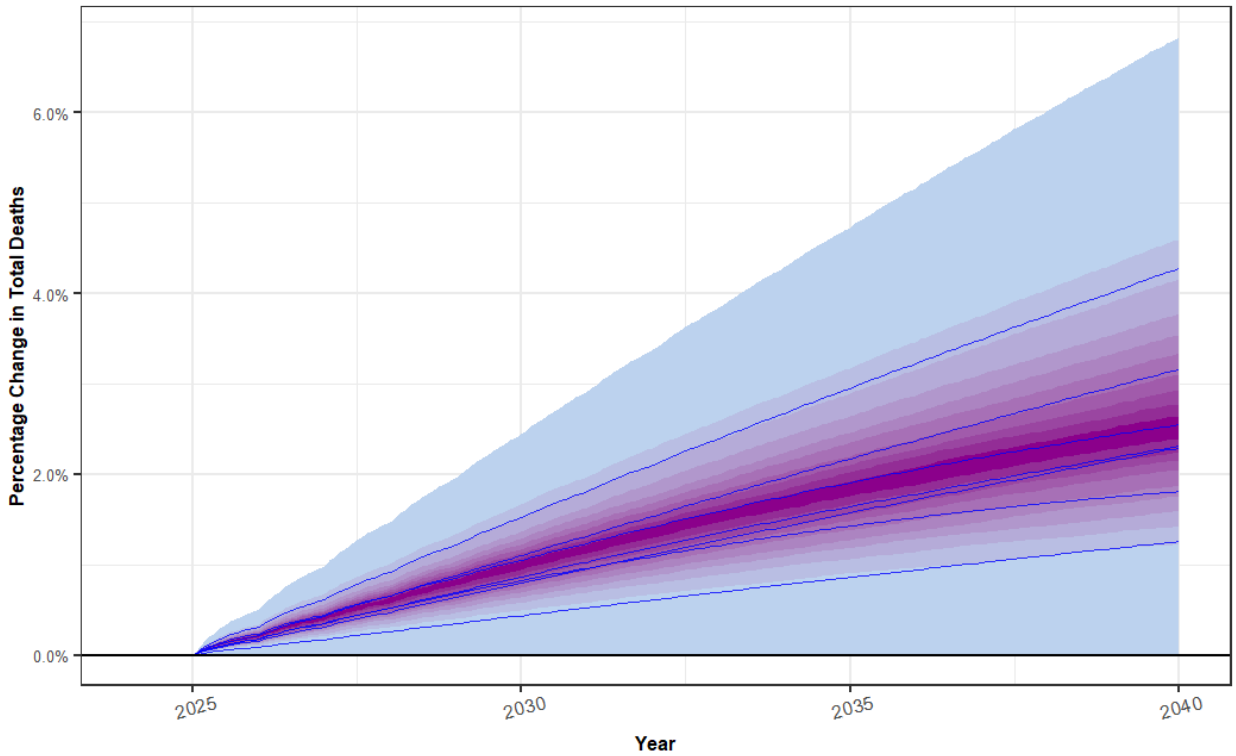
(Figure 3.3b). Overall, these changes in prevalence and mortality result in an estimated increase in demand for albuterol by 1.5 percent to 3 percent (Figure 3.3c).

Figure 3.3a. Results of Asthma/Albuterol Model: Projected Percentage Change in Asthma Prevalence Compared to Baseline Under All Climate Change Scenarios and All Age Groups, 2024–2040



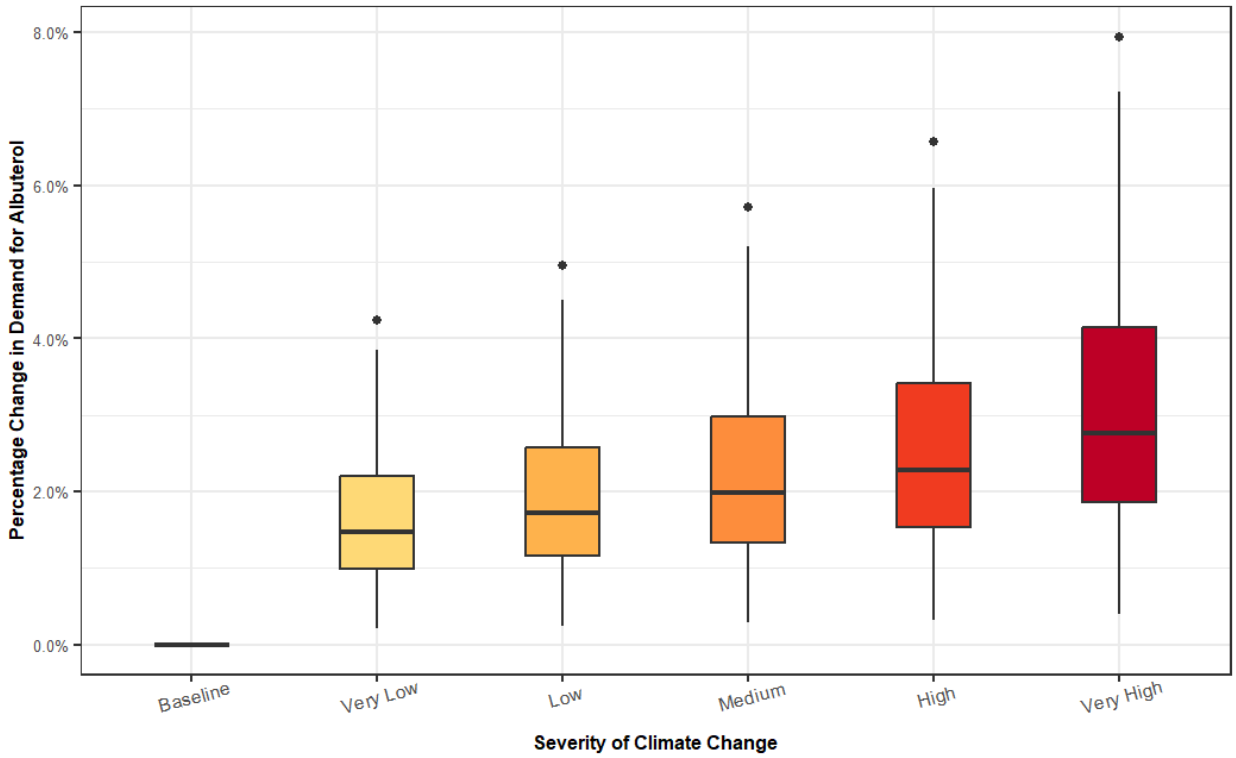
NOTE: Yellow and orange areas = range of projected prevalence estimates under selected climate scenarios; orange = more likely trajectory, yellow = less likely trajectory. Blue lines = randomly selected model runs.

Figure 3.3b. Results of Asthma/Albuterol Model: Projected Percentage Change in Total Deaths Compared to Baseline Under All Climate Change Scenarios and All Age Groups, 2024–2040



NOTE: Blue and violet areas = range of projected total deaths under selected climate scenarios; violet = more likely trajectory, blue = less likely trajectory. Blue lines = randomly selected model runs.

Figure 3.3c. Results of Asthma/Albuterol Model: Predicted Percentage Change in Demand for Albuterol Across All Age Groups (2040)



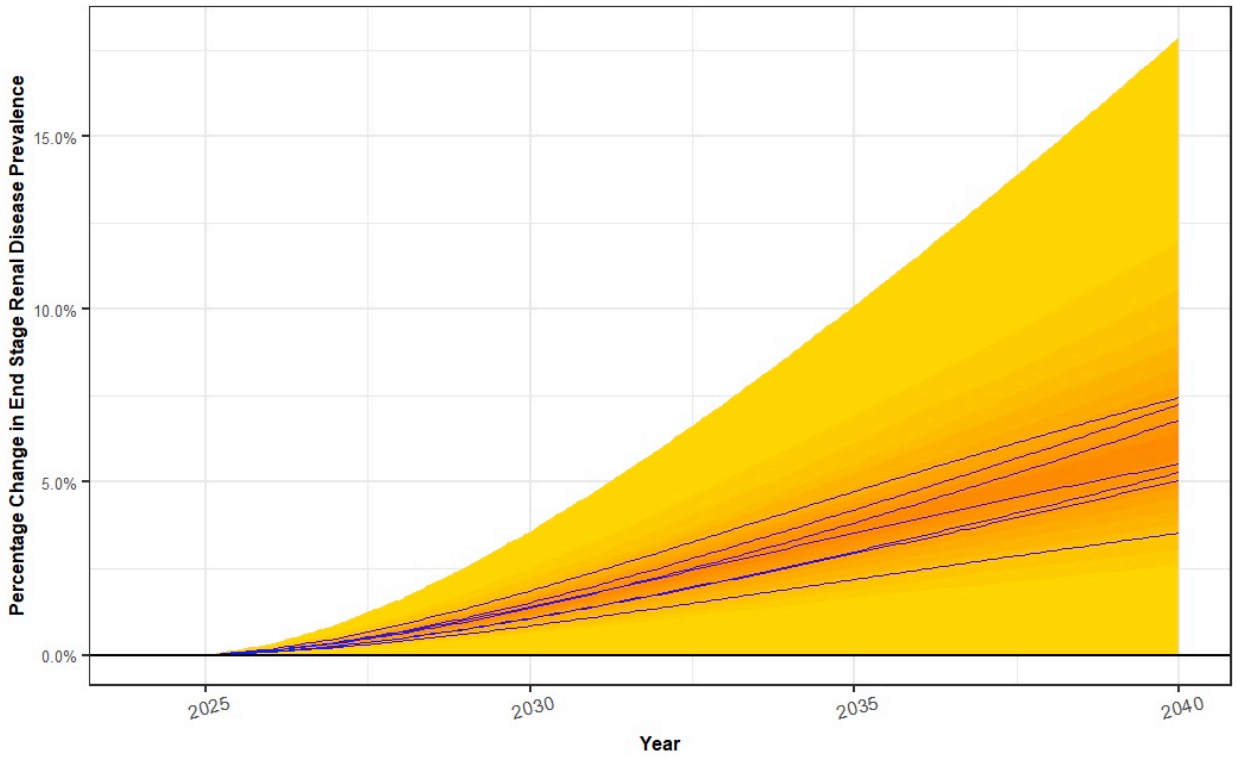
As Figure D.2 in Appendix D shows, the impact of climate change on asthma prevalence varies by age group. In younger age groups (ages 0 to 4 and 5 to 14 years), the relative decrease or stabilization in asthma prevalence seen under the baseline scenario (without climate change) is disrupted. Climate change may prevent these decreases, potentially maintaining or even increasing prevalence in these age groups. In the 15 to 24 year age group, where prevalence peaks in the baseline scenario, climate change could prolong or intensify these peaks. For individuals aged 25 years and older, climate change is projected to significantly increase asthma prevalence, surpassing baseline expectations due to both exacerbation effects and demographic shifts. In contrast, for the older age group (65+ years), climate change may lead to a decrease in asthma prevalence, primarily due to increased mortality rates. Changes in demand for albuterol by age group would be expected to mirror the changes in prevalence.

Climate Change and Demand for Heparin

Figures 3.4a–3.4c present the results of the ESRD/heparin model. Aggregated across all age groups (Figure 3.4a), overall prevalence is estimated to increase relative to the baseline scenario. Aggregate deaths from ESRD and other causes are expected to rise under all climate change scenarios, driven by increased disease-specific and general mortality (Figure 3.4b). Overall,

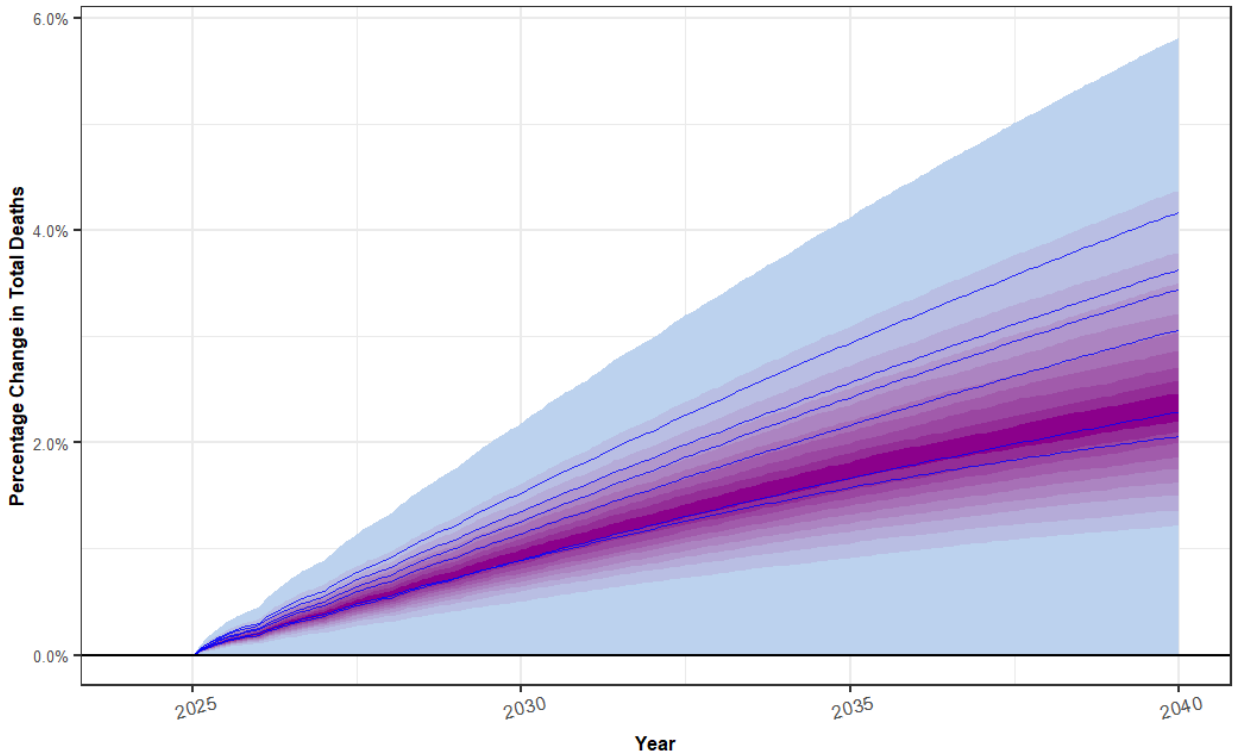
these changes in prevalence and mortality result in an estimated increase in demand for heparin by 4.4 percent to 8.5 percent (Figure 3.4c).

Figure 3.4a. Results of End-Stage Renal Disease/Heparin Model: Projected Percentage Change in ESRD Prevalence Compared to Baseline Under All Climate Change Scenarios and All Age Groups, 2024–2040



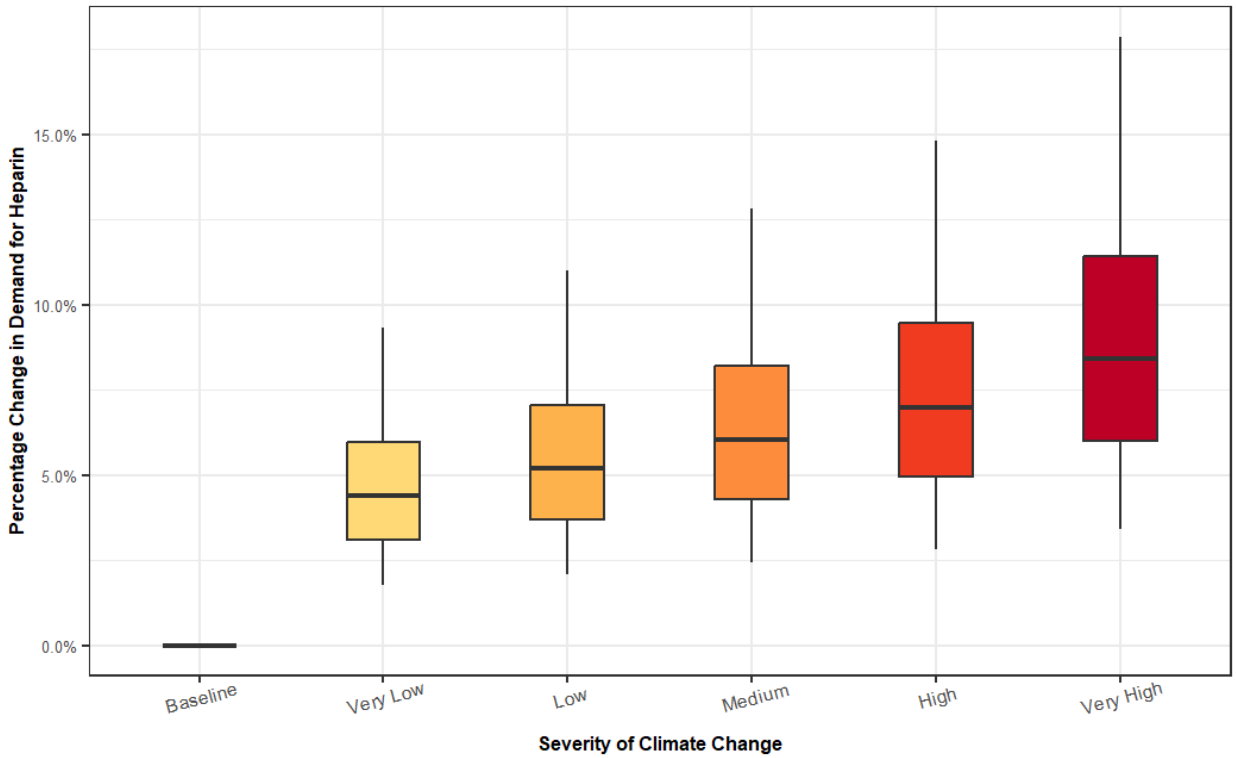
NOTE: Yellow and orange areas = range of projected prevalence estimates under selected climate scenarios; orange = more likely trajectory, yellow = less likely trajectory. Blue lines = randomly selected model runs.

Figure 3.4b. Results of End-Stage Renal Disease/Heparin Model: Projected Percentage Change in Total Deaths Compared to Baseline Under All Climate Change Scenarios, 2024–2040



NOTE: Blue and violet areas = range of projected total deaths under selected climate scenarios; violet = more likely trajectory, blue = less likely trajectory. Blue lines = randomly selected model runs.

Figure 3.4c. Results of End-Stage Renal Disease/Heparin Model: Predicted Percentage Change in Demand for Heparin Across All Age Groups (2040)

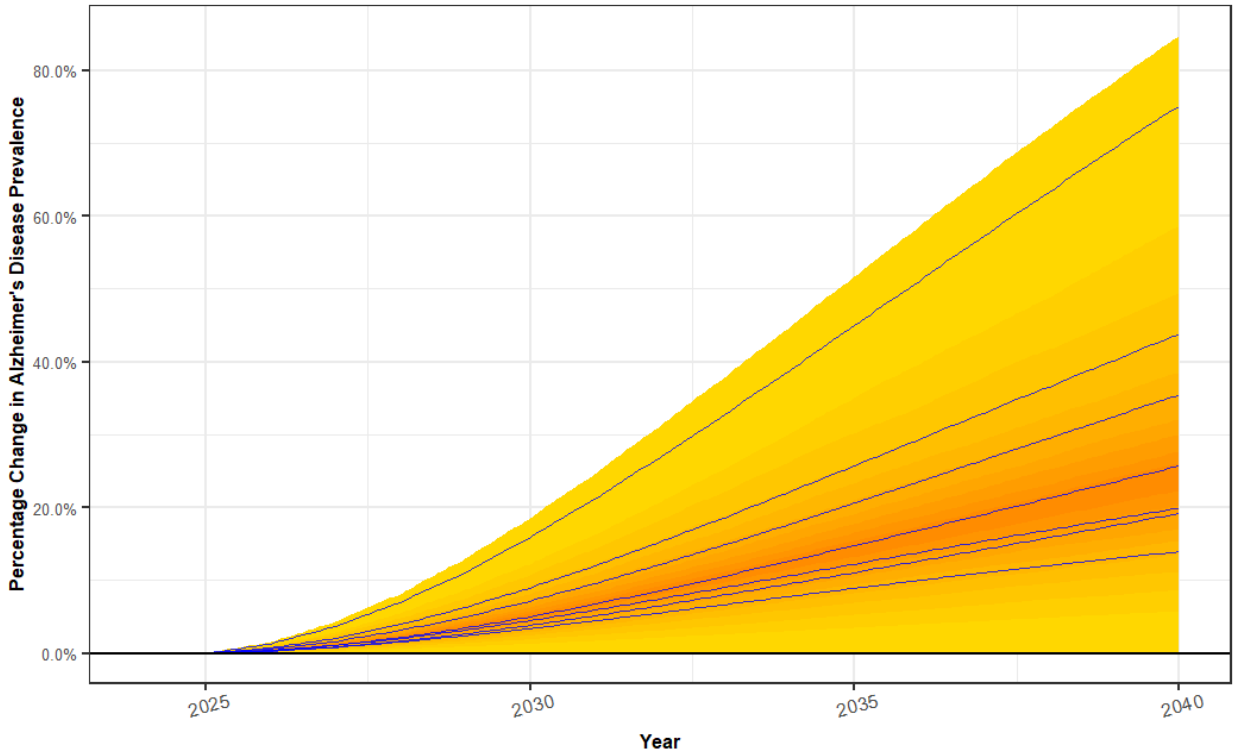


Under the baseline scenario, ESRD is expected to increase in prevalence across all age groups, particularly among individuals over the age of 45 years (Appendix D, Figure D.3). Climate change amplifies this trend, maintaining higher prevalence rates even in the face of increased mortality due to climate impacts. Unlike CVD, the incidence rate of ESRD has been rising, which contributes to sustained and exacerbated prevalence under climate change scenarios. Changes in estimated demand for heparin by age group would be expected to mirror the changes in prevalence.

Climate Change and Demand for Donepezil

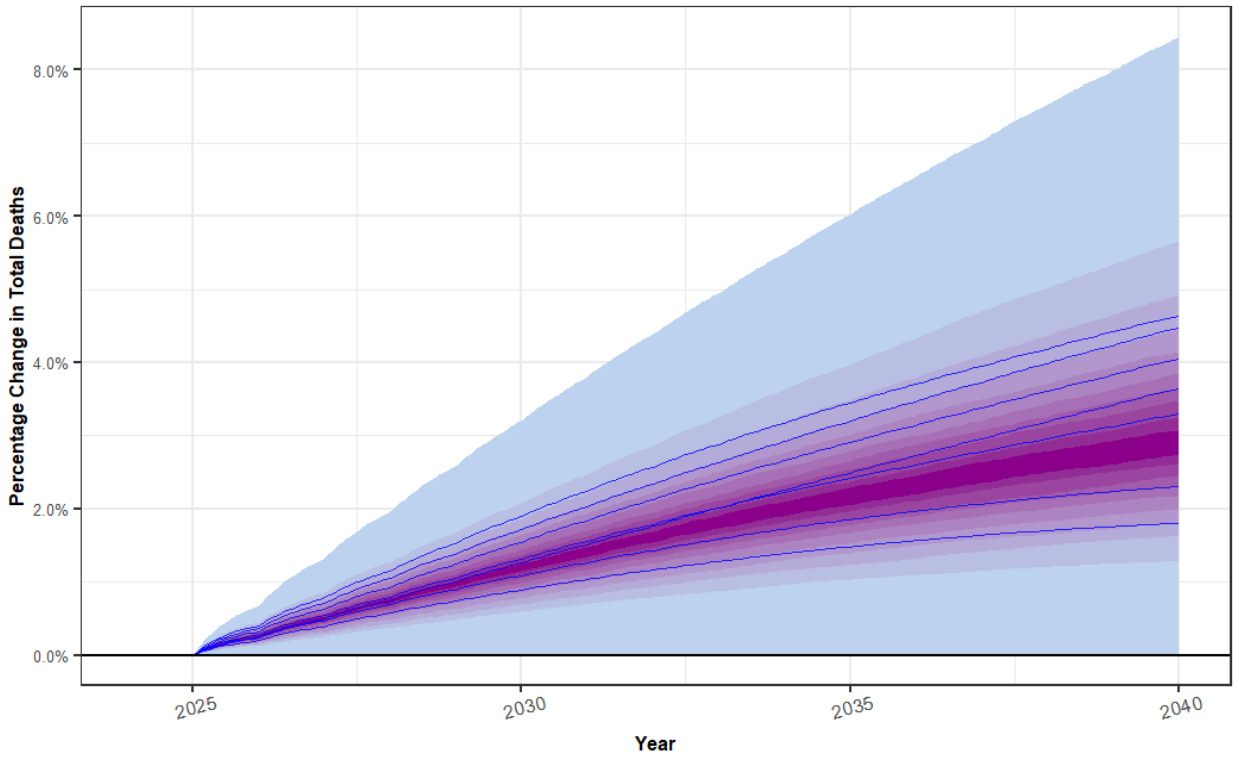
Figures 3.5a–3.5c present the results of the Alzheimer's/donepezil model. Aggregated across all age groups (Figure 3.5a), overall prevalence is expected to increase relative to the baseline scenario. Aggregate deaths from Alzheimer's and other causes are expected to rise under all climate change scenarios, driven by increased disease-specific and general mortality (Figure 3.5b). Due to the substantial increase in Alzheimer's disease prevalence, the demand for donepezil is expected to rise significantly, especially under climate change scenarios (Figure 3.5c). Overall demand for donepezil is projected to increase by 17.5 percent to 33.1 percent compared to baseline increases.

Figure 3.5a. Results for Alzheimer's Disease/Donepezil Model: Projected Percentage Change in Alzheimer's Disease Prevalence Compared to Baseline Under All Climate Change Scenarios and All Age Groups, 2024–2040



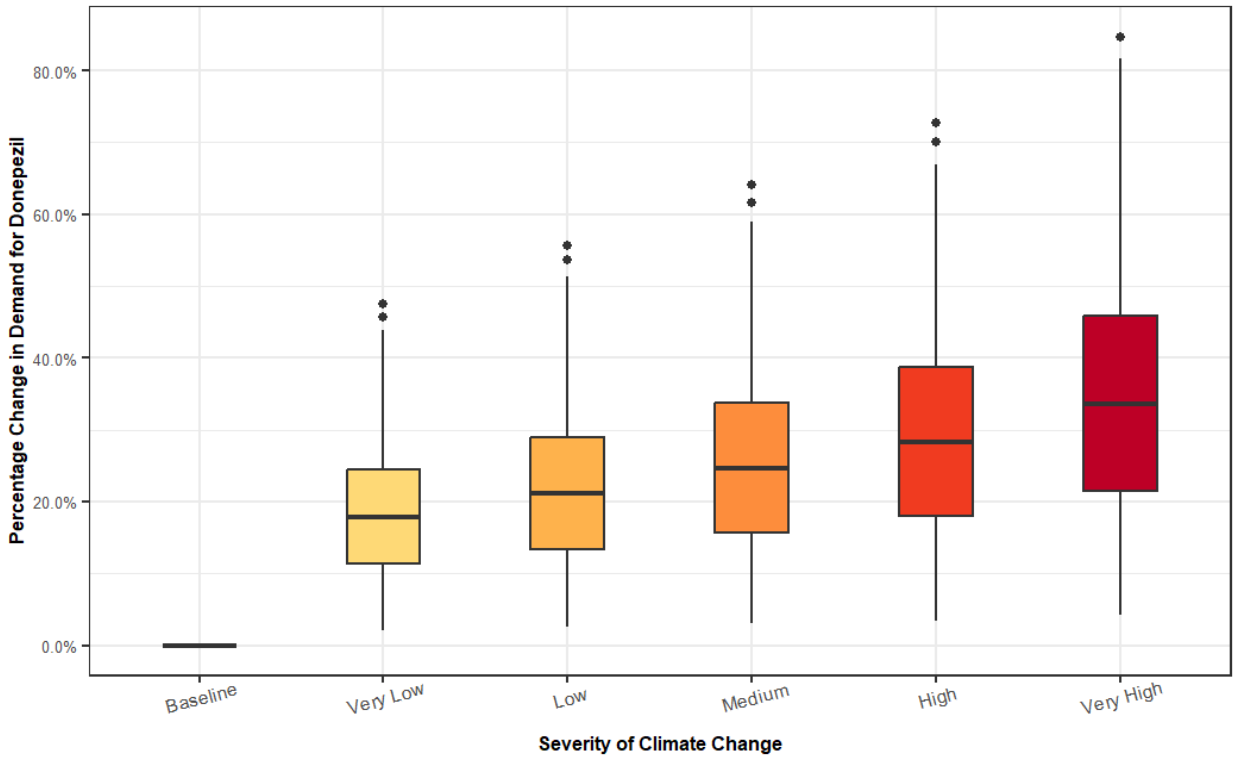
NOTE: Yellow and orange areas = range of projected prevalence estimates under selected climate scenarios; orange = more likely trajectory, yellow = less likely trajectory. Blue lines = randomly selected model runs.

Figure 3.5b. Results for Alzheimer's Disease/Donepezil Model: Projected Percentage Change in Total Deaths Compared to Baseline Under All Climate Change Scenarios, 2024–2040



NOTE: Blue and violet areas = range of projected total deaths under selected climate scenarios; violet = more likely trajectory, blue = less likely trajectory. Blue lines = randomly selected model runs.

Figure 3.5c. Results for Alzheimer's Disease/Donepezil Model: Predicted Percentage Change in Demand for Donepezil Across All Ages (2040)



Our model for Alzheimer's disease focused only on older age groups (55+ years). Prevalence and mortality are expected to increase among all age groups modeled (Appendix D, Figures D.4 and D.8).

Chapter 4. Discussion and Future Directions

Discussion

From our environmental scan, we identified the following types of medical conditions that are climate-vulnerable: maternal-fetal health, CVD, asthma, COPD, water- and food-borne infectious diseases, fungal infections, vector-borne illnesses, mental health, cancer, stroke, Alzheimer's disease and other neurodegenerative diseases, kidney disease, and diabetes. Many of these conditions are among the most common chronic conditions in the United States or among the top ten leading causes of death in the country.

The majority of the articles from our environmental scan focused on the impact of climate change on maternal-fetal health, CVD, asthma, COPD, vector-borne diseases, and CKD. The environmental scan also revealed that drugs used to treat many of these conditions have experienced past and/or current shortages. Our review revealed a significant knowledge gap regarding the impact of climate change on the demand for drugs to treat these and other conditions.

Many of the environmental scan articles included a discussion of the variability of climate change effects among different populations and geographic locations, highlighting the importance of keeping this variation in mind when considering climate-mitigating strategies so that resource planning is conducted with the highest-risk and highest-demand populations in mind. Furthermore, the shifting demographics of the U.S. population in the coming decades, particularly the aging population, will have a significant impact on how climate change interacts with health and drug demand in the future.

We evaluated the demand for one drug used to treat each of the four medical conditions under study: CVD, asthma, ESRD, and Alzheimer's disease. Our systems dynamics model estimates significant changes in drug demand across all age groups under various climate change scenarios. As climate change intensifies, the model projects that drug demand will generally increase, except in cases where higher mortality rates lead to a decrease in demand. The model captures the combined effects of these factors, particularly how increased incidence and mortality due to climate change affect disease prevalence—and hence drug demand. This selection process is indirect, involving a shift in the age profile or distribution of disease. There is a dynamic interplay within each age group between increased incidence and increased mortality, which ultimately determines not only the prevalence for the given age group but also for subsequent older age groups.

The concept of *selection effect* is key to understanding how climate change influences disease prevalence outcomes—and ultimately drug demand. *Selection effect* refers to how changes in mortality rates under climate change reshape the composition of disease-affected

populations. For CVD, increased mortality due to climate change disproportionately affects those in advanced disease stages, stabilizing or reducing prevalence in older age groups (65+ years), despite rising incidence rates. Similarly, asthma shows exacerbated prevalence in younger age groups because of heightened incidence and exacerbation, while higher mortality rates among severe cases in older age groups might stabilize or reduce prevalence over time.

In contrast, ESRD demonstrates sustained prevalence increases across all age groups under climate change, driven by a rising baseline incidence. Despite elevated mortality rates, the persistently high incidence of ESRD outweighs these effects, resulting in continued or exacerbated prevalence trends. This understanding of selection effects is crucial for anticipating future disease burdens and drug demand amid evolving environmental conditions. It emphasizes the need for health care and medical supply chain strategies that adapt, not only to disease incidence and mortality, but also to the dynamic shifts in disease prevalence driven by demographic changes and climate impacts.

Future Directions

The results of our systems dynamic model need to be interpreted in the context of the previously outlined model limitations (see Chapter 3). Future work should assess how these limitations may bias the estimates and explore ways to address these limitations in future iterations of the model.

According to our literature review, existing models developed to predict the impact of climate change on future disease prevalence use various underlying assumptions, and evaluate impact on differing geographic units, time frames, or populations, which makes comparison of projected prevalence estimates across models (including comparison to our model) challenging. Our model is the first national-level model designed to predict drug demand changes under future climate scenarios. Building on our work, future research can develop a blueprint for climate change and health model inputs to create methodological consistency across studies and allow for cross-model comparisons.

Future versions of this model, which informs demand for drugs or medical products in response to health outcomes of climate, can focus on U.S. regions and populations at highest risk for climate-related weather events. Furthermore, future models can account for chronic disease progression or severity (and resultant impact on drug demand) and account for complex climate events where multiple extreme weather events need to be concurrently accounted for. The current model focuses on chronic conditions and assumes that people with these conditions will remain on the modeled drugs. Future work should examine acute conditions affected by climate change, such as Valley Fever and other infectious diseases, and short-term demand for related drugs. Importantly, future models should evaluate drug supply-demand dynamics and account for various drugs that can be interchangeably used to treat a given condition. As far as the effect of extreme temperature on health is concerned, most studies focused on extreme heat. Future

studies should also focus on better understanding the effect of extreme cold weather on health and related drug demand.

With the model's estimations, policymakers, manufacturers, suppliers, health care providers, and other key stakeholders may be able to have a clearer view of the potential anticipated future drug demand—and necessary innovations or strategies required to mitigate increased demand—under varying climate conditions. This could help trigger proactive strategies to build supply chain resiliency through advance planning—such as stockpiling, ensuring the availability of multiple supply chains for certain high-demand drugs, and on-shoring production, where appropriate. Ultimately, the model could be used to inform policies to mitigate climate change's impact on demand by ensuring sufficient drug supply under various future climate scenarios.

Appendix A. Environmental Scan Search Strategy

Table A.1. Search Strategy of PubMed Database

Set No.	Search	No. of results
1	"United States"[tiab] OR "U.S."[tiab] OR "US"[tiab] OR "USA"[tiab] OR "U.S.A."[tiab] OR Alabama[tiab] OR Alaska[tiab] OR Arizona[tiab] OR Arkansas[tiab] OR California[tiab] OR Colorado[tiab] OR Connecticut[tiab] OR Delaware[tiab] OR "District of Columbia"[tiab] OR Florida[tiab] OR Georgia[tiab] OR Hawaii[tiab] OR "Hawai i"[tiab] OR Idaho[tiab] OR Illinois[tiab] OR Indiana[tiab] OR Iowa[tiab] OR Kansas[tiab] OR Kentucky[tiab] OR Louisiana[tiab] OR Maine[tiab] OR Maryland[tiab] OR Massachusetts[tiab] OR Michigan[tiab] OR Minnesota[tiab] OR Mississippi[tiab] OR Missouri[tiab] OR Montana[tiab] OR Nebraska[tiab] OR Nevada[tiab] OR "New Hampshire"[tiab] OR "New Jersey"[tiab] OR "New Mexico"[tiab] OR "New York"[tiab] OR "North Carolina"[tiab] OR "North Dakota"[tiab] OR Ohio[tiab] OR Oklahoma[tiab] OR Oregon[tiab] OR Pennsylvania[tiab] OR "Rhode Island"[tiab] OR "South Carolina"[tiab] OR "South Dakota"[tiab] OR Tennessee[tiab] OR Texas[tiab] OR Utah[tiab] OR Vermont[tiab] OR Virginia[tiab] OR Washington[tiab] OR "West Virginia"[tiab] OR Wisconsin[tiab] OR Wyoming[tiab] OR Huntsville[tiab] OR Montgomery[tiab] OR Anchorage[tiab] OR Fairbanks[tiab] OR Tafuna[tiab] OR Phoenix[tiab] OR Tucson[tiab] OR "Little Rock"[tiab] OR Fayetteville[tiab] OR "Los Angeles"[tiab] OR "San Diego"[tiab] OR Denver[tiab] OR "Colorado Springs"[tiab] OR Bridgeport[tiab] OR Stamford[tiab] OR Wilmington[tiab] OR Jacksonville[tiab] OR Miami[tiab] OR Atlanta[tiab] OR Columbus[tiab] OR Honolulu[tiab] OR Boise[tiab] OR Chicago[tiab] OR Aurora[tiab] OR Indianapolis[tiab] OR "Fort Wayne"[tiab] OR "Des Moines"[tiab] OR "Cedar Rapids"[tiab] OR Wichita[tiab] OR "Overland Park"[tiab] OR Louisville[tiab] OR Lexington[tiab] OR "New Orleans"[tiab] OR "Baton Rouge"[tiab] OR Baltimore[tiab] OR Boston[tiab] OR Worcester[tiab] OR Detroit[tiab] OR "Grand Rapids"[tiab] OR Minneapolis[tiab] OR "Kansas City"[tiab] OR Billings[tiab] OR Missoula[tiab] OR Omaha[tiab] OR Lincoln[tiab] OR "Las Vegas"[tiab] OR Nashua[tiab] OR Newark[tiab] OR "Jersey City"[tiab] OR Albuquerque[tiab] OR "Las Cruces"[tiab] OR Charlotte[tiab] OR Raleigh[tiab] OR Fargo[tiab] OR Bismarck[tiab] OR Dandan[tiab] OR Cleveland[tiab] OR Tulsa[tiab] OR Portland[tiab] OR Salem[tiab] OR Philadelphia[tiab] OR Pittsburgh[tiab] OR "San Juan"[tiab] OR Bayamon[tiab] OR Providence[tiab] OR Warwick[tiab] OR Charleston[tiab] OR "Sioux Falls"[tiab] OR "Rapid City"[tiab] OR Nashville[tiab] OR Memphis[tiab] OR Houston[tiab] OR "San Antonio"[tiab] OR "Salt Lake City"[tiab] OR "West Valley City"[tiab] OR Burlington[tiab] OR Chesapeake[tiab] OR Seattle[tiab] OR Spokane[tiab] OR Huntington[tiab] OR Milwaukee[tiab] OR Madison[tiab] OR Cheyenne[tiab] OR Casper[tiab] OR "United States"[Mesh] OR "Puerto Rico"[Mesh] OR Guam[Mesh] OR "Los Angeles"[Mesh] OR "San Francisco"[Mesh] OR "Chicago"[Mesh] OR "New York City"[Mesh] OR "Baltimore"[Mesh] OR "Philadelphia"[Mesh] OR "Boston"[Mesh] OR "New Orleans"[Mesh]	2,155,158
2	(asthma*[tiab] OR "Asthma"[Mesh])	208,271
3	(albuterol*[tiab] OR "albuterol sulfate"[tiab] OR "albuterol ipratropium"[tiab:~1] OR Levalbuterol[tiab] OR Proventil[tiab] OR Salbutamol[tiab] OR Sultanol[tiab] OR "Salmeterol Xinafoate"[tiab] OR Ventolin[tiab] OR "Fluticasone Salmeterol"[tiab] OR "Formoterol Fumarate"[tiab] OR "Albuterol"[Mesh])	14,969
4	#1 AND #2 AND #3 AND (2013/12/31:2024/12/31[pdat]) AND (english[Filter])	118
5	"heart failure*"[tiab] OR "heart attack*"[tiab] OR "myocardial failure*"[tiab] OR "myocardial infarction*"[tiab] OR "myocardial ischemia"[tiab] OR "Heart Failure"[Mesh] OR "Myocardial Infarction"[Mesh] OR "Myocardial Ischemia"[Mesh] OR "Cardiomyopathies"[MAJR] OR stroke[tiab] OR strokes[tiab] OR "cerebrovascular disease*"[tiab] OR "cerebrovascular disorder*"[tiab] OR "cerebrovascular accident*"[tiab] OR "Stroke"[Mesh] OR "Cerebrovascular Disorders"[Mesh]	1,381,791
6	Metoprolol[tiab] OR Toprol*[tiab] OR Lopressor*[tiab] OR "Metoprolol"[Mesh]	9,127
7	#1 AND #5 AND #6 AND (2013/12/31:2024/12/31[pdat]) AND (english[Filter])	47
8	Coccidioidomycosis[tiab] OR Coccidiomycosis[tiab] OR "Coccidioides infection"[tiab:~1] OR "Coccidioides infections"[tiab:~1] OR Coccidioidal[tiab] OR "San Joaquin Valley Fever"[tiab] OR "Coccidioidomycosis"[Mesh]	4,014

Set No.	Search	No. of results
9	Amphotericin[tiab] OR Amphocil[tiab] OR “Amphotericin B”[Mesh]	27,692
10	#1 AND #8 AND #9 AND (2013/12/31:2024/12/31[pdat]) AND (english[Filter])	23
11	(“chronic kidney disease*”[tiab] OR “chronic kidney insufficienc*”[tiab] OR “chronic renal insufficienc*”[tiab] OR “chronic renal failure*”[tiab] OR “chronic kidney failure*”[tiab] OR “chronic kidney disorder*”[tiab] OR “chronic kidney injur*”[tiab] OR “chronic renal injur*”[tiab] OR “end stage kidney disease*”[tiab] OR “end stage renal disease*”[tiab] OR dialysis[tiab] OR hemodialys*[tiab] OR “hemodiafiltration”[tiab] OR “renal dialysis”[tiab] OR “Renal Insufficiency, Chronic”[Mesh] OR “Kidney Failure, Chronic”[Mesh] OR “Renal Dialysis”[Mesh])	328,277
12	(heparin*[tiab] OR LMWH*[tiab] OR Dalteparin[tiab] OR Enoxaparin[tiab] OR Nadroparin[tiab] OR Tinzaparin[tiab] OR Heparin[Mesh])	117,002
13	#1 AND #11 AND #12 AND (2013/12/31:2024/12/31[pdat]) AND (english[Filter])	47
14	(Alzheimer*[tiab] OR “Alzheimer Disease”[Mesh])	215,257
15	(Donepezil[tiab] OR “Donepezil”[Mesh] OR Aricept[tiab] OR Galantamin*[tiab] OR Nivalin[tiab] OR Reminyl[tiab] OR “Galantamine”[Mesh] OR Rivastigmine[tiab] OR Exelon[tiab] OR Rivastigmine[Mesh])	8,265
16	#1 AND #14 AND #15 AND (2013/12/31:2024/12/31[pdat]) AND (english[Filter])	79

Table A.2. Search Strategy of CINAHL Database

Set No.	Search	No. of Results
1	(TI “United States” OR AB “United States”) OR (TI U.S. OR AB U.S.) OR (TI USA OR AB USA) OR (TI U.S.A. OR AB U.S.A.) OR (TI Alabama OR AB Alabama) OR (TI Alaska OR AB Alaska) OR (TI Arizona OR AB Arizona) OR (TI Arkansas OR AB Arkansas) OR (TI California OR AB California) OR (TI Colorado OR AB Colorado) OR (TI Connecticut OR AB Connecticut) OR (TI Delaware OR AB Delaware) OR (TI “District of Columbia” OR AB “District of Columbia”) OR (TI Florida OR AB Florida) OR (TI Georgia OR AB Georgia) OR (TI Hawaii OR AB Hawaii) OR (TI “Hawai i” OR AB “Hawai i”) OR (TI Idaho OR AB Idaho) OR (TI Illinois OR AB Illinois) OR (TI Indiana OR AB Indiana) OR (TI Iowa OR AB Iowa) OR (TI Kansas OR AB Kansas) OR (TI Kentucky OR AB Kentucky) OR (TI Louisiana OR AB Louisiana) OR (TI Maine OR AB Maine) OR (TI Maryland OR AB Maryland) OR (TI Massachusetts OR AB Massachusetts) OR (TI Michigan OR AB Michigan) OR (TI Minnesota OR AB Minnesota) OR (TI Mississippi OR AB Mississippi) OR (TI Missouri OR AB Missouri) OR (TI Montana OR AB Montana) OR (TI Nebraska OR AB Nebraska) OR (TI Nevada OR AB Nevada) OR (TI “New Hampshire” OR AB “New Hampshire”) OR (TI “New Jersey” OR AB “New Jersey”) OR (TI “New Mexico” OR AB “New Mexico”) OR (TI “New York” OR AB “New York”) OR (TI “North Carolina” OR AB “North Carolina”) OR (TI “North Dakota” OR AB “North Dakota”) OR (TI Ohio OR AB Ohio) OR (TI Oklahoma OR AB Oklahoma) OR (TI Oregon OR AB Oregon) OR (TI Pennsylvania OR AB Pennsylvania) OR (TI “Rhode Island” OR AB “Rhode Island”) OR (TI “South Carolina” OR AB “South Carolina”) OR (TI “South Dakota” OR AB “South Dakota”) OR (TI Tennessee OR AB Tennessee) OR (TI Texas OR AB Texas) OR (TI Utah OR AB Utah) OR (TI Vermont OR AB Vermont) OR (TI Virginia OR AB Virginia) OR (TI Washington OR AB Washington) OR (TI “West Virginia” OR AB “West Virginia”) OR (TI Wisconsin OR AB Wisconsin) OR (TI Wyoming OR AB Wyoming) OR (TI Huntsville OR AB Huntsville) OR (TI Montgomery OR AB Montgomery) OR (TI Anchorage OR AB Anchorage) OR (TI Fairbanks OR AB Fairbanks) OR (TI Tafuna OR AB Tafuna) OR (TI Phoenix OR AB Phoenix) OR (TI Tucson OR AB Tucson) OR (TI “Little Rock” OR AB “Little Rock”) OR (TI Fayetteville OR AB Fayetteville) OR (TI “Los Angeles” OR AB “Los Angeles”) OR (TI “San Diego” OR AB “San Diego”) OR (TI Denver OR AB Denver) OR (TI “Colorado Springs” OR AB “Colorado Springs”) OR (TI Bridgeport OR AB Bridgeport) OR (TI Stamford OR AB Stamford) OR (TI Wilmington OR AB Wilmington) OR (TI Jacksonville OR AB Jacksonville) OR (TI Miami OR AB Miami) OR (TI Atlanta OR AB Atlanta) OR (TI Columbus OR AB Columbus) OR (TI Honolulu OR AB Honolulu) OR (TI Boise OR AB Boise) OR (TI Chicago OR AB Chicago) OR (TI Aurora OR AB Aurora) OR (TI Indianapolis OR AB Indianapolis) OR (TI “Fort Wayne” OR AB “Fort Wayne”) OR (TI “Des Moines” OR AB “Des Moines”) OR (TI “Cedar Rapids” OR AB “Cedar Rapids”) OR (TI Wichita OR AB Wichita) OR (TI “Overland Park” OR AB “Overland Park”) OR (TI Louisville OR AB Louisville) OR (TI Lexington OR AB Lexington) OR (TI “New Orleans” OR AB “New Orleans”) OR (TI “Baton Rouge” OR AB “Baton Rouge”) OR (TI Baltimore OR AB	972,684

Set No.	Search	No. of Results
	Baltimore) OR (TI Boston OR AB Boston) OR (TI Worcester OR AB Worcester) OR (TI Detroit OR AB Detroit) OR (TI "Grand Rapids" OR AB "Grand Rapids") OR (TI Minneapolis OR AB Minneapolis) OR (TI "Kansas City" OR AB "Kansas City") OR (TI Billings OR AB Billings) OR (TI Missoula OR AB Missoula) OR (TI Omaha OR AB Omaha) OR (TI Lincoln OR AB Lincoln) OR (TI "Las Vegas" OR AB "Las Vegas") OR (TI Nashua OR AB Nashua) OR (TI Newark OR AB Newark) OR (TI "Jersey City" OR AB "Jersey City") OR (TI Albuquerque OR AB Albuquerque) OR (TI "Las Cruces" OR AB "Las Cruces") OR (TI Charlotte OR AB Charlotte) OR (TI Raleigh OR AB Raleigh) OR (TI Fargo OR AB Fargo) OR (TI Bismarck OR AB Bismarck) OR (TI Dandan OR AB Dandan) OR (TI Cleveland OR AB Cleveland) OR (TI Tulsa OR AB Tulsa) OR (TI Portland OR AB Portland) OR (TI Salem OR AB Salem) OR (TI Philadelphia OR AB Philadelphia) OR (TI Pittsburgh OR AB Pittsburgh) OR (TI "San Juan" OR AB "San Juan") OR (TI Bayamon OR AB Bayamon) OR (TI Providence OR AB Providence) OR (TI Warwick OR AB Warwick) OR (TI Charleston OR AB Charleston) OR (TI "Sioux Falls" OR AB "Sioux Falls") OR (TI "Rapid City" OR AB "Rapid City") OR (TI Nashville OR AB Nashville) OR (TI Memphis OR AB Memphis) OR (TI Houston OR AB Houston) OR (TI "San Antonio" OR AB "San Antonio") OR (TI "Salt Lake City" OR AB "Salt Lake City") OR (TI "West Valley City" OR AB "West Valley City") OR (TI Burlington OR AB Burlington) OR (TI Chesapeake OR AB Chesapeake) OR (TI Seattle OR AB Seattle) OR (TI Spokane OR AB Spokane) OR (TI Milwaukee OR AB Milwaukee) OR (TI Madison OR AB Madison) OR (TI Cheyenne OR AB Cheyenne) OR (TI Casper OR AB Casper) OR (MH "United States+") OR (MH "Puerto Rico") OR (MH "Guam")	
2	(TI asthma* OR AB asthma*) OR (MH "Asthma+")	50,490
3	(TI albuterol* OR AB albuterol*) OR (TI "albuterol sulfate" OR AB "albuterol sulfate") OR (TI "albuterol ipratropium" OR AB "albuterol ipratropium") OR (TI Levalbuterol OR AB Levalbuterol) OR (TI Proventil OR AB Proventil) OR (TI Salbutamol OR AB Salbutamol) OR (TI Sultanol OR AB Sultanol) OR (TI "Salmeterol Xinafoate" OR AB "Salmeterol Xinafoate") OR (TI Ventolin OR AB Ventolin) OR (TI "Fluticasone Salmeterol" OR AB "Fluticasone Salmeterol") OR (TI "Formoterol Fumarate" OR AB "Formoterol Fumarate") OR (MH "Albuterol")	3,086
4	S1 AND S2 AND S3 Limits: 2013 – 2024; English; Academic Journals	58
5	(TI "heart failure*" OR AB "heart failure*") OR (TI "heart attack*" OR AB "heart attack*") OR (TI "myocardial failure*" OR AB "myocardial failure*") OR (TI "myocardial infarction*" OR AB "myocardial infarction*") OR (TI "myocardial ischemia" OR AB "myocardial ischemia") OR (MH "Heart Failure+") OR (MH "Myocardial Infarction+") OR (MH "Myocardial Ischemia+") OR (MM Cardiomyopathies+) OR (TI stroke OR AB stroke) OR (TI strokes OR AB strokes) OR (TI "cerebrovascular disease*" OR AB "cerebrovascular disease*") OR (TI "cerebrovascular disorder*" OR AB "cerebrovascular disorder*") OR (TI "cerebrovascular accident*" OR AB "cerebrovascular accident*") OR (MH "Stroke+")OR (MH "Cerebrovascular Disorders")	325,693
6	(TI Metoprolol OR AB Metoprolol) OR (TI Toprol* OR AB Toprol*) OR (TI Lopressor* OR AB Lopressor*) OR (MH "Metoprolol")	1,457
7	S1 AND S5 AND S6 Limits: 2013 – 2024; English; Academic Journals	25
8	(TI Coccidioidomycosis OR AB Coccidioidomycosis) OR (TI Coccidiomycosis OR AB Coccidiomycosis) OR (TI "Coccidioides infection*" OR AB "Coccidioides infection*") OR (TI Coccidioidal OR AB Coccidioidal) OR (TI "San Joaquin Valley Fever" OR AB "San Joaquin Valley Fever") OR (MH "Coccidioidomycosis")	601
9	(TI Amphotericin OR AB Amphotericin) OR (TI Amphocil OR AB Amphocil) OR (MH "Amphotericin B")	2,759
10	S1 AND S8 AND S9 Limits: 2013 – 2024; English; Academic Journals	4
11	(TI "chronic kidney disease*" OR AB "chronic kidney disease*") OR (TI "chronic kidney insufficienc*" OR AB "chronic kidney insufficienc*") OR (TI "chronic renal insufficienc*" OR AB "chronic renal insufficienc*") OR (TI "chronic renal failure*" OR AB "chronic renal failure*") OR (TI "chronic kidney failure*" OR AB "chronic kidney failure*") OR (TI "chronic kidney disorder*" OR AB "chronic kidney disorder*") OR (TI "chronic kidney injur*" OR AB "chronic kidney injur*") OR (TI "chronic renal injur*" OR AB "chronic renal injur*") OR (TI "end stage kidney disease*" OR AB "end stage kidney disease*") OR (TI "end stage renal disease*" OR AB "end stage renal disease*") OR (TI dialysis OR AB dialysis) OR (TI hemodialys* OR AB hemodialys*) OR (TI hemodiafiltration OR AB hemodiafiltration) OR (TI "renal dialysis" OR AB	70,277

Set No.	Search	No. of Results
	"renal dialysis") OR (MH "Renal Insufficiency, Chronic+") OR (MH "Kidney Failure, Chronic") OR (MH "Dialysis") OR (MH "Dialysis Patients")	
12	(TI heparin* OR AB heparin*) OR (TI LMWH* OR AB LMWH*) OR (TI Dalteparin OR AB Dalteparin) OR (TI Enoxaparin OR AB Enoxaparin) OR (TI Nadroparin OR AB Nadroparin) OR (TI Tinzaparin OR AB Tinzaparin) OR (MH "Heparin+") OR (MH "Heparin, Low-Molecular-Weight") OR (MH "Dalteparin Sodium") OR (MH "Tinzaparin Sodium")	16,005
13	S1 AND S11 AND S12Limits: 2013 – 2024; English; Academic Journals	14
14	(TI Alzheimer* OR AB Alzheimer*) OR (MH "Alzheimer's Disease")	53,037
15	((TI Donepezil OR AB Donepezil) OR (TI Aricept OR AB Aricept) OR (TI Galantamin* OR AB Galantamin*) OR (TI Nivalin OR AB Nivalin) OR (TI Reminyl OR AB Reminyl) OR (TI Rivastigmine OR AB Rivastigmine) OR (TI Exelon OR AB Exelon) OR (MH "Donepezil") OR (MH "Galanthamine") OR (MH "Rivastigmine")	2,388
16	S1 AND S14 AND S15 Limits: 2013 – 2024; English; Academic Journals	26

Table A.3. Search Strategy of Web of Science Database

Set No.	Search	No. of results
1	TI=("United States" OR "U.S." OR "USA" OR "US" OR "U.S.A." OR Alabama OR Alaska OR Arizona OR Arkansas OR California OR Colorado OR Connecticut OR Delaware OR "District of Columbia" OR Florida OR Georgia OR Hawaii OR "Hawai i" OR Idaho OR Illinois OR Indiana OR Iowa OR Kansas OR Kentucky OR Louisiana OR Maine OR Maryland OR Massachusetts OR Michigan OR Minnesota OR Mississippi OR Missouri OR Montana OR Nebraska OR Nevada OR "New Hampshire" OR "New Jersey" OR "New Mexico" OR "New York" OR "North Carolina" OR "North Dakota" OR Ohio OR Oklahoma OR Oregon OR Pennsylvania OR "Rhode Island" OR "South Carolina" OR "South Dakota" OR Tennessee OR Texas OR Utah OR Vermont OR Virginia OR Washington OR "West Virginia" OR Wisconsin OR Wyoming OR Huntsville OR Montgomery OR Anchorage OR Fairbanks OR Phoenix OR Tucson OR "Little Rock" OR Fayetteville OR "Los Angeles" OR "San Diego" OR Denver OR "Colorado Springs" OR Bridgeport OR Stamford OR Wilmington OR Jacksonville OR Miami OR Atlanta OR Honolulu OR Boise OR Chicago OR Indianapolis OR "Fort Wayne" OR "Des Moines" OR "Cedar Rapids" OR Wichita OR "Overland Park" OR Louisville OR "New Orleans" OR "Baton Rouge" OR Baltimore OR Boston OR Detroit OR "Grand Rapids" OR Minneapolis OR "Kansas City" OR Billings OR Missoula OR Omaha OR "Las Vegas" OR Nashua OR "Jersey City" OR Albuquerque OR "Las Cruces" OR Raleigh OR Fargo OR Cleveland OR Tulsa OR Portland OR Salem OR Philadelphia OR Pittsburgh OR "San Juan" OR Charleston OR "Sioux Falls" OR "Rapid City" OR Nashville OR Memphis OR Houston OR "San Antonio" OR "Salt Lake City" OR "West Valley City" OR Burlington OR Seattle OR Spokane OR Milwaukee) OR AB=("United States" OR "U.S." OR "USA" OR "U.S.A." OR Alabama OR Alaska OR Arizona OR Arkansas OR California OR Colorado OR Connecticut OR Delaware OR "District of Columbia" OR Florida OR Georgia OR Hawaii OR "Hawai i" OR Idaho OR Illinois OR Indiana OR Iowa OR Kansas OR Kentucky OR Louisiana OR Maine OR Maryland OR Massachusetts OR Michigan OR Minnesota OR Mississippi OR Missouri OR Montana OR Nebraska OR Nevada OR "New Hampshire" OR "New Jersey" OR "New Mexico" OR "New York" OR "North Carolina" OR "North Dakota" OR Ohio OR Oklahoma OR Oregon OR Pennsylvania OR "Rhode Island" OR "South Carolina" OR "South Dakota" OR Tennessee OR Texas OR Utah OR Vermont OR Virginia OR Washington OR "West Virginia" OR Wisconsin OR Wyoming OR Huntsville OR Montgomery OR Anchorage OR Fairbanks OR Phoenix OR Tucson OR "Little Rock" OR Fayetteville OR "Los Angeles" OR "San Diego" OR Denver OR "Colorado Springs" OR Bridgeport OR Stamford OR Wilmington OR Jacksonville OR Miami OR Atlanta OR Honolulu OR Boise OR Chicago OR Indianapolis OR "Fort Wayne" OR "Des Moines" OR "Cedar Rapids" OR Wichita OR "Overland Park" OR Louisville OR "New Orleans" OR "Baton Rouge" OR Baltimore OR Boston OR Detroit OR "Grand Rapids" OR Minneapolis OR "Kansas City" OR Billings OR Missoula OR Omaha OR "Las Vegas" OR Nashua OR "Jersey City" OR Albuquerque OR "Las Cruces"	1,878,497

Set No.	Search	No. of results
	OR Raleigh OR Fargo OR Cleveland OR Tulsa OR Portland OR Salem OR Philadelphia OR Pittsburgh OR “San Juan” OR Charleston OR “Sioux Falls” OR “Rapid City” OR Nashville OR Memphis OR Houston OR “San Antonio” OR “Salt Lake City” OR “West Valley City” OR Burlington OR Seattle OR Spokane OR Milwaukee)	
2	TI=(asthma*) OR AB=(asthma*)	190,596
3	TI=(albuterol* OR “albuterol sulfate” OR “albuterol ipratropium” OR Levalbuterol OR Proventil OR Salbutamol OR Sultanol OR “Salmeterol Xinafoate” OR Ventolin OR “Fluticasone Salmeterol” OR “Formoterol Fumarate”) OR AB=(albuterol* OR “albuterol sulfate” OR “albuterol ipratropium” OR Levalbuterol OR Proventil OR Salbutamol OR Sultanol OR “Salmeterol Xinafoate” OR Ventolin OR “Fluticasone Salmeterol” OR “Formoterol Fumarate”)	11,641
4	(#1 AND #2 AND #3) AND (PY==(“2024” OR “2023” OR “2022” OR “2021” OR “2020” OR “2019” OR “2018” OR “2017” OR “2016” OR “2015” OR “2014” OR “2013”) AND DT==(“ARTICLE” OR “REVIEW” OR “EARLY ACCESS”) AND LA==(“ENGLISH”))	57
5	TI=(“heart failure*” OR “heart attack*” OR “myocardial failure*” OR “myocardial infarction*” OR “myocardial ischemia” OR cardiomyopath* OR stroke OR strokes OR “cerebrovascular disease*” OR “cerebrovascular disorder*” OR “cerebrovascular accident*”) OR AB=(“heart failure*” OR “heart attack*” OR “myocardial failure*” OR “myocardial infarction*” OR “myocardial ischemia” OR cardiomyopath* OR stroke OR strokes OR “cerebrovascular disease*” OR “cerebrovascular disorder*” OR “cerebrovascular accident*”)	876,631
6	TI=(Metoprolol OR Toprol* OR Lopressor*) OR AB=(Metoprolol OR Toprol* OR Lopressor*)	8,204
7	(#1 AND #5 AND #6) AND (PY==(“2024” OR “2023” OR “2022” OR “2021” OR “2020” OR “2019” OR “2018” OR “2017” OR “2016” OR “2015” OR “2014” OR “2013”) AND DT==(“ARTICLE” OR “REVIEW” OR “EARLY ACCESS”) AND LA==(“ENGLISH”))	19
8	TI=(Coccidioidomycosis OR Coccidiomycosis OR “Coccidioides infection*” OR Coccidioidal OR “San Joaquin Valley Fever”) OR AB=(Coccidioidomycosis OR Coccidiomycosis OR “Coccidioides infection*” OR Coccidioidal OR “San Joaquin Valley Fever”)	2,355
9	TI=(Amphotericin* OR Amphocil) OR AB=(Amphotericin* OR Amphocil)	20,068
10	(#1 AND #8 AND #9) AND (PY==(“2024” OR “2023” OR “2022” OR “2021” OR “2020” OR “2019” OR “2018” OR “2017” OR “2016” OR “2015” OR “2014” OR “2013”) AND DT==(“ARTICLE” OR “REVIEW” OR “EARLY ACCESS”) AND LA==(“ENGLISH”))	16
11	TI=(“chronic kidney disease*” OR “chronic kidney insufficienc*” OR “chronic renal insufficienc*” OR “chronic renal failure*” OR “chronic kidney failure*” OR “chronic kidney disorder*” OR “chronic kidney injur*” OR “chronic renal injur*” OR “end stage kidney disease*” OR “end stage renal disease*” OR dialysis OR hemodialys* OR “hemodiafiltration” OR “renal dialysis”) OR AB=(“chronic kidney disease*” OR “chronic kidney insufficienc*” OR “chronic renal insufficienc*” OR “chronic renal failure*” OR “chronic kidney failure*” OR “chronic kidney disorder*” OR “chronic kidney injur*” OR “chronic renal injur*” OR “end stage kidney disease*” OR “end stage renal disease*” OR dialysis OR hemodialys* OR “hemodiafiltration” OR “renal dialysis”)	271,362
12	TI=(heparin* OR LMWH* OR Dalteparin OR Enoxaparin OR Nadroparin OR Tinzaparin) OR AB=(heparin* OR LMWH* OR Dalteparin OR Enoxaparin OR Nadroparin OR Tinzaparin)	91,914
13	(#1 AND #11 AND #12) AND (PY==(“2024” OR “2023” OR “2022” OR “2021” OR “2020” OR “2019” OR “2018” OR “2017” OR “2016” OR “2015” OR “2014” OR “2013”) AND DT==(“ARTICLE” OR “REVIEW” OR “EARLY ACCESS”) AND LA==(“ENGLISH”))	35
14	TI=(Alzheimer*) OR AB=(Alzheimer*)	211,663
15	TI=(Donepezil OR Aricept OR Galantamin* OR Nivalin OR Reminyl OR Rivastigmine OR Exelon) OR AB=(Donepezil OR Aricept OR Galantamin* OR Nivalin OR Reminyl OR Rivastigmine OR Exelon)	8,701
16	(#1 AND #14 AND #15) AND (PY==(“2024” OR “2023” OR “2022” OR “2021” OR “2020” OR “2019” OR “2018” OR “2017” OR “2016” OR “2015” OR “2014” OR “2013”) AND DT==(“ARTICLE” OR “REVIEW” OR “EARLY ACCESS”) AND LA==(“ENGLISH”))	62

NOTE: Web of Science Core Collection: Science Citation Index Expanded (SCI-EXPANDED), Social Sciences Citation Index (SSCI), Emerging Sources Citation Index (ESCI).

Table A.4. Search Strategy of Grey Literature

Search Parameter	Details
Any of these words	“drug utilization” | “drug usage” | “prescription statistic*” | “prescribed drug statistic*” | “total purchase*” | “drug shortage*” | “drug prescriptions statistical data”
This exact word or phrase	((Albuterol* OR “albuterol sulfate” OR “albuterol ipratropium” OR Levalbuterol OR Proventil OR Salbutamol OR Sultanol OR “Salmeterol Xinafoate” OR Ventolin OR “Fluticasone Salmeterol” OR “Formoterol Fumarate”) AND asthma) Metoprolol OR Toprol* OR Lopressor* OR “Metoprolol” (Amphotericin OR Amphocil OR “Amphotericin B”) AND (“San Joaquin Valley Fever”[tiab] OR Coccidioidomycosis) ((Heparin* OR Enoxaparin OR Nadroparin OR Tinzaparin) AND (“kidney disease” OR hemodialysis)) ((Donepezil OR Aricept OR Galantamine OR Nivalin OR Reminyl OR Rivastigmine OR Exelon) AND Alzheimer)
Limited to these site domains (.gov, .org)	AAP, AHRQ, AMA, CDC, FDA, HHSEPA, IOM/NAM, IQVIA, National Academies, NSF, WHO
Year limits	2014–2024

Appendix B. Technical Model Details

This appendix provides additional technical details on the structure of the model to supplement the methods as written in Chapter 3. Specific details on data sources, inputs, and transformations are available in Appendix C.

Model Design

Given the age-structured nature of our model, we maintain separate compartments, also known as state variables, for each clinical state within each age group. Specifically, we denote T_i as the population diagnosed with a given disease, for example, CVD, and receiving treatment in age group i. H_i represents the healthy population in age group i, and D_i denotes the deceased population in age group i. These compartments, T_i, H_i, and D_i, represent the different conditions individuals can be in over time. The state variables are updated as time (denoted by t) progresses in the model simulation.

The dynamics of our model are governed by a set of coupled ODEs. These equations determine how individuals move between different compartments over time. They also account for demographic changes, such as births and migration. In our model, the rate at which individuals enter the healthy population via birth or migration for age group i is denoted by π_i. The rate at which individuals age from one group to the next (for example, from age group i to age group $i + 1$) is denoted by α_i.

For simplicity, we assume that no individuals are born with a given disease and that immigrants do not enter the system already diagnosed with a disease. Our model explicitly accounts for aging within both the healthy and diagnosed populations as part of the demographic dynamics.

New cases of a disease (incidence) are represented by the movement of individuals from the Healthy Population to the Diagnosed and Treated Population. This transition is governed by age-specific hazard rates, denoted by λ_i, which represents the annual risk of a healthy individual developing and being diagnosed with a disease. Deaths within each age group i are accounted for by two rates: the all-other-cause mortality rate (μ_{Oi}) and the disease-specific mortality rate (μ_{Ti}), both of which can change over time (t). For our baseline scenario, these rates are based on existing U.S. Census Bureau projections (U.S. Census Bureau, undated). For our climate change scenarios, these rates are adjusted to reflect the impact of extreme weather events related to climate change.

Although our model uses annual rates for input parameters, we convert these to daily rates (i.e., divide by 365) since our model operates on a daily time scale. This conversion allows us to

capture the dynamics of disease progression and treatment more accurately on a finer, day-to-day basis.

Based on the described state variables and transition rates, our model is formulated by the following set of coupled ODEs (1) through (3):

$$\frac{dH_i}{dt} = \pi_i - (\lambda_i + \mu_{Oi})H_i + (\alpha_{i-1}H_{i-1} - \alpha_i H_i) \text{ (1)}$$

$$\frac{dT_i}{dt} = \lambda_i H_i - (\mu_{Oi} + \mu_{Ti})T_i + (\alpha_{i-1}T_{i-1} - \alpha_i T_i) \text{ (2)}$$

$$\frac{dD_i}{dt} = \mu_{Oi}(H_i + T_i) + \mu_{Ti}T_i \text{ (3).}$$

These interconnected ODEs are numerically integrated in R version 4.2.2 using the deSolve package (Soetaert, Petzoldt, and Setzer, 2010).

Informing the Baseline Model

Population Dynamics

Our chosen approach enabled us to describe and reproduce baseline demographic projections over time. We aggregated raw Census data related to deaths, net migration, and population into specified age groups, based on a combination of disease-specific factors and the format in which incidence and mortality data were reported (see Appendix C). Using this aggregated data, we defined inflow rates (including births and net migration) and outflow rates (including predicted deaths by age group) to create Census-based projections. For projected births, we used annual totals aggregated across all demographics (e.g., race), without further breakdown by factors such as gender or age group. For deaths and net migration, the data were aggregated by specified age groups, ensuring that projections accounted for demographic categories such as race and gender within those groups. Finally, total population projections were compiled to support model development, providing key insights into population dynamics across age groups and demographic factors as they evolve over time.

Following a self-consistency verification, we used our forecast for total deaths by age group from 2024 to 2040 to extract mortality scaling factors for each age group, $s_i(t)$. Here, t represents the time in years since our initial year of 2024. Initially, $s_i(t = 0)$ is set to one for 2024, meaning no adjustment is needed for the base year. As we project into future years, $s_i(t)$ adjusts to reflect changing mortality trends. Mathematically, the scaling factor $s_i(t)$ is given by $s_i(t) = \frac{D_i(t)}{N_i(t)} \cdot \frac{N_i(0)}{D_i(0)}$, where $N_i(t)$ and $D_i(t)$ are Census-provided populations and deaths in age group i in year t. By definition, $s_i(0) = 1$ for all age groups. These scaling factors are integrated into our ODE model to adapt mortality rates over time, ensuring that our model accurately reflects projected demographic dynamics and is consistent with actual population trends.

We also incorporated U.S. life tables from the Human Mortality Database to estimate aging rates and for verification purposes (Human Mortality Database, undated-a). While the Census provides annual predictions of deaths by age, offering detailed insights into demographic trends over time, the U.S. life tables offer comprehensive mortality data adjusted for underreporting, age misreporting, and other biases, ensuring accurate mortality rates across different age groups. These tables also aggregate mortality data for both genders, providing gender-neutral mortality rates essential for demographic modeling. We estimated the aging rate for how individuals transition from one age group to the next, α_i by computing l_x, which represents the number of individuals out of 100,000 who survive to each age x, based on the life table mortality rate m_x for each year. By summing these l_x values for each age group, we determine the total number of survivors within that group, ensuring that we account for the cumulative survival of the cohort up to that age. The proportion for the last age in each group indicates the annual fraction of individuals aging out of that age group transitioning to the next.

Informing the Disease-Specific Rates

After establishing the baseline demographic rates in our model, the next step involves incorporating disease-specific inputs, including initial conditions (i.e., the populations of healthy individuals and those diagnosed with the disease) and transition rates for each age group. After estimating disease prevalence, we distributed the total population $N_i(0)$ of each age group into those diagnosed with the disease, denoted as $T_i(0)$, and the healthy population, denoted as $H_i(0)$. Therefore, the prevalence for age group i is simply given by $T_i(0)/N_i(0)$.

Equally important to establishing baseline inputs is determining the initial disease-specific mortality rates, $\mu_{Ti}(0)$, and hazard rates, $\lambda_i(0)$, for each age group. These rates are pivotal for forecasting how disease prevalence will evolve over time. We derived the disease-specific mortality rates from various sources and adjusted to match our age groupings (see Appendix C).

Having obtained the initial values for $T_i(0)$ and $H_i(0)$ from the prevalence data and the disease-specific mortality rates, $\mu_{Ti}(0)$, for each age group, we proceeded to estimate the initial age group-specific all-other-cause mortality rates, $\mu_{Oi}(0)$. This estimation was derived from the all-cause mortality given by the Census data, denoted as $\frac{D_i(0)}{N_i(0)}$, which must equal the sum of all-other-cause mortality applied to the healthy population $H_i(0)$ and the combined all-other-cause and disease-specific mortality applied to the diseased population $T_i(0)$. Mathematically, this relationship is expressed by equation (5):

$$\mu_{Oi}(0)H_i(0) + [\mu_{Oi}(0) + \mu_{Ti}(0)]T_i(0) = D_i(0) \qquad (5).$$

This equation essentially balances the contributions of mortality from other causes (i.e., not the disease of interest) from both the healthy population (H_0) and the diagnosed population (T_0)

against the total deaths (D_0) observed in the initial year. Solving this equation (equation (6)) provides an estimate of the initial all-other-cause mortality $\mu_{Oi}(0)$, which is crucial for accurately modeling the overall mortality dynamics within each age group in subsequent years.

$$\mu_{Oi}(0) = \frac{D_i(0) - \mu_{Ti}(0)T_i(0)}{N_i(0)} \qquad (6).$$

Incidence data, or historic data on prevalence trends by age group, can be used to estimate the initial hazard rates $\lambda_i(0)$. When further accounting for demographic aging dynamics, this relationship is mathematically expressed by equation (7):

$$[\mu_{Oi}(0) + \mu_{Ti}(0) + \alpha_i]T_i(0) = \lambda_i(0)H_i(0) + \alpha_{i-1}T_{i-1}(0) \qquad (7)$$

Rearranging this equation, we have equation (8),

$$\lambda_i(0) = \{[\mu_{Oi}(0) + \mu_{Ti}(0) + \alpha_i]T_i(0) - \alpha_{i-1}T_{i-1}(0)\}/H_i(0) \quad (8)$$

Having obtained the baseline initial disease-specific mortality rates, $\mu_{Ti}(0)$, all-other-cause mortality rates, $\mu_{Oi}(0)$, and hazard rates, $\lambda_i(0)$, for each age group, we then project these values for future years. To ensure consistency with Census population projections, we assume that the relationship (or ratio) of disease prevalence between the age groups remains stationary over time. Under this assumption, the projected values for each future year t are given by: $\mu_{Oi}(t) = s_i(t)\mu_{Oi}(0)$, $\mu_{Ti}(t) = s_i(t)\mu_{Ti}(0)$ and $\lambda_i(t) = s_i(t)\lambda_i(0)$. Here, $s_i(t)$ is the scaling factor that adjusts for changes in overall mortality trends observed in the Census data for age group i. By applying these scaling factors, we ensure that our model remains aligned with demographic dynamics and accurately reflects future population changes.

Verification of Population Dynamics, Initial Conditions, and Baseline Rates Input

We conducted a self-consistency verification that involved comparing the population growth dynamics derived from integrating births, deaths, migration, and aging data against historic Census-provided population growth data. We found that errors across all age groups remained within ± 2 percent, and over time the positive and negative errors balanced each other out, confirming that our demographic projections closely match Census data by the end of the study period and validating this aspect of our model.

We also conducted a self-consistency verification of the initial conditions and baseline rates. We used the initial conditions along with all our initial baseline rate inputs and their expected changes over time and entered these into our model with numerically integrated model ODEs.

This aimed to ensure that the ODE-generated population dynamics were consistent with the Census projections. We found excellent agreement between the model's projections and the Census data with errors ± 0.3 percent.

Fine-Tuning Incidence Rates for 2024 Baseline Prevalence Projections

In our modeling of the four diseases, we fine-tuned the baseline scenario (i.e., no climate change effects) incidence rates to ensure that our 2040 prevalence estimates aligned closely with other models available in the literature that forecast future disease prevalence without incorporating the impact of climate change. To achieve target 2040 prevalence for the baseline scenario, we modified incidences rather than mortalities, as disease-specific mortality data are generally more precise than incidence data. Here are the specific adjustments made for each disease, as shown in Table 3.1.

- For CVD, we adjusted the estimated incidence rate to reflect a projected increase in prevalence from 9.8 percent in 2015 to 14.0 percent in 2040. This adjustment corresponds to a 43-percent increase in prevalence from the 2024 baseline scenario to 2040 (i.e., 14.0 percent/9.8 percent) (Ortendahl et al., 2019).
- For asthma, we adjusted the estimated incidence rate to reflect an assumed 5 percent increase in prevalence by 2040 relative to 2024 in the baseline scenario. This estimate was informed by existing projections that forecast a rise in asthma prevalence among people under age 18 from 8 percent to 14 percent by 2090 (Neumann et al., 2019). Using the upper bound estimate (14 percent), we assumed a linear trend and estimated a 5 percent increase by 2040.
- For ESRD, we adjusted the incidence rate to reflect an assumed 34-percent increase in prevalence from the 2024 baseline scenario to 2040 based on global trends and adjusted for the specific demographic and health care context of the United States (CDC, 2023; GBD Chronic Kidney Disease Collaboration, 2020).
- For Alzheimer's disease, we adjusted the incidence rate to reflect an assumed 45-percent increase in prevalence by 2040 relative to 2024 in the baseline scenario. This projection was based on global trends and adjusted for the specific demographics and health care context of the United States (Institute for Health Metrics and Evaluation, undated; Akushevich et al., 2023).

Appendix C. Model Inputs and Transformations

The text below describes the sources, transformations, and assumptions for all the inputs to the model.

Global Temperature Projections

No changes from source (Fyfe et al., 2021). Global temperature projections are drawn from five illustrative climate change scenarios. Emissions estimates vary between the scenarios depending on socio-economic assumptions, levels of climate change mitigation, and air pollution controls.

Global Temperature Changes Projections Relative to 2024

Because our model treats 2024 as the baseline year, we converted the global temperature projections corresponding to each climate change scenario used in the model into a relative value to the 2024 temperature. We achieved this for each scenario by subtracting the temperature for 2024 from the temperature values for all subsequent years up to 2040.

Temperature-Climate Links

Relationship between Global and U.S. temperatures: EPA (undated-c) provided temperature data dating back to 1901 for changes in U.S. and global mean temperatures relative to each of their respective long-term average temperatures. These two series were converted from Fahrenheit to degrees Celsius.

Following this conversion, we constructed a linear regression as follows with change in U.S. mean annual temperature as the outcome variable:

$$US\ temperature\ change = \beta_1 * Global\ temperature\ change\ +\ intercept\ +\ error$$

The coefficient β_1 represents the change in the mean annual U.S. temperature for a 1-degree Celsius increase in the mean annual global surface temperature.

U.S. temperature changes and extreme heat days: EPA (undated-a) provided decadal data for the average annual heatwave frequency, duration, season, and intensity. To get the average number of extreme heat days in a year, we used the following equation:

$$Average\ annual\ extreme\ heat\ days = Annual\ heat\ wave\ frequency * Annual\ heat\ wave\ duration$$

Following this calculation, we constructed a linear regression as follows with the number of extreme heat days as the outcome variable:

$$Number\ of\ annual\ extreme\ heat\ days = \beta_2 * US\ temperature\ change\ +\ intercept\ +\ error$$

The coefficient β_2 represents the change in the annual number of extreme heat days for a 1-degree Celsius increase in the mean annual U.S. temperature.

U.S. temperature changes and hurricanes: EPA (undated-b) provided data for the annual incidence of hurricanes that make landfall in the United States. We constructed a linear regression as follows with the number of hurricanes making landfall in the United States as the outcome variable:

$$Number\ of\ hurricanes\ making\ landfall\ in\ the\ United\ States = \beta_3 * US\ temperature\ change\ +\ intercept\ +\ error$$

The coefficient β_3 represents the change in the annual number of hurricanes making landfall in the United States for a 1 degree Celsius increase in the mean annual U.S. temperature.

U.S. temperature changes and air quality: Our chosen metrics for measuring air quality are the concentration of particulate matter (PM2.5) and ground-level ozone. However, when observing the raw temporal trends for these two pollutants, we observed an overall decline due to improving overall air quality in the recent past. Wildfires, which have a demonstrated link to climate change (U.S. Geological Survey, undated), are linked to increased emissions of particulate matter and ozone. Therefore, instead of directly relating temperature rise in the United States with PM2.5 and ozone, we related temperature increases with wildfire extent as a first step, and then related changes in wildfire extent to changes in the concentration of PM2.5 and ground-level ozone.

1. EPA (undated-e) provided annual data for wildfire extent in acres and we converted this series into millions of acres by dividing each datapoint by 1,000,000. Then we constructed a linear regression as follows with wildfire extent as the outcome variable:

   $$Wildfire\ extent = \beta_4 * US\ temperature\ change\ +\ intercept\ +\ error$$

   The coefficient β_4 represents the change in wildfire extent in millions of acres for a 1-degree Celsius increase in the mean annual U.S. temperature.

2. Next, we found a model (Burke et al., 2021) in the literature that suggested that 25 percent of PM2.5 emissions in 2020 were attributable to wildfires. We assumed that there is a linear relationship between wildfire extent and PM2.5 emissions, and thus divided EPA's PM2.5 concentrations for 2020 (EPA, undated-f) by the wildfire extent in 2020 (in millions of acres), and then multiplied the results by 0.25 to estimate PM2.5 emissions produced per million acres burnt by wildfires. We divided the result by 10 to standardize the change in PM2.5 concentration to 10s of $\mu g/m^3$ which are the units used between exposure to PM2.5 and all-cause mortality, disease mortality, and disease incidence. For simplicity, we assumed that the ratio of wildfire extent to PM2.5 emissions will remain stable and PM2.5 will change linearly as wildfire extent changes in response to climate change.
3. We found another model (Jaffe et al., 2008) in the literature that estimated an increase in ground-level ozone emissions by 2 parts per billion (ppb) for every million acres of

wildfire extent. We divided this result here by 10 to standardize the units to 10s of ppb. We have assumed a static relationship between wildfire extent and ground-level ozone for simplicity.

Baseline Medical Conditions

Cardiovascular Disease

In alignment with the data sources, we used six input age groups for this model: 18–24, 25–44, 45–54, 55–64, 65–74, and 75+ years.

1. *CVD mortality:* To calculate the baseline mortality for CVD, we used data from the CDC's WONDER system that tracks mortality statistics (CDC, undated-c). We filtered the data by cause of death corresponding to ICD Chapter I00-I00 codes (Diseases of the Circulatory System) and age. For age, we chose to filter by single-year age groups in order to standardize the age groups with the CVD prevalence data sourced from elsewhere. We then collated the data from single-year age groups to create larger age groups. For instance, the source returned the deaths and total population for individuals aged 18 years, 19 years, 20 years etc. We created the age group 18-24 by summing up the total deaths among the single age-groups between age 18 and age 24, summing the total population of the single-year age groups between age 18 and age 24, then divided the former by the latter and multiplied by 100,000 to get the average mortality rate for age group 18–24 in terms of deaths per 100,000 individuals. This process was repeated to create all the CVD mortality age groups. However, since the age groups created using these data did not necessarily line up with the age groups we were using in our model, we needed to interpolate and obtain mortality rates for our chosen groups. This was done by fitting our mortality rates as calculated from the CDC data to a polynomial. The dataset did not report population statistics for individuals 85 and older. Therefore, we applied the death rate for ages 75 to 84 to individuals aged 85+ years.
2. *CVD incidence:* We were unable to find data on CVD incidence, however historic prevalence data by age group shows that CVD prevalence has remained relatively stationary over the past decade. Based on this information, and assuming stationary demographic dynamics, we assumed that the deaths that deplete the CVD-diagnosed population would need to be balanced by the equivalent inflow of newly diagnosed (incident) CVD cases. Therefore, we chose to use CVD baseline mortality estimates as a proxy for CVD baseline incidence in the model.
3. *CVD prevalence:* We used self-reported prevalence data from the CDC (undated-e), which reported the prevalence of CVD for each age group in percentage of adults. The CDC data were not provided according to the same age groups as our model; therefore, we used a fourth-order polynomial fitting technique to adjust the CDC prevalence data to align with our age groups. We converted this series to cases per 100,000 individuals by multiplying each datapoint by 1,000.

End-Stage Renal Disease

In alignment with the data sources, we used five input age groups for this model: 0–17, 18–44, 45–64, 65–74, and 75+ years.

1. *ESRD mortality:* For the baseline mortality of ESRD, we used the mortality rate in deaths per 1,000 person-years from the U.S. Renal Data System's 2023 Annual Data Report (NIDDK, undated-a; NIDDK, 2023). Data from the U.S. Renal Data System were not provided according to the same age groups as our model; therefore, we used a fourth-order polynomial fitting technique on the logarithm of mortality rates to adjust the ESRD mortality data to align with our age groups. The report mentioned that the majority of patients were observed for a period of one year, so we assumed this mortality rate to be equivalent to deaths per 1,000 patients. We converted this estimate into individual deaths by dividing each mortality rate by 1,000, then multiplied the results by the corresponding prevalence of ESRD for each age group in cases per 100,000 individuals. Mortality data were unavailable for the 0–17 years age group.
2. *ESRD incidence:* For the baseline incidence of ESRD, we used incidence data from the U.S. Renal Data System's 2023 Annual Data Report (NIDDK, undated-a; NIDDK, 2023). We converted this series to cases per 100,000 individuals by dividing each datapoint by 10 for each age group. Data from the U.S. Renal Data System were not provided according to the same age groups as our model; therefore, we used a fourth-order polynomial fitting technique to adjust the U.S. Renal Data System prevalence data to align with our age groups.
3. *ESRD prevalence:* For the baseline prevalence of ESRD, we used prevalence data from the U.S. Renal Data System's 2023 Annual Data Report (NIDDK, undated-a; NIDDK, 2023). We converted this series to cases per 100,000 individuals by dividing each datapoint by 10 for each age group. Data from the U.S. Renal Data System were not provided according to the same age groups as our model; therefore, we used a fourth-order polynomial fitting technique to adjust the U.S. Renal Data System prevalence data to align with our age groups.

Asthma

In alignment with the data sources, we used seven input age groups for this model: 0–4, 5–14, 15–19, 20–24, 25–34, 35–64, and 65+ years.

1. *Asthma mortality:* To calculate the baseline mortality for asthma, we used CDC underlying cause of death data (CDC, undated-c), for ICD-10 codes J45–J46 (asthma). We converted this series from the death rate per 1,000,000 individuals to deaths per 100,000 individuals by dividing each datapoint by 10.

   The age cutoffs differed between the prevalence and mortality data for the age groups 5–14, 15–19, and 20–24 years, and the age groups 5–11, 12–17, and 18–24 years, respectively. We assumed that these data would not differ significantly, therefore we used the age groups from the prevalence dataset for the mortality data in the model. The CDC data were not provided according to the same age groups as our model; therefore, we used a fourth-order polynomial fitting technique on the logarithm of mortality rates to adjust the asthma mortality data to align with our age groups.
2. *Asthma incidence:* We were unable to find data on asthma incidence, however historic prevalence data by age group show that asthma prevalence has remained relatively stationary over the past decade. Based on this information, and assuming stationary demographic dynamics, we assumed that the deaths that deplete the asthma-diagnosed population would need to be balanced by the equivalent inflow of newly diagnosed

(incident) asthma cases. Therefore, we chose to use asthma baseline mortality estimates as a proxy for asthma baseline incidence in the model.

3. *Asthma prevalence:* To calculate baseline prevalence of asthma, we used self-reported prevalence data from the CDC (CDC, undated-d) for each age group in percentage of individuals. We assumed this to equate to cases per 100 individuals and converted this series to cases per 100,000 individuals by multiplying each datapoint by 1,000. The CDC data were not provided according to the same age groups as our model; therefore, we used a fourth-order polynomial fitting technique to adjust the CDC prevalence data to align with our age groups.

Alzheimer's Disease

We sourced the mortality, prevalence, and incidence data for Alzheimer's disease from the Alzheimer's Association's "Alzheimer's Disease Facts and Figures" report (2024). Data were available for all three disease characteristics for the 65–74, 75–84 and 85+ years age groups. The source also provided mortality data for the 45–54 and 55–64 years age groups, and prevalence data for the 30–64 years age group.

1. *Alzheimer's disease mortality:* Our source provided mortality data in deaths per 100,000 individuals and no further transformations were required.
2. *Alzheimer's disease incidence:* Our source recorded incidence data for Alzheimer's disease in percentage of individuals, which we interpreted as cases per 100 individuals. To convert these figures into cases per 100,000 individuals, we multiplied each incidence data point by 1,000.
3. *Alzheimer's disease prevalence:* For age groups 65–74, 75–84, and 85+ years, prevalence data were recorded in percentage of individuals, which we interpreted as cases per 100 individuals. To convert these data into cases per 100,000 persons, we multiplied each datapoint by 1,000. The source also reported the prevalence for age group 30–64 years in cases per 100,000 individuals, so no further transformations were required.

Disease-Climate Links

Hurricane affected proportion of the U.S. population: To account for the proportion of the United Stated that is affected by hurricanes, we developed a scaling factor to adjust each of the hurricane-related inputs below by the proportion of the total U.S. population (328.24 million) (Johnson, 2019) that resides in the most hurricane-prone regions (60.2 million) (Cohen, 2019) according to 2019 U.S. Census estimates, as below:

$$\frac{60.2\ million}{328.24\ million} = 0.185534974$$

We assumed that the populations of both the hurricane-prone regions and the United States as a whole will grow at similar rates and that this proportion will remain constant over the study period.

Climate and All-Cause Mortality

1. *Extreme heat:* We found a source in the literature (Anderson and Bell, 2011) that reported a 3.74 percent (95% CI 2.29–5.22) increase in all-cause mortality due to a heat wave. To obtain the percentage increase in all-cause mortality for each extra day of extreme heat, we divided by the average length of a heatwave in the 2020s (4.3 days) (Johnson, 2019; EPA, undated-a).
2. *Hurricanes:* We found a source in the literature (Huang et al., 2023) that reported the relative risk for deaths due to exposure to a cyclone or hurricane as 1.09 (95% CI 1.04–1.13), which can be interpreted as an estimated increase in the risk of mortality of 9 percent, with the true mortality risk most likely falling between 4 and 13 percent. To account for the affected proportion of the United States, we scaled down by multiplying these figures by 0.185534974.
3. *PM2.5:* We found a source in the literature (Wang et al., 2020) that reported the relative risk for total deaths due to exposure to an additional 10 $\mu g/m^3$ of PM2.5 as 1.05 (95% CI 1.044–1.056). These can be interpreted as an estimated increase in mortality risk of 5 percent, with the true risk of mortality most likely falling between 4.4 and 5.6 percent.
4. *Ozone:* We found a source in the literature (Kim, Kim, and Kim, 2020) that reported the hazard ratio for total deaths due to exposure to an additional 10 ppb of ozone as 1.01 (95% CI 1.01–1.01). These can be interpreted as an estimated increase in mortality of 1 percent, with the true value most likely also falling within the 1 percent range. Due to the need to provide a varied confidence interval for sampling during the simulations, we adjusted the upper and lower bounds of the percentage interpretation to 0.99 percent to 1.01 percent, respectively.

Climate and Cardiovascular Disease Mortality

1. *Extreme heat:* We found a source in the literature (Khatana, Werner, and Groeneveld, 2022) that reported the percent increase in CVD mortality due to exposure to an additional day of extreme heat as 0.12 percent (95% CI 0.04–0.21).
2. *Hurricanes:* We found a source in the literature (Huang et al., 2023) that reported the relative risk for CVD-related deaths due to exposure to a cyclone or hurricane as 1.14 (95% CI 0.99–1.3), which can be interpreted as an estimated increase in the risk of mortality of 14 percent per cyclone or hurricane. To account for the affected proportion of the United States, we scaled down by multiplying these figures by 0.185534974.
3. *PM 2.5:* We found a source in the literature (Manisalidis et al., 2020) that reported the relative risk for cardiovascular deaths due to exposure to an additional 10 $\mu g/m^3$ of PM2.5 as 1.088 (95% CI 1.078–1.098), which can be interpreted as an estimated increase in the risk of mortality of 8.8 percent, with the true increased risk of mortality most likely falling between 7.8 percent to 9.8 percent.
4. *Ozone:* We found a source in the literature (Wang et al., 2020) that reported the hazard ratio for CVD-related deaths due to exposure to an additional 10 ppb of ozone as 1.03 (95% CI 1.01–1.06), which can be interpreted as an estimated increase in mortality of 3 percent, with the most likely true increase in mortality falling between 1 percent to 6 percent.

Climate and Cardiovascular Disease Incidence

1. *Extreme heat:* We found a source in the literature (Singh et al., 2024) that reported the relative risk of CVD morbidity due to a heat wave as 1.008 (95% CI 0.998–1.017), which can be interpreted as an estimated increase of 0.8 percent, with the true change in morbidity most likely falling between–0.2 percent and 1.7 percent. To obtain the percentage increase in all-cause mortality for each extra day of extreme heat, we divided these figures by the average length of a heatwave in the 2020s (4.3 days).
2. *Hurricanes:* We were unable to find data that directly related hurricanes to changes in the incidence of CVD. However, we did find a source in the literature (Swerdel et al., 2014) that reported the attributable rate ratio of myocardial infarctions specifically due to hurricanes or cyclones as 1.22 (95% CI 1.16–1.28), which we assume to be similar to the percentage increase in CVD overall. Therefore, these figures can be interpreted as an increase in CVD incidence of 22 percent, with the true increase in CVD incidence most likely falling between 16 percent and 28 percent. To account for the affected proportion of the United States, we scaled down by multiplying these figures by 0.185534974.
3. *PM2.5:* We found a source in the literature (Xi et al., 2022) that reported the hazard ratio for CVD incidence due to exposure to an additional 10 $\mu g/m^3$ of PM2.5 as 1.03 (95% CI1.02–1.04), which can be interpreted as an estimated increase in CVD incidence of 3 percent, with the true change in CVD incidence most likely falling between 2 percent and 4 percent.
4. *Ozone:* We found a source in the literature (Wu et al., 2022) that reported the percentage increase in CVD incidence due to exposure to an additional 10 ppb of ozone as 1.42 percent (95% CI 0.14–2.73).

Climate and End-Stage Renal Disease Mortality

1. *Extreme heat:* We found a source in the literature (Blum et al., in press) that reported the hazard ratio of ESRD mortality due to an extreme heat event as 1.18 (95% CI 1.15–1.20). This can be interpreted as an increase in ESRD mortality of 18 percent, with the true increase in mortality most likely falling between 15 percent and 20 percent. To obtain the percentage increase in ESRD mortality for each extra day of extreme heat, we divided these figures by the average length of a heatwave in the 2020s (4.3 days) according to the EPA (undated-a).
2. *Hurricanes:* We found a source in the literature (Blum et al., 2022) that reported the hazard ratio for ESRD-related deaths due to exposure to a cyclone or hurricane as 1.13 (95% CI 1.06–1.22), which can be interpreted as an estimated increase in mortality of 13 percent, with the true increase in mortality most likely falling between 6 percent and 22 percent. To account for the affected proportion of the United States, we scaled down by multiplying these figures by 0.185534974.
3. *PM2.5:* We found a source in the literature (Xi et al., 2020) that reported the relative risk for ESRD-related deaths due to exposure to an additional 10 $\mu g/m^3$ of PM2.5 as 1.01 (95% CI 1.001–1.019), which can be interpreted as an estimated increase in mortality of 1 percent, with the true risk of death most likely falling between 0.1 percent and 1.9 percent.
4. *Ozone:* We found a source in the literature (Kim et al., 2024) that reported the hazard ratio for ESRD-related deaths due to exposure to an additional 10 ppb of ozone as 1.012

(95% CI 1.008–1.017), which can be interpreted as an estimated increase in mortality of 1.2 percent, with the true value most likely falling between 0.8 percent and 1.7 percent.

Climate and End-Stage Renal Disease Incidence

1. *Extreme heat:* We were unable to find data that directly related change in the incidence of ESRD with heat waves. However, we did find a source in the literature (Bobb et al., 2014) that reported the relative risk of ESRD-related hospitalizations due to a heat wave as 1.14 (95% CI 1.06–1.23), which we interpreted as an increase in ESRD-related morbidity of 14 percent. To obtain the percentage increase in ESRD incidence for each extra day of extreme heat, we divided these figures by the average length of a heat wave in the 2020s (4.3 days) according to the EPA (undated-a).
2. *Hurricanes:* We found a source in the literature (Howard et al., 2012) that reported the percentage of excess renal-related hospitalizations due to a hurricane as 3 percent (95% CI 2.86–3.7). To account for the affected proportion of the United States, we scaled down by multiplying these figures by 0.185534974.
3. *PM2.5:* We found a source in the literature (Wathanavasin et al., 2024) that reported the odds ratio for ESRD incidence due to exposure to an additional 10 $\mu g/m^3$ of PM2.5 as 1.16 (95% CI 1.00–1.36), which can be interpreted as an estimated increase in incidence of 16 percent, with the true change most likely falling between of 0 percent and 36 percent.
4. *Ozone:* We found a source in the literature (Kim et al., 2024) that reported the hazard ratio for ESRD incidence due to exposure to an additional 10 ppb of ozone as 1.049 (95% CI 1.044–1.054), which can be interpreted as an estimated increase in incidence of 4.9 percent, with the true change most likely falling between 4.4 percent and 5.4 percent.

Climate and Asthma Mortality

1. *Extreme heat:* We found a source in the literature (Cheng et al., 2019) that reported the relative risk of asthma mortality due to a heat wave as 1.08 (95% CI 1.01–1.160) which can be interpreted as an estimated increase in asthma mortality of 8 percent, with the true change most likely falling between 1 percent and 16 percent. To obtain the percentage increase in asthma-related mortality for each extra day of extreme heat, we divided these figures by the average length of a heatwave in the 2020s (4.3 days) according to the EPA (undated-a).
2. *Hurricanes:* We found a source in the literature (Huang et al., 2023) that reported the percentage change in respiratory deaths due to exposure to a cyclone or hurricane as 1.3 percent (95% CI 0.2–2.4). To account for the affected proportion of the United States, we scaled down by multiplying these figures by 0.185534974.
3. *PM2.5:* We found a source in the literature (Song et al., 2022) that reported the percentage change in asthma-related deaths due to exposure to an additional 10 $\mu g/m^3$ of PM2.5 as 2.39 percent (95% CI 0.05–4.78).
4. *Ozone:* We found a source in the literature (Kim, Kim, and Kim, 2020) that reported the hazard ratio for asthma-related deaths due to exposure to an additional 10 ppb of ozone as 1.04 (95% CI 1.01–0.07), which can be interpreted as an estimated increase in mortality of 4 percent, with the true change most likely falling between 1 percent and 7 percent.

Climate and Asthma Incidence

1. *Extreme heat:* We were unable to find data that directly measured the relationship between extreme heat and change in asthma incidence, therefore we used a source in the literature (Soneja et al., 2016) that reported the odds ratio of same-day hospitalizations for asthma due to an extreme heat day as 1.03 (95% CI 1.00–1.07), which can be interpreted as an estimated increase in asthma morbidity of 3 percent, with the true change most likely falling between 0 percent and 7 percent.
2. *Hurricanes:* We were unable to find data that directly measured the relationship between extreme heat and change in asthma incidence, therefore we used a source in the literature (Makrufardi et al., 2023) that reported the relative risk for asthma events due to exposure to a cyclone or hurricane as 1.5 (95% CI 0.93–2.43), which can be interpreted as an estimated increase in asthma morbidity of 50 percent, with the true change in morbidity most likely falling between -7 percent and 143 percent. To account for the affected proportion of the United States, we scaled down by multiplying these figures by 0.185534974.
3. *PM2.5:* We found a source in the literature (Khalili et al., 2018) that reported the odds ratio for asthma diagnosis due to exposure to an additional 5.9 $\mu g/m^3$ of PM2.5 as 1.08 (95% CI 1.0–1.15), which can be interpreted as an estimated increase in asthma incidence of 8 percent, with the true change in incidence most likely falling between 0 percent and 15 percent. To obtain the change in incidence due to exposure to an additional 10 $\mu g/m^3$ of PM2.5, we divided these figures by 5.9 and multiplied the results by 10.
4. *Ozone:* We were unable to find data that directly measured the relationship between exposure to ozone and change in asthma incidence, therefore we used a source in the literature (Li et al., 2019) that reported the relative risk for asthma exacerbations due to exposure to an additional 10 $\mu g/m^3$ of ozone as 1.014 (95% CI 1.005–1.024). These can be interpreted as an estimated increase in asthma incidence of 1.4 percent, with the true change in asthma incidence most likely falling between 0.5 percent and 2.4 percent. To standardize the units to 10 ppb of ozone, we multiplied these figures by 1.996 as 1 ppb of ozone is equivalent to 1.996 $\mu g/m.^3$

Climate and Alzheimer's Disease Mortality

1. *Extreme heat:* We found a source in the literature (Yin et al., 2023) that reported the relative risk of death due to an extreme heat day among patients with Alzheimer's disease as 1.3 (95% CI 1.23–1.38), which can be interpreted as an estimated increase in Alzheimer's mortality of 30 percent, with the true change in mortality risk most likely falling between 23 percent and 38 percent.
2. *Hurricanes:* We found data in the literature (Bell et al., 2023) that reported the relative risk of death due to hurricane exposure among patients with Alzheimer's disease or other related dementias as 1.08 (95% CI 1.07–1.09), which can be interpreted as an estimated increase in mortality among patients with Alzheimer's disease of 8 percent, with the true change in risk of death most likely falling between 7 percent and 9 percent. To account for the affected proportion of the United States, we scaled down by multiplying these figures by 0.185534974.
3. *PM2.5:* We were unable to find specific data for the effect of PM2.5 on the risk of death among patients with Alzheimer's disease, but we found a study in the literature (Wang et

al., 2022) that assessed the impact of PM 2.5 exposure on mortality among Medicare beneficiaries; since this population also accounts for the vast majority of Alzheimer's patients, we assumed that the percentage changes in mortality due to the effect of PM2.5 would be similar. The study reported the hazard ratio for total mortality due to exposure to an additional 2.63 μg/m^3 of PM2.5 as 1.025 (95% CI 1.023–1.027), which estimates a mortality increase of 2.5 percent, with the true mortality change most likely falling between 2.3 percent and 2.7 percent. These units were standardized with our other PM2.5 variables and converted into effect per 10 μg/m^3 of PM2.5 by dividing by 2.63 and multiplying the results by 10.

4. *Ozone:* We were unable to find specific data for the effect of ground-level ozone on Alzheimer's patient mortality, but we found one study in the literature that assessed the impact of ozone exposure on dementia mortality (Zhao et al., 2021). We assumed that these percentage changes would be similar. This source reported the hazard ratio for dementia related deaths due to exposure to an additional 10.1 ppb of ozone as 1.08 (95% CI 1.06–1.10), which can be interpreted as an estimated increase in mortality of 8 percent, with the true change in mortality most likely falling between 6 percent and 10 percent. We divided the percentages by 10.1 and multiplied the results by 10 to convert them into effect per 10 ppb of ozone.

Alzheimer's Disease Incidence

1. *Extreme heat:* We were unable to find data that directly investigated the impact of extreme heat exposure on Alzheimer's disease incidence, however we found a source in the literature (Xu et al., 2019) that reported the percentage increase in Alzheimer's-related hospitalizations due to a heat wave as 51 percent (95% CI 2.0–126.0). To obtain the percentage increase in Alzheimer's related hospitalizations for each extra day of extreme heat, we divided these figures by the average length of a heat wave in the 2020s (4.3 days) according to the EPA (undated-a).
2. *Hurricanes:* We were unable to find data that directly investigated the impact of hurricane exposure on Alzheimer's incidence, however, we found a source (Bell et al., 2021) in the literature that reported the incidence rate ratio for all-cause hospital admissions among Medicare beneficiaries during a hurricane. We assume that these rates will be similar. The study reported the admissions rate ratio as 1.23 (95% CI 1.22–1.24), which can be interpreted as an estimated increase in of 23 percent, with the true change in admissions most likely falling between 22 percent and 24 percent. To account for the affected proportion of the United States, we scaled down by multiplying these figures by 0.185534974.
3. *PM2.5:* We found a source in the literature (Yang et al., 2022) that reported the hazard ratio for Alzheimer's disease incidence due to exposure to an additional 10 μg/m^3 of PM2.5 as 1.05 (95% CI 1.01–1.10), which can be interpreted as an estimated increase in the incidence of Alzheimer's disease of 5 percent, with the true change in incidence most likely falling between 1 percent and 10 percent.
4. *Ozone:* We found a source in the literature (Jung, Lin, and Hwang, 2015) that reported the hazard ratio for Alzheimer's disease incidence due to exposure to an additional 9.63 ppb of ozone as 1.06 (95% CI 1.00–1.12), which can be interpreted as an estimated increase in incidence of 6 percent, with the true change in incidence most likely falling

between 0 percent and 12 percent. We divided the percentages by 9.63 and multiplied the results by 10 to standardize the units to 10 ppb of ozone.

Human Mortality Database U.S. Life Table

We used data from the Total (both sexes), 1x1, Life Tables dataset as provided by the Human Mortality Database. No changes were made to the source data (Human Mortality Database, undated).

U.S. Births

To project births in the U.S. between 2024 and 2040, we used data from the "Projected Births by Sex, Race, and Hispanic Origin for the United States: 2023 to 2100" dataset as projected by the U.S. Census "2023 National Population Projections." No changes were made to the source data (U.S. Census Bureau, undated).

U.S. Deaths

To project deaths in the U.S. between 2024 and 2040, we used data from the "Projected Deaths by Single Year of Age, Sex, Race, and Hispanic Origin for the United States: 2023 to 2100" dataset as projected by the U.S. Census "2023 National Population Projections." No changes were made to the source data (U.S. Census Bureau, undated).

U.S. Net Migration

To project net migration to the U.S. between 2024 and 2040, we used data from the "Projected Net International Migration by Single Year of Age, Sex, Race, and Hispanic Origin for the United States: 2023 to 2100" dataset as projected by the U.S. Census "2023 National Population Projections." No changes were made to the source data (U.S. Census Bureau, undated).

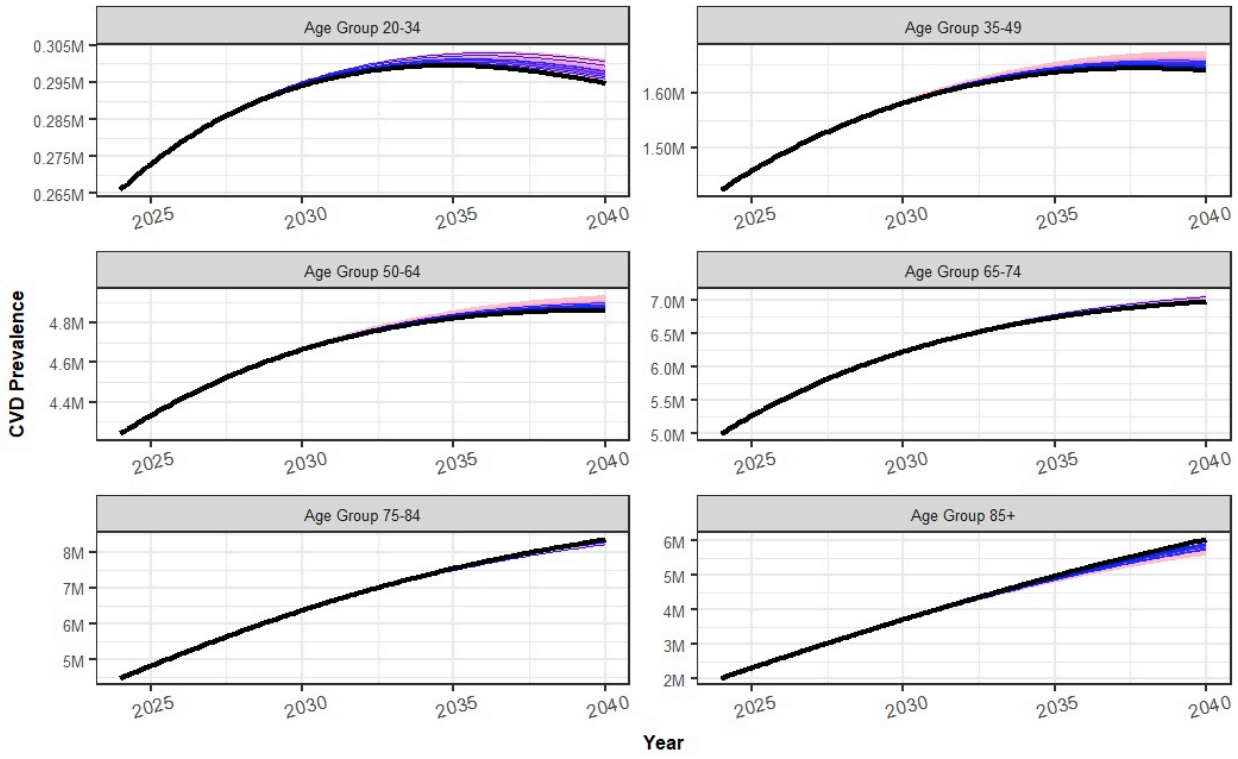
U.S. Total Population

To project the total population of the U.S. between 2024 and 2040, we used data from the "Projected Population by Single Year of Age, Sex, Race, and Hispanic Origin for the United States: 2022 to 2100" dataset as projected by the U.S. Census "2023 National Population Projections." No changes were made to the source data (U.S. Census Bureau, undated).

Appendix D. Projected Prevalences and Percentage Changes in Deaths by Age Group for Each Condition

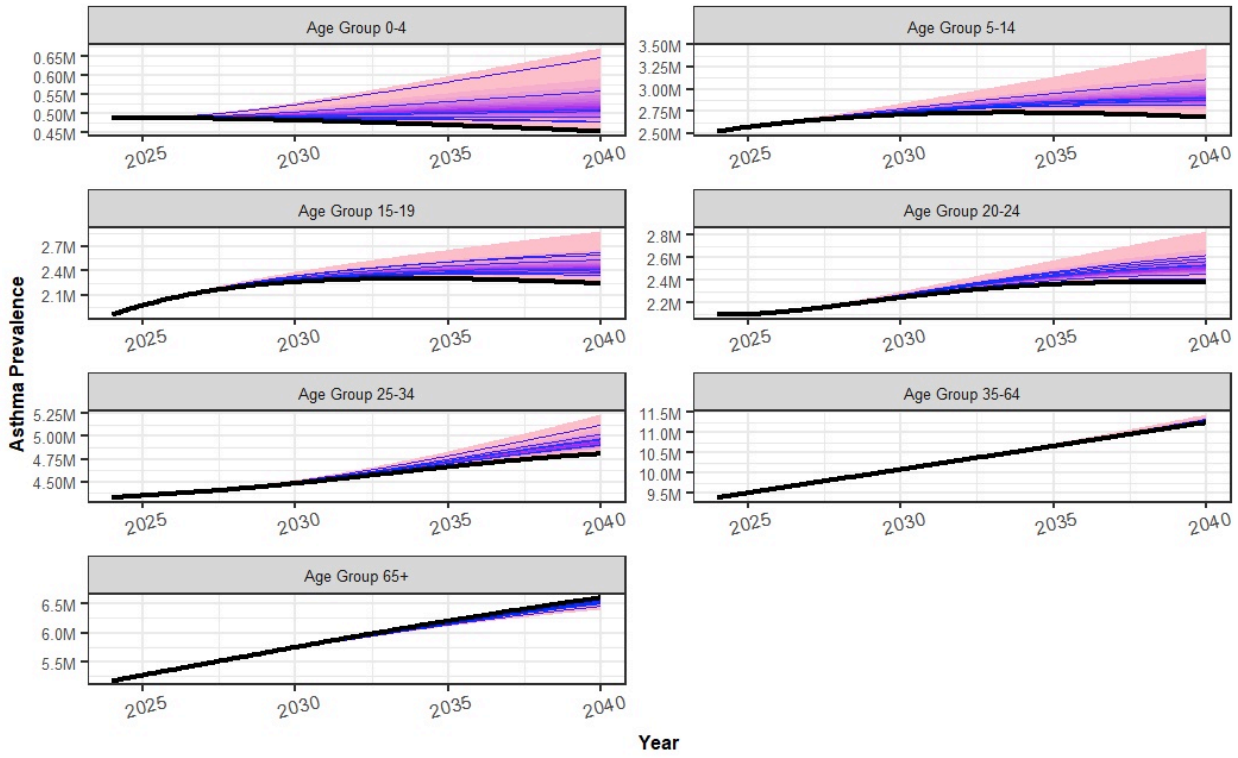
Figures D.1–D.4 show the projected prevalence from the initial year (2024) to the final year (2040) for each of the four sampled medical conditions, with each age group displayed in separate panels. The baseline prevalence trajectory is represented by a bold black line, indicating how the prevalence of each disease would change over time without the influence of climate change effects. The pink and purple bands illustrate the range of projected prevalence trajectories under the modeled climate change scenarios, from least severe to most severe. These scenarios incorporate varying inputs within their uncertainty ranges, describing how extreme weather events, influenced by climate change, affect incidence and mortality rates. The concentration of purple in the fan indicates where the median of these trajectories lies, and the pink areas depict the less likely trajectories.

Figure D.1. CVD Prevalence Projections Compared to Baseline Under All Climate Change Scenarios by Age Group, 2024–2040



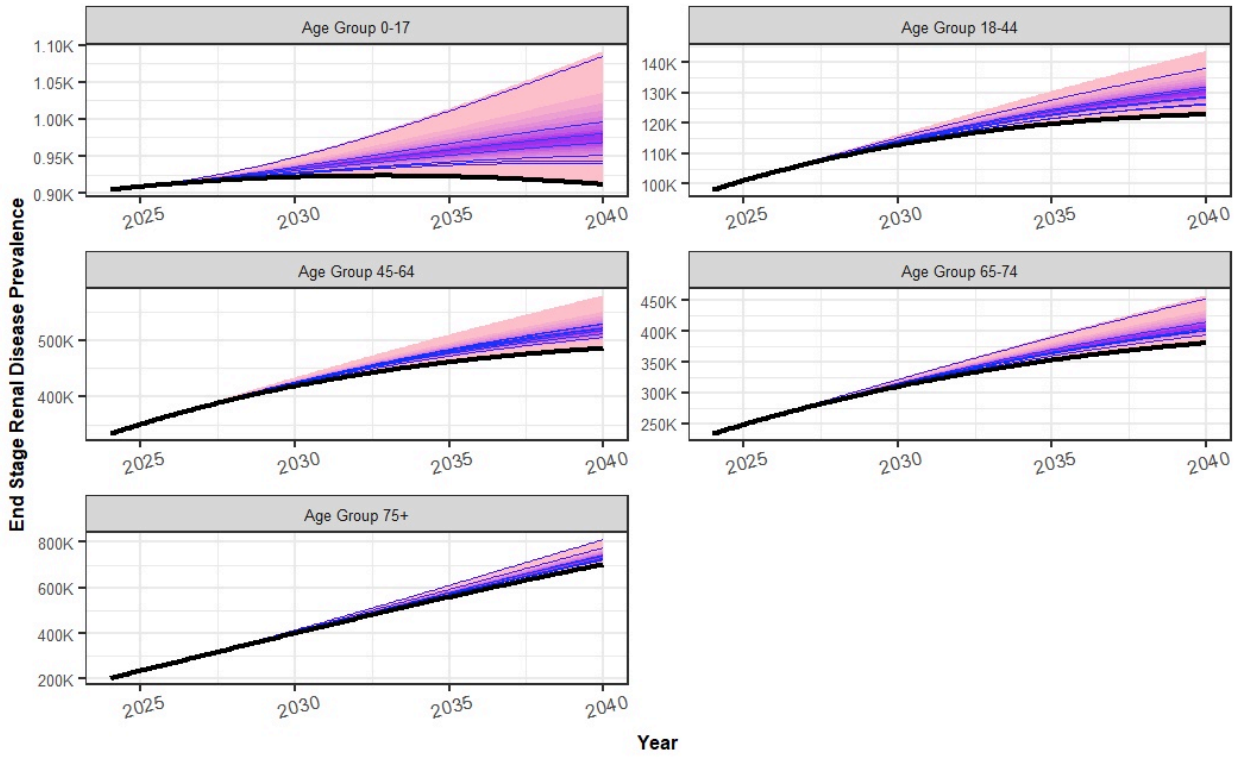
NOTE: Pink and purple areas = range of projected prevalence estimates under selected climate scenarios; purple = more likely trajectory, pink = less likely trajectory. Bold black line = baseline scenario; blue lines = randomly selected model runs.

Figure D.2. Asthma Prevalence Projections Compared to Baseline Under All Climate Change Scenarios by Age Group, 2024–2040



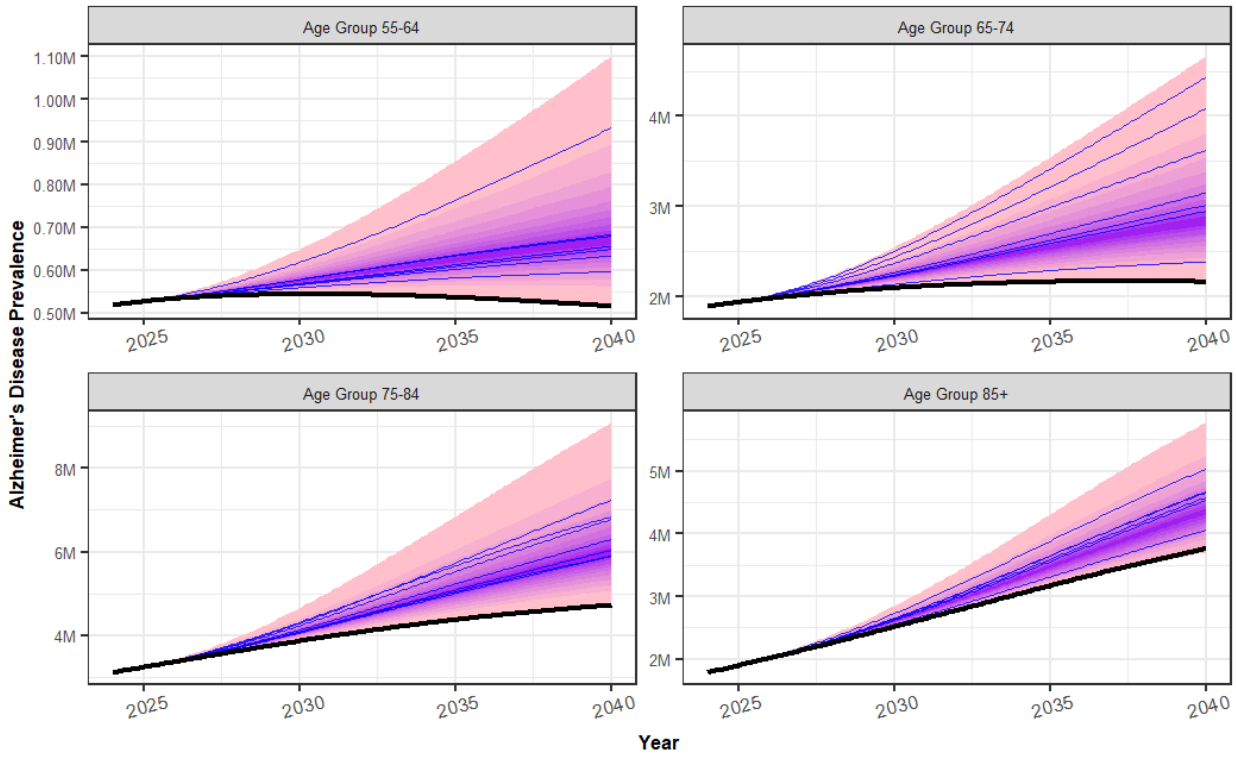
NOTE: Pink and purple areas = range of projected prevalence estimates under selected climate scenarios; purple = more likely trajectory, pink = less likely trajectory. Bold black line = baseline scenario; blue lines = randomly selected model runs.

Figure D.3. End-Stage Renal Disease Prevalence Projections Compared to Baseline Under All Climate Change Scenarios by Age Group, 2024–2040



NOTE: Pink and purple areas = range of projected prevalence estimates under selected climate scenarios; purple = more likely trajectory, pink = less likely trajectory. Bold black line = baseline scenario; blue lines = randomly selected model runs.

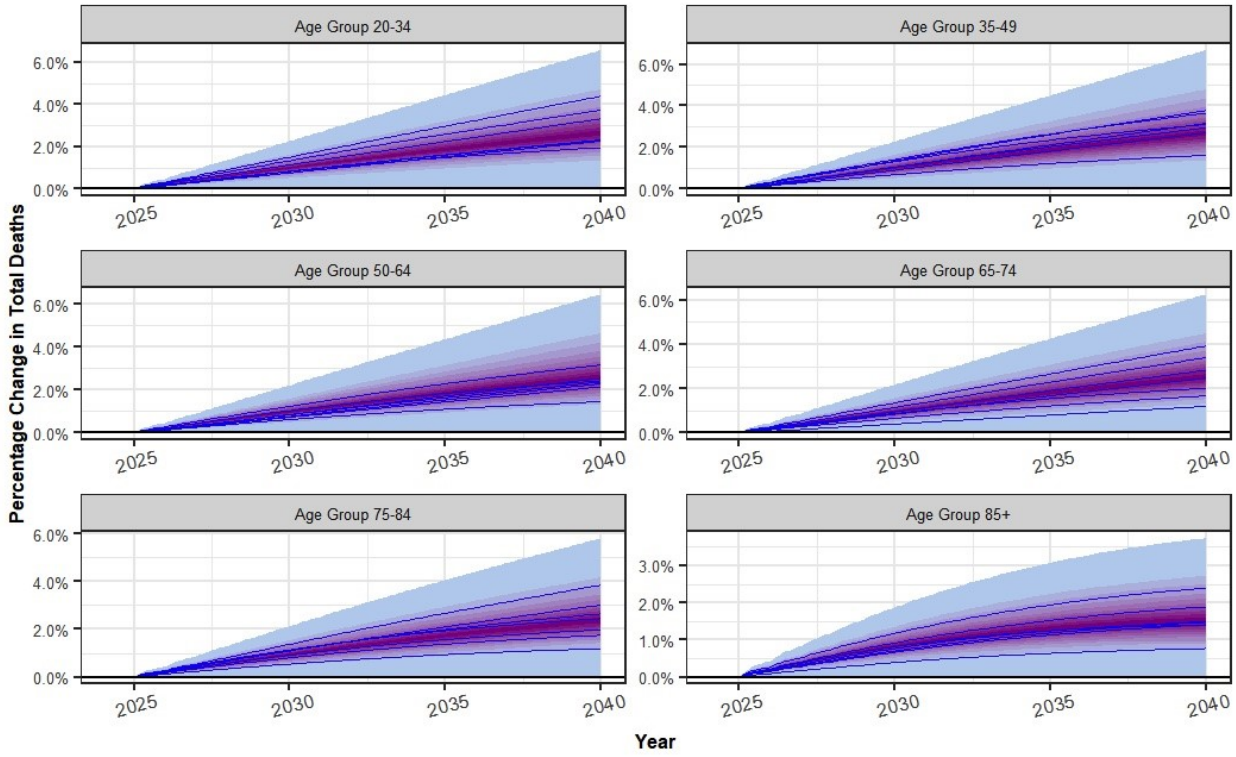
Figure D.4. Alzheimer's Disease Prevalence Projections Compared to Baseline Under All Climate Change Scenarios by Age Group, 2024–2040



NOTE: Pink and purple areas = range of projected prevalence estimates under selected climate scenarios; purple = more likely trajectory, pink = less likely trajectory. Bold black line = baseline scenario; blue lines = randomly selected model runs.

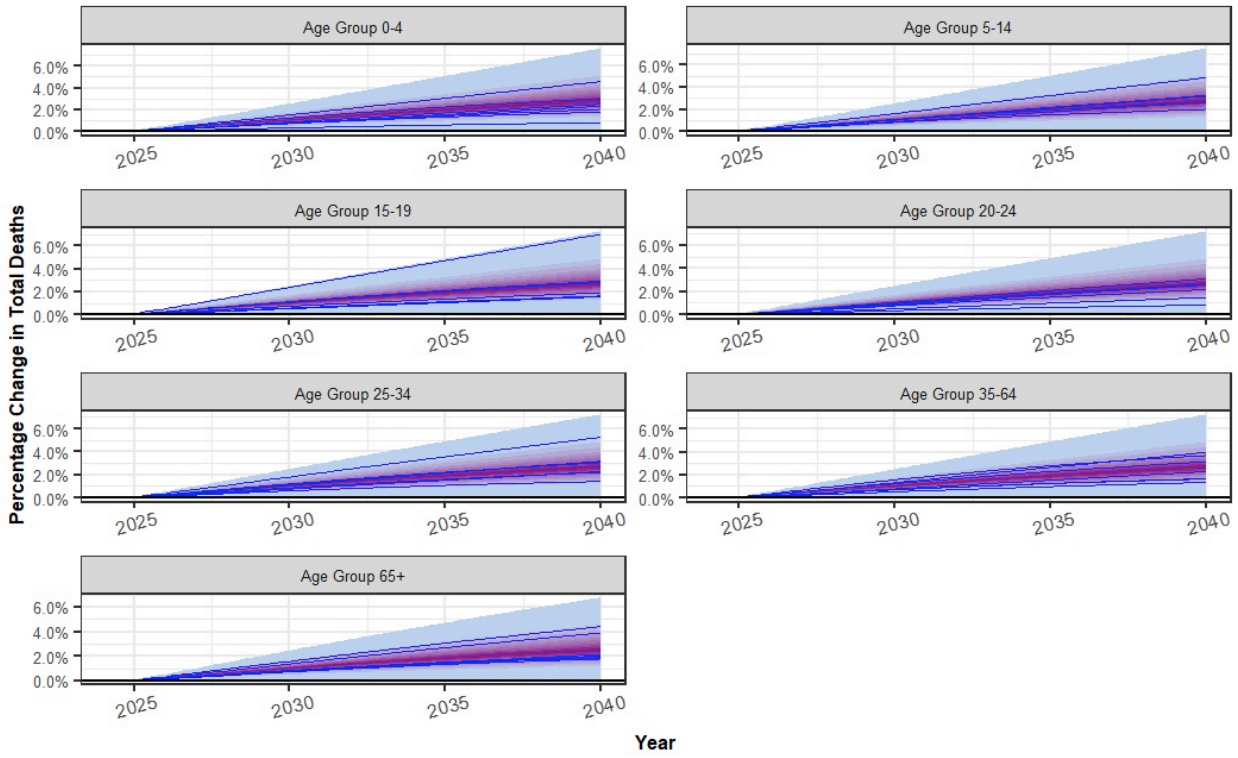
Figures D.5–D.7 show projected percentage change in total deaths compared to the baseline scenarios under all climate change scenarios by age group from 2024 to 2040 for each of the conditions modeled.

Figure D.5. Results of Cardiovascular Disease/Metoprolol Model: Projected Percentage Change in Total Deaths Compared to Baseline Under All Climate Change Scenarios by Age Group, 2024–2040



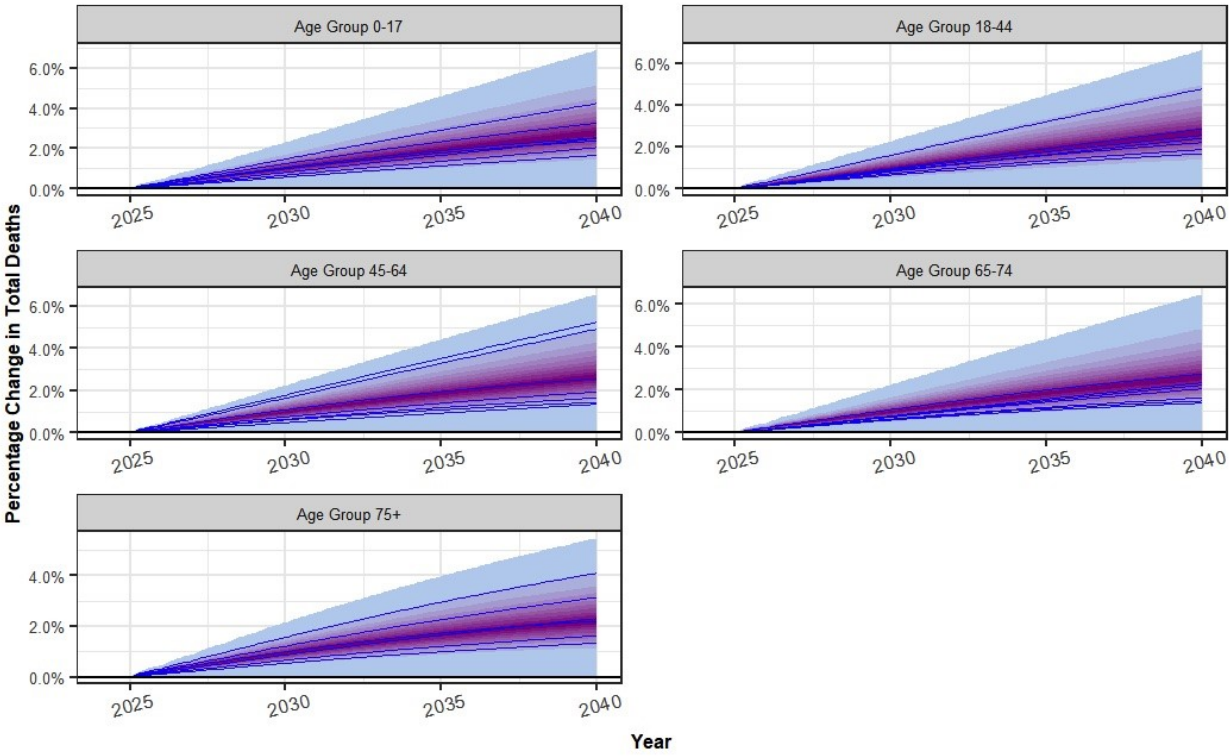
NOTE: Blue and violet areas = range of projected total deaths under selected climate scenarios; violet = more likely trajectory, blue = less likely trajectory. Blue lines = randomly selected model runs.

Figure D.6. Results of Asthma/Albuterol Model: Projected Percentage Change in Total Deaths Compared to Baseline Under All Climate Change Scenarios by Age Group, 2024–2040



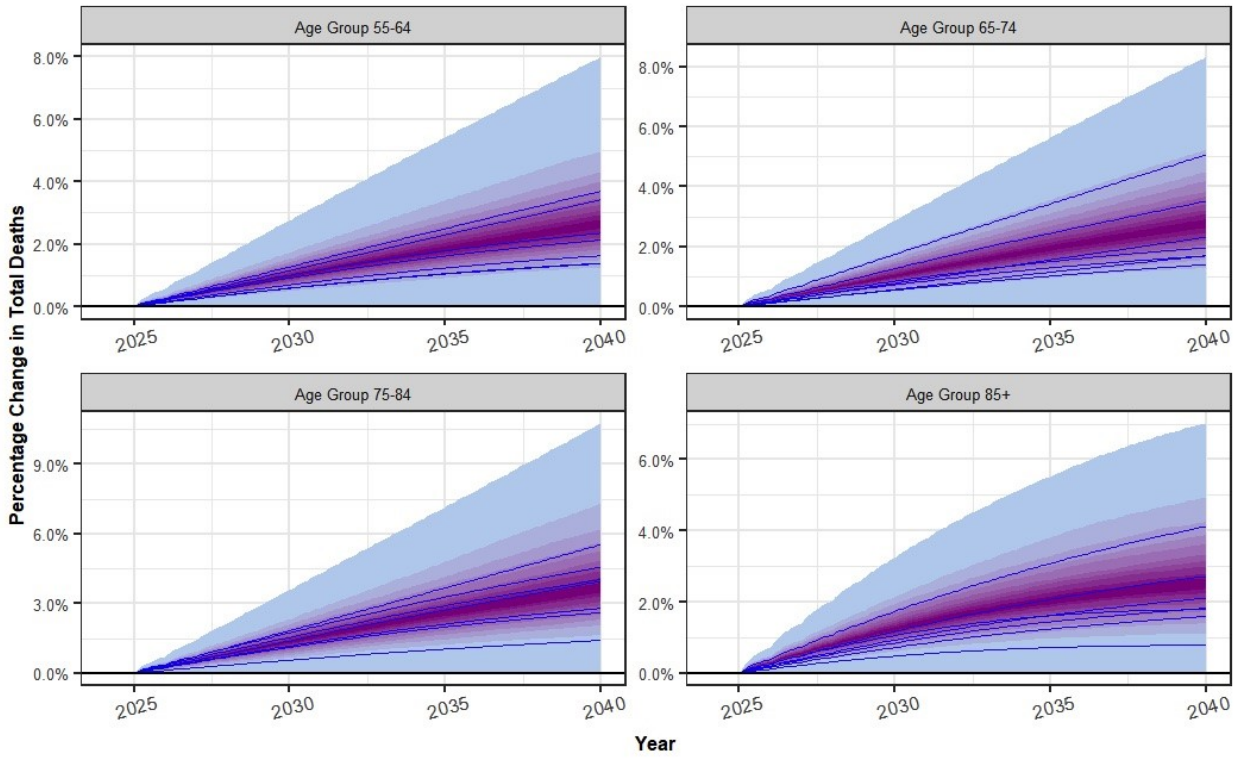
NOTE: Blue and violet areas = range of projected total deaths under selected climate scenarios; violet = more likely trajectory, blue = less likely trajectory. Blue lines = randomly selected model runs.

Figure D.7. Results of End-Stage Renal Disease/Heparin Model: Projected Percentage Change in Total Deaths Compared to Baseline Under All Climate Change Scenarios by Age Group, 2024–2040



NOTE: Blue and violet areas = range of projected total deaths under selected climate scenarios; violet = more likely trajectory, blue = less likely trajectory. Blue lines = randomly selected model runs.

Figure D.8. Results of Alzheimer's/Donepezil Model: Projected Percentage Change in Total Deaths Compared to Baseline Under All Climate Change Scenarios by Age Group, 2024–2040



NOTE: Blue and violet areas = range of projected total deaths under selected climate scenarios; violet = more likely trajectory, blue = less likely trajectory. Blue lines = randomly selected model runs.

Abbreviations

AHRQ	Agency for Healthcare Research and Quality
BMI	body mass index
CDC	Centers for Disease Control and Prevention
CKD	chronic kidney disease
COPD	chronic obstructive pulmonary disease
COVID-19	coronavirus disease 2019
CVD	cardiovascular disease
ED	emergency department
EPA	Environmental Protection Agency
ESRD	end-stage renal disease
FDA	Food and Drug Administration
GHG	greenhouse gases
HHS	U.S. Department of Health and Human Services
ICD	International Classification of Diseases
IPCC	Intergovernmental Panel for Climate Change
ODE	ordinary differential equations
PM2.5	particulate matter 2.5
ppb	parts per billion
RRT	renal replacement therapy
SSP	Shared Socioeconomic Pathway
WHO	World Health Organization

References

Abadi, Azar M., Yeongjin Gwon, Matthew O. Gribble, Jesse D. Berman, Rocky Bilotta, Mike Hobbins, and Jesse E. Bell, "Drought and All-Cause Mortality in Nebraska from 1980 to 2014: Time-Series Analyses by Age, Sex, Race, Urbanicity and Drought Severity," *Science of the Total Environment*, Vol. 840, 2022.

Akushevich, I., A. Yashkin, M. Kovtun, J. Kravchenko, K. Arbeev, and A. I. Yashin, "Forecasting Prevalence and Mortality of Alzheimer's Disease Using the Partitioning Models," *Experimental Gerontology*, Vol. 174, 2023.

Alexeeff, Stacey E., Gabriele G. Pfister, and Doug Nychka, "A Bayesian Model for Quantifying the Change in Mortality Associated with Future Ozone Exposures Under Climate Change," *Biometrics*, Vol. 72, 2016.

Al-Shihabi, Fatima, Anna Moore, and Tahseen A. Chowdhury, "Diabetes and Climate Change," *Diabetic Medicine*, Vol. 40, 2023.

Alzheimer's Association, "What Is Alzheimer's Disease?" webpage, undated. As of August 28, 2024:
https://www.alz.org/alzheimers-dementia/what-is-alzheimers

Alzheimer's Association, "2024 Alzheimer's Disease Facts and Figures," *Alzheimer's and Dementia*, Vol. 20, No. 5, May 2024.

American Heart Association, "What Is Cardiovascular Disease?" webpage, undated. As of August 28, 2024:
https://www.heart.org/en/health-topics/consumer-healthcare/what-is-cardiovascular-disease

Anderson, G. Brooke, and Michelle L. Bell, "Heat Waves in the United States: Mortality Risk during Heat Waves and Effect Modification by Heat Wave Characteristics in 43 U.S. Communities," *Environmental Health Perspectives*, Vol. 119, 2011.

Archer, Elizabeth J., Craig Baker-Austin, Timothy J. Osborn, Natalia R. Jones, Jaime Martínez-Urtaza, Joaquín Trinanes, James D. Oliver, Felipe J. Colón González, and Iain R. Lake, "Climate Warming and Increasing Vibrio Vulnificus Infections in North America," *Scientific Reports*, Vol. 13, 2023.

Arias, P.A., N. Bellouin, E. Coppola, R. G. Jones, G. Krinner, J. Marotzke, V. Naik, M. D. Palmer, G.-K. Plattner, J. Rogelj, et al., "Technical Summary," in V. Masson-Delmotte, P. Zhai, A. Pirani, S. L. Connors, C. Péan, S. Berger, N. Caud, Y. Chen, L. Goldfarb, M. I. Gomis, M. Huang, K. Leitzell, E. Lonnoy, J. B. R. Matthews, T. K. Maycock, T. Waterfield, O. Yelekçi, R. Yu, and B. Zhou, eds., *Climate Change 2021: The Physical Science Basis. Contribution of Working Group I to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change*, Cambridge University Press, 2021.

Bell, Sue Anne, Theodore J. Iwashyna, Xingyu Zhang, Bingxin Chen, and Matthew A. Davis, "All-Cause Hospitalizations After Large-Scale Hurricanes Among Older Adults: A Self-Controlled Case Series Study," *Prehospital and Disaster Medicine*, Vol. 36, 2021.

Bell, Sue Anne, Marie Lynn Miranda, Julie P. W. Bynum, and Matthew A. Davis, "Mortality After Exposure to a Hurricane Among Older Adults Living with Dementia," *JAMA Network Open*, Vol. 6, 2023.

Berberian, Alique G., David J. X. Gonzalez, and Lara J. Cushing, "Racial Disparities in Climate Change–Related Health Effects in the United States," *Current Environmental Health Reports*, Vol. 9, 2022.

Blum, Matthew F., Yijing Feng, G. Brooke Anderson, Dorry L. Segev, Mara McAdams-Demarco, and Morgan E. Grams, "Hurricanes and Mortality Among Patients Receiving Dialysis," *Journal of the American Society of Nephrology*, Vol. 33, 2022.

Blum, Matthew F., Yijing Feng, Cascade P. Tuholske, Byoungjun Kim, Mara A. McAdams Demarco, Brad C. Astor, and Morgan E. Grams, "Extreme Humid-Heat Exposure and Mortality Among Patients Receiving Dialysis," *American Journal of Kidney Diseases*, in press.

Bobb, Jennifer F., Ziad Obermeyer, Yun Wang, and Francesca Dominici, "Cause-Specific Risk of Hospital Admission Related to Extreme Heat in Older Adults," *JAMA*, Vol. 312, 2014.

Bongioanni, Paolo, Renata Del Carratore, Silvia Corbianco, Andrea Diana, Gabriella Cavallini, Silvia M. Masciandaro, Marco Dini, and Roberto Buizza, "Climate Change and Neurodegenerative Diseases," *Environmental Research*, Vol. 201, 2021.

Burke, Marshall, Anne Driscoll, Sam Heft-Neal, Jiani Xue, Jennifer Burney, and Michael Wara, "The Changing Risk and Burden of Wildfire in the United States," *Proceedings of the National Academy of Sciences*, Vol. 118, 2021.

Carnes, Bruce A., David Staats, and Bradley J. Willcox, "Impact of Climate Change on Elder Health," *The Journals of Gerontology: Series A*, Vol. 69, 2014.

CDC—*See* Centers for Disease Control and Prevention.

Centers for Disease Control and Prevention, "Heart Disease Facts," webpage, undated-a. As of August 28, 2024: https://www.cdc.gov/heart-disease/data-research/facts-stats/index.html

Centers for Disease Control and Prevention, "Heat and Pregnancy," webpage, undated-b. As of August 28, 2024: https://www.cdc.gov/extreme-heat/risk-factors/heat-and-pregnancy.html

Centers for Disease Control and Prevention, "Leading Causes of Death," webpage, undated-c. As of August 28, 2024: https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm

Centers for Disease Control and Prevention, "Most Recent National Asthma Data," webpage, undated-d. As of August 28, 2024: https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm

Centers for Disease Control and Prevention, *Chronic Kidney Disease in the United States, 2023*, May 2023.

Cheng, Jian, Zhiwei Xu, Hilary Bambrick, Vanessa Prescott, Ning Wang, Yuzhou Zhang, Hong Su, Shilu Tong, and Wenbiao Hu, "Cardiorespiratory Effects of Heatwaves: A Systematic Review and Meta-Analysis of Global Epidemiological Evidence," *Environmental Research*, Vol. 177, 2019.

Clayton, Susam "Climate Change and Mental Health," *Current Environmental Health Reports*, Vol. 8, No. 1, 2021.

ClevelandClinic, "Cardiovascular Disease," webpage, undated. As of August 28, 2024: https://my.clevelandclinic.org/health/diseases/21493-cardiovascular-disease

Cohen, Daryl, "94.7M Americans Live in Coastline Regions," *America Counts: Stories*, U.S. Census Bureau, July 15, 2019.

Cronin, Robert E., and Robert F. Reilly, "Unfractionated Heparin for Hemodialysis: Still the Best Option," *Seminars in Dialysis*, Vol. 23, 2010.

Davis, Robert E., Elizabeth K. Driskill, and Wendy M. Novicoff, "The Association between Weather and Emergency Department Visitation for Diabetes in Roanoke, Virginia," *International Journal of Biometeorology*, Vol. 66, 2022.

Debbage, Neil, and J. Marshall Shepherd, "The Urban Heat Island Effect and City Contiguity," *Computers, Environment and Urban Systems*, Vol. 54, 2015.

Edelson, Paul J., Rachel Harold, Joel Ackelsberg, Jeffrey S. Duchin, Steven J. Lawrence, Yukari C. Manabe, Matt Zahn, and Regina C. Larocque, "Climate Change and the Epidemiology of Infectious Diseases in the United States," *Clinical Infectious Diseases*, Vol. 76, 2023.

Einzinger, Patrick, Ruth Leskovar, and Claudia Wytrzens, "A Comparison of System Dynamics and Markov Models for Cost-Effectiveness Analysis of Chronic Diseases," in *Proceedings of the International Workshop on Innovative Simulation for Health Care*, Backfrieder, Bruzzone, Longo, Novak, Rosen, eds., 107-14, DIME Università di Genova, 2012.

EPA—*See* U.S. Environmental Protection Agency.

FDA—*See* U.S. Food and Drug Administration.

Federal Emergency Management Agency, "Hurricane," webpage, undated. As of August 28, 2024:
https://community.fema.gov/ProtectiveActions/s/article/Hurricane

Flores, Aaron B., Timothy W. Collins, Sara E. Grineski, and Jayajit Chakraborty, "Disparities in Health Effects and Access to Health Care Among Houston Area Residents After Hurricane Harvey," *Public Health Reports*, Vol. 135, 2020.

Fuchs, Flávio D., and Paul K. Whelton, "High Blood Pressure and Cardiovascular Disease," *Hypertension*, Vol. 75, 2020.

Fyfe, J., B. Fox-Kemper, R. Kopp, and G. Garner, "Summary for Policymakers of the Working Group I Contribution to the IPCC Sixth Assessment Report—Data for Figure SPM.8 (v20210809)," NERC EDS Centre for Environmental Data Analysis, 2021. As of August 28, 2024:
https://dx.doi.org/10.5285/98af2184e13e4b91893ab72f301790db

Gasparrini, Antonio, Yuming Guo, Masahiro Hashizume, Eric Lavigne, Antonella Zanobetti, Joel Schwartz, Aurelio Tobias, Shilu Tong, Joacim Rocklöv, Bertil Forsberg, Michela Leone, Manuela De Sario, Michelle L. Bell, Yue-Liang Leon Guo, Chang-Fu Wu, Haidong Kan, Seung-Muk Yi, Micheline De Sousa Zanotti Stagliorio Coelho, Paulo Hilario Nascimento Saldiva, Yasushi Honda, Ho Kim, and Ben Armstrong, "Mortality Risk Attributable to High and Low Ambient Temperature: A Multicountry Observational Study," *The Lancet*, Vol. 386, 2015.

GBD Chronic Kidney Disease Collaboration, "Global, Regional, and National Burden of Chronic Kidney Disease, 1990–2017: A Systematic Analysis for the Global Burden of Disease Study 2017," *The Lancet*, Vol. 395, No. 10225, February 29, 2020.

Gorris, Morgan E., Kathleen K. Treseder, Charles S. Zender, and James T. Randerson, "Expansion of Coccidioidomycosis Endemic Regions in the United States in Response to Climate Change," *GeoHealth*, Vol. 3, No. 10, October 2019.

Gronlund, Carina J., Kyle P. Sullivan, Yonathan Kefelegn, Lorraine Cameron, and Marie S. O'Neill, "Climate Change and Temperature Extremes: A Review of Heat- and Cold-Related Morbidity and Mortality Concerns of Municipalities," *Maturitas*, Vol. 114, 2018.

Guirguis, Kristen, Rupa Basu, Wael K. Al-Delaimy, Tarik Benmarhnia, Rachel E. S. Clemesha, Isabel Corcos, Janin Guzman-Morales, Brittany Hailey, Ivory Small, Alexander Tardy, Devesh Vashishtha, Joshua G. Zivin, and Alexander Gershunov, "Heat, Disparities, and Health Outcomes in San Diego County's Diverse Climate Zones," *GeoHealth*, Vol. 2, 2018.

Gutierrez, Miguel Pardinas, Paquita Zuidema, Mehdi Mirsaeidi, Michael Campos, and Naresh Kumar, "Association Between African Dust Transport and Acute Exacerbations of COPD in Miami," *Journal of Clinical Medicine*, Vol. 9, 2020.

Ha, Sandie, Kelly Nguyen, Danping Liu, Tuija Männistö, Carrie Nobles, Seth Sherman, and Pauline Mendola, "Ambient Temperature and Risk of Cardiovascular Events at Labor and Delivery: A Case-Crossover Study," *Environmental Research*, Vol. 159, 2017.

Harvard Medical School, "Target Heart Rate on a Beta Blocker," webpage, undated. As of August 28, 2024: http://www.health.harvard.eduwww.health.harvard.edu/heart-health/target-heart-rate-on-a-beta-blocker

HHS—*See* U.S. Department of Health and Human Services.

Homer, Jack B., and Gary B. Hirsch, "System Dynamics Modeling for Public Health: Background and Opportunities," *American Journal of Public Health*, Vol. 96, 2006.

Howard, David, Rebecca Zhang, Yijian Huang, and Nancy Kutner, "Hospitalization Rates Among Dialysis Patients During Hurricane Katrina," *Prehospital and Disaster Medicine*, Vol. 27, 2012.

Howard, Luke, *The Climate of London*, [1883] 2012.

Huang, Wenzhong, Yuan Gao, Rongbin Xu, Zhengyu Yang, Pei Yu, Tingting Ye, Elizabeth A. Ritchie, Shanshan Li, and Yuming Guo, "Health Effects of Cyclones: A Systematic Review and Meta-Analysis of Epidemiological Studies," *Environmental Health Perspectives*, Vol. 131, 2023.

Human Mortality Database, "U.S.A. Total Population," webpage, undated. As of August 28, 2024: https://www.mortality.org/Country/Country?cntr=USA

Iman, Ronald L., Jon C. Helton, and James E. Campbell, "An Approach to Sensitivity Analysis of Computer Models: Part II—Ranking of Input Variables, Response Surface Validation, Distribution Effect and Technique Synopsis," *Journal of Quality Technology*, Vol. 13, 1981.

Institute for Health Metrics and Evaluation, "Global Burden of Disease (GBD)," webpage, undated. As of August 28, 2024: https://www.healthdata.org/research-analysis/gbd

IPCC—*See* Intergovernmental Panel on Climate Change.

Jaffe, Dan, Duli Chand, Will Hafner, Anthony Westerling, and Dominick Spracklen, "Influence of Fires on O3 Concentrations in the Western US," *Environmental Science & Technology*, Vol. 42, 2008.

Johnson, Sandra Leigh, "New Estimates Show U.S. Population Growth Continues to Slow," *America Counts: Stories*, U.S. Census Bureau, December 30, 2019.

Jung, Chau-Ren, Yu-Ting Lin, and Bing-Fang Hwang, "Ozone, Particulate Matter, and Newly Diagnosed Alzheimer's Disease: A Population-Based Cohort Study in Taiwan," *Journal of Alzheimer's Disease*, Vol. 44, 2015.

Khalili, Roxana, Scott M. Bartell, Xuefei Hu, Yang Liu, Howard H. Chang, Candice Belanoff, Matthew J. Strickland, and Verónica M. Vieira, "Early-Life Exposure to PM2.5 and Risk of Acute Asthma Clinical Encounters Among Children in Massachusetts: A Case-Crossover Analysis," *Environmental Health*, Vol. 17, 2018.

Khatana, Sameed Ahmed M., Rachel M. Werner, and Peter W, Groeneveld. 2022, "Association of Extreme Heat and Cardiovascular Mortality in the United States: A County-Level Longitudinal Analysis from 2008 to 2017," *Circulation*, Vol. 146, 2022.

Kim, Ejin, Hyuk Huh, Yongwon Mo, Jae Yoon Park, Jiyun Jung, Hajeong Lee, Sejoong Kim, Dong Ki Kim, Yon Su Kim, and Chun Soo Lim, "Long-Term Ozone Exposure and Mortality in Patients with Chronic Kidney Disease: A Large Cohort Study," *BMC Nephrology*, Vol. 25, 2024.

Kim, Sun-Young, Esther Kim, and Woo Jin Kim, "Health Effects of Ozone on Respiratory Diseases," *Tuberculosis and Respiratory Diseases*, Vol. 83, 2020.

Kolbe, Allison, and Trini Beleche, *Linking Medical Product Manufacturing Locations with Natural Hazard Risk: Implications for the Medical Product Supply Chain*, Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services July 2024.

Kovesdy, Csaba P., "Epidemiology of Chronic Kidney Disease: An Update 2022," *Kidney International Supplements*, Vol. 12, 2022.

Leffers, Jeanne M., "Climate Change and Health of Children: Our Borrowed Future," Jopurnal of Pediatric Health Care, Vol. 35, No. 1, 2022.

Levi, Marcel, "Hemostasis and Thrombosis in Extreme Temperatures (Hypo- and Hyperthermia)," *Seminars in Thrombosis and Hemostasis*, 2018.

Levy, Karen, Shanon M. Smith, and Elizabeth J. Carlton, "Climate Change Impacts on Waterborne Diseases: Moving Toward Designing Interventions," *Current Environmental Health Reports*, June 2019.

Li, Xing, Qing Chen, Xueyan Zheng, Yongzhi Li, Min Han, Tao Liu, Jianpeng Xiao, Lingchuan Guo, Weilin Zeng, Junfeng Zhang, and Wenjun Ma, "Effects of Ambient Ozone Concentrations with Different Averaging Times on Asthma Exacerbations: A Meta-Analysis," *Science of The Total Environment*, Vol. 691, 2019.

Limaye, Vijay S., Wendy Max, Juanita Constible, and Kim Knowlton, "Estimating the Health-Related Costs of 10 Climate-Sensitive U.S. Events During 2012," *GeoHealth*, Vol. 3, 2019.

Lin, Cynthia, Timothy Wade, and Elizabeth Hilborn, "Flooding and Clostridium Difficile Infection: A Case-Crossover Analysis," *International Journal of Environmental Research and Public Health*, Vol. 12, 2015.

Lynch, Victoria D., and Jeffrey Shaman, "Waterborne Infectious Diseases Associated with Exposure to Tropical Cyclonic Storms, United States, 1996–2018," *Emerging Infectious Diseases*, Vol. 29, 2023.

Makrufardi, Firdian, Amja Manullang, Desy Rusmawatiningtyas, Kian Fan Chung, Sheng-Chieh Lin, and Hsiao-Chi Chuang, "Extreme Weather and Asthma: A Systematic Review and Meta-Analysis," *European Respiratory Review*, Vol. 32, 2023.

Manisalidis, Ioannis, Elisavet Stavropoulou, Agathangelos Stavropoulos, and Eugenia Bezirtzoglou, "Environmental and Health Impacts of Air Pollution: A Review," *Frontiers in Public Health*, Vol. 8, 2020.

Masson-Delmotte, V., P. Zhai, A. Pirani, S. L. Connors, C. Péan, S. Berger, N. Caud, Y. Chen, L. Goldfarb, M. I. Gomis, M. Huang, K. Leitzell, E. Lonnoy, J. B. R. Matthews, T. K. Maycock, T. Waterfield, O. Yelekçi, R. Yu, and B. Zhou, eds., *Climate Change 2021: The Physical Science Basis. Contribution of Working Group I to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change*, Cambridge University Press, 2021.

Mazidi, Mohsen, and John R. Speakman, "Predicted Impact of Increasing Average Ambient Temperature over the Coming Century on Mortality from Cardiovascular Disease and Stroke in the USA," *Atherosclerosis*, Vol. 313, 2020.

Medical News Today, "Metoprolol, Oral Tablet," webpage, undated. As of August 28, 2024: https://www.medicalnewstoday.com/articles/metoprolol-oral-tablet#about

Monaghan, Andrew J., Sean M. Moore, Kevin M. Sampson, Charles B. Beard, and Rebecca J. Eisen, "Climate Change Influences on the Annual Onset of Lyme Disease in the United States," *Ticks and Tick-Borne Diseases*, Vol. 6, 2015.

Monsour, Molly, Emily Clarke-Rubright, Wil Lieberman-Cribbin, Christopher Timmins, Emanuela Taioli, Rebecca M Schwartz, Samantha S. Corley, Anna M Laucis, and Rajendra A Morey, "The Impact of Climate Change on the Prevalence of Mental Illness Symptoms," *Journal of Affective Disorders*, March 2022.

Morgado, Michele E., Chengsheng Jiang, Jordan Zambrana, Crystal Romeo Upperman, Clifford Mitchell, Michelle Boyle, Amy R. Sapkota, and Amir Sapkota, "Climate Change, Extreme Events, and Increased Risk of Salmonellosis: Foodborne Diseases Active Surveillance Network (FoodNet), 2004–2014," *Environmental Health*, Vol. 20, 2021.

NASEM—*See* National Academies of Science, Engineering, and Medicine.

National Academies of Science, Engineering, and Medicine, *Building Resilience into the Nation's Medical Product Supply Chains*, 2022.

National Center for Biotechnology Information, "PubChem Compound Summary for CID 2083, Albuterol," webpage, undated-a. As of August 28, 2024: https://pubchem.ncbi.nlm.nih.gov/compound/Albuterol

National Center for Biotechnology Information, "PubChem Compound Summary for Heparin," webpage, undated-b. As of August 28, 2024: https://pubchem.ncbi.nlm.nih.gov/compound/Heparin

National Center for Health Statistics, "Mortality in the United States, 2022," *NCHS Data Brief*, No. 492, March 2024.

National Institute of Diabetes and Digestive and Kidney Diseases, "Kidney Disease Statistics for the United States, Fast Facts on Kidney Disease," webpage, undated-a. As of August 28, 2024: https:// www.niddk.nih.gov/health-information/health-statistics/kidney-disease

National Institute of Diabetes and Digestive and Kidney Diseases, "What Is Chronic Kidney Disease?" webpage, undated-b. As of August 28, 2024: https://www.niddk.nih.gov/health-information/kidney-disease/chronic-kidney-disease-ckd/what-is-chronic-kidney-disease

National Institute of Diabetes and Digestive and Kidney Diseases, *End Stage Renal Disease*, 2023.

National Institute on Aging, "How Is Alzheimer's Disease Treated?" webpage, undated. As of August 28, 2024: https://www.nia.nih.gov/health/alzheimers-treatment/how-alzheimers-disease-treated

National Kidney Foundation, "Hemodialysis," webpage, undated. As of August 28, 2024: https://www.kidney.org/atoz/content/hemodialysis#:~:text=In%20a%20dialysis%20center%2C%20hemodialysis,for%20shorter%20hours%20each%20time

National Oceanic and Atmospheric Administration, "Wildfire Climate Connection, " webpage, last updated July 24, 2023. As of September 4, 2024: https://www.noaa.gov/noaa-wildfire/wildfire-climate-connection

National Oceanic and Atmospheric Administration, National Centers for Environmental Information, "U.S. Climate Summary for June 2024," July 11, 2024.

Neumann, James E., Susan C. Anenberg, Kate R. Weinberger, Meredith Amend, Sahil Gulati, Allison Crimmins, Henry Roman, Neal Fann, and Patrick L. Kinney, "Estimates of Present and Future Asthma Emergency Department Visits Associated with Exposure to Oak, Birch, and Grass Pollen in the United States," *GeoHealth*, Vol. 3, 2019.

Next Foundry for American Biotechnology, Advanced Regenerative Manufacturing Institute, and Nexight Group, *Essential Medicines Supply Chain and Manufacturing Resilience Assessment*, U.S. Department of Health and Human Services, May 2022.

NIDDK—*See* National Institute of Diabetes and Digestive and Kidney Diseases.

NOAA—*See* National Oceanic and Atmospheric Administration.

Ortendahl, Jesse D., Allison L. Diamant, Peter P. Toth, Dasha Cherepanov, Amanda L. Harmon, and Michael S. Broder, "Protecting the Gains: What Changes Are Needed to Prevent a Reversal of the Downward Cardiovascular Disease Mortality Trend?" *Clinical Cardiology*, Vol. 42, 2019.

Parker, Eva Rawlings, "The Influence of Climate Change on Skin Cancer Incidence: A Review of the Evidence," *International Journal of Women's Dermatology*, Vol. 7, 2021.

Rasking, Leen, Kenneth Vanbrabant, Hannelore Bové, Michelle Plusquin, Katrien De Vusser, Harry A. Roels, and Tim S. Nawrot, "Adverse Effects of Fine Particulate Matter on Human Kidney Functioning: A Systematic Review," *Environmental Health*, Vol., 21, 2022.

Remigio, Richard V., Chengsheng Jiang, Jochen Raimann, Peter Kotanko, Len Usvyat, Frank W. Maddux, Patrick Kinney, and Amir Sapkota, "Association of Extreme Heat Events with Hospital Admission or Mortality Among Patients with End-Stage Renal Disease," *JAMA Network Open*, Vol. 2, 2019.

Rice, R. Byron, Katie Boaggio, Nicole E. Olson, Kristen M. Foley, Christopher P. Weaver, Jason D. Sacks, Stephen R. McDow, Amara L. Holder, and Stephen D. Leduc, "Wildfires Increase Concentrations of Hazardous Air Pollutants in Downwind Communities," *Environmental Science and Technology*, Vol. 57, 2023.

Rowland, Sebastian T., Amelia K. Boehme, Johnathan Rush, Allan C. Just, and Marianthi-Anna Kioumourtzoglou, "Can Ultra Short-Term Changes in Ambient Temperature Trigger Myocardial Infarction?" *Environment International*, Vol. 143, 2020.

Salas, R. N., L. G. Burke, J. Phelan, G. A. Wellenius, E. J. Orav, and A. K. Jha, "Impact of Extreme Weather Events on Healthcare Utilization and Mortality in the United States," *Nature Medicine*, Vol. 30, 2024.

Singh, Nidhi, Ashtyn Tracy Areal, Susanne Breitner, Siqi Zhang, Stefan Agewall, Tamara Schikowski, and Alexandra Schneider, "Heat and Cardiovascular Mortality: An Epidemiological Perspective," *Circulation Research*, Vol. 134, 2024.

Soetaert, Karline, Thomas Petzoldt, and R. Woodrow Setzer, "Solving Differential Equations in R: PackagedeSolve," *Journal of Statistical Software*, Vol. 33, 2010.

Soneja, Sutyajeet, Chengsheng Jiang, Jared Fisher, Crystal Romeo Upperman, Clifford Mitchell, and Amir Sapkota, "Exposure to Extreme Heat and Precipitation Events Associated with Increased Risk of Hospitalization for Asthma in Maryland, U.S.A," *Environmental Health*, Vol. 15, 2016.

Song, Jian, Zhen Ding, Hao Zheng, Zhiwei Xu, Jian Cheng, Rubing Pan, Weizhuo Yi, Jing Wei, and Hong Su, "Short-Term PM1 and PM2.5 Exposure and Asthma Mortality in Jiangsu Province, China: What's the Role of Neighborhood Characteristics?" *Ecotoxicology and Environmental Safety*, Vol. 241, 2022.

Stella, A. B., A. Galmonte, M. Deodato, S. Ozturk, J. Reis, and P. Manganotti, "Climate Change and Global Warming: Are Individuals with Dementia—Including Alzheimer's Disease—at a Higher Risk?" *Current Alzheimer's Research*, Vol. 20, 2023.

Straight Nursing, "All Aboard for Albuterol," webpage, undated. As of August 28, 2024: https://straightanursingstudent.com/albuterol-administration/

Sun, Jian, Joshua S. Fu, Kan Huang, and Yang Gao, "Estimation of future $PM_{2.5}$- and Ozone-Related Mortality over the Continental United States in a Changing Climate: An Application of High-Resolution Dynamical Downscaling Technique," *Journal of the Air & Waste Management Association*, Vol. 65, 2015.

Sun, Shengzhi, Keith R. Spangler, Kate R. Weinberger, Jeff D. Yanosky, Joseph M. Braun, and Gregory A. Wellenius, "Ambient Temperature and Markers of Fetal Growth: A Retrospective Observational Study of 29 Million U.S. Singleton Births," *Environmental Health Perspectives*, Vol. 127, No. 6, 2019.

Swerdel, Joel N., Teresa M. Janevic, Nora M. Cosgrove, and John B. Kostis, "The Effect of Hurricane Sandy on Cardiovascular Events in New Jersey," *Journal of the American Heart Association*, Vol. 3, 2014.

Tavera Busso, Iván, Ana Carolina Mateos, Luis Isaías Juncos, Norma Canals, and Hebe Alejandra Carreras, "Kidney Damage Induced by Sub-Chronic Fine Particulate Matter Exposure," *Environment International*, Vol. 121, Part 1, December 2018.

Tee Lewis, P. Grace, Weihsueh A. Chiu, Ellu Nasser, Jeremy Proville, Aurora Barone, Cloelle Danforth, Bumsik Kim, Jolanda Prozzi, and Elena Craft, "Characterizing Vulnerabilities to Climate Change Across the United States," *Environment International*, Vol. 172, 2023.

Tsao, C. W., A. W. Aday, Z. I. Almarzooq, "Heart Disease and Stroke Statistics—2023 Update: A Report From the American Heart Association," *Circulation*, 2023.

U.S. Census Bureau, "Population Projections," webpage, undated. As of August 28, 2024: https://www.census.gov/programs-surveys/popproj.html

U.S. Department of Health and Human Services, "Extreme Heat," webpage, undated. As of August 28, 2024: https://www.hhs.gov/climate-change-health-equity-environmental-justice/climate-change-health-equity/climate-health-outlook/extreme-heat/index.html

U.S. Environmental Protection Agency, "Climate Change Indicators: Heatwaves," webpage, undated-a. As of August 28, 2024: https://www.epa.gov/climate-indicators/climate-change-indicators-heat-waves

U.S. Environmental Protection Agency, "Climate Change Indicators: Tropical Cyclone Activity," webpage, undated-b. As of August 28, 2024: https://www.epa.gov/climate-indicators/climate-change-indicators-tropical-cyclone-activity

U.S. Environmental Protection Agency, "Climate Change Indicators: U.S. and Global Temperature," webpage, undated-c. As of August 28, 2024: https:/www.epa.gov/climate-indicators/climate-change-indicators-us-and-global-temperature

U.S. Environmental Protection Agency, "Climate Change Indicators: Weather and Climate," webpage, undated-d.

U.S. Environmental Protection Agency, "Climate Change Indicators: Wildfires," webpage, undated-e. As of August 28, 2024: https://www.epa.gov/climate-indicators/climate-change-indicators-wildfires

U.S. Environmental Protection Agency, "Particulate Matter (PM2.5) Trends," webpage, undated-f. As of August 28, 2024: https://www.epa.gov/air-trends/particulate-matter-pm25-trends

U.S. Food and Drug Administration, "FY25 Legislative Proposals," 2024. As of August 28, 2024: https://www.fda.gov/media/176924/download?attachment#:~:text=The%20FY%202025%20budget%20includes,%2C%20medical%20devices%2C%20and%20foods

U.S. Geological Survey, "Wildfire and Climate Change," webpage, undated. As of August 28, 2024: https://www.usgs.gov/science-explorer/climate/wildfire

Vergadi, Eleni, Glykeria Rouva, Maria Angeli, and Emmanouil Galanakis, "Infectious Diseases Associated with Desert Dust Outbreaks: A Systematic Review," *International Journal of Environmental Research and Public Health*, Vol. 19, 2022.

Wang, Bingyu, Ki-Do Eum, Fatemeh Kazemiparkouhi, Cheng Li, Justin Manjourides, Virgil Pavlu, and Helen Suh, "The Impact of Long-Term PM2.5 Exposure on Specific Causes of Death: Exposure-Response Curves and Effect Modification Among 53 Million U.S. Medicare Beneficiaries," *Environmental Health*, Vol. 19, 2020.

Wang, Yifan, Siyao Xiao, Yuhan Zhang, Howard Chang, Randall V. Martin, Aaron Van Donkelaar, Audrey Gaskins, Yang Liu, Pengfei Liu, and Liuhua Shi, "Long-Term Exposure to PM2.5 Major Components and Mortality in the Southeastern United States," *Environment International*, Vol. 158, 2022.

Wathanavasin, Wannasit, Athiphat Banjongjit, Jeerath Phannajit, Somchai Eiam-Ong, and Paweena Susantitaphong, "Association of Fine Particulate Matter (PM2.5) Exposure and Chronic Kidney Disease Outcomes: A Systematic Review and Meta-Analysis," *Scientific Reports*, Vol. 14, 2024.

Wettstein Z. S., and A. Vaidyanathan, "Psychotropic Medication Prescriptions and Large California Wildfires," *JAMA Network Open*, Vol. 7, No. 2, 2024.

Wilgus, May-Lin, and Maryum Merchant, "Clearing the Air: Understanding the Impact of Wildfire Smoke on Asthma and COPD," *Healthcare*, Vol. 12, 2024.

World Health Organization, "Standard Classification of Medical Conditions," webpage, undated. As of August 28, 2024: https://www.who.int/observatories/global-observatory-on-health-research-and-development/classifications/health-categories

Wu, Keyu, Hung Chak Ho, Hong Su, Cunrui Huang, Hao Zheng, Wenyi Zhang, Junwen Tao, Mohammad Zahid Hossain, Yunquan Zhang, Kejia Hu, Min Yang, Qiyue Wu, Zhiwei Xu, and Jian Cheng, "A Systematic Review and Meta-Analysis of Intraday Effects of Ambient Air Pollution and Temperature on Cardiorespiratory Morbidities: First Few Hours of Exposure Matters to Life," *eBioMedicine*, Vol. 86, 2022.

Xi, Y., D. B. Richardson, A. V. Kshirsagar, T. J. Wade, L. Wyatt, G. C. Peterson, and A. G. Rappold. 2020. "Ambient PM2.5 Exposure and Mortality in U.S. End Stage Renal Disease Patients Receiving In-Center Hemodialysis: 2008–2014," *ISEE Conference Abstracts*, 2020.

Xi, Yuzhi, David B. Richardson, Abhijit V. Kshirsagar, Timothy J. Wade, Jennifer E. Flythe, Eric A. Whitsel, Geoffrey C. Peterson, Lauren H. Wyatt, and Ana G. Rappold, "Effects of Short-Term Ambient PM2.5 Exposure on Cardiovascular Disease Incidence and Mortality Among U.S. Hemodialysis Patients: A Retrospective Cohort Study," *Environmental Health*, Vol. 21, 2022.

Xu, Zhiwei, Shilu Tong, Jian Cheng, Yuzhou Zhang, Ning Wang, Yuqi Zhang, Alimila Hayixibayi, and Wenbiao Hu, "Heatwaves, Hospitalizations for Alzheimer's Disease, and Postdischarge Deaths: A Population-Based Cohort Study," *Environmental Research*, Vol. 178, 2019.

Yang, Li, Wenjie Wan, Caiyan Yu, Cheng Xuan, Pinpin Zheng, and Jing Yan, "Associations Between PM2.5 Exposure and Alzheimer's Disease Prevalence Among Elderly in Eastern China," *Environmental Health*, Vol. 21, 2022.

Yin, Peng, Ya Gao, Renjie Chen, Wei Liu, Cheng He, Junwei Hao, Maigeng Zhou, and Haidong Kan, "Temperature-Related Death Burden of Various Neurodegenerative Diseases Under Climate Warming: A Nationwide Modelling Study," *Nature Communications*, Vol. 14, 2023.

Zhang, Yunquan, Qianqian Xiang, Yong Yu, Zhiying Zhan, Kejia Hu, and Zan Ding, "Socio-Geographic Disparity in Cardiorespiratory Mortality Burden Attributable to Ambient Temperature in the United States," *Environmental Science and Pollution Research*, Vol. 26, 2019.

Zhao, Naizhuo, Lauren Pinault, Olaniyan Toyib, Jennifer Vanos, Michael Tjepkema, and Sabit Cakmak, "Long-Term Ozone Exposure and Mortality from Neurological Diseases in Canada," *Environment International*, Vol. 157, 2021.