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Review

Colliding crises: The global diabetes pandemic meets climate change—A scoping review



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ABSTRACT

Introduction: Climate change poses myriad threats to human health, including deleterious impacts on chronic diseases such as diabetes mellitus. A scoping review was conducted to clarify the current state of knowledge regarding climate change impacts on the incidence, progression, complications, and management of diabetes. *Methods:* Literature was searched across PubMed, EMBASE, and Web of Science combining terms related to "climate change" and "diabetes". In addition, the *Journal of Climate Change and Health* was hand searched. Primary-source, peer-reviewed human studies were included in the analysis. Animal studies, plant-based research, studies focused upon pollution, and review articles were excluded.

Results: Seventy-three articles met the inclusion criteria. Articles predominantly focused upon heat-related health effects, noting linkage to deteriorating glycemic control, increased mortality, and more frequent emergency room visitations. While studies examined mortality linked to heat, cold, and natural disasters, a notable proportion failed to specify precise causes of death. Significant data gaps were identified regarding climate impacts on diabetes-related complications and non-glycemic metabolic outcomes as well as impacts on pediatric, gestational, and type 1 diabetes. Few studies focused upon low and middle-income countries where climate impacts are predicted to be greatest.

Conclusion: Various manifestations of climate change are linked to multiple adverse outcomes among those with diabetes. However, current data is sparse regarding climate impacts on vulnerable populations, diabetes-related complications, and geographic regions most vulnerable to climate change that are also experiencing the greatest rise in diabetes rates. Mitigating the impact of climate change on those with diabetes requires closing these data gaps.

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1. Introduction

The last several decades have witnessed a dramatic increase in the rates of diabetes mellitus across the globe. In 2021, 537 million adults

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were estimated to have diabetes worldwide, and this number was projected to grow to a staggering 783 million by the year 2045 [1]. The impacts of this are potentially devastating to both individuals and healthcare systems. Diabetes is a leading cause of adult blindness, kidney failure, and non-traumatic amputations; it is also a potent driver of cardiovascular disease, a principal contributor to mortality [2]. In addition to the profound impacts on individual morbidity and mortality, the economic toll of the disease is enormous. In the United States alone, the total annual economic burden of diabetes is estimated to be \$412.9 billion [3], and globally, total diabetesrelated health expenditures are projected to reach a staggering \$1.05 trillion by 2045 [1]. The addition of factors that could amplify the burden of diabetes or its complications, such as climate change, could be truly devastating, yet they remain understudied.

Climate change impacts health through multiple direct and indirect pathways, including increased exposure to extreme heat; disruptions to infrastructure from extreme weather events; increased vector-borne, water-related, and food-related diseases, and other factors [4,5]. According to the Intergovernmental Panel on Climate Change Sixth Assessment Report, 3.3 to 3.6 billion people globally are highly vulnerable to climate change [6], while the World Bank estimates that the number of people exposed to extreme weather events, including heat waves, floods, droughts, and cyclones, increased from 4.0 billion in 2010 to 4.5 billion in 2019 [7]. The health impacts of these events are potentially catastrophic, with the World Health Organization projecting that climate change could be responsible for an additional 250,000 annual deaths between 2030 and 2050 arising from undernutrition, malaria, diarrhea, and heat stress alone [8].

Based upon the pathophysiology of diabetes, its adverse impacts on physiology, and the complexities of its treatment, there is significant *a priori* potential for climate change to amplify the impacts of diabetes on individuals and healthcare systems. Biological factors include the contribution of diabetes to chronic kidney disease (CKD) and osmotic diuresis that can lead to abnormal fluid handling and dehydration, factors likely to be exacerbated by extreme heat and disrupted access to drinking water [9], which can further worsen glucose homeostasis in those with diabetes [10]. During heat waves, patients with diabetes are at a higher risk of adverse cardiovascular events, including myocardial infarctions, compared to healthy individuals [9]. Diabetes is also associated with the development of various neuropathies, including autonomic dysfunction [11], which can impair thermoregulation [12], rendering those with diabetic neuropathy more sensitive to temperature extremes. From the perspective of health delivery, the need to refrigerate insulin and other anti-diabetic medications amplifies the vulnerability of those on these medications to disruptions in electrical supply or dislocation arising from extreme weather events and natural disasters. Thus, from both individual and systems perspectives, those with diabetes are predicted to be especially vulnerable to disruptions induced by climate change.

Both diabetes and climate change exert unequal impacts across society. The impact of climate change on health is predicted to exhibit marked disparities based upon geographic region [5], with additional disparate impacts on low income and some communities of color, immigrant groups, Indigenous Peoples, children and pregnant women, older adults, vulnerable occupational groups, people with disabilities, and persons with chronic medical conditions, including diabetes [4]. Critically, those regions predicted to experience the greatest increase in diabetes rates are also expected to experience some of the most severe impacts of climate change [13]. These include regions such as Southeast Asia, the Middle East and North Africa, and sub-Saharan Africa that are projected to see increases in diabetes prevalence from 2021 to 2045 of 68%, 87%, and 134%, respectively [1].

Understanding how climate change impacts diabetes development, its associated complications, and the provision of care for those with the disease will be critical for building resilient systems that protect the well-being of those living with diabetes. The purpose of this targeted scoping review was to assess the current state of knowledge connecting various manifestations of climate change with diabetes rates, complications, and mortality to both identify critical data gaps and to provide a platform for synthesizing knowledge that can be used to address these colliding crises.

2. Materials and methods

The search was executed on 10 July 2023 in three databases: PubMed, Web of Science, and Embase. The search was supported by a medical librarian and included terms related to climate change and diabetes (Supplemental Table 1). The search was iterative, with new terms added as they were found throughout the search process. Only the most recent literature was included in the search set, resulting in date filters for all three databases of 1 January 2018 to 10 July 2023. In addition, The Journal of Climate Change and Health was handsearched from March 2021 to August 2023. Inclusion criteria encompassed studies investigating the impact of extreme environmental conditions [including heat, cold, and natural disasters (specifically, flooding, tropical storms, cyclones, typhoons, hurricanes, and wildfires)] on individuals affected by diabetes (including those with type 1, type 2, gestational, and pediatric/juvenile diabetes). Primarysource, peer-reviewed human studies were the focus of this analysis. Animal studies, plant-based research, studies focused upon pollution, and review articles were excluded. All abstracts were uploaded to the systematic review software Covidence (Melbourne, Australia). The screening process included two stages to determine the relevance of the identified studies: title and abstract screening followed by full text review. All articles were screened by two reviewers at each stage to ensure they met the inclusion criteria. In the event of any disagreement, discrepancies were resolved through discussion and consensus between the reviewers.

Data from each article that was selected for review was extracted (*Supplemental Table 2*). For all extracted studies, key findings were incorporated into a matrix to classify articles into three general categories of climate change effects: heat-related health effects, cold-related health effects, and natural disasters. Articles were then further organized into seven sub-categories: glycemic control, non-glycemic metabolism, diabetes-related complications, non-diabetes-related complications, healthcare utilization, mortality, and others. Articles in each of the sub-categories were organized based upon whether they pertained to type 1 diabetes, type 2 diabetes, or gestational diabetes. If no distinction was made between type 1 or type 2 diabetes, the article was categorized under both. Some articles were classified under more than one category. Each article was also categorized based on the country studied, with each country classified by the World Bank's income-level criteria [14].

3. Results

Initially, 2,789 articles were identified: PubMed (817), Web of Science (257), Embase (1713), and *The Journal of Climate Change and Health* (2). Upon removal of duplicates, 1,991 unique articles underwent title and abstract screening, and 158 of these articles were included in the full-text review. Of those 158 articles, 73 articles met the inclusion criteria, were included in the analysis (Fig. 1), and were subsequently classified (Table 1).

3.1. Geographic distribution of data

We analyzed the geographic distribution of study populations included across all 73 articles (Fig. 2). Studies from the United States were the most common (23 publications) followed by 9 studies evaluating impacts in Puerto Rico. China and Canada contributed 8 articles each, while all other countries provided 3 articles or fewer

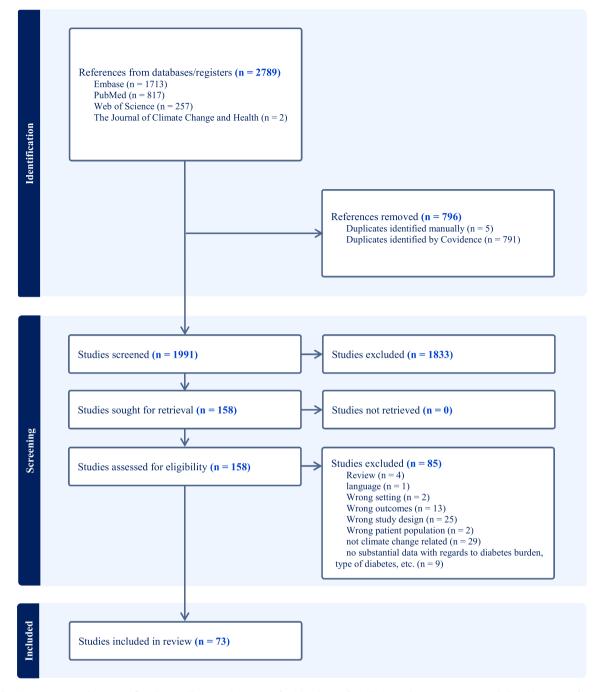


Fig. 1. Article selection strategy. This PRISMA flow diagram illustrates the process of article selection for inclusion in this scoping review, including the number of studies identified and retained at each stage of the review process.

(Table 2). Several articles reported data from more than one country, while two included global data [15,16]. Of note, the majority of studies focused on high-income countries (59), with fewer studies from middle-income countries (21), and no studies from low-income countries.

3.2. Impacts on metabolic physiology

To understand the impact of climate change on diabetes, we first examined studies assessing the impact of extreme heat, extreme cold, and natural disasters on glycemic control. Non-glycemic metabolism was also evaluated; however, no articles met the criteria for classification into this category (Table 1).

3.2.1. Extreme heat and cold

A cross-sectional investigation exploring the effects of exposure to long-term temperature variability amongst elderly Chinese individuals revealed an increase in the prevalence of common diseases such as cardiovascular disease, cerebrovascular disease, and asthma, but did not associate heat nor cold with diabetes [17]. In contrast, a US cohort study found increased rates of hospital admissions for diabetic ketoacidosis (DKA) and hypoglycemia during both extreme hot and cold weather [18]. Interestingly, the association of extreme cold with DKA admissions was greater than the impact of extreme heat in this study, while hypoglycemia admissions were similarly increased for both extreme heat and cold [18]. Similar effects were also observed among Japanese adults, where heat exposure was associated with a higher risk of hospital admissions for DKA and hypoglycemia as well

Conceptual organization of climate change and diabetes-related parameters. Studies were categorized based upon the specific climate-based impacts they assessed and the diabetes-related outcomes analyzed. Studies that analyzed individuals with both type 1 and type 2 diabetes were included in both columns. Of note, only three articles specifically looked at type 1 diabetes, a noted deficit in the available data. For discussion purposes, glycemic control and non-glycemic metabolism were grouped together in the text as were diabetes-related and non-diabetes related complications. A1c, hemoglobin A_{1c}; CKD, chronic kidney disease; DKA, diabetic ketoacidosis; DM, diabetes; DR, diabetic retinopathy; HHS, hyperosmolar hyperglycemic state.

Climate Based Impacts	Diabetes Related Outcomes	Type I DM (A)	Type II DM (B)	Gestational DM (C)
(1) Heat-Related Health Effect	(1a) Glycemic control (ex. worsening A1c, increase incidence of HHS/DKA, hyper/hypo- glycemia)		5	3
	(1b) Non-glycemic metabolism (ex. lipid derangements)	0	0	0
	(1c) DM-related complications (ex. CKD, worsening DR)	1	2	0
	(1d) Non-DM related complications (ex. dehydration, acute kidney injury, altered mental status, others)	7	11	1
	(1e) Healthcare utilization	4	10	0
	(1f) Mortality	10	12	0
	(1g) Others	2	4	1
(2) Cold-Related Health Effect	(2a) Glycemic control (ex. worsening A1c, increase incidence of HHS/DKA, hyper/hypo- glycemia)	1	2	2
	(2b) Non-glycemic metabolism (ex. lipid derangements)	0	0	0
	(2c) DM-related complications (ex. CKD, worsening DR)	0	0	0
	(2d) Non-DM related complications (ex. dehydration, acute kidney injury, altered mental status, others)	2	5	0
	(2e) Healthcare utilization	1	2	0
	(2f) Mortality	4	5	0
	(2g) Others	0	0	1
(3) Natural disasters	(3a) Glycemic control (ex. worsening A1c, increase incidence of HHS/DKA, hyper/hypo- glycemia)	3	7	0
	(3b) Non-glycemic metabolism (ex. lipid derangements)	0	0	0
	(3c) DM-related complications (ex. CKD, worsening DR)	0	0	0
	(3d) Non-DM related complications (ex. dehydration, acute kidney injury, altered mental status, others)	3	5	2
	(3e) Healthcare utilization	4	6	1
	(3f) Mortality	4	4	0
	(3g) Others	1	1	1

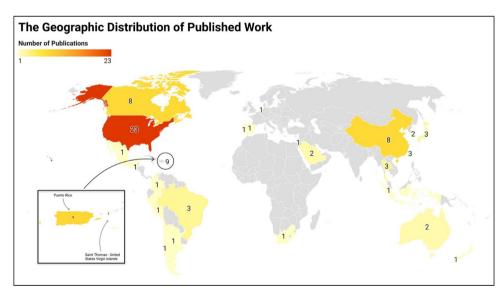


Fig. 2. Geographic distribution of articles examining the intersection of climate change and diabetes. The distribution of articles is shown in this map, which highlights the relative paucity of data from middle-income countries and the lack of data from low-income countries.

as hyperosmolar hyperglycemic state [19]. Heat exposure during the hot season in Brazil was similarly linked to a heightened risk of diabetes-related hospitalizations, including diabetic coma and DKA [20]. Specifically, every 5°C rise in daily mean temperature was associated with a 6% increase in hospitalizations, an effect particularly notable among individuals aged 80 years or older [20]. Increased hemoglobin A1c (HBA_{1c}) levels were linked to rising ambient temperatures in a Saudi study in which each 1°C increase in average weekly temperature was associated with a 0.007% HbA1c increase [21].

3.2.2. Natural disasters

While no significant differences were found in mean HbA_{1c} levels before and after Hurricane Matthew, a higher period prevalence of DKA was identified following the hurricane's impact on North Carolina in the US [22]. Similarly, a single-center analysis in New Orleans, Louisiana, revealed a significantly higher diabetes prevalence in their cohort after Hurricane Katrina [23,24]. Puerto Rico, a Caribbean island frequently thrashed by hurricanes, has been the focus of several studies examining the impact of natural disasters. For example, two

Geographic distribution of studies. The articles analyzed were categorized based on the country studied and classified according to the World Bank's income-level criteria [14]. A majority of the available data came from highincome countries, with less data from middle-income countries, and no data available for low-income countries. Note: several articles reported data from more than one country, while two included global data [15,16].

Level of Income	Country	Number of Publications
High-Income Countries	USA	23 [18,22–24,33,43,44,46–51,53,54,63,68,71,73–75,81,103]
	Puerto Rico	9 [25-27,62,66,67,81,104,105]
	Canada	8 [38,39,76,82-85,106]
	Japan	3 [19,31,34]
	Australia	2 [45,77]
	Saudi Arabia	2 [21,36]
	South Korea	2 [32,65]
	Chile	1 [63]
	Israel	1 [78]
	Netherlands	1 [41]
	New Zealand	1 [63]
	Portugal	1 [57]
	Spain	1 [107]
	St. Thomas (USVI)	1 [52]
	Taiwan	3 [29,69,70]
Middle-Income Countries	China	8 [17,30,40,56,60,63,64,72]
	Brazil	3 [20,59,63]
	Thailand	3 [15,35,80]
	Argentina	1 [58]
	Colombia	1 [63]
	Guatemala	1 [63]
	Indonesia	1 [42]
	Mexico	1 [63]
	Peru	1 [28]
	South Africa	1 [63]
Low-Income Countries	None	No Studies

studies reported increases in both HbA_{1c} levels and diabetes incidence after Hurricanes Maria and Irma [25,26]. Another study in Puerto Rico after Hurricane Maria found that post-hurricane participants had lower rates of diabetes and were less likely to have medical insurance [27], prompting investigators to hypothesize that residents of lower socioeconomic status and with chronic illnesses were more likely to emigrate in the post-hurricane period. Finally, a study conducted in Peru found that floods were associated with a three-fold increased incidence of hypertension and diabetes amongst 544 displaced families [28].

3.3. Impacts on diabetes-associated and other health complications

Articles were analyzed for associations linking climate changerelated factors with diabetes-associated complications, including retinopathy, nephropathy, neuropathy, and cardiovascular disease, as well as other medical complications.

3.3.1. Extreme heat and cold

A study from Taiwan linked low temperatures to an increased likelihood of Emergency Room (ER) visits for cardiac arrest among patients with a history of cardiovascular disease and hypertension, but not among those with a history of DM [29]. Another study conducted in China demonstrated an increase in acute myocardial infarction admissions among patients with diabetes with both extremes of high and low temperatures [30]. A Japanese study identified diabetes as a comorbidity that enhances the risk of admissions for acute cardiovascular diseases linked to temperature variability [31]. They observed a 2.07 % increase in heart failure admissions per 1°C rise in temperature among patients with diabetes, compared to a 0.61% increase in those without diabetes [31]. Among US Medicaid beneficiaries, admissions for sudden cardiac arrest or ventricular arrhythmias were higher during both cold and hot temperature extremes for those with type 2 diabetes (T2D) [18]. A Korean study identified a significant association between both high and low temperatures and ER

visits for ischemic stroke, including among patients with diabetes [32]. A study assessing susceptibility to heat-related illnesses (HRI) among US Veterans found that Black and American Indian/Alaska Native Veterans were disproportionately more likely to be diagnosed with HRI [33]. Similarly, a study in Japan evaluating individuals who worked in factories, construction, fire stations, or as traffic guards showed that those with impaired glucose tolerance were more susceptible to HRI [34]. Additionally, elderly Thai farmers with hypertension, diabetes, or heart disease were more likely to perceive hot conditions while working outdoors [35]. Finally, a Saudi study identified diabetes as the most prevalent comorbidity among Hajj participants who developed heatstroke and heat exhaustion [36].

Hear rate variability (HRV) is a measure of cardiac fitness [37]. A study comparing HRV during exercise at elevated temperatures between young individuals with and without T1D found a more pronounced reduction in HRV among those with type 1 diabetes, particularly with vigorous exercise, which may indicate increased cardiac risk [38]. These data highlight potential differences in cardiovascular response to heat between individuals with and without diabetes [38]. Importantly, the authors noted that these findings may suggest that vigorous exercise in hot environments may pose enhanced risks for those with T1D. Intriguingly, a study of physically active older adults found that those with well-controlled T2D had levels of cardiovascular strain and hyperthermia comparable to their non-diabetic counterparts when exposed to three hours of passive heating, suggesting similar capacities to dissipate heat during brief periods of extreme temperatures [39]. Intriguingly, these data may also indicate that improved glycemic control may protect against heat-induced complications; however, this requires formal study.

Regarding microvascular complications, extreme humidity was identified as a trigger for the onset of painful diabetic neuropathy among patients with diabetes, with women and patients under the age of 65 years particularly susceptible [40]. Another analysis using data from the Global Burden of Disease Study spanning the years 1990 to 2019 highlighted that hypertension and diabetes were the primary causes of CKD deaths associated with non-optimal temperatures, with males and older adults having heightened vulnerability [15].

3.3.2. Natural disasters

Two studies examining the aftermath of Hurricane Katrina found an increased prevalence of coronary artery disease and increased incidence of acute myocardial infarction up to 14 years after the storm. Diabetes drives cardiovascular disease development, and the prevalence of diabetes was markedly higher in the post-hurricane versus pre-hurricane cohorts used in these analyses [23,24].

3.4. Impacts on healthcare utilization

In addition to evaluating the impacts of climate factors on acute diabetes-associated complications, studies examining diabetesrelated healthcare utilization were evaluated.

3.4.1. Extreme heat and cold

Increased hospital admissions for diabetes-related complications due to heat exposure have been documented in studies conducted in the US, Australia, Brazil, Indonesia, The Netherlands, and Japan [18 -20,41-45]. For example, one study found that on days above 30°C, the proportion of diabetes-related visits increased between 20.9% and 24.7% [42]. Higher temperatures were also associated with increased admissions for dehydration, ischemic stroke, and primary diabetes [44]. Moreover, higher temperatures were associated with an increase in emergency response calls in the US, particularly among Black patients with diabetes [46]. Patients taking angiotensin converting enzyme inhibitors, angiotensin-receptor blockers, insulin, antipsychotics, or with a history of CKD were found to have a higher likelihood of hospitalization for heat stroke [41,43]. A study conducted in Australia determined that temperature significantly contributed to a substantial number of hospital admissions and associated healthcare costs for temperature-related diseases, which included diabetes [45]. Importantly, a future climate scenario consistent with Representative Concentration Pathway 8.5 was projected to increase hospital admissions, lengths of stay, and costs by 2.2%, 8.4%, and 7.7%, respectively, by mid-century [45]. In a separate study, patients with end-stage renal disease experienced an increased risk of hospital admission upon exposure to heat events, particularly those with a pre-existing diagnosis of diabetes [47]. A study conducted in the US demonstrated a U-shaped relationship between ER visits and temperature for those with diabetes, with increased ER visits resulting during both unusually warm and cold days [48]. The increased risk of ER visits during cold events was greater than that observed for warm events, with cold waves increasing the odds of ER visits by up to 11% [48]. Additionally, periods of high temperatures were associated with increased acute care utilization for patients with chronic conditions, including diabetes [49].

3.4.2. Natural disasters

Two US studies examined the health impacts following Hurricanes Katrina and Rita among elderly Medicare beneficiaries with diabetes [50,51]. One study reported increased ER visits and longer hospital stays, while the other noted significant declines in screening rates for diabetes and diabetes-associated complications (e.g., HbA1c, urinary microalbumin, cholesterol, and retinal exams) that persisted for up to three years after the hurricanes. In the US Virgin Islands (USVI), there was a substantial increase in patients seeking care for diabetes-related issues following Hurricanes Irma and Maria, with 55% of visits attributable to diabetes or related illnesses [52]. Patients with diabetes were more likely to seek medical attention during the post-hurricane period, particularly patients who were Black, often for non-urgent complaints [52]. Additionally, an analysis of US Federal Emergency Management Agency records following eight different hurricanes revealed an overall increase in hospitalizations for all causes, including those associated with diabetes [53]. Furthermore, Medicare beneficiaries with diabetes were found to be less likely to fill their prescriptions after Hurricane Irma made landfall [54].

3.5. Impacts on mortality

Diabetes is a leading driver of global mortality, directly causing 1.5 million deaths worldwide in 2019 with an additional 460,000 deaths arising from diabetes-associated kidney disease [55]. Thus, we examined studies for data linking climate change to diabetes-associated mortality.

3.5.1. Extreme heat and cold

Two studies, one conducted in China and the other in Portugal, assessed the impact of climate change on temperature-related mortality, revealing that both low and high temperatures elevate the risk of mortality [56,57]. Heatwaves are linked to excess deaths as well as an increased risk of diabetes-related mortality [58,59], effects that are particularly pronounced with higher heatwave intensity and with impacts greater in rural compared to urban areas [60,61]. Increased vulnerability to heat stress was especially noted among women, individuals with less education, and the elderly [58-60]. Conversely, increased levels of greenery are linked to reduced heat-related mortality [61]. Additionally, pre-existing diabetes was found to increase mortality risk associated with extreme heat events among patients with end-stage renal disease [47]. A study from Puerto Rico revealed increased mortality resulting from heat; while stroke and cardiovascular diseases were the primary causes of deaths associated with high temperatures, 4.5% of mortality was attributed to diabetes [62].

Two analyses of the Global Burden of Disease Study in 2019 were performed to evaluate the impact of non-optimal temperatures on mortality. Diabetes-related mortality increased in response to both below and above threshold temperatures, with cold-attributable mortality exceeding that of heat-attributable mortality [63]. Additionally, between 1990 and 2019, the number of deaths attributed to type 2 diabetes due to non-optimal temperatures rose by over 136% [16]. Another analysis of data from the Global Burden of Disease Study noted that CKD resulting from hypertension and diabetes was the primary cause of kidney disease deaths associated with non-optimal temperatures, with men and older adults being more vulnerable [15]. A study conducted in China revealed that both low and high relative humidity were associated with increased all-cause mortality as well as mortality due to cardiovascular diseases and chronic obstructive pulmonary disease; however, only low relative humidity was linked to an increased risk of diabetes-associated mortality [64].

Cold temperatures were associated with increased all-cause and cause-specific deaths, including diabetes-associated mortality [57]. Another study from Korea revealed that cold spells were linked to increased hospital admissions and greater mortality due to diabetes across various demographic groups; these associations were more pronounced with longer and more intense periods of cold [65].

3.5.2. Natural disasters

Two separate studies from Puerto Rico examining the impact of Hurricane Maria uncovered evidence of excess mortality, with some deaths linked to diabetes [66,67], with one of the studies specifically noting higher mortality rates among men compared to women, particularly among those aged 60 years or older [66]. As mentioned above, among seniors with type 1 or type 2 diabetes in the southern US, all-cause mortality increased both immediately and up to a decade after Hurricanes Katrina and Rita [68]. Among patients dependent on dialysis, men aged 45–75 years, along with patients with diabetes or a history of cerebrovascular disease, experienced significantly higher mortality rates in areas moderately affected by Typhoon Morakot, which hit Taiwan in 2009 [69]. Extending beyond

dialysis patients, another study showed increased mortality among those with a history of ischemic heart disease in the most severely affected areas, with mortality significantly increased among those with diabetes [70]. Another investigation focusing on US Medicare beneficiaries with a diagnosis of diabetes in Louisiana, Mississippi, Texas, and Alabama during 2005, the period of Hurricanes Katrina and Rita, identified increased mortality associated with both heart disease and nephritis [68].

3.6. Diabetes in pregnancy and pregnancy-related outcomes

Our search identified five articles that investigated the impact of climate change on diabetes in pregnancy. Two studies revealed a heightened risk of developing gestational diabetes (GDM) following exposure to extremely high temperatures during specific gestational periods [71,72]. Additionally, exposure to extremely low temperatures during other gestational periods was also associated with increased GDM risk [71,72]. Extreme heat events were also correlated with pregnancy complications, such as threatened or spontaneous abortion, in women with both pre-existing diabetes and GDM [73], with Blacks and women of lower socioeconomic status being particularly vulnerable. Finally, Hurricane Sandy was found to contribute to an increase in overall pregnancy complications and a higher rate of emergency room visits [74,75].

In Canada, Project Ice Storm was initiated to investigate the repercussions of *in utero* exposure to different levels of prenatal maternal stress following the 1998 Quebec Ice Storm. Adolescents who experienced the storm while in utero displayed urinary metabolomic profiles associated with deleterious alterations in amino acid metabolism, protein biosynthesis, and energy metabolism that may predict the development of metabolic disorders [76]. In Australia, a study examining the urinary metabolomes of 4-year-old children who experienced the 2011 Queensland flood while in utero found that higher prenatal stress correlated with changes in metabolites linked to protein synthesis, energy metabolism, and carbohydrate metabolism, effects that may similarly presage the development of metabolic disorders later in life [77]. Studies are now needed to assess how the metabolomic changes in both of these studies translate into health outcomes in these populations. A matched nested case-control study from Israel examining environmental exposures during gestation found that higher exposure to solar radiation, a parameter indirectly influenced by climate change, may be associated with a greater likelihood of developing type 1 diabetes [78]. In agreement with the Developmental Origins of Health and Disease Hypothesis that posits that the risk of chronic diseases, including diabetes, is enhanced by stressors during critical windows of development [79], these data collectively indicate that climate-related factors may influence the developmental programming of energy metabolism and diabetes risk; however, more studies are needed.

3.7. Other health-related metrics and outcomes

Diabetes is a complex metabolic disorder that is characterized by dysregulated metabolic cross-talk between multiple tissues that often requires treatment with anti-diabetic agents that require specific storage conditions. The use of anti-diabetic agents that require refrigeration raises concerns that disruptions in the supply of electricity from climate events may impair diabetes care. Indeed, to address these concerns, a Thai study evaluated the effectiveness of alternative cooling devices for insulin storage in hot-humid environments without refrigeration. Traditional low-cost cooling methods, such as wet sand or soil-filled clay pots, were found to lower storage temperatures to near room temperature, enabling insulin storage in resource-limited areas without the need for refrigeration [80]. In addition to medication storage, an analysis of the impacts of three major Atlantic hurricanes (one each in Texas, Florida, and Puerto Rico) on those with T1D revealed hurricane-induced disruptions in access to insulin and diabetes supplies [81]. Of note, each hurricane exhibited unique meteorological characteristics (e.g., flooding, high winds) that created distinct challenges that local providers and volunteers needed to address; furthermore, in some instances social media was critical in identifying individuals in need. Collectively, these data highlight the need for existing and deployable infrastructure to address climate-related risks for those living with diabetes.

Normal energy metabolism requires the regulated action of multiple organs coordinated, in part, by various circulating factors. In a series of studies, the impact of prolonged moderate-intensity exercise on various serum proteins under both temperate and hot temperatures was examined. Notably, Klotho concentrations remained stable during exercise in a temperate setting but increased in older men with hypertension during heat-induced exercise [82]. Similarly, serum irisin levels showed no change with exercise in a temperate environment but increased in older men with hypertension and T2D during exercise under hot conditions [83]. However, when irisin levels were compared between controls and individuals with T1D, the temperature-dependent increase was observed only in the control group [84]. Additionally, increases in serum EMAP-II concentrations were similar between healthy older men and those with hypertension; however, older men with T2D did not exhibit the normal increase in EMAP-II following prolonged exertion in the heat [85]. These data suggest that circulating factors regulating metabolism are responsive to heat stress, with potentially differential responses based on diabetes status. Further work is required to understand how these and other endocrine alterations can be used as biomarkers to study and treat climate-related impacts on metabolic health.

4. Discussion

We identified 73 primary articles exploring the impact of climate change and its manifestations on diabetes risk and outcomes. The data indicate several concerning links, including increased diabetesrelated complications and mortality as well as greater healthcare utilization arising from exposure to extreme temperatures and natural disasters. Some data indicate that climate change may worsen glycemia, although the cumulative data was somewhat inconclusive. Collectively, these findings indicate that those with diabetes may be especially vulnerable to the adverse impacts of climate change; however, significant data gaps remain.

We identified a key deficiency in data from regions experiencing the greatest increases in diabetes rates that are also at heightened risk of climate impacts. Using the regional classification employed by the International Diabetes Federation (IDF) [1], we found that a considerable proportion of current data originated from the North America and Caribbean region (33 articles or 41.2% of the total) followed by 23 articles (28.8%) from the Western Pacific region and 17 publications (21.2%) from South and Central America. Few articles were from Europe (4 articles, 5%) or the Middle East and North Africa (2 articles, 2.5%). Only one article was identified from the Africa region (1.25%), and none from the South-East Asia region (Table 3). According to IDF estimates, the regions predicted to have the greatest increase in diabetes prevalence from 2021 to 2045 are Africa (134% increase); the Middle East and North Africa (87% increase); and South-East Asia (68% increase) [1], all regions under- or unrepresented in our dataset. Similarly, despite central Asia being among the regions experiencing some of the most extreme temperature changes [86], no articles were identified with data representative of this area. Overall, our analysis revealed that the currently available data disproportionately comes from high-income countries (Table 2) and fails to capture global regions with the fastest rising diabetes rates (Table 3).

For this review, several articles related to "natural disasters" deemed unrelated to climate change were excluded; these included articles exploring the impacts of earthquakes or tsunamis on

Regional diabetes rates in relation to the geographic distribution of studies examining the impact of climate change on diabetes parameters. Total adult (ages 20–79 years) diabetes cases and age-adjusted comparative prevalence of adult diabetes for the years 2021 and 2045 were obtained from the International Diabetes Federation's Diabetes Atlas [1].

Geographic Region	Adults (20–79 years) with Diabetes [Total Number (Age-Adjusted Comparative Prevalence)]		Projected Percent Increase in Total Adult Diabetes Cases	Number of Climate x Diabetes Publications (Percentage) [References]
	2021	2045 (projected)	2021 to 2045	
Africa	24 million (5.3%)	55 million (5.6%)	134%	1 (1.25%) [63]
Middle East & North Africa	73 million (18.1%)	136 million (20.4%)	87%	2 (2.5%) [21,36]
South-East Asia	90 million (10.0%)	152 million (11.3%)	68%	0 (0%)
South & Central America	32 million (8.2%)	49 million (9.8%)	50%	17 (21.25%) [20,25–28,58,59,62,63,66,67,81,104,105]
Worldwide	537 million (9.8%)	784 million (11.2%)	46%	2 [15,16]
Western Pacific	206 million (9.9%)	260 million (11.5%)	27%	23 (28.75%) [17,19,29–32,34,35,40,42,45,56,60,61,63–65,69,70,72,77,80]
North American & Caribbear	. ,	63 million (14.2%)	24%	33 (41.25%) [18,22–24,33,38,39,43,44,46–54,63,68,71,73–76,81 -85,103,106]
Europe	61 million (7.0%)	69 million (8.7%)	13%	4 (5%) [41,57,78,92]

diabetes-related outcomes. While unrelated to climate change, these articles enhance our understanding of how migration and displacement impact diabetes care, serving as a vital resource for climate change preparedness. For example, a systematic review assessing the impact of sudden-onset natural disasters on diabetes care identified multiple articles related to earthquakes and hurricanes [87]. Their analysis identified worsening glycemic control among those with diabetes that was attributable to factors such as evacuation, poor diets, and post-traumatic stress; all of which are factors also associated with natural disasters linked to climate change. In particular, forced migrations arising from extreme weather events underscore the value in examining data on earthquake and tsunami impacts to prepare those with diabetes for potential disruptions arising from climate change.

Several articles found associations between climate change factors and an increased incidence and/or exacerbation of pregnancy-associated diabetes [71–75]. According to the IDF, the global estimated prevalence of GDM is 14.0%, with the highest rates observed in the Middle East, North Africa, and South-East Asia [88]. The IDF also identified these regions as having the highest projected increase in diabetes incidence by 2045 [1], suggesting a probable corresponding rise in the GDM incidence as well. GDM is linked to various adverse pregnancy outcomes, including premature delivery, birth injury, need for intensive neonatal care, and preeclampsia [89] as well as an increased long-term risk of developing diabetes in both mothers and offspring [90]. Fully elucidating the impact of GDM and other climate changeinduced maternal stressors (e.g., disruptions in nutrition, psychosocial stress, displacement, loss of access to healthcare) on metabolic and other health-related outcomes in both mothers and their offspring is of paramount importance, as they may further accelerate the already disturbing increases in global diabetes rates.

Multiple notable data gaps were identified in this analysis. This includes an absence of recent data on diabetes in children. While our initial aim was to assess healthcare outcomes in the pediatric population, no relevant articles were identified. Over 227,000 incident cases of childhood diabetes were estimated to occur globally in 2019, a 39.4% increase from 1990; North Africa and the Middle East experienced the greatest increase at over two-fold [91]. While overall childhood diabetes mortality has decreased globally, there was a 58.11% increase in diabetes-associated mortality among countries with a low Sociodemographic Index [91]. Importantly, in this analysis published after our search, the authors concluded that nonoptimal, high, and low temperatures were all key risk factors for diabetes-associated mortality

in children [91]. Given that children possess proportionately higher body surface areas and are thus more susceptible to extreme temperature fluctuations, this is not surprising. There is a significant need for more studies examining the impact of climate change on children with diabetes. In addition to data gaps in pediatric diabetes, a paucity of studies examined associations of climate change on the microvascular complications of diabetes, including neuropathy, nephropathy, and retinopathy. Such data is critical as it is likely that extreme temperatures and natural disasters will exacerbate underlying kidney disease, while underlying diabetic neuropathy is likely to render those with this diabetes-associated complication especially vulnerable to extreme temperatures due to impairments in thermoregulation.

While many studies examined included individuals with T1D in their analyses, there was little data specifically examining the impact of climate change on those with T1D [38,81,84,92], an especially vulnerable subset of those with diabetes. Furthermore, some of the studies included did not differentiate between T1D and T2D in their study populations [23,36,63]. T1D afflicted 8.4 million individuals globally in 2021, with 13.5–17.4 million individuals predicted to have the disease by 2040; notably, the largest increases in T1D are projected to occur in low- and lower-middle-income countries [93]. Care of T1D is complicated by the absolute need for exogenous insulin, an injectable treatment requiring refrigeration that is thus sensitive to disruptions in electricity supplies and displacement stemming from climate events. Further work is needed in this area given the special vulnerabilities of this patient population.

Several additional areas also require further study. These include assessing the impacts of acute climate change manifestations on healthcare delivery and the utility of interventions that promote resiliency to mitigate disruptions in diabetes care arising from extreme events. These include efforts to develop alternatives to formal refrigeration [80] as well as more thermally-stable preparations of anti-diabetic medications. Also critical is leveraging knowledge of previous natural disasters to identify and organize local resources to address the impact of climate-related events on the care of those with diabetes; this should include leveraging non-traditional forms of communication such as social media for outreach to vulnerable individuals [81]. Developing and implementing such systems will be critical in the face of growing climate change threats.

The current state of evidence clearly shows that climate change threatens human health. As such, healthcare can no longer be confined by the four walls of the clinic room or surgical suite. Rather, the healthcare system and affiliated institutions must take a more holistic

Stakeholder engagement required to address climate threats to metabolic health and to assist those living with diabetes. Addressing the various threats of climate change to those living with diabetes as well as those at risk of developing diabetes and other metabolic disorders requires holistic and coordinated engagement across the full spectrum of healthcare engagement.

Stakeholder	Requisite Engagement and Action	
Patients	 Learn about potential health threats from climate change and how climate change may threaten self-care. Work with healthcare providers and other entities to develop action plans to ensure access to medications and other supplies needed for diabetes self-care in the event of climate-mediated disruptions. 	
	 Discuss climate change and other environmental health threats with providers. Engage with elected representatives and advocate for policies and practices that: 1) ensure access to healthcare during emergencies; and 2) reduce greenhouse gas emissions and other environmental health threats. 	
Healthcare Providers	 Reduce household greenhouse gas emissions whenever feasible but appreciate that effective action requires systems change.t Recognize that extreme temperatures, natural disasters, and other manifestations of climate change can adversely affect metabolic health. 	
	 Understand that those living with diabetes are vulnerable to the impacts of climate change. Appreciate that those living with type 1 diabetes and others who are dependent on insulin may be especially vulnerable to climate-mediated disruptions in access to medications and diabetes supplies. 	
	 Assist patients in the development of action plans to fortify access to medications and other self-care resources in the event of natural disasters or other climate-mediated disruptions in care. Provide guidance on the health threats of extreme weather events and ways for patients to protect themselves. 	
	 Advocate for health systems to: 1) develop comprehensive strategies to reduce greenhouse gas emissions; and 2) implement emergency management strategies that protect access to healthcare during extreme weather events and natural disasters. Advocate for public policies that protect against environmental health threats. 	
Hospitals and Clinics	 Implement strategies to reduce direct and indirect greenhouse gas emissions. Develop emergency management practices that protect access to healthcare during extreme weather events and natural 	
	disasters.Prioritize emergency management practices that target patients and communities that are especially vulnerable to climate disruptions, including those living with diabetes or in under-resourced communities.	
	 Deploy strategies to inform patients of climate-mediated health threats in real-time, including during extreme weather events. Ensure their providers are acquainted with the health threats of climate change while providing them with resources for patient and self-education. 	
Pharmacies and Other For-Profit Healthcare Entities	 Reduce direct and indirect greenhouse gas emissions. Invest in climate-resilient infrastructure to ensure access to care during extreme weather events. 	
	 Develop and deploy emergency management practices that rapidly respond to natural disasters, including mobile infrastructure that can provide access to essential medications such as insulin. Ensure access to emergency resources in vulnerable communities including low-income communities and communities of color. 	
Healthcare Education	 Ensure access to emergency resources in vulnerable communities, including low-income communities and communities of color Incorporate climate change and its impacts on health into medical, nursing, pharmacy, and other curricula. Include climate and other environmental health risks in all discussions of the social and structural determinants of health. 	
Professional Societies	 Encourage and empower healthcare trainees to be environmental health advocates. Incorporate climate change and other environmental health threats into clinical practice guidelines. Develop educational resources about climate change for patients and providers. 	
Governments	 Advocate for government investments to reduce greenhouse gas emissions and to study the impacts of the various manifestations of climate change on human health, including diabetes. Invest in research to: 1) understand the physiological impact of climate change-mediated health threats (e.g., heat stress); 2) 	
	develop approaches and interventions to mitigate those risks; 3) devise techniques and approaches to make medical devices and medications (including insulin) resistant to climate threats (including extreme temperatures); and 4) develop new technologies to reduce greenhouse gas emissions and other drivers of climate change.	
	 Incentivize and deploy available technologies that reduce greenhouse gas emissions at scale. Implement policies that bolster private sector investments in efforts to reduce greenhouse gas emissions and other environmental health threats. 	
	 Invest in emergency preparedness that ensures continuous access to healthcare during disasters, including in vulnerable communities. 	
	Develop policies that protect workers most vulnerable to climate change, including farm and construction workers among others.Provide the public with early warning systems to alert them to the threats of extreme weather while providing them with	
	Provide the public with early warning systems to alert them to the threats of extreme weather while providing them with resources to protect themselves.Work internationally to develop global strategies to combat the global threat of climate change.	
	 Adopt an "Environment-In-All-Policies" approach to policymaking that ensures environmental risks, including those imposed by climate change, are incorporated into all public policy, including healthcare, economic, and defense policies as well as urban planning and others. 	
Non-Governmental Organizations	• Advocate for local, state, federal, and international efforts that reduce greenhouse gas emissions or otherwise protect the public from the ravages of climate change.	
	 Promote policies that specifically protect vulnerable individuals and communities from climate change. Educate stakeholders on the threats of climate change to human health. Ensure laws are enacted and justly enforced that protect the public from environmental health threats. 	

and activistic approach to this unprecedented threat to human health (Table 4). Healthcare providers must acquaint themselves with the burgeoning evidence linking climate change to adverse health effects and appreciate how climactic factors influence disease development and complications. Moreover, it will be critical to leverage this emerging knowledge to provide anticipatory guidance for how patients can protect themselves from the worst impacts, including approaches to avoid the adverse effects of excessive temperatures

and proper medication storage to ensure its safety and efficacy [94]. Educating healthcare providers on climate change impacts and solutions should begin early with incorporation into professional school curricula for doctors, nurses, pharmacists, and others [95,96]. Federal funding for climate-related research ranging from the biology of heat stress to dissemination and implementation science will be crucial for building the mechanistic knowledge and public health infrastructure needed to meet the climate change threat [97]. Armed with

increasing knowledge and concern for our patients, healthcare providers must also become advocates for local, state, and federal policies that address the drivers of climate change. They must work locally to reduce the carbon footprint of their own hospitals and clinics while also looking outward to advocate for the global initiatives that can address the challenge of this global problem. In the realm of diabetes, this is especially critical given the collision of climate change and rising diabetes rates in low- and middle-income countries that have fewer resources to meet this challenge on their own. Finally, while prioritizing efforts to lower greenhouse gas emissions and reduce the risks of climate change, healthcare providers, health systems, government agencies, non-governmental organizations, and for-profit companies must work together to develop comprehensive, integrated emergency preparedness plans to respond quickly, efficiently, and justly to extreme temperatures, natural disasters, and other manifestations of climate change. The lives of those with or at risk for diabetes will depend on these efforts.

The present analysis has several limitations, including temporal constraints imposed by the five-year retrospective analysis that may have resulted in earlier publications being missed. Given the dramatic increase in climate science over the last few years, however, a significant proportion of the relevant literature was likely captured. Importantly, the current study was also limited to a subset of climate change impacts, namely extreme heat, extreme cold, and natural disasters. Key areas that were excluded from this analysis included impacts of climate change on nutrition, a key contributor to diabetes pathogenesis and a central focus of non-pharmaceutical treatment. Climate change poses significant challenges to food access and availability while also diminishing the nutritional value of foods, as has been observed resulting from hurricanes Matthew and Florence [22]. Finally, studies that focused on the impact of environmental pollution on diabetes outcomes were a priori excluded despite substantial evidence of a connection [98-101]. Fossil fuel burning generates significant pollution and drives climate change, while climate change conversely can amplify pollution. Beyond energy generation, fossil fuels are key elements in the production of plastics, which are also linked to diabetes risk [102]. Studies are required to understand the interconnected relationships between climate change, pollution, and diabetes, including potential positive feedback loops that may amplify disease burden and complications. Despite these limitations the current analysis has several notable strengths, including a comprehensive assessment of evidence across three databases, robust complementary search terms, and critical appraisal of associations based upon multiple climate- and diabetes-associated subcategories. Overall, this work provides evidence that climate change is linked to diabetes development, care, and complications.

5. Conclusions

While notable data gaps remain in our understanding of climate change impacts on specific types and complications of diabetes as well as the impact of climate change on geographic regions disproportionately burdened by climate change and diabetes, current data clearly indicate that various manifestations of climate change adversely affect those living with diabetes. With global temperatures and diabetes rates rising concordantly, these data reinforce the critical need to understand and address the impacts of these two colliding crises to protect human health.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: RMS declares he has received honoraria from CVS/Health, which are unrelated to this manuscript. All other authors have no relevant disclosures. The views expressed in this article are those of the authors and do not necessarily reflect the positions or policies of the Department of Veterans Affairs, the Department of Defense, or the United States government.

CRediT authorship contribution statement

Julienne Sanchez Perez: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. Holly Hudson: Writing - review & editing, Writing - original draft, Visualization, Validation, Resources, Methodology, Formal analysis, Data curation, Conceptualization. Julia Araneta: Investigation. Brandon Bedell: Visualization, Investigation. Ama de-Graft Aikins: Methodology, Conceptualization. Lara R. Dugas: Writing - review & editing, Writing - original draft, Visualization, Validation, Methodology, Formal analysis, Conceptualization. Mennaallah Eid: Investigation, Formal analysis. Youssof Eshac: Investigation. Maria Fariduddin: Investigation, Formal analysis. Muddasir Fariduddin: Investigation. Karen Jong: Investigation, Formal analysis. Thandi Kapwata: Writing review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Conceptualization. Amy Luke: Writing - review & editing, Writing - original draft, Visualization, Validation, Methodology, Formal analysis, Conceptualization. Tina Moazezi: Investigation. Daniel Ruiz: Writing - review & editing, Visualization, Validation, Formal analysis, Conceptualization. Nadia Sweis: Writing - original draft, Visualization, Validation, Investigation, Formal analysis, Conceptualization. Kasra Tayebi: Investigation. Dirin Ukwade: Investigation. Lidan Zhao: Writing - review & editing, Visualization, Conceptualization. Robert M. Sargis: Writing - review & editing, Writing - original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation. Conceptualization.

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Supplementary materials

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