MORTALITY RISING: A REVIEW OF THE HUMAN HEALTH CONSEQUENCES OF GLOBAL CLIMATE CHANGE

by

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Jon Runyeon

The objective of this review is to assess the projected health risks associated with climate variability. Primary studies pertaining to the health consequences of skin cancer, cataract incidence, and immunosuppression were used to explore the projected increased incidence of these conditions under the conditions associated with ozone depletion. A similar strategy was used to show the cardiovascular and respiratory risks associated with direct thermal stress and ambient air pollution, and the increased incidence of vector-borne and waterborne diseases present with geographic climate variability. In closing, a section of this review was designed to explore current public health infrastructure intended to protect at-risk populations and to use this analysis to identify what strategies should be prioritized in current public health practices. This paper will combine the two fields of global health and ecology studies, to which this thesis will attribute most of its significance and relevance. With enough appropriate data and correlation done within the research field, preventative global health measures could potentially improve preparedness levels for given illness outbreaks.

Acknowledgements

I would first like to thank Professor Runyeon for not only inspiring this research, but for agreeing to embark on this strenuous yet rewarding journey with me, and for having the utmost confidence that I would succeed. I would also like to thank Professor Carey and Professor Halliwill for standing on my committee and for being the inspiring educators and researchers they are. To Kyle, Dalton, Emily, Erin, Molly, and Kevin, and the rest of the beautiful humans who supported me and made me laugh these past four years, college would have been one boring ride without all of you. Thank you Adria for always believing in me and giving me the wisdom and joy you did during this journey. And last but most certainly not least, thank you to my wonderful family, without whom my education and opportunity to write this would never have been a reality.

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Climate Change: An Introduction

Greenhouse Gases

Established in 1988 by the World Meteorological Organization and the United Nations Environment Programme, the Intergovernmental Panel on Climate Change (IPCC) was formed for the purpose of providing regular reports and analyses on the changes and mitigation influenced by climate change. In a report from 1997, the IPCC published the projection that the Earth would undergo a variety of climactic changes as a result of the combined forces of greenhouse gas emission and other anthropogenic factors (8). According to the United States Environmental Protection Agency (EPA), the primary greenhouse gases include carbon dioxide, methane, nitrous oxide, and fluorinated gases. In 2013, these gas emissions totaled 6,673 million metric tons, representing a 6% increase since the initial recordings in 1990 (51).

The primary greenhouse gas emitted as the result of human activity is carbon dioxide, which has shown at atmospheric concentration increase of approximately 7% since 1990 (52). Nitrous oxide emission, which is typically the result of agricultural practices, has also shown to be threatening to climate change variables with an increase by 8%. However, the most notable increase in greenhouse gas emissions is the 73% increase in fluorinated gas concentration. These gases are most commonly emitted by various commercial, industrial, and household practices. The sectors responsible for the largest shares of emissions are electricity and transportation, respectively.

A Global Warming Potential (GWP) is calculated for each greenhouse gas and is representative of the duration a particular gas will remain in the atmosphere, as well as how strongly that gas is able to absorb energy. Gases determined to have a higher GWP value will absorb more energy than those with a lower value. Greenhouse gases with higher GWP values, such as the primary greenhouse gases stated previously, have been attributed to the warming of the earth's atmosphere due to their high GWP value and energy capacity.

As a result of increasing greenhouse gas emissions, average global temperature is estimated to increase by 1.4-5.8 °C within the next century (8). In addition, sea levels are predicted to rise by 15-95 cm within the same period of time. This prediction will also likely result in increased global precipitation as well as expand the equatorial tropic zone.

Water

Reliable and clean water sources are critical to sustaining the health of human populations and crucial to larger systemic forces like agriculture, energy, manufacturing, trade, and recreation. Increased temperature results in increased evaporation and drought in some regions while simultaneously having the effect of increased precipitation and tropic expansion in others due to atmospheric carrying capacity. Ocean temperature, similar to the temperature of land, will continue to rise as well due to increased atmospheric temperature and decreased ice cover. According to a report by the IPCC, the ocean's heat content has increased by an average of 14.5×10^{22}J between the years 1955-1998 (4). This equates to an average temperature increase of approximately 0.037 °C in about forty years. The specific implications of this warming, however, are unique.

When water warms, it expands, which has contributed to sea level rise. Further, the earth's icecaps are melting and will continue to gradually contribute to the ocean's global volume as well. According to the EPA, minimum arctic ice cover, typically lowest in the month of September, reached the lowest extent ever recorded in September 2012 (51). The month of March yields the highest arctic ice coverage, on average, for which ice cover extent has slowly been decreasing (figure 1).

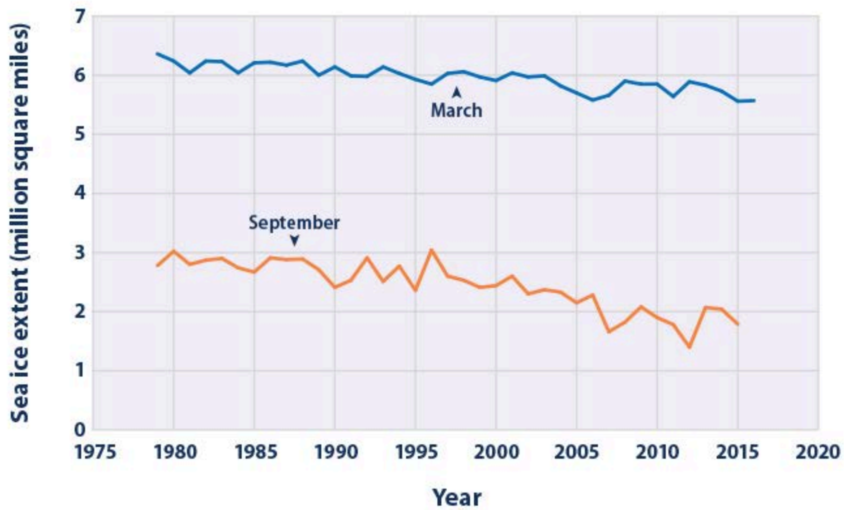

Figure 1: Monthly average arctic ice coverage for March and September

Figure Source: NSIDC (National Snow and Ice Data Center). 2016. Sea ice data image archive. Accessed May 2016. http://nsidc.org/data/seaice_index/archives.html.

In 2015, sea ice extent for the month of March reached a new low, approximately 7% below the 1981-2010 average for the month (36). This increased temperature and consequential sea level rise are projected to have negative health consequences related to rainfall patterns, waterborne disease, and ecosystem toxicity.

Ozone Depletion and Ultraviolet Radiation

Another significant atmospheric change occurring in response to the accumulation of the mentioned greenhouse gases is ozone (O_3) depletion (29). This critical gas is found in the Earth's troposphere, its closest atmospheric level, as well as the stratosphere, which extends 6-30 miles from the Earth's surface and provides a protective chemical covering to ultraviolet (UV) radiation. Ozone's chemical destruction is specifically due to increased concentrations of ozone-depleting substances (ODS) such as chlorofluorocarbons (CFCs), hydrochlorofluorocarbons (HCFCs), methyl chloroform, halons, and carbon tetrachloride (52). When these substances are emitted, often by human machinery that utilizes the chemicals, their degradation is slow enough that they will often not break down until the force of UV radiation acts on them within the stratosphere. At this point, ODS deplete ozone levels through the release of chlorine and bromine resulting from the chemical breakdown.

While ozone accumulation can be harmful in terms of air pollution close to the Earth's surface, it acts as a protective barrier at a further proximity within the stratosphere. With the chemical thinning of ozone in the stratosphere, increased concentrations of UV radiation are able to reach the Earth's surface. UV Radiation exists in three primary forms determined by wavelength: UV-A (320-400 nm), UV-B (290-320 nm), and UV-C (100-290 nm) (51). High doses of UV are threatening to both agricultural and human health. The cellular damage caused by UV radiation has been strongly correlated with increasing incidence of conditions such as immunosuppression and increased susceptibility to infectious disease, skin cancer, cataract formation, and others (31). Admittedly, the extent of this reach is challenging to quantify on a global scale due to the cascade of secondary effects UV radiation exposure is likely to have as well.

The purpose of this work is to introduce global climate change and show the numerous studies and cases that support the positive correlation between global warming and human mortality. The evidence in support of this argument is strong. This work integrates and represents a holistic review of the significant cases of climate variability that have posed major threats to human health. The climate research and projections performed within the field of environmental studies and human health should contribute to finding and implementing preventative global health measures that could strengthen preparedness levels for natural disasters, disease outbreak, and incidence of negative health consequences and infections within high-risk populations.

Methods

Articles were collected from the databases of PubMed, Google Scholar, Web of Science, and the University of Oregon Library. Early searches were conducted using a varied combination of search terms such as “health consequences, climate change” or “ozone depletion, human mortality” including others with terms pertaining to specific health consequences. Additionally, articles were sought out by reviewing literature and various cited references that were used to protect and support research. Articles unable to be obtained through this means were requested and obtained through interlibrary loan. Article search was limited to those published in English between the years of 1975 and 2016. Primary case studies as well as secondary review style articles were collected and saved electronically following thorough review and organization by health area. Articles were further divided into categories according to the specific health complication to which they pertained. For example, the subheading of “UV Radiation” was further segmented to the categories of skin cancer, cataract incidence, and immunosuppression. This systematic organization is also represented in a hierarchical table of the selection process for this review (figure 2).

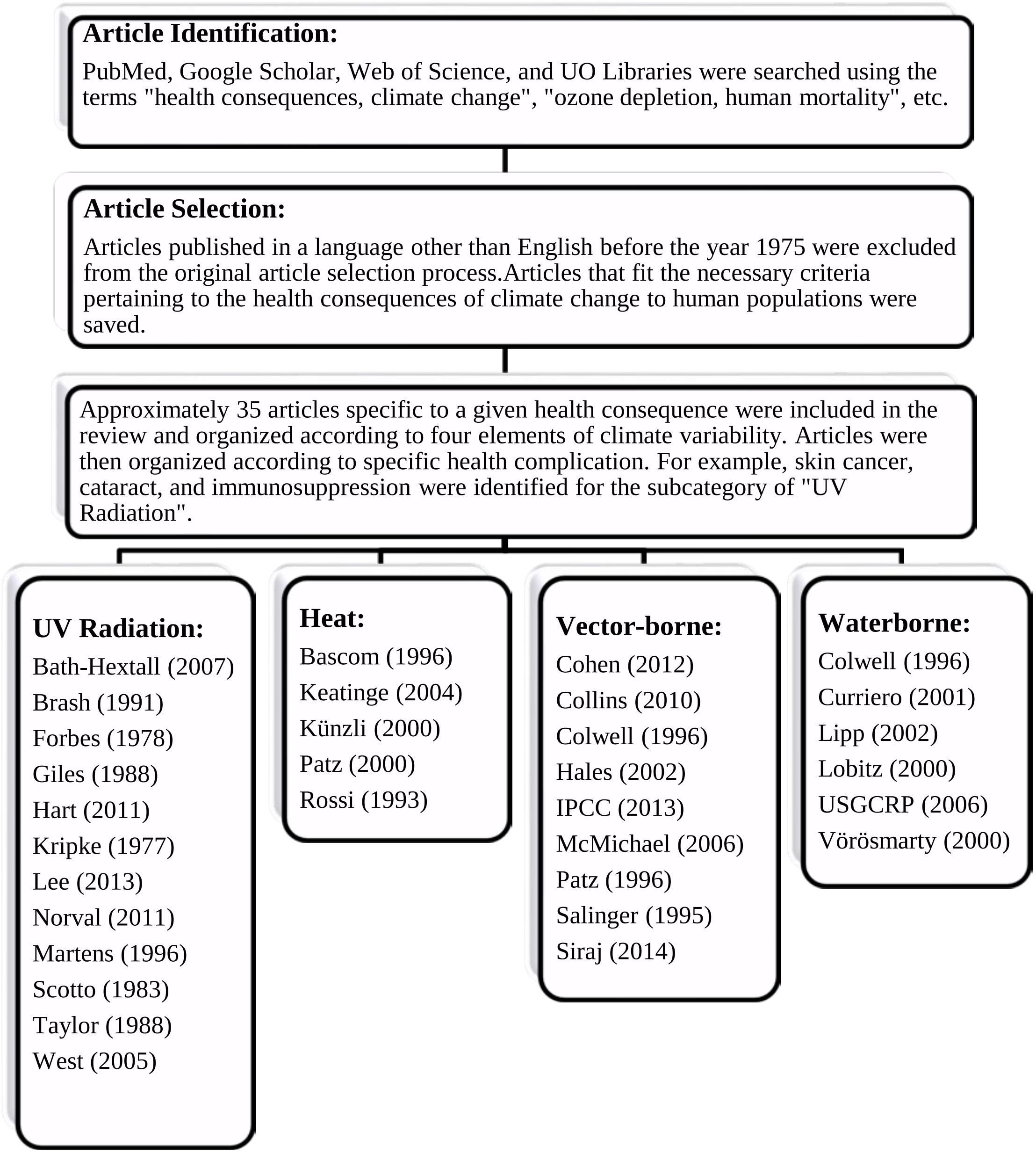

Figure 2: Flowchart of the article selection and organization process

UV Radiation and Mortality

In limited doses, the exposure of human skin to UV radiation can be beneficial. For example, short-term exposure to limited doses of radiation can lead to increased vitamin D synthesis. That said, the negative health consequences that have been associated with increased exposure to UV radiation include but are not limited to skin cancer formation, cataract incidence, suppression of the immune system, and premature aging. As introduced, climate change has been linked with ozone depletion and therefore higher concentrations of the sun's UV rays reaching the earth's surface. Due to the composition of the wavelengths, the most threatening UV rays are UVA and UVB. It is critically important to consider the major health consequences associated with ozone depletion due to the effect they will undoubtedly have on human mortality in the future.

Skin Cancer

An adverse effect of UV radiation, specifically UVA and UVB radiation as identified, is the increasing risk associated with skin cancer. Further, there is a confirmed causal relationship between UV radiation and incidence of squamous cell carcinoma in those exposed to high concentrations of it (15, 54). Skin cancer formation occurs in response to DNA damage within skin cells, typically caused by lengthened or concentrated exposure to UV radiation from varied light sources. More specifically, UVB light has the potential to disrupt sequential reproductive enzyme copying due to a disruption in genetic strand sequence, or mutated base pairing that results in pyrimidine dimers.

Squamous cell carcinoma (SCC) is known to be the most directly caused and perpetuated form of skin cancer specifically by sunlight exposure relative to other cancers such as basal cell carcinoma or melanoma (5). SCC is typically seen on the most commonly sun-exposed areas of the body such as the head, neck, face, etc. This skin cancer is notable because population-level incidence increases toward the equator (44). This is due to the consistently high level of UV exposure present at the equator relative to the rest of the globe. Another factor contributing to varied UV radiation worldwide are areas of "thinned" ozone or locations where ozone holes are present. In addition, UV Radiation is also more threatening at high altitudes where the atmosphere is thinner, providing lessened protection from UV rays.

One such thinned ozone area where it is possible to see a correlation with increased incidence of SCC is Australia, the country where skin cancer incidence is the highest recorded worldwide (17). A study was done on the projected increases in skin cancer incidences due to stratospheric ozone depletion in both Australia and the Netherlands along with the qualification that skin cancer incidence is statistically higher in higher age distributions due to UV accumulation over time (31). The study looked at a calculated projection based on an integrative model of stratospheric ozone data for the two regions.

Ultimately, the study showed a linear increase in anticipated skin cancer cases for the Netherlands and Australia. In addition, the study stated that, due to model projections concluded by the study, this hypothesized skin cancer incidence is not reversible. It is also possible to see the clear correlation between aging and increased susceptibility to cancer development, as represented by the straight line on the included graph (figure 3). That said, it is also important to note the adapted dashed line in the figure, which represents that same population but at a halved UV exposure.

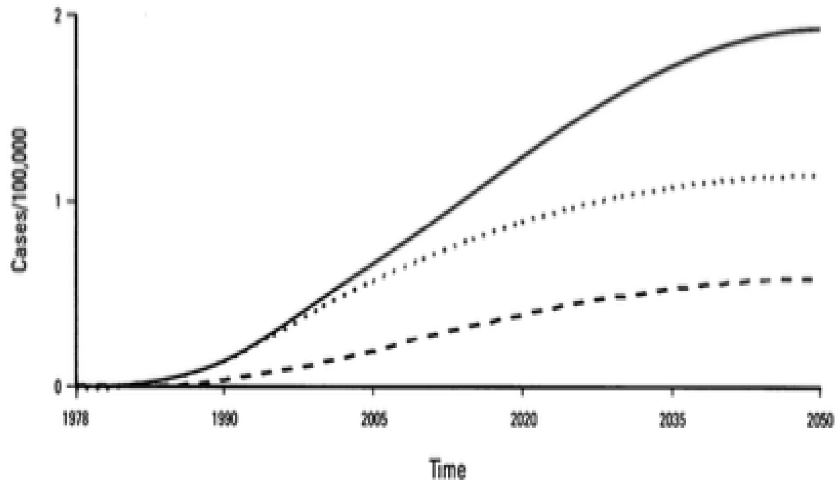

Figure 3: Projected squamous cell carcinoma incidence in Australia

This graph represents future projection for excess skin cancer rates per 100,000 for Australia extrapolated to the year 2050 under three potential conditions. The projected conditions included rates as projected as a result of the Copenhagen Amendments to the Montreal Protocol with a constant population (dotted line), an aging Australian population (straight line), and an aging Australian population with a 50% decrease of UV exposure (dashed line).

Figure Source: Martens, W. J. "Health impacts of climate change and ozone depletion: an ecoepidemiologic modeling approach." *Environmental Health Perspectives* 106.Suppl 1 (1998): 241.

A similar assessment, one of the first to study skin cancer incidence in Asia, was done on the projected skin cancer morbidity in Korea (26). This study quantitatively projected skin cancer incidence rate by analysis of radiation amplification factor (RAF) as well as an assortment of dose-response models to estimate changes in cancer incidence as a result of expected increases in UV concentration. According to a predicted 10% yearly decrease in ozone concentration, the study expects approximately 1312-1630 cases of skin cancer associated with climate changes based on its determined amplification factor (AF), which represents the relationship between ozone depletion and cancer incidence.

With a greater focus on existing data over projected calculations, a database study conducted within population-based cohorts sought to identify trends existing in the population related to basal cell carcinoma (BCC) diagnosis (3). Between the years 1996 and 2003 there was a 3% yearly increase in BCC diagnosis according to the Health Improvement Network database that the study utilized for sampling. When the study was published in 2007, it was estimated that 53,000 new cases of BCC would be diagnosed in the UK every year following with an expected estimation increase with each year. These studies, along with the calculations made to predict future incidence within certain populations, helps to identify skin cancer not only as a current threat to human health, but one that will likely continue to worsen for years to come.

Cataract

Cataract formation occurs in the eyes due to excessive protein buildup that results in a clouding of the lens. This clouding typically prevents light from passing through the lens of the eye and results in obstructed vision in patients. Specifically, the cataract is formed by an accumulation of compacted lens cells following the development of newer cells that form on the perimeter of the lens. According to the World Health Organization (WHO), cataract formation is the leading cause of blindness worldwide (6). Exposure to UV radiation is known and concluded by countless epidemiological studies as a critical risk factor for cortical cataract development.

There are three primary categories of cataract: cortical, nuclear, and posterior subscapular (34). Cortical cataract formation has been strongly linked with UV radiation exposure, while little evidence exists in relation to the other two forms of age-related cataract. More specifically, cataract development in human eyes is strongly influenced by UVB radiation, which is known to be more damaging to biological tissue than UVA due to its wavelength.

A study was conducted on watermen who worked in Chesapeake Bay with the intention to investigate the relationship between UV radiation and cataract formation (48). The predicted ocular exposure was calculated for the 838 men in the study to estimate an annual exposure from the time each participant was 16. This was determined by a self-reported occupational history as well as lab and field observations to determine average sun exposure levels. Development of both cortical and nuclear cataract was present in 340, or about 40%, of the participants. The study also concluded that those with annual exposure within the upper quartile of all study participants had a 3.3-times increased risk of cataract development compared with those in lower exposure quartiles. Perhaps most significant from the results of the study, individuals with cortical cataract formation had a 21% higher average exposure to UV-B radiation.

Another study was conducted to model the projected consequences for U.S. cataract cases that would result from a given percentage of ozone depletion. The numbers were determined using longitudinal data and the dose-dependent relationship between UV radiation and cataract formation incidence collected from the Salisbury

Eye Evaluation Project (42). Within a theoretical range of 5-20% ozone depletion, the authors of the U.S. study predict 167,000-830,000 additional cases of cortical cataract by the year 2050 (56). Additionally, this study found that there was an increase in cataract precedence associated with ageing populations, African-American populations, and female sex. Further, cataract formation is socially and epidemiologically unique from other conditions associated with ozone depletion due to the fact that cataract affects African-American communities at a higher frequency than it does Caucasian populations, who are typically at a 10- to 100-fold greater susceptibility to skin cancer (56).

Due to recent significant ozone depletion that has resulted from global warming and increased greenhouse gas emission, increasing concentrations of UV radiation are reaching the Earth's surface. Consequently, this shift is resulting in damage to various ecosystems, agricultural development, and human health across the globe.

Immunosuppression

Another consequence of ozone depletion has been observed recently in relation to the suppression of adaptive immune response. Unlike innate immune response, which is characterized by nonspecific immune defense in individuals, adaptive immunity occurs in response to specific microorganisms and a subsequent T cell response. T cells act to facilitate immune response to a given antigen by secreting appropriate immune "mediators" (33). In short, the simple process of immunosuppression happens in response to the interaction of UV radiation on the skin's cutaneous mediators. From this interaction, cell-mediated immunity, specifically the body's T cell response, is ultimately suppressed. There has been increasing support as of late connecting increased

UV radiation exposure to immunosuppression including negative effects related to vaccination effectiveness, the pathogenesis of infectious and autoimmune diseases, and tumor rejection incidence (13). Though the extent to which UV radiation influences these consequences is still relatively unexplored, there are studies that have evaluated the likely causation that continues to persist in susceptible populations.

The first significant evidence published in regards to UV-induced immunosuppression is thought to have been that by Kripke and colleagues. Their study linked UV radiation in mice to weakened antitumor immune responses (24). UV-induced tumors were transplanted to healthy mice as well as those who had received concentrated doses of UV radiation. The tumors were rejected in immunocompetent mice, however immunosuppression was present in UV irradiated mice due to the fact that the tumors transplanted in these mice grew following transplant. Similar reactions have been observed in human immune responses as well in relation to tumor-related antigens (35).

What is perhaps most significant to note about radiation-induced immunosuppression is that it is not limited to exposure site. In other words, the effects of immunosuppression due to UV radiation are seen systemically, not just on the surface of the skin. A study was conducted to assess the extent to which increased concentrations of UV exposure affected the effectiveness of vaccination, specifically the hepatitis B vaccine (47). A number of participants in the study, prior to their hepatitis B vaccine, were subjected to several consecutive days of UVB exposure. The study revealed that no significant changes had been observed in cellular or humoral immunity responses. However, the study did demonstrate immunosuppression as a result of UVB exposure in the decreased activity of killer cells as well as the suppression of diphenylcyclopropenone sensitivity of the skin. The results of this study are significant because they reveal that there is an element of immunosuppression that results from increased exposure to UVB radiation.

It is relatively simple to understand the relationship between ozone depletion and increased UV radiation to the earth's surface. The extent to which this UV radiation has the potential to cause significant consequences to human health is more challenging to assess due to regional variability, insufficient data collection within high-risk populations, and numerous other compounding variables. This brief introduction to those known consequences of UV radiation calls for validation of the idea that climate change is not only a crisis that will affect seemingly isolated events that harm the environment, but truly has the potential to cause catastrophic illness to the human population.

Heat-Related Mortality

As previously introduced, the direct causes for climate change and increasing global temperature can be attributed to the depletion of ozone that continues to be the result of greenhouse gas emission to the atmosphere. Though a myriad of health consequences related to increased UV irradiation are directly correlated with the depletion of ozone, there are different health consequences being perpetuated simply by the secondary effect of increased rising temperatures and global heat wave incidence alone. Generally, there is a set temperature for which mortality rates are lowest in populations (32). Upon drastic deviation from this optimal zone, death rates increase (figure 4). Consequently, there has been a gradual shift in public health concern from cold-related mortality rates, which do continue to be higher, to a new precedent that prioritizes the increasing rates of heat-related mortality that could be logically attributed to the projected global temperature increase of 1.4-5.8°C (32). Figure 4 represents a schematic of how increased global temperature would influence annual mortality.

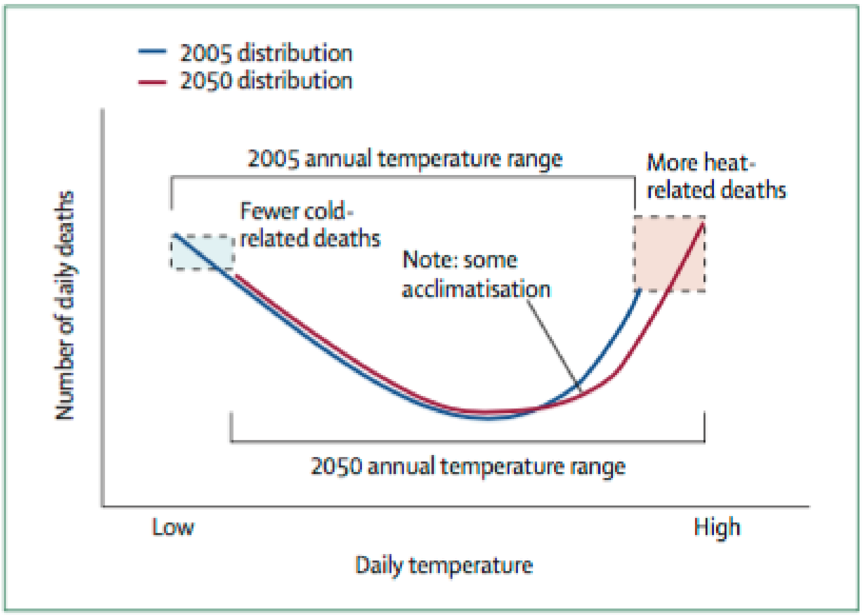

Figure 4: U-shaped relation of temperature and mortality in 2005 and the predicted shift for the year 2050

This figure illustrates a predicted increase in heat-related deaths for the year 2050 and indicates that these deaths would outweigh the averted cold-related deaths that are predicted for the same year.

Figure Source: McMichael, Anthony J., Rosalie E. Woodruff, and Simon Hales. "Climate change and human health: present and future risks." *The Lancet* 367.9513 (2006): 859-869.

When discussing heat-related mortality it is important to consider several qualifying factors in terms of its effects. Heat-related mortality spikes in human populations in extreme cases of heat waves as well as with the increasing annual temperature we are projected to experience globally in years to come. Additionally, heat-related mortality disproportionately affects ageing populations and psychiatric patients due to the physiological processes responsible for the specific cause of mortality (22). Mortality as it relates to increased temperature is typically attributed to hyperthermia, under which the body will become too warm for homeostatic balance to naturally be maintained or regained, leading to the chemical destruction and denaturing of vital proteins. Psychiatric patients and others who are prescribed psychoactive drugs that may require anticholinergic or narcotic responses are at increased risk due to the drug's effect of impairing thermoregulatory responses such as sweating (22).

The cardiovascular system is at increased risk under thermal stress due to the increased likelihood of cerebral and coronary thrombosis, again particularly in older populations (22). Thromboses that occur as a result of warmer weather are due physiologically to the hemoconcentration that results from excessive salt and water loss in heat. Additionally, increased strain on the heart due to a necessity of thermoregulatory blood circulation can frequently lead to cardiovascular complications in those with weakened systems prior to the thermal stress. Additionally, these health consequences can happen simultaneously with common heat illnesses such as heat exhaustion or heat stroke (22).

Respiratory Health

In addition to the increased risk to populations with prior existing cardiovascular conditions, those with chronic respiratory diseases are at a similar risk under increased thermal stress. In addition, according to the Air Pollution and Respiratory Health Branch (APRHB) of the CDC, the two major environmental threats to respiratory health are ozone and particle pollution. The presence of ozone at ground-level elevation could have the effect of worsening current respiratory conditions (39). Ozone has the effect of deteriorating healthy lung tissue, restricting respiratory function, and often results in heightened sensitivity of lung tissue to irritation by other pollutants and chemicals.

Secondary effects of these conditions can lead to acute or chronic chest pain, coughing, congestion, and can aggravate previous conditions (2). Though it could seem that the impending threat climate change poses to the average individual may be small, the impact future climactic variability will have on public health will be significant for many reasons.

Human respiratory health is very closely tied with regional air quality. Due to climate change, many populations live in areas with air quality that does not meet global health standards due to air pollutant concentrations. Within the United States alone there were 107 million people living in counties that could not meet national quality standards for at least one pollutant in 1997 (39). Due to primarily anthropogenic forces contributing to the increased demand for fuel combustion in the past two decades, it could reasonably be concluded that this number has increased. A study published in 2000 was done in order to assess the impact of traffic-related air pollution on public health in Austria, France, and Switzerland. This study found that air pollution caused 6% of total deaths per year (25). In addition, the research team concluded that approximately half of pollution-related morbidity were attributed to traffic, which was also correlated with high incidence of chronic and episodic bronchitis, as well as about 0.5 million asthma attacks yearly.

According to several studies and ongoing research, asthma is projecting to be a respiratory condition of increasing incidence within populations of pollutant-dense regions. Correlation between pollutant levels and meteorological factors such as temperature are known to exhibit correlation with incidence of hospital admittance due to respiratory complication (41). As previously identified, global temperature is projected to rise significantly over the next century. In addition, air pollutants associated with greenhouse gas emission, other anthropogenic factors, and climate variability will undoubtedly have similar correlating effects. The primary and secondary effects, along with the consequences to those with preexisting respiratory illness, of decreased air quality has the potential to continue increasing mortality within regions that will undoubtedly be susceptible to climate variability in coming years.

Additional factors that increase the risk of health complications under extreme thermal stress include living in urban environments, mostly due to the “heat island effect” of heat retention in inner-city environments, or living in housing that is not considered thermally efficient (32). These factors, along with the risks associated with older populations and those living with existing cardiovascular, psychological, and respiratory conditions have the likely potential to result in increased overall mortality rates in populations susceptible to extreme thermal stress.

Vector-borne Disease

Infectious diseases are physiological disorders that result from interaction and transmission with another organism such as bacteria, viruses, fungi, or parasites. For this review, the intention is to specifically explore the outbreaks of several diseases transmitted primarily by poikilothermic arthropods, specifically the culicidae, or mosquito. Increasing rates in global disease transmission has been linked primarily with diseases transmitted by the culicidae. This disease transmission is currently being researched due to the potential connection present between outbreak and climate change (14). Specifically, this should stand as an abridged assessment of the recent outbreaks of several vector-borne diseases including malaria and dengue hemorrhagic fever (DHF), both transmitted by culicidae.

According to the Intergovernmental Panel on Climate Change (IPCC) we should anticipate global temperature increases averaging 1.4-5.8 °C within the next 100 years (32). Not only does this pose a threat to human health in terms of heat-related morbidity rates and natural disaster recurrence, but alters mosquito localization to effect in a higher susceptibility in certain populations to experience disease outbreak. Studies have pointed to malaria and DHF as being resurging vector-borne diseases of particular importance and of high public health priority due to their threat (18). That said it is nearly impossible to quantify the extent to which infectious disease has been exacerbated by climate variability due to the secondary and tertiary health effects that could result.

Due to recent changes in average global temperatures within given regions, mosquito populations have recently undergone a new age of globalization that is placing them in regions where their threat is seemingly new, or resurging (21). This same phenomenon is occurring simultaneously with hosts as well. The ecological development and spread of infrastructure such as urbanization, irrigation, deforestation, and others have resulted in the effect of increased or diversified vector densities in new geographical settings (18). In addition, increasing temperature is a crucial determinant in transmission rates for some of these diseases. In cases of malaria, for example, both globalization and temperature change are majorly responsible for a multitude of malaria resurgence cases. Climate change not only has the effect of creating more tropical habitats and therefore more potential regions for mosquitos to inhabit, but it also has a unique effect on vector development. Studies have been conducted that consistently show a correlation between warmer temperatures and the available window of vector development in the lifecycle of mosquitos (45). Simply put, due to the effects of climate change on the physiology of the culicidae, possible periods for transmission can occur over a greater window of time.

Malaria

Malaria has been of particular public health concern as of late due to its implications at high altitude environments. Areas of increased importance are the highlands of East Africa and South America in regions where malaria is of heightened risk. Typically, due to decreased temperatures at higher altitude and the combined restriction on insect physiology due to the insect’s natural temperate habitat, these highlands have historically provided protection, in a way, from malaria incidence within densely populated high-altitude communities, such as those found in Ethiopia or Colombia. More recently, however, global temperatures at these high altitudes have been higher on average, allowing for vectors to access and thrive in new environments within populations that have not previously been exposed to the threat. A study performed a comparison between the spatial distributions of malaria incidence with the elevation gradient of the region in order to identify long-term trends with the disease (46). This study found that the average altitude for malaria case incidence increased with mean temperature reports. Further, this same study found that within both the identified regions malaria cases spiked in the uniquely warm years of 1997 and 2002 at these higher altitudes. The study found strong correlation between the variables of cumulative cases and altitude, median altitude and mean temperature, and median altitude, mean temperature, and year within both Ethiopia and Colombia (figure 5). Because these regions are isolated geographically yet exist within a similar altitudinal plane, this study is able to illustrate the importance of climate variability in vector distribution at a global scale, particularly in high-risk highland populations.

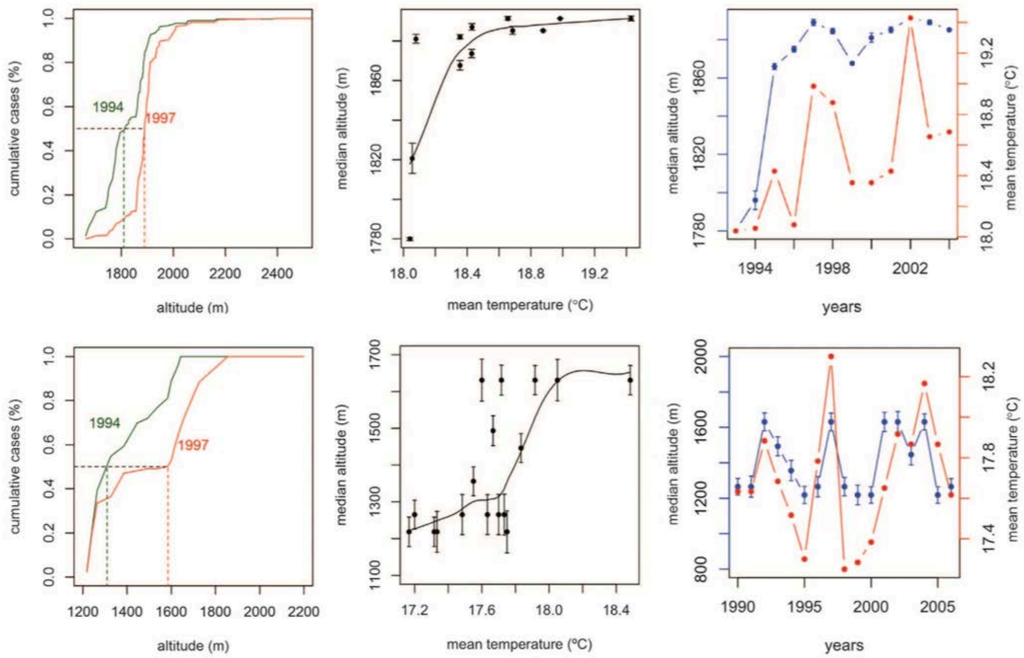

Figure 5: Graphical representation of malaria outbreak incidence in Ethiopia and Colombia as it correlates with altitude and mean temperature across years

Ethiopia (top row) and Colombia (bottom row) have seen a shift in malaria incidence to increasingly high altitudes that could not ecologically support the vector-borne disease prior to recent years. These graphs show the strong positive correlation between malaria outbreak, temperature, and altitude as they have been recorded in recent decades.

Figure Source: Siraj, A. S., et al. "Altitudinal changes in malaria incidence in highlands of Ethiopia and Colombia." *Science* 343.6175 (2014): 1154-1158.

Despite growing evidence in support of the contributions that climate change has made in vector borne disease transmission, there is also evidence that supports the claim that malaria's resurgence is due to weakened systemic support for malaria programs in affected regions. A review published on the assessment of the causes of malaria resurgence included a review of possible causation attributed to three major causes (9). According to the review, incidences of disease resurgence were primarily attributed to the weakening of malaria programming, the intrinsic potential for malaria transmission, as well as some cases being correlated with developed resistance.

Malaria is not a new infectious disease by any means. Its disastrous effects have already been observed for years. Its reach, however, has the capability to extend further than it ever has before. Incidence has increased and even newly appeared in latitudes and altitudes where malaria was never before a threat due to ambient air warming and climate variability. Malaria claims approximately two million lives yearly, a figure that is predicted to increase by one million based on current climate trends and assumptions (11). This exponential expansion would result in unprecedented effects in terms of population health as well as systemic development.

Dengue and Dengue Hemorrhagic Fever

Dengue or Dengue Hemorrhagic Fever (DHF) emerged as a global disease and threat around the 1950s. There is no present cure known for the disease, and it continues to infect approximately 400 million people annually, almost exclusively living in equatorial tropic regions (6). According to the World Health Organization, Dengue Fever claims approximately 22,000 lives yearly of the total 2.5 billion people who live within regions that could support the transmission of the disease. Further, the disease is currently endemic in at least 100 countries. Interestingly, prior to 1981 there were no laboratory-confirmed cases of DHF within North or South America. Between that time and 2003, however, most countries within these two continents have experienced outbreak.

A contributing phenomenon that has been correlated with the resurgence of vector borne diseases and warrants consideration in this review is El Niño Southern

Oscillation (ENSO). This element of climate variability occurs over a 2-7 year period and is especially responsible for approximately 40% of temperature and rainfall variation in the Pacific each cycle (43). An article published on the correlation between Dengue Hemorrhagic Fever (DHF) outbreak in the South Pacific and ENSO occurrence with a positive correlation of r_s=0.58, (figure 5) (19).

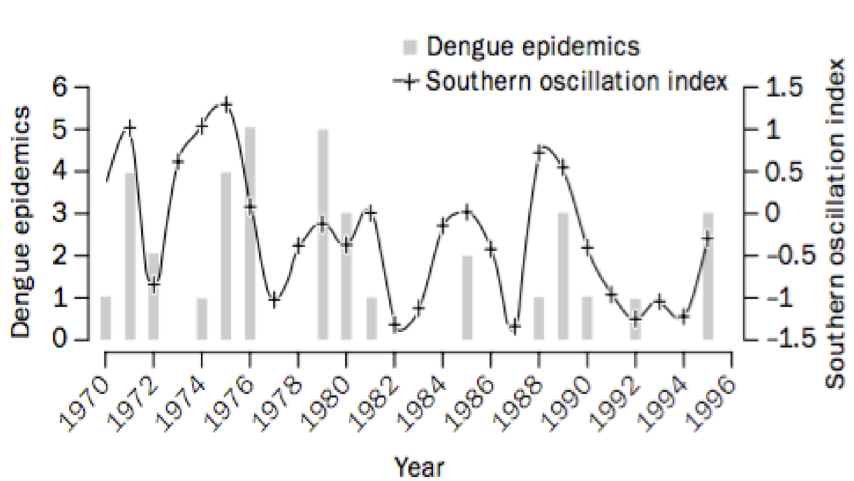

Figure 6: Relation between dengue epidemics and Southern oscillation index value

This figure is a representation of the correlating trend between the Southern oscillation index (represented by the straight line) and Dengue epidemics in the South Pacific (gray bars). The graph represents a positive correlation with an r value of 0.58.

Figure Source: Hales, S., P. Weinstein, and A. Woodward. "Dengue fever epidemics in the South Pacific: driven by El Niño southern oscillation?." *The Lancet* 348.9042 (1996): 1664-1665.

Though the existence of ENSO may appear to partially invalidate the intention of this review due to its cyclical nature, it should be considered that, though this study shows somewhat of a correlation between ENSO and DHF outbreaks in the South Pacific, outbreaks of DHF have been gradually increasing on a global scale over the past few decades. Further, the apparent correlation represented by Figure 6 is not completely consistent, nor does it show strong statistical correlation. Furthermore, within the same review climate change is identified as a global trend responsible for this increase (19). It should be noted further, that year-to-year ENSO variability is heavily impacted by climate change and is even projected to strengthen with global warming (10). Factors like warming ocean temperature and trade winds in the effected regions have the potential to influence the variance and strength with which ENSO affects regional climate.

It is important to consider the global impact of climate change and its potential influence on vector-borne disease outbreak. Another article investigated a similar correlation that involved relating global DHF risk with long-term vapor pressure recordings in order to model average humidity and assess the geographical limits for disease risk. The article states that in 1990, about twelve years before the article's publication, approximately 30% of the world's population lived in geographic regions with a DHF infection risk of at least 50% (20). Researchers then modeled a projection of future population and humidity values due to predicted climate change and global warming. Findings from the calculations predict an estimated 50-60% of the global population to be living in a geographic region that puts them at risk of DHF infection (20).

Zika Virus

Perhaps most pertinent to current events and at the forefront of public health priorities today is the curious Zika outbreak within various equatorial regions as of late. There is little concretely known about Zika virus, its symptoms, transmission, and reach due to the newness of the disease. The first case in the world's most recent outbreak is said to have come out of Easter Island in March 2014 and has since been reported vastly throughout countries at equatorial latitude and beyond due to population mobility and global travel (1). This virus is especially pertinent to this review and is included due to the fact that Zika virus is known to be transmitted by the *Aedes aegypti* mosquito and is done only under warm equatorial-like climates, much like malaria and DHF. The *Health Map* organization has developed a variety of maps and timelines to represent the recent Zika outbreak and current surveillance efforts pertaining to its spread. The organization designed a representation of specific regions with high levels of environmental suitability for the virus, indicated by the color red, from which it is possible to see the significant equatorial pattern and reach due to expanding tropical regions (figure 7).

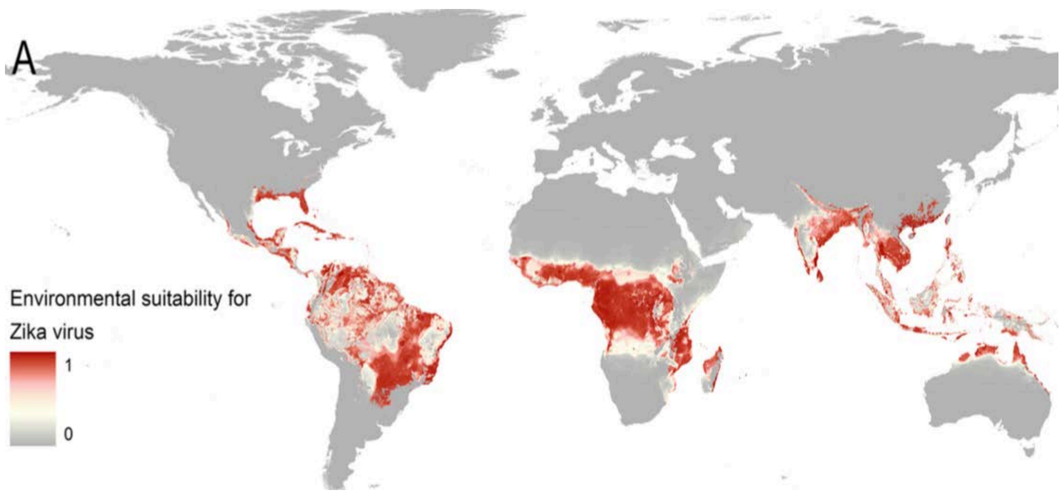

Figure 7: Geographical representation of the environments suitable to support Zika

The environmental suitability as determined by disease and climactic surveillance is indicated by a range from most suitable (indicated by red) to not suitable (gray). It is possible to see the concentration within the equatorial region, as well as the slight expansion outside of it due to recent climate shifts.

Figure Source: "2016 Zika Outbreak." Health Map. Boston Children's Hospital, n.d. Web. 15 May 2016. <http://www.healthmap.org/zika/#timeline>.

Waterborne Disease

A final element of climate variability that warrants assessment is the earth's water supply and its effect on waterborne disease transmission. Waterborne disease outbreak is particularly interesting because it is often threatening within regions that host high incidence of vector-borne disease as well. Simply put, increasing water levels can facilitate waterborne disease transmission as well as encourage vector expansion and transmission due to the creation of more tropical habitats within which they are able to thrive. The three major water-related changes of detriment to human health can be simplified to increased and varied rainfall patterns, flooding and its relation to sea level rise, and general temperature increase of the world's water sources (49). On a global scale, flooding and heavy periods of rain can often be followed by peeks in population-wide infection outbreak, whereas this trend is not commonly assumed in the global west unless water infrastructure has been contaminated or damaged directly. The major organisms responsible for the transmission of waterborne disease are helminthes, protozoa, algae, and bacteria. The organism from which most waterborne diseases stem is bacterium. Bacterial waterborne diseases include cholera, cyanobacteria, typhoid, and salmonellosis, to name a few.

Vibrio

In addition to toxic algae, the U.S. Global Change Research Program identified the naturally occurring waterborne pathogen *vibrio* as being particularly threatening to human health. The bacterium is especially likely to thrive within water temperatures above 59°F, the major reason its threat is projected to be exacerbated by global warming. General vibrio infections have as much as tripled in the United States since

1996 (50). This is projected to only increase in coming years due to the increased exposure to contaminated water sources that will accompany global warming and water level rise. Perhaps most pressing to the future of public health, vibrio is the bacterium responsible for the more widely recognized diseases and infections of greater incidence in recent decades, perhaps most notably is that of cholera.

Cholera

The most evidence in terms of climate-related disease spread that currently exists typically pertains to international cholera incidence (11). Cholera is a devastating diarrheal disease that was first linked to water in the 1850s by John Snow in London (27). Though traditionally conceptualized as an ancient disease, *V. cholerae* persists and has resurged in many tropical regions as of late. Though primarily associated with tropical warmer climates at equatorial latitude, the bacterium could theoretically live in any body of water. Interestingly, studies have been done that strongly suggest cholera to have a symbiotic relationship or correlation with zooplankton, which further suggests it to have certain vector borne characteristics (27). In terms of its correlation with climate variability and ocean warming specifically, cholera endemic periods have been shown not only to correlate with *V. cholerae* presence in water sources, but increased water temperatures and zooplankton density as well (28). This relationship is especially significant due to the implications it has for expected seasonality as well as what could potentially be prevented using recorded and projected cycles of ENSO.

Water Vulnerability

Though this review is primarily an assessment of the direct health consequences of climate variability and global warming, water vulnerability is a crucial aspect of human society that will also be threatened. With rapid population expansion and development, freshwater resources continue to be depleted and exposed to potential contamination. Water vulnerability is an important consideration within this review given that increased population growth is correlated with increased water pollution and ultimately has the effect of increasing incidence of waterborne disease (55). The secondary and tertiary effects of climactic variability will likely be just as threatening, if not more so on a systemic level, to the longevity and health of a human's life.

In Conclusion: Ecoepidemiology

The intention of this review is to stand as a validation of climate change as a major global health concern. Emerging diseases and physiological conditions that result from the epidemiological impacts of climate change will continue to challenge and impede global health progress for populations around the world. Ecoepidemiology, or the interaction of the ecosystem on human health, must be considered and prioritized as an emerging field and a call for mobilization in public health prevention measures. This thesis carefully considers the human health consequences of major factors of climactic change including global warming, ozone depletion, equatorial tropic expansion, and water pattern variability. The World Health Organization (WHO) estimated that by the year 2000, approximately 150,000 deaths could be attributed directly to the impacts of climate change (16). These assessments of human mortality demonstrate the significance of global warming as a major threat to global health. Due to the numerous correlations, it is important to consider, as well as potentially evaluate, the public health infrastructure currently in place to respond to such threats to human life.

Prevention and Surveillance Principles

Effective public health initiatives as they relate to global climate change must focus on prevention. Prevention exists as a programming mechanism in three forms: primary, secondary, and tertiary (16). The idea of primary prevention relies on protecting populations completely from illness, injury, outbreak, or other negative health outcomes. Relevant clinical examples of this include large-scale vaccination and immunization efforts in particularly high-risk regions. In relation to climate change specifically, this would depend more on ecological mitigation efforts. In other words, a focus on how to slow or reverse the harmful impacts, as identified in this work, of climate change. In the context of ecological variability, secondary prevention pertains to adaptation and anticipation of given projected health outcomes. For example, the combination of malarial treatment centers implemented alongside a community mosquito net distribution in a region with high malaria morbidity would both be adapting to a current outbreak as well as attempting to mitigate future infection on a large scale. The final category of public health prevention, or tertiary prevention, has a primary focus on an attempt to restore health in those already affected by a given disease.

With events that cannot be accurately or precisely predicted, the field of public health preparedness is particularly important. Actions taken in this field in relation to climate change are of dire importance due to the fact that events like disease outbreak or natural disaster occurrence cannot be anticipated, yet will potentially have disastrous effects on human health should there not be preparedness measures taken. Disease and climactic surveillance become increasingly important in this lens due to the fact that these preparedness strategies cannot exist without data and projections that come about through careful and intentional surveillance of events already known to be detrimental to human health.

The concept of surveillance is of increasing importance within the field of public health, as global climate change becomes an international priority. Though surveillance would not be effective in preventing inevitable conditions or susceptibility, it would be especially relevant in cases such as infectious disease control. Surveillance, when used within the sphere of global health, refers to the consistent monitoring, tracking, and educated prediction of climactic shifts and regional outbreak. Effective surveillance relies heavily on data collection in order to inform potential intervention as well as prevention with the risk of global emergencies such as natural disasters or disease outbreak. As this work has intended to illustrate, the two epidemics are not typically independent of the other.

This relationship between surveillance and preparedness is supplemented and supported by the precautionary principle, by which much policy and law pertaining to environmental sustainability has been supported (40). Interestingly, the principle is commonly used to protect the environment from drastic human intervention. Within the context of this work, however, it will be used to address and support preparedness for the consequences of climate change on human mortality. The precautionary principle could be used to assess risk and implement policy in the potential case of a malaria outbreak, for example.

When it comes to natural disasters and disease outbreak, such as what we are currently seeing with Zika in South America, the urgency of unexpected disaster overwhelms governmental systems and the medical communities that must respond. According to the Center for Research on the Epidemiology of Disasters (CRED), unexpected climactic events accounted for approximately 90% of disaster-related fatalities between the years of 1970 and 1999 (12). This discussion is not to say that public health is lacking when it comes to preparedness surrounding climate variability and global warming, but to suggest that it could be stronger. In terms of current public health infrastructure, a variety of programs are in place or in the process of being developed that promote prevention, but could potentially be strengthened if implemented with the priority of climactic preparedness.

Several strategies that support this shift within the field of public health include those that emphasize risk reduction as well as those with a focus on fostering resiliency (23). These two principles are especially impactful because they have the potential to facilitate the other. Human vulnerability could be decreased by risk management in the form of building safer and cleaner homes, medical institutions, schools, and so on. In theory, this would then perpetuate human resiliency not only in the stronger health practices of the individual, but also in the systemic security of a stronger infrastructure. Global health programs should not be operating based on an expect-the-worst mindset, but if that possibility is brought to the forefront of policy and program implementation with the added understanding of climate change's impact on human health, future disasters could potentially be less catastrophic for population morbidity.

The Future of Human Health

Based on projections of future trends by the IPCC, public health officials should expect to see increased incidence of heat waves, heavy precipitation events, areas affected by drought, and sea level elevation in coming years (37). The scientific community is in agreement that global climate change is a phenomenon that is acting to facilitate events of climactic variability and therefore, as this paper has assessed, will continue based on projections to cause unfortunate health consequences to human populations. This thesis specifically assesses the increased incidence of skin cancer, cataract formation, and immunosuppression in populations as it correlates with ozone depletion. In addition, direct thermal stress was investigated due to its relation to direct cardiovascular and respiratory conditions, particularly in high-risk populations, during periods of particularly high temperatures. Finally, outbreak and infection instigated by vector and waterborne disease are shown to have a strong relation to the expanding equatorial tropic zone as a result of overall warming within the region.

It should be noted that this thesis stands as an assessment of the direct physiological effects of climate change on human populations as a direct effect of gradual climate shifts. The indirect effects of any of these identified elements of climate variability, however, are likely numerous and not fully understood. For example, mental wellness is an area of public health that has more recently gained momentum as a medical priority. In the aftermath of natural disasters, the variability of which correlates strongly with global warming trends, mental illness incidence will likely always follow in affected areas. Preparedness efforts should take the indirect consequences such as this into account as well.

It is vital that global climate change be considered a threat to human health. These two fields within the scientific community not only coexist within one system, but also are dependent on the other for sustained longevity. Human mortality is not independent of climate change, and therefore cannot continue to be thought of as such. Funding efforts in order to prioritize preparedness for the unexpected yet undoubtedly impending outbreaks and disease incidence that will come with prolonged climate variability is just a start. An adjusted perspective on global health programs and the power of climate change is needed within these fields as well. If one cannot support the politics of environmental conservation, human health should motivate a unanimous mobilization of efforts with the vision to mitigate the threat of climate variability.

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