The Impact of Climate Change on Human Health and Pharmaceuticals

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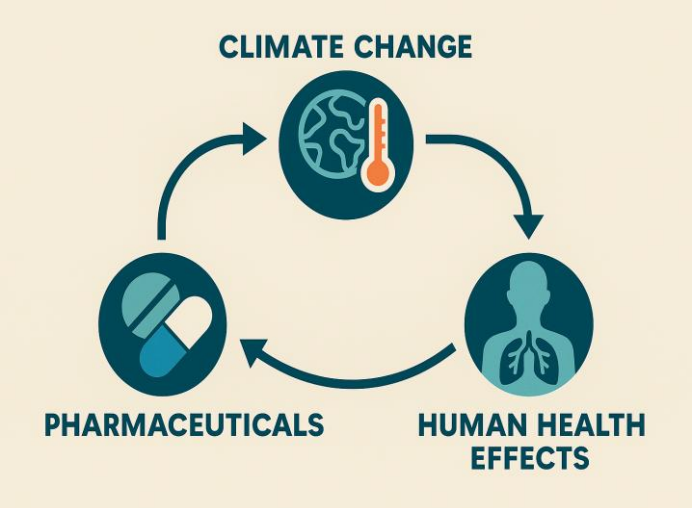
Graphical Abstract



Abstract

Climate change and air pollution affect every major organ system, altering both the presentation of disease and patient responses to pharmaceutical treatments. However, existing knowledge on how patients, healthcare professionals, and governments should prepare for these challenges is fragmented. Climate change contributes to premature mortality, increased morbidity, and exacerbation of pre-existing conditions across cardiovascular, respiratory, renal, gastrointestinal, neurological, endocrine, and dermatological systems.

Emerging evidence shows that climate variables, particularly temperature and humidity, can directly affect medication stability, bioavailability, and pharmacokinetics. For example, elevated temperatures may degrade active pharmaceutical ingredients, while humidity can accelerate the disintegration of hygroscopic tablets, increasing the risk of dose dumping and adverse events. Extreme weather events may also disrupt pharmaceutical supply chains, compounding risks to patient care.

This review synthesises evidence to (i) identify diseases, populations, and medications most affected by climate change, and (ii) anticipate how pharmaceutical interventions will need to adapt. The findings highlight the urgent need for integrated research exploring the interplay between climate change, therapeutic response, and drug safety to support resilient, climate-ready healthcare systems.

Introduction

Climate change (CC) is one of the major global concerns for human health [1]. Beyond its effects on the physical environment, CC significantly disrupts interconnected systems essential to human well-being, including societal, economic, and healthcare systems [2]. The United Nations Framework Convention on Climate Change (UNFCCC) defines CC as "a change of climate which is attributed directly or indirectly to human activity that alters the composition of the global atmosphere, and which is in addition to natural climate variability observed over comparable time periods" [3]. Human-induced CC has accelerated the frequency and severity of climate hazards and extreme weather, thereby surpassing the variability expected from natural climatic processes. According to the Intergovernmental Panel on Climate Change's (IPCC) Sixth Assessment Report (AR6), the risks associated with CC are emerging faster than anticipated, and their magnitude will be severe owing to global warming [4].

There is an overwhelming consensus that human activities that emit greenhouse gas (GHG) are the primary driver of modern CC [5]. This was also stated by the IPCC 2, it is unequivocal that human influence has warmed the atmosphere, ocean, and land" [4]. These human activities include industrialisation, burning fossil fuels, deforestation, transportation emissions, and waste disposal. As a result, levels of GHGs such as carbon dioxide continue to rise. This increase in GHGs contributes significantly to global warming, altering atmospheric, terrestrial, and oceanic systems[6]. Consequently, this leads to rising sea levels, extreme heat, more frequent extreme weather events, including wildfires, heavy precipitation and floods, droughts, storms (including tropical cyclones), and temperature extremes, as well as compound events (multivariate and concurrent extremes), such as heatwaves and droughts [7].

CC and extreme weather events have wide-ranging consequences affecting healthcare, forestry, tourism, the economy, agriculture, and biodiversity [1]. An array of literature has linked CC and extreme events to increased incidence or exacerbation of diseases across cardiovascular, respiratory, renal, and gastrointestinal systems, as well as morbidity and premature mortality [8]. Extreme events such as hurricanes, floods, droughts, and wildfires have been associated with worsening or onset of mental health disorders, including anxiety, depression, acculturation stress, post-traumatic stress disorder (PTSD), and suicide [9]. Moreover, the increased frequency and severity of extreme conditions also threaten water quality, contributing to water-borne and food-borne diseases and malnutrition [10].

Emerging evidence suggests that CC affects medication effectiveness and safety. By directly altering the integrity of medicines, it may reduce efficacy and lead to adverse effects. Elevated temperatures can accelerate the degradation of active pharmaceutical ingredients (API). This may lead to reduced bioavailability and subsequently diminished therapeutic effects [11, 12]. Similarly, humidity can accelerate the degradation of hygroscopic drugs, potentially leading to reduced efficacy, dose dumping, and adverse effects [11]. In addition, extreme weather events may affect pharmaceutical patient care by disrupting the medicines supply chain, including production, transportation, and storage [12, 13].

Physiological changes associated with heat exposure may alter organ perfusion and pharmacokinetic parameters, including absorption, distribution, metabolism, and elimination. These changes may affect medication effectiveness and clinical outcomes. A recent systematic review has revealed that CC complicates the management of epilepsy. High temperatures and

humidity affect the stability of anti-seizure medications, alter pharmacokinetics, and directly increase susceptibility to seizures due to heat stress and dehydration [11]. Furthermore, elevated temperatures cause heat-induced local vasodilation, increased blood flow to the skin, and reduced perfusion of internal organs. For example, reduced hepatic perfusion significantly reduces the hepatic clearance of certain drugs, which may result in drug accumulation and increased risk of toxicity [14].

Despite substantial research on the health impact of CC [1, 15-19], research exploring the impact of CC on therapeutic response and potential drug toxicities remains limited and fragmented. Therefore, this review consolidates evidence to examine the impact of CC on human health and to evaluate how climate variables may influence the safety, efficacy, and quality of pharmaceutical treatments (Figure 1). By integrating recent data, this review aims to identify high-risk diseases, populations, and medications, and to highlight areas where further research is urgently needed to support climate-resilient healthcare systems.

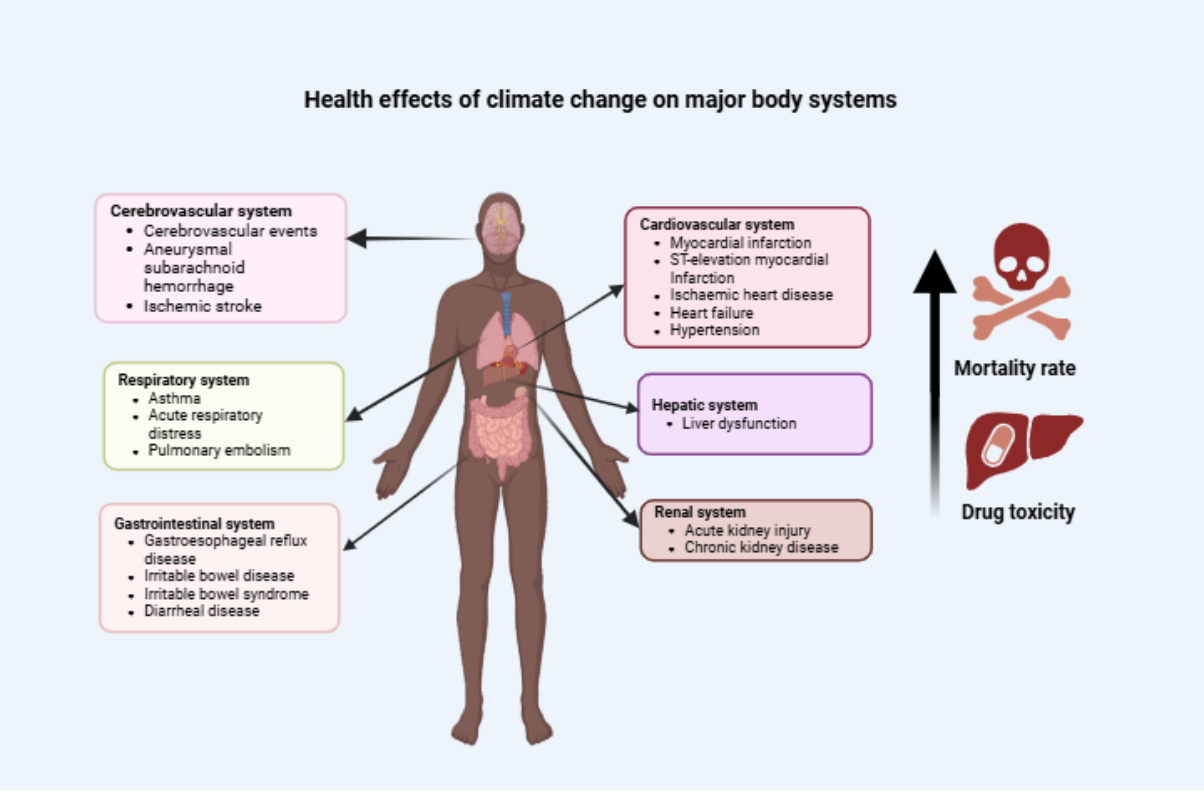


Figure 1. Illustrates potential climate change-induced disease changes per major system organ classes. Created using https://BioRender.com.

Major organ systems affected by climate change.

Cardiovascular system

Seven studies examined the relationship between CC variables and cardiovascular diseases CVDs. Three studies observed a non-linear relationship between both cold and hot temperatures and increased risk of acute myocardial infarction (MI) [20-23]. Cold temperatures had more pronounced acute MI effects in females [21], while significantly increasing the incidence of ST-elevation myocardial Infarction (STEMI) in males compared to females [22].

Both cold and heat were associated with increased risk of hospitalisation and mortality from cardiovascular and respiratory diseases across all ages. Females experienced significantly higher mortality from heat-induced cardiovascular and respiratory diseases compared to males, and the effects were more pronounced in older adults. was associated with increased risk of hospitalisation for diseases affecting arteries, arterioles, and capillaries, and ischaemic heart disease was associated with increased risk of hospitalisation for diseases affecting arteries, arterioles, and capillaries, and for ischaemic heart disease. Furthermore, an increased risk of mortality from hypertension and heart failure was observed. Conversely, cold exposure increased the risk of hospitalisation for heart failure and mortality from acute MI [23]. In addition, a study investigating the direct and urine-electrolyte-mediated effects of temperature on blood pressure (BP) found that ambient temperature lowers BP through physiological effects, with minimal indirect effects from electrolytes, including sodium, potassium, calcium, and magnesium [24].

Two studies explored the adverse effects of floods and wildfires on cardiovascular outcomes. Sunohara et al. found that floods were associated with a significantly increased risk of CVDs and cerebrovascular diseases, two weeks after the flood disaster. In addition, patients with heart failure presented with significantly elevated systolic and diastolic BP at the time of hospitalisation [25]. In contrast, a study investigating the effects of wildfire smoke on CVDs observed an increased risk of all-cause CVDs across different lag times. Particularly, individuals aged 65 years and above were at the highest risk of MI and ischemic heart disease. Dense smoke was strongly associated with heat failure; all levels of smoke density were associated with hypertension, while medium and dense smoke were also associated with increased pulmonary embolism risk among individuals aged 65 years and above [26].

Cerebrovascular system

Several studies have investigated how climate variables influence cerebrovascular events. Zhu et al. and Salam et al. found a positive association between high temperature and acute ischemic stroke [27, 28]. Notably, Zhu et al. reported that this association was evident from one hour after exposure and attenuated over time, and found that gender, age, smoking, and alcohol had no significant modifying effect [26]. On the other hand, Huang et al. demonstrated that low temperatures were attributed to an increased risk of aneurysmal subarachnoid hemorrhage [29]. Salam et al. found a positive linear association between temperature and ischemic stroke in a study conducted in Qatar's desert climate with high year-round solar exposure [30]. In contrast, a non-linear relationship between ultraviolet radiation (UVR) and ischemic stroke admissions was observed, with both high and low UVR associated with reduced risks of ischemic stroke admissions over a lag time of 0 to 10 days [31]. The diverging results may be due to long-term exposure to high solar radiation in Qatar compared to Harbin, Northeast China, which has moderate solar exposure. Furthermore, Wu et al. also noted a protective effect of UVR in adults aged 65 years or younger and in females [31]. Additionally, Salam et al. observed an inverse association between ischemic stroke incidence and both atmospheric pressure and relative humidity [30]. However, a significant positive association between maximum daily atmospheric pressure and incidence of aneurysmal subarachnoid hemorrhage was reported in China [29].

Respiratory system

An association between temperature on respiratory diseases has been well established [23, 27, 32-35]. Higher temperatures were associated with an increased risk of asthma hospitalisation [34, 35], and respiratory-related emergency room visits, with males and individuals aged 20–59 years particularly affected [34]. Zhu et al. reported that lower temperature and a sudden decline in temperature between neighbouring days are associated with a significantly higher risk of asthma exacerbation. Furthermore, males, individuals aged above 40 years, and those with a body mass index (BMI) above 25 kg/m^2 were at a higher risk [27].

Chen et al. reported that temperature has a U-shaped association with adult asthma hospitalisation across a 30-day lag period [33]. Furthermore, Chen et al. identified that extreme cold had more pronounced effects than extreme heat; among adults, women, and the elderly were significantly vulnerable to both extremes [33]. Similarly, Achebak et al. found

that women had significantly higher mortality from heat-induced cardiovascular and respiratory diseases compared to men, and the impact was more evident in older adults [23].

In children, Cheng et al. observed increased risk of respiratory disease admissions on days with high temperature (above 32 °C), combined with elevated ambient formaldehyde (12–14 × 10^{15} molecules/cm^2) compared to ambient formaldehyde alone [36]. Blando et al. reported that wildfire smoke was associated with a significant decrease in peak flow measurements one year after each wildfire event, with women and black patients experiencing the highest average peak flow measure decrease [37].

Renal system

Five studies investigated the renal adverse effects of CC; among them, four focused on occupational heat-exposure studies, and one was a community-based population study. Heat exposure significantly reduced the estimated glomerular filtration rate (eGFR) among factory workers compared to controls over the work shift [38]. Similarly, Nicolas et al. reported a comparable trend among migrant seasonal farm workers (MSFWs) in Mexico [39]. A multinational community-based population study reported that exposure to ambient heat independently accelerates decline in eGFR by –0.9% annually in individuals with established chronic kidney disease (CKD) [40]. In Saudi Arabia, construction workers exposed to high ambient temperatures showed a significantly increased albumin-to-creatinine ratio (ACR) throughout the summer months, with some workers developing new-onset albuminuria and CKD [41]. In addition, a Florida-based study among agricultural workers reported a positive association between heat exposure and acute kidney injury (AKI) on at least one workday during the study [42].

Gastrointestinal system

Five studies examined the effects of CC on the gastrointestinal (GI) system. Seo et al. reported that sunshine exposure significantly increased the risk of utilising medical care for gastroesophageal reflux disease (GERD), while wind speed was significantly associated with lower medical care usage. Notably, there was a 6-day lag time for sunshine and a 9-day lag time for wind speed [43]. In Korea, higher sun exposure showed a protective effect against paediatric irritable bowel disease (IBD) [44].

A Japanese study reported that floods significantly exacerbated and triggered a new onset of irritable bowel syndrome (IBS) among flood victims. This was demonstrated by a notable

increase in the number of ramosetron, polycarbophil calcium, and mepenzolate bromide for victims immediately after the disaster [45]. In Bangladesh, the Water, Sanitation, Hygiene (WASH) Benefits Trial revealed that heavy rainfall and higher temperatures are associated with increased incidence of diarrheal disease among children, likely due to exposure to enteric pathogens [46]. Isler et al. investigated GI manifestations in patients with heatstroke and found that 18.5% developed at least one GI symptom, including diarrhoea, flatulence, nausea/vomiting, and bloody stools, during the intensive care unit (ICU) stay. Older patients and those with low Glasgow Coma Scale (GCS) scores were most likely to experience GI symptoms. Furthermore, patients exhibiting at least one GI symptom developed kidney injury, liver dysfunction, and central nervous system (CNS) damage, had longer ICU stay, and were less likely to tolerate enteral nutrition (EN) therapy [47].

Mortality rate

Multiple studies investigated the association between mortality rate and different temperature metrics (daily air temperature, maximum air temperature, average temperature, and mean temperature). Among these, the majority focused on all-cause mortality as the primary measure [48-62], while a few investigated the impact of temperature on specific causes of mortality. These include MI mortality rate [63], type 2 diabetes (T2D) mortality rate [64], hypertension mortality rate [65], stroke mortality rate [66, 67], CVD mortality rate [68], and coronavirus disease (COVID-19) mortality rate [69]. In another study, Açıktepe et al. found that median air pressure and median humidity significantly increased the cardiovascular mortality, whereas air pressure and humidity variability (fluctuations) showed protective effects [70].

High temperatures were consistently associated with increased risk of all-cause mortality [48, 49, 51, 55, 57, 58, 61] as well as mortality from T2D [64], hypertension [65], and stroke [67]. On the other hand, cold temperatures increased the risk of (MI) mortality rate [63]. Four studies reported that both cold and elevated temperatures are associated with increased risk of all-cause mortality [50, 52-54, 56]. Moreover, both cold and high temperatures were associated with increased risk of mortality from stroke [66], CVD [68], and the COVID-19 disease [69].

The collective scientific evidence demonstrates that climate change poses a threat to human well-being and planetary health. Evidence across major systems, cardiovascular, cerebrovascular, renal, and gastrointestinal systems, shows that CC is a broad physiological stressor. Heat exposure consistently emerges as a central mechanism, driving dehydration,

electrolyte imbalance, haemoconcentration, and increased metabolic demand. All these clinical presentations increase the risk of acute events such as MI, arrhythmias, stroke, and AKI or exacerbate preexisting conditions such as diabetes, CKD, IBS, and IBD, and increase morbidity and mortality. In addition, other co-exposures such as air pollution, poor water quality, and food insecurity disproportionately impact individuals with pre-existing disease, the elderly, and socioeconomically disadvantaged populations. Overall, the evidence demonstrates that the impact of CC is not limited to a single organ but rather a complex phenomenon that affects multiple physiological systems.

Direct Impact of Climate Change on Pharmaceuticals

Drug stability, pharmacokinetics, and pharmacodynamic changes

Extreme temperature can directly alter the physicochemical properties of pharmaceutical products, thereby disrupting their pharmacokinetic and pharmacodynamic properties [11]. This has a significant impact on the stability of pharmaceuticals. Medications are formulated to be stable within specific temperature ranges; thus, any deviation from these ranges will accelerate degradation of the pharmaceutical product, which in turn will alter the product's shelf-life and overall effectiveness. Similarly, humidity plays a role, as it accelerates the degradation of hygroscopic drugs, potentially leading to reduced efficacy, dose dumping, and adverse effects [71]. A recent case report in the Philippines described melted sodium valproate tablets following exposure to extreme, unseasonal heat of 42°C and high humidity. Sodium valproate is generally stable at high temperatures; however, it is hygroscopic, making it susceptible to degradation in humid environments [72]. Furthermore, a patient developed generalised convulsive status epilepticus following the use of water-exposed carbamazepine, and this was marked by decreased serum level of carbamazepine during admission. Pharmaceutical analysis demonstrated a reduction in mean dissolution from >80% to 16% at 60 min for moisture-exposed carbamazepine tablets compared with dry carbamazepine tablets [73]. A study in Italy found that improper storage (exposed to heat, light, and humidity) of levothyroxine tablets was linked to refractory hypothyroidism [74].

Kaplan et al. report that in resource-limited settings, with limited access to appropriate cold chain facilities, heat-sensitive pharmaceuticals, such as vaccines, insulin, and blood products, are most likely to degrade during extreme heat. This will compromise the quality, safety, and

efficacy of the pharmaceutical products. In addition, there is a potential increased risk of post-partum haemorrhage owing to the use of unstable oxytocin in settings with limited access to adequate cold chain [12].

Together, these climatic stressors highlight the need to strengthen pharmaceutical formulation, packaging, and labelling requirements, as well as the storage and distribution of climate-sensitive pharmaceutical products. Furthermore, there is a need for proper patient counselling on the appropriate storage of these medications.

Direct impact of climate change on human health in relation to pharmaceuticals

Higher temperatures have been linked to increased mortality rates from type 2 diabetes (T2D) [64], hypertension [65], cerebrovascular events [66, 67] cardiovascular diseases [68], and COVID-19 mortality rate [69]. Heat exposure induces a series of physiological responses, including increased core temperature, cardiovascular stress (increased heart rate and cardiac output), haemoconcentration, increased blood viscosity, reduced central blood volume, renal hypoperfusion, electrolyte imbalance, and dehydration. These directly affect cardiovascular and renal function [75, 76]. In addition, this will alter pharmacokinetic parameters, including absorption, distribution, metabolism, and excretion. Subsequently, this will reduce bioavailability and efficacy and increase the risk of adverse drug reactions (Figure 2).

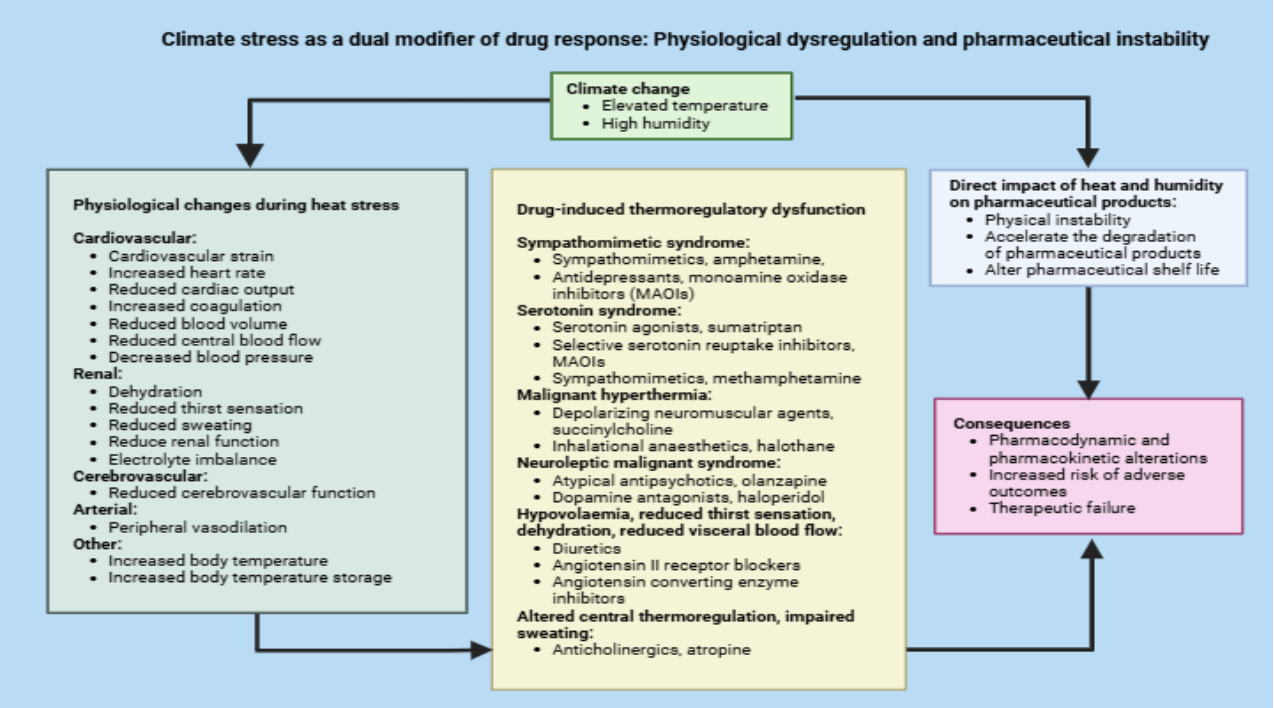


Figure 2. The diagram illustrates how climate change stressors, by disrupting thermoregulation, cause physiological changes and drug-induced thermoregulatory dysfunction. In parallel, climate stressors accelerate pharmaceutical degradation and alter formulation performance, collectively modifying drug safety, efficacy, and therapeutic outcomes. Created using https://BioRender.com

It is well known that heat exposure disrupts normal thermoregulatory function. This is particularly detrimental in heat-sensitive individuals, including the elderly, oncology patients, and those living with chronic conditions. Often, these individuals use multiple medications from different therapeutic classes, some of which are known to interfere with thermoregulation [77]. These drug classes include antidepressants, antipsychotics, anticonvulsants, benzodiazepines, opioids, antidiabetics, novel oral anticoagulants, diuretics, angiotensin II receptor blockers, angiotensin converting enzyme inhibitors, and anticholinergics [78]. Interestingly, prior studies have reported diverging findings. In France, a pharmacovigilance study reported more heat-related adverse drug reactions among the elderly during heat wave periods compared to non-heat wave periods [79]. Conversely, a US study found no increased risk of hospitalisation among the elderly during heatwave periods, compared with warm months. Thus, such medications do not have synergistic effects during heatwave events [80]. Indeed, the interplay between drug-induced thermoregulatory dysfunction and heat stress needs to be elucidated, particularly in relation to clinical outcomes and potential adverse events.

Studies have shown that high ambient temperatures consistently increase the risk of emergency department visits and hospitalisation due to drug poisoning, alcohol-related disorders, and substance use disorders. A German study reported that elevated temperatures compared to mild temperatures increase the frequency and severity of acute severe poisoning from opioids, sedatives/hypnotics, other multiple drugs, and alcohol, with varying severity. All other drugs demonstrated a significant association, while the association with alcohol was not significant [81]. In New York State, a longitudinal study described a linear relationship between an increase in temperature and alcohol-related and substance-related disorders (cocaine and cannabis) across most temperatures, with a lag of 0–6 days for alcohol-related disorders and 0-3 days for substance-related disorders [82]. Similarly, Noris-Sarma et al. and Yoo et al. reported that short-term exposure to high temperatures significantly increased the risk of emergency department visits for mental disorders, including substance abuse [82, 83]. Furthermore, Yoo et al. found no significant association with cold temperatures [84]. In addition, Chang et al. reported that short-term exposure to elevated temperatures increased the risk of use and overdose of amphetamines, cocaine, and opioids [85]. Chang et al. and Noris-Sarma et al. found that males were at high risk of substance-related disorders during high temperature exposure compared to females [83, 85]. Furthermore, Chang et al. revealed that non-Hispanic individuals were at a lower risk of amphetamine related emergency department visits compared to Hispanic groups. Socioeconomic disparities were the probable cause of the risk differences rather than biological differences [85]. Contrary to this, Parks et al. and Yoo et al. found that age, gender, and social vulnerability factors did not have any modifying effects on the substance-related disorders outcomes [82, 84].

Furthermore, Sklebar et al. reported that the therapeutic effects of some medications can be increased during heatwaves, which can increase the risk of adverse drug reactions. For example, nitro-glycerine could lead to hypotension [14]. In addition, revealed that there is an increased risk of hypoglycaemia in diabetic patients using subdermal insulin in warm weather conditions [86]. Recently, Gulcebi et al. described a decrease in serum phenytoin concentration levels in people living with epilepsy during summer days compared to other seasons in a hot and humid setting. Similarly, in Denmark, the same pattern was noticed during unusually hot days. Furthermore, high ultraviolet light intensity and high vitamin D levels have been associated with lower serum levels of sirolimus and tacrolimus during the hot summer months [11]. A summary of representative CC-impacted drug molecules is shown in Figure 3.

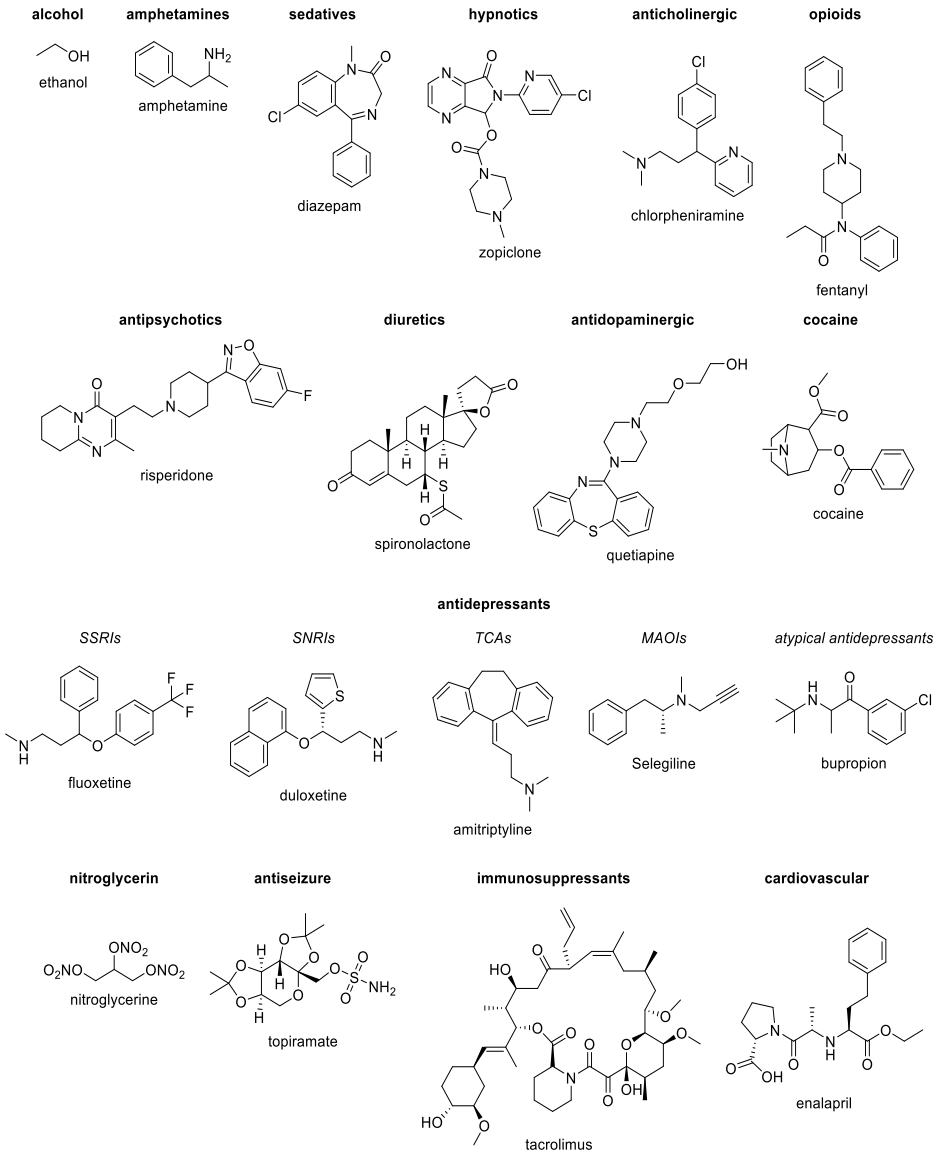


Figure 3. Examples of representative drug molecules from the highlighted drug classes affected by climate change in their efficacy or toxicity profiles in human health.

Policy implications, regulatory, and clinical practice

Climate change and extreme weather events directly or indirectly cause various physiological changes, exacerbating existing conditions or increasing the incidence of new ones. Vulnerable groups, such as low-income individuals, the elderly, women, and children, ethnic groups, indigenous people, and people with disability, continue to be disproportionately affected by CC [2]. It is projected that extreme weather events, including heatwaves, will increase in frequency, duration, and intensity. Heatwaves induce heat stress alters pharmacokinetics and pharmacodynamics. Heat-sensitive individuals, including the elderly, oncology patients, and those living with chronic conditions, are at a higher risk of worsening diseases, diminished

drug efficacy, and increased risk of adverse drug effects. It is therefore imperative that clinical guidelines be updated to incorporate these risks. Clinicians should receive adequate training to identify drug classes that interfere with thermoregulation, conduct therapeutic monitoring, and make temporary dose adjustments during heat waves. Moreover, they should offer personalised patient education on recognising heat-related illnesses and on reducing the risk of drug-induced thermoregulatory issues, along with specific precautions for medications during heat exposure.

There is an urgent need for high-resolution, large-population cohort studies that include multiple climate change variables to fully understand the impact of climate change on pharmacotherapy. Furthermore, pharmacovigilance systems should link meteorological data to adverse event reporting to enable real-time risk identification and facilitate real-world data analysis, thereby complementing cohort studies.

Extreme temperature and humidity directly alter the physicochemical properties and stability of pharmaceutical products, thereby disrupting their pharmacokinetic and pharmacodynamic properties. This is particularly a major concern for climate-sensitive pharmaceutical products; therefore, strict cold-chain management should be implemented throughout the product lifecycle. Most current stability testing protocols are based on historical temperature data, which may not accurately reflect the current frequency and intensity of heatwaves. Therefore, national medicines regulatory agencies need to review their requirements in line with current and projected temperatures and humidity. Mandatory labelling updates for medicines linked to thermoregulation dysfunction. Increased industry investment in climate-resilient pharmaceutical formulations should be prioritised to safeguard public health in a warming climate. In addition, in resource-limited settings, local manufacturing should be prioritised to reduce dependence on the cold chain and associated costs.

Conclusions

This review provides an up-to-date synthesis of how climate change affects human health and pharmaceutical safety across multiple systems. The evidence highlights which diseases, patient groups, and medications are most vulnerable to climate-related stressors, offering essential insight into how healthcare practices and pharmaceutical interventions must evolve in a warming world. Overall, the current literature reveals a substantial knowledge gap regarding how climate change will alter drug safety, efficacy, stability, and patient outcomes. There is an urgent need for integrated, multidisciplinary research to understand these interactions and to

support the development of climate-resilient healthcare and pharmaceutical systems. Strengthening this evidence base will be essential to ensuring safe and effective treatments for diverse populations as global climatic conditions continue to shift.

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