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Association between extreme ambient heat exposure and diabetes-related hospital admissions and emergency department visits: A systematic review

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Abstract

Background and objectives: Diabetes is an increasing public health concern worldwide. The impact of extreme heat exposure on diabetes healthcare utilization such as diabetes-related hospital admissions and emergency department (ED) visits was understudied although extreme temperature exposure was linked with diabetes mortality. In addition, very few systematic reviews have been conducted in this field. This review aims to systematically evaluate the currently available evidence on the association between extreme ambient heat exposure and hospital admissions/ED visits for diabetes and the vulnerable population to heat extremes.

Methods: A systematic literature review was conducted by using the keywords/terms “ambient temperature or heatwave or heat wave or extreme temperature or high temperature effect ” and “diabetes morbidity or diabetes hospital admissions or diabetes emergency room visits ” for available publications until August 2022. The heat exposure was categorized into four groups using difference definitions. The outcomes were diabetes-related hospital admissions/ED visits. A meta-analysis was performed to estimate the pooled effects of relative risk (RR)/odds ratio (OR) and 95% confidence intervals (CI) for each of the associations of interest.

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Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Declaration of Competing Interest
The authors declare that they have no competing interests.

Results: Eighteen articles were selected from forty full-text, English written papers based on the inclusion and exclusion criteria. The overall pooled effect of excessive heat on diabetes, across all groups, was 1.045 (95% CI 1.024–1.066). The pooled effects for each exposure group were significant/borderline significant. Additionally, the pooled effect of the RR/OR was 1.100 (95% CI: 1.067–1.135) among adults aged 65 years or older. The most controlled confounders were air pollutants. The commonly listed limitation in those studies was misclassification of exposure.

Conclusions: The body of evidence supports that ambient extreme heat exposure is associated with diabetes-related hospital admissions/ED visits. Additionally, adults 65 years of age or older with diabetes are vulnerable to heat extremes. Future studies should consider controlling for various biases and confounders.

Keywords

Extreme ambient heat; Diabetes; Systematic review

Introduction

Diabetes is a common chronic disease. It affects 34.2 million people, or about 10.5% of the US population (Centers for Disease Control and Prevention, National Diabetes Statistics Report 2020). In New York State (NYS), an estimated 1.7 million adults have been diagnosed with diabetes (New York State Department of Health, Diabetes New York State Adults 2018, Shaw et al., 2010, Zimmet et al., 2014). Diabetes is not only common worldwide, it is also a very costly disease (Zhang et al., 2010). In 2017 in the U.S., the estimated direct and indirect costs of diagnosed diabetes was $327 billion, which reflects a 26% increase over the five-year period from 2012 to 2017 (American Diabetes Association 2018). The common risk factors for the development of diabetes are genes, obesity, inactivity, diet, toxins, and seasonality (Bilous and Donnelly, 2010). Over time, high blood glucose damages nerves and blood vessels, leading to macrovascular and microvascular complications such as heart disease, stroke, blindness, kidney disease, and lower extremity amputations (Bilous and Donnelly, 2010). It has been reported that the complications resulting from diabetes are the major causes for diabetes-related disability and premature death (Bilous and Donnelly, 2010). Diabetes and its associated complications are also significant sources of hospitalization and medical expenditures (American Diabetes Association 2018).

Global climate change has led to an increase in the frequency and severity of weather extremes including extreme heat and heatwaves (Rossati, 2017). It has been reported that extreme ambient heat exposure is associated with diabetes mortality (Basagaña et al., 2011, Gasparrini et al., 2012, Stafoggia et al., 2006, Kim et al., 2015, Oudin Åström et al., 2015, Isaksen et al., 2016, Li et al., 2017, Méndez-Lázaro et al., 2018, He et al., 2020). Despite diabetes mortality being a critical health endpoint, studying mortality alone captures only the most severe cases and underestimates the larger public health impact of diabetes. Therefore, studying diabetes-related healthcare utilization, such as hospital admissions and emergency department (ED) visits is critical for understanding the public health impacts of diabetes. Although some studies have tested the association between extreme ambient heat exposure and diabetes-related hospital admissions and ED visits (Green et al., 2010, Ostro et al., 2010, Pudpong and Hajat, 2011, Wang et al., 2012, Basu et al., 2012, Vaneckova and Bambrick, 2013, Wilson et al., 2013, Bobb et al., 2014, Wang and Lin, 2014, Bai et al., 2016, Winquist et al., 2016, Chen et al., 2017, Ogbomo et al., 2017, Sherbakov et al., 2018, Campbell et al., 2019, Xu et al., 2019, Xu et al., 2019, Jiang et al., 2021), the findings were inconsistent. The definition of exposure varied from study to study. In addition, very few systematic reviews have been performed in this field (Song et al., 2021, Moon, 2021). The objectives of this review are to 1) systematically evaluate the currently available evidence on the association between extreme ambient heat exposure and diabetes healthcare utilization, defined as hospital admissions and ED visits for diabetes; and 2) identify the populations most vulnerable to excessive heat.

Methods

Data sources

The eligible articles were identified from the electronic databases: PubMed, Cochrane Library, and the University at Albany (UAlbany) Libraries. PubMed and Cochrane Library are commonly used data sources for literature searches. UAlbany Libraries provide access to many online data sources for students, faculty, and staff at UAlbany. The reference lists from the selected articles were also searched as a data source.

Search strategy

The keywords/terms used for the search were “ambient temperature or heatwave or heat wave or extreme temperature or high temperature effect” and “diabetes morbidity or diabetes hospital admissions or diabetes emergency room visits” No specific filtration was applied in searching the databases PubMed and Cochrane Library. Only a few articles were identified through Cochrane Library using the above keyword combinations. The filtration was applied at searching the UAlbany Library to limit articles so that they are from peer-reviewed journals, use English language, and contain diabetes or environmental science as the subject. The duplicated records were identified by using the “find” function in Microsoft Word. A majority of non-qualified studies were filtered out through title and abstract screening. The final studies that are included in our analysis were confirmed by the assessment of full-text articles. We conducted the literature search for all the available publications until August 2022.

Ambient heat exposure grouping and diabetes definition

In this systematic review, heat exposure was categorized into the following four groups based on the difference of exposure definitions described in a previous review (Song et al., 2021): 1) group 1: exposure was measured as continuous variable for per unit increase of ambient temperature (*e.g.*, per 5°C increase of daily mean temperature); 2) group 2: exposure was assessed as a comparison between categorized hot days and reference days based on the specific cut-off points selected by the authors (*e.g.*, hot (32°C) vs. reference (18°C) days); 3) group 3: exposure was classified as the ambient temperature above vs. below a heat threshold (*e.g.*, ≥ 95^{th} vs. < 95^{th} percentiles); and 4) group 4: exposure was defined as above the 90^{th}, 95^{th}, 97^{th}, 98^{th}, or 99^{th} percentiles consecutively for at least two days (*e.g.*, ≥ 95^{th} percentiles for two consecutive days). In summary, exposure groups 1 to 3 were used to compare exposures' continuous changes or excessive heat vs. references, whereas exposure group 4 is relevant to the exposure duration to excessive heat. Apparent temperature (AT) was calculated as AT (°C) = − 2.653 + (0.994* temperature (°C)) + (0.0153* (dew point temperature (°C))^2) (Green et al., 2010, Ostro et al., 2010, Basu et al., 2012) or AT (°C) = −1.3 + (0.92* temperature (°C)) + (2.2* water vapor pressure (kPa)) (Chen et al., 2017).

The term "diabetes" was defined as any hospital admissions, ED visits, or out-patient visits related to any diabetes diagnosis. Diabetes ascertainment was conducted based on the *International Classification of Disease, 9th Revision (ICD-9)* code 250 and *10th Revision* (ICD-10) codes E10-E14. We studied both type 1 and type 2 diabetes because they are the most common forms of diabetes, which contribute to about 97% of all diagnosed diabetes (Bullard et al., 2018).

Inclusion and exclusion criteria

The inclusion criteria were: 1) All primary diabetes defined above; 2) Exposures to extreme heat ambient temperature and/or heatwaves; 3) Diabetes-related hospital admissions and/or ED visits; 4) studies that evaluated the association between excessive heat exposure and diabetes-related hospital admissions and/or ED visits; and 5) English articles and articles from peer-reviewed journals. The exclusion criteria were: 1) Exposures to indoor or workplace high temperature, other weather extremes, or seasonality; 2) Hospital admissions and/or ED visits due to other diseases or all-cause but not diabetes-specific; and 3) Review articles. The number of eligible articles at each selection stage are presented in Fig. 1.

Data collection and calculation

The following data were collected from the eligible studies: the first author's last name, publication year, study title, study population including sample size, source(s) of data, country, duration of study, study type, exposures, outcomes, key findings, and major limitations. Sums, counts, and percentages were calculated for the selected measures. The authors applied a random-effect model to conduct the meta-analysis to evaluate the pooled effect of excessive heat-diabetes association for each exposure group. For group 1, the percent (%) increase in excess risk of diabetes was transformed to a relative risk (RR)/odds ratio (OR) using the formula (% increase in excess risk of diabetes/100% +1). The pooled effect was then converted back to % increase in excess risk of diabetes by transforming the aforementioned formula when an estimate of a pooled effect of the RR was obtained (i.e., (RR-1)*100%). The estimates of pooled effects were reported as the % increase in excess risk of diabetes with a 95% confidence interval (CI) for group 1, and a RR with a 95% CI for the other groups of exposure and selected indicators. The analysis was performed using R software (version 4.2.1; R Development Core Team).

Results

Description of study selection

As shown in Fig. 1, initially 1,407 records were identified from PubMed, Cochrane Library, UAlbany Libraries, and through searches of identified papers' reference lists. After removing duplicated records, 1,035 records went through title and abstract screening of eligibility based on the inclusion/exclusion criteria. Finally, eighteen studies were included in the systematic review from the full-text assessment of forty articles.

Characteristics of the studies included

The characteristics of the eighteen studies were summarized in Table 1. Nine studies (50%) were conducted in the U.S. (Green et al., 2010, Ostro et al., 2010, Basu et al., 2012, Bobb et al., 2014, Winquist et al., 2016, Chen et al., 2017, Ogbomo et al., 2017, Sherbakov et al., 2018, Jiang et al., 2021), five (27.8%) in Australia (Wang et al., 2012, Vaneckova and Bambrick, 2013, Wilson et al., 2013, Campbell et al., 2019, Xu et al., 2019), one (5.6%) in Brazil (Xu et al., 2019), one (5.6%) in Canada (Bai et al., 2016), one (5.6%) in China (Wang and Lin, 2014), and one (5.6%) in Thailand (Pudpong and Hajat, 2011) including a total of at least 2,331,929 patients from 1999 to 2016 in the selected studies published between 2010 and 2022. Of the included studies, ten of them (55.6%) used a time stratified case-crossover study design (Green et al., 2010, Ostro et al., 2010, Wang et al., 2012, Basu et al., 2012, Vaneckova and Bambrick, 2013, Wilson et al., 2013, Ogbomo et al., 2017, Campbell et al., 2019, Xu et al., 2019, Xu et al., 2019) and eight of them (44.4%) employed a time series study design (Pudpong and Hajat, 2011, Bobb et al., 2014, Wang and Lin, 2014, Bai et al., 2016, Winquist et al., 2016, Chen et al., 2017, Sherbakov et al., 2018, Jiang et al., 2021). Among the eighteen studies, ten studies (55.6%) reported excessive heat effects (Green et al., 2010, Ostro et al., 2010, Pudpong and Hajat, 2011, Basu et al., 2012, Vaneckova and Bambrick, 2013, Wang and Lin, 2014, Bai et al., 2016, Winquist et al., 2016, Xu et al., 2019, Jiang et al., 2021), five studies (27.8%) reported heatwave effects (Wang et al., 2012, Bobb et al., 2014, Chen et al., 2017, Campbell et al., 2019, Xu et al., 2019), and three studies (16.7%) reported both excessive heat and heatwave effects (Wilson et al., 2013, Ogbomo et al., 2017, Sherbakov et al., 2018) on diabetes-related hospital admissions/ED visits. For exposure indicators, thirteen studies (72.2%) assessed air temperatures (Pudpong and Hajat, 2011, Wang et al., 2012, Vaneckova and Bambrick, 2013, Wilson et al., 2013, Bobb et al., 2014, Wang and Lin, 2014, Bai et al., 2016, Winquist et al., 2016, Ogbomo et al., 2017, Sherbakov et al., 2018, Xu et al., 2019, Xu et al., 2019, Jiang et al., 2021), three studies (16.7%) assessed apparent temperatures (AT) (Green et al., 2010, Ostro et al., 2010, Basu et al., 2012), one study (5.6%) tested both air and apparent temperatures (Chen et al., 2017), and one study (5.6%) measured the Excess Heat Factor index (Campbell et al., 2019). For outcomes, ten studies (55.6%) evaluated diabetes-related hospital admissions (Green et al., 2010, Ostro et al., 2010, Vaneckova and Bambrick, 2013, Wilson et al., 2013, Bobb et al., 2014, Bai et al., 2016, Ogbomo et al., 2017, Sherbakov et al., 2018, Xu et al., 2019, Xu et al., 2019), five studies (27.8%) explored diabetes-related ED visits (Wang and Lin, 2014, Winquist et al., 2016, Chen et al., 2017, Campbell et al., 2019, Jiang et al., 2021), one study (5.6%) assessed both diabetes-related outpatient visits and hospital admissions (Pudpong and Hajat, 2011), one study (5.6%) evaluated diabetes-related emergency hospital admissions (Wang et al., 2012), and one study (5.6%) measured diabetic hospitalization originating with an ED visit at the same day (Basu et al., 2012). Furthermore, six (33.3%) of the total selected studies investigated age related to the excessive heat-diabetes association (Wang et al., 2012, Basu et al., 2012, Wilson et al., 2013, Winquist et al., 2016, Ogbomo et al., 2017, Xu et al., 2019). Very few studies evaluated other socio-demographic factors such as gender, race, and ethnicity etc. in relation to the association of interest.

Ambient temperature and diabetes

Temperature as a continuous variable—The individual and pooled results for six prior papers using temperature as a continuous variable were presented in Exposure group 1 table in Fig. 2. The excess risk of diabetes-related hospital admissions increased from 2.8% to 4.3% (range of 95% CI: 0.6–6.2%) per 10°F (5.6°C) increase in daily mean apparent temperature (ATmean) from 1999 to 2008 in California, USA (Green et al., 2010, Ostro et al., 2010, Basu et al., 2012). A positive increase in the excess risk of diabetes-related hospital admissions (% increase = 1.8%, 95% CI: 0.9–2.8%) was also observed for per 10°F (5.6°C) increase in daily maximum apparent temperature (ATmax) from 1999 to 2005 in California, USA (Ostro et al., 2010). However, a 10°F (5.5°C) increase in daily minimum apparent temperature (ATmin) was not associated with a significant increase (1.7%, 95% CI: −0.8–4.2%) for the risk of diabetes-related hospital admissions (n = 1 study) (Ostro et al., 2010). Using the daily mean ambient temperature (Tmean) as an indicator, Xu et al. (2019) (Xu et al., 2019) found that the risk of diabetes-related hospital admissions increased 6% corresponding to per 5°C increase in Tmean from 2000 to 2015 in Brazil (95% CI: 4.0–7.0%). Pudpond and Hajat (2011) (Pudpong and Hajat, 2011) reported that the risk of diabetes-related out-patient visits increased 26.3% (95% CI: 7.1–49.0%) per 1°C increase in Tmean above the threshold of 29°C from 2002 to 2006 in Chiang Mai, Thailand. On the other hand, they did not find a significant increase in hospital admissions for diabetes associated with a 1°C increase in Tmean.

Extreme heat vs. references—The results for the association of interest comparing exposures between categorized hot and reference days were showed in Exposure group 2 table in Fig. 2. The estimated RR for diabetes-related hospital admissions was 1.30 (95% CI: 1.06–1.58) in comparing exposures to the 99^{th} vs. 11^{th} percentiles of Tmean from 1996 to 2013 in Ontario, Canada (Bai et al., 2016). A significant RR for diabetes-related ED visits (RR = 1.03, 95% CI: 1.01–1.06) was observed in comparing exposures to the 75^{th} vs. 25^{th} percentiles of daily ambient maximum temperature (Tmax) from 1993 to 2012 in Atlanta, USA (Winquist et al., 2016). Furthermore, the adjusted RRs of diabetes-related hospital admissions/ED visits were 1.69 (95% CI 1.09–2.61) and 1.06 (95% CI 1.03–1.09) in comparing exposures to hot days (32°C) vs. reference days (18°C) from 2000 to 2009 in Taipei, China (Wang and Lin, 2014) and exposures to hot days (26°C) vs. mild days (20°C) from 1999 to 2009 in California, USA (Sherbakov et al., 2018), respectively. Other associations of interest studied in this exposure group were not statistically significant.

The associations of interest obtained from four studies for comparing exposures above vs. below a heat threshold were presented in Exposure group 3 table in Fig. 2. The positive associations between diabetes-related hospital admissions and exposure to the 95^{th} percentile of Tmean/Tmax ($\geq 95^{th}$ vs. $< 95^{th}$ / $\geq 95^{th}$ vs. $\leq 95^{th}$ percentiles) were estimated as the OR = 1.06 (95% CI: 1.02–1.10) from 1991 to 2009 (Vaneckova and Bambrick, 2013) and OR = 1.12 (95% CI: 1.06–1.18) from 1997 to 2010 (Wilson et al., 2013) in Sydney, Australia but not in Michigan, USA (Ogbomo et al., 2017). In addition, the association between diabetes-related ED visits and exposure to the 95th percentile of daily ambient minimum temperature (Tmin) (> 95th vs. ≤ 95th percentiles) was not significant (OR = 1.009, 95% CI: 0.996–1.021) in Atlanta, USA (Jiang et al., 2021). The similar inconsistent pattern was also found in the association between diabetes-related hospital admissions and exposure to the 99th percentile of Tmean/Tmax (≥ 99th vs. < 99th / ≥ 99th vs. ≤ 99th percentiles). The positive associations of interest were reported as OR = 1.12 (95% CI: 1.04–1.20) (Vaneckova and Bambrick, 2013) and OR = 1.16 (95% CI: 1.03–1.30) in Sydney, Australia (Wilson et al., 2013) but not in Michigan, USA (Ogbomo et al., 2017).

Heat exposure duration—In terms of heat exposure duration (Exposure group 4 table in Fig. 2), both Wilson (2013) (Wilson et al., 2013) and Xu Z. (2019) (Xu et al., 2019) teams found a positive association between diabetes-related hospital admissions and exposure to heatwaves. Wilson et al. (2013) (Wilson et al., 2013) estimated the positive association of interest as OR = 1.07 (95% CI: 1.01–1.14) or OR = 1.14 (95% CI: 1.01–1.29) when defining heatwaves as above the 95th or 99th percentile of Tmax for 3-day moving average, respectively, from 1997 to 2010 in Sydney, Australia. Xu Z. et al. (2019) (Xu et al., 2019) calculated the positive association of interest as OR = 1.18 (95% CI: 1.01–1.39) or OR = 1.37 (95% CI: 1.11–1.69) when defining heatwaves as above the 95th or 97th percentile of Tmean for at least 2 consecutive days, respectively, from 2005 to 2013 in Brisbane, Australia. However, no other significant associations of interest were identified in the remaining fifteen different heatwave-diabetes associations. In these associations, the heatwaves were either defined based on a specific ambient temperature (*e.g.*, 37°C) in Brisbane, Australia (a case-crossover study investigated one heatwave-diabetes association) (Wang et al., 2012) or various percentiles for selected temperature indicators. More specifically, the heatwaves were defined as above the 90th percentile of Tmean for at least 2 consecutive days in Brisbane, Australia (a case-crossover study evaluated one heatwave-diabetes association) (Xu et al., 2019); above the 95th percentile of Tmean for at least 2 consecutive days in California, USA (a time-series study examined one heatwave-diabetes association) (Sherbakov et al., 2018) and in Brisbane, Australia (a case-crossover study tested one heatwave-diabetes association) (Xu et al., 2019), respectively; above the 95th percentile of the Excess Heat Factor index for 3 consecutive in Tasmania, Australia (a case-crossover study tested one heatwave-diabetes association) (Campbell et al., 2019); above the 97th percentile of Tmean for 2 to 4 consecutive days in Michigan, USA (a case-crossover study tested three heatwave-diabetes associations) (Ogbomo et al., 2017) and for at least 2 consecutive days in Brisbane, Australia (a case-crossover study tested one heatwave-diabetes association) (Xu et al., 2019); above the 98th percentile of ATmean, ATmax, ATmin, Tmean, Tmax, or Tmin for at least 2 consecutive days in Atlanta, USA (a time-series study examined six different heatwave-diabetes associations) (Chen et al., 2017); and above the 99th percentile of Tmean for at least 2 consecutive days in USA (a time-series study evaluated one heatwave-diabetes association) (Bobb et al., 2014) and in Brisbane, Australia (a case-crossover study tested one heatwave-diabetes association) (Xu et al., 2019), respectively.

The overall pooled effect of all the associations examined was 1.045 (95% CI: 1.024–1.066) (top table in Fig. 2). For a total of forty excessive heat-diabetes associations examined in all selected studies, about half (n = 18) of them showed a significant association of interest. Furthermore, among twenty-one of the heat-diabetes associations tested in the studies that belong to exposure groups 1 to 3, 66.7% (n = 14) of them showed a significant association of interest with the pooled effect = 1.054 (95% CI: 1.027–1.083) (top table in Fig. 2). On the other hand, among nineteen of the heatwave-diabetes associations tested in the selected studies that belong to exposure group 4, 21.1% (n = 4) of them showed a significant association of interest. The group-specific exposure tables in Fig. 2 show that the pooled effect of the % increase in excess risk for diabetes in group 1 was 3.76 (95% CI: 1.64–5.91) from eight heat-diabetes associations investigated in five studies, whereas the pooled effects of the RR/OR were 1.134 (95% CI: 0.996–1.292), 1.054 (95% CI: 1.008–1.103), and 1.029 (95% CI: 0.997–1.062) related to exposure group 2 (from five associations evaluated in four studies), group 3 (from eight associations tested in four studies), and group 4 (from nineteen associations examined in eight studies), respectively.

Pooled effects by different heat indicators, study designs, and locations—The pooled effects of the associations of interest are presented in Table 2. The pooled effect of the associations examined was significantly positive for either apparent temperature (RR = 1.028, 95% CI: 1.017–1.038) or air temperature (RR = 1.059, 95% CI: 1.030–1.089) as the indicator. More specifically, the pooled effects of the associations were 1.038 (95% CI: 1.027–1.049), 1.017 (95% CI: 1.008–1.027), 1.021 (95% CI: 0.998–1.044), 1.069 (95% CI: 1.030–1.110), 1.067 (95% CI: 1.014–1.122), and 0.993 (95% CI: 0.956–1.031) for ATmean, ATmax, ATmin, Tmean, Tmax, and Tmin, respectively.

The pooled effect of the associations tested was significant for the exposure defined as above vs. below the 99th percentile (RR = 1.106, 95% CI: 1.017–1.203 in exposure group 3). However, the pooled effect of the associations was not significant for the exposure defined as above vs. below the 95th (RR = 1.044, 95% CI: 0.989–1.102) or 97th (RR = 0.97, 95% CI: 0.85–1.11) percentile, respectively. On the other hand, the pooled effect of the associations of interest was significant for the exposure defined as above the 95th (RR = 1.096, 95% CI: 1.017–1.182) or 99th (RR = 1.083, 95% CI: 1.010–1.161) percentile for at least two consecutive days (exposure group 4). No significant pooled results were found for the exposure defined as above the 90th, 97th, or 98th percentile in this exposure group. When combining both exposure groups, we observed a similar pattern as in exposure group 4. The pooled effect of the associations was statistically significant for the 95th (RR = 1.064, 95% CI: 1.018–1.112) or 99th (RR = 1.101, 95% CI: 1.053–1.151) percentile rather than the 90th, 97th, or 98th percentile as the heat threshold indicator.

In terms of the study design, we observed the significant/borderline significant pooled associations in the selected studies using either the case-crossover (RR = 1.056, 95% CI: 1.032–1.080) or time-series (RR = 1.036, 95% CI: 0.996–1.077) study design. We also found most of the pooled effects were significant for the associations examined in Australia (RR = 1.105, 95% CI: 1.069–1.142), Brazil (RR = 1.06, 95% CI: 1.04–1.07), Canada (RR = 1.176, 95% CI: 1.013–1.364), China (RR = 1.69, 95% CI: 1.09–2.61), and USA (RR = 1.021, 95% CI: 1.011–1.032) but not in Thailand (RR = 1.153, 95% CI: 0.955–1.393).

Heat exposure–diabetes association by demographic—Since six (33.3%) out of all selected studies assessed the excessive heat-diabetes association among older adults, we summarized the age-related findings in Fig. 3. As reported in Fig. 3, Basu et al. (2012) (Basu et al., 2012) found that older adults aged 65 years or older showed a higher % increase in excess risk of diabetes-related hospital admissions associated with per 5.6°C increase in ATmean (7.0%, 95% CI: 2.9–11.3%) compared to those aged 19–64 years from 2005 to 2008 in California, USA. Wilson et al. (2013) (Wilson et al., 2013) also found that older adults aged 65 years or older had a higher OR of diabetes-related hospital admissions (OR = 1.12, 95% CI 1.03–1.21) in comparing exposures to Tmax > 95^{th} vs. ≤ 95^{th} percentiles from 1997 to 2010 in Sydney, Australia. In addition, the strongest association between heat exposure (75^{th} vs. 25^{th} percentiles in Tmax) and diabetes-related ED visits was discovered among patients who were 65 years of age or older (RR = 1.05, 95% CI: 1.01–1.10) from 1993 to 2012 in Atlanta, USA (Winquist et al., 2016). Furthermore, Xu R. et al. (2019) (Xu et al., 2019) observed the strongest association between heat exposure (per 5°C increase in Tmean) and diabetes-related hospital admissions among older adults aged 80 years or older (OR = 1.18, 95% CI: 1.13–1.23) compared to other age groups from 2000 to 2015 in Brazil. In contrast, Wang et al. (2012) (Wang et al., 2012) or Ogbomo et al. (2017) (Ogbomo et al., 2017) did not observe the age differences in the heatwave-diabetes or heat-diabetes association, respectively. Overall, the pooled effect of the RR/OR was 1.100 (95% CI: 1.067–1.135) among older adults aged 65 years or older from ten excessive heat-diabetes associations tested in six studies.

Among reviewed studies, few of them evaluated the effects of race/ethnicity on the association between excessive heat exposure and hospital admissions/ED visits for diabetes (Green et al., 2010, Basu et al., 2012, Ogbomo et al., 2017). Basu et al. (2012) (Basu et al., 2012) reported that the excess risk of hospital admissions increased 7.6% (95% CI: −0.1–17.0%) among Asians compared with Whites in California, USA. On the other hand, Green et al. (2010) (Green et al., 2010) did not show their results but mentioned in the discussion that they did not observe any effects of race/ethnicity on the association of interest. Ogbomo et al. (2017) (Ogbomo et al., 2017) also did not detect any significant associations between excessive heat exposure and diabetes-related hospital admissions in Whites (OR = 0.98, 95% CI: 0.79–1.22) and in non-Whites (OR = 0.96, 95% CI: 0.81–1.13) from 2000 to 2009 in Michigan, USA. No significant differences were reported for other socio-demographic factors.

Confounding factors—Table 1 shows among the eighteen studies, the commonly controlled confounding factors were air pollutants (n = 11 studies, 61.1%) including O_3, $PM_{2.5}$, SO_2, CO, NO_2, and PM_{10}, followed by holidays (n = 9 studies, 50.0%), day of the week and time trends (n = 7 studies, respectively, 38.9%, all in time-series studies), and dewpoint temperature (n = 4 studies, 22.2%). Relative humidity (RH) was directly controlled in seven studies (38.9%) and was also controlled within apparent temperatures in four studies (22.2%). In addition to these confounders, between-month variation, autoregressive term, periods of hospital participation, rain, wind speed, seasonality, and influenza admission were adjusted in those studies with a time-series design. On the other hand, since socio-demographic factors were automatically controlled in studies with a case-crossover design (n = 10 studies, 55.6%), they were not specifically mentioned in these studies.

Limitations and alternative strategies listed in prior articles—As reported in Table 1, the most common limitation listed in the articles was potential misclassification of exposure because of ecologic exposure assessment (n = 9, 50.0%). To address this limitation, the authors employed a strategy to only select those patients whose residential zip codes were within a certain distance of a temperature monitor. However, the radius between residence and the temperature monitor station varied among the studies from 10 to 55 km. Some authors discussed that the misclassification of exposure could be non-differential. Lack of patients' sociodemographic information, air conditioning (AC) usage, and/or activity patterns (n = 6, 33.3%) were other common limitations listed in those studies. No clear strategies were proposed to address these limitations. The authors argued that AC usage might not be an issue in their studies. For example, Green et al. (2010) (Green et al., 2010) reported that many coastal homes did not have AC. Therefore, they did not control AC in their study because it was less likely of a confounder. On the other hand, the AC ownership was 94% in Atlanta (Chen et al., 2017). Thus, the authors thought it could be less problematic in their research. Potential misclassification of outcomes was a concern in two of those studies (11.1%). The authors recommended using the ICD code to categorize health outcomes across several health centers and hospitals to minimize this bias (Pudpong and Hajat, 2011). Additionally, including elective admissions in the analysis was described as a limitation in two studies (11.1%). The authors expected to observe a stronger association if it was possible to use a reliable set of unplanned admissions (Vaneckova and Bambrick, 2013). The limitations such as lack of controlling for confounders, not conducting a sensitivity analysis, or lack of stratified analysis were also mentioned in the reviewed studies. The explanations for those limitations were proposed as lack of data access (Ogbomo et al., 2017, Xu et al., 2019) or not necessary to do so based on previous and their own studies (Winquist et al., 2016). Finally, the limitation of generalization was also mentioned in some studies (Wang et al., 2012, Chen et al., 2017, Xu et al., 2019). The authors suggested it occurred due to small sample sizes or their studies being conducted in one city with specific conditions. However, no strategies were proposed to minimize this limitation.

Discussion

Extreme heat exposure and diabetes

In this systematic review, we observed a consistently significant/borderline significant association between extreme heat exposure and diabetes-related hospital admissions/ED visits despite the variations for definitions of extreme heat exposure, measurement of meteorological factors, and study designs in the selected studies. Among a total of forty excessive heat-diabetes associations examined, eighteen of them showed a significant result. In addition, the overall pooled effect of the RR/OR for these associations of interest was statistically significant, which is consistent with previous findings. Song et al. (2021) (Song et al., 2021) and Moon (2021) (Moon, 2021) conducted a systematic review and meta-analysis to evaluate the impact of extreme temperature on diabetes morbidity and mortality. They also found that the overall pooled effect of the RR/OR for the association of interest was significant in their reviews. Furthermore, the strength of the pooled effect was similar between our review and prior studies. The positive findings in our review were obtained from the studies conducted in different countries around the world, and so were the studies performed by Song et al. and Moon. On the other hand, unlike our review and Song's review that were mainly focused on diabetes-related hospital admissions/ED visits, Moon also assessed the health outcomes such as consultations for diabetes in general practice, diabetes comorbidity, and self-reported health conditions in a survey (Moon, 2021).

Bradford Hill criteria are used as evidence to determine causality from all the epidemiological studies reviewed. The Hill's criteria include nine principles: strength of the association, consistency of findings, specificity of the association, temporal sequence of association, biological gradient, biological plausibility, coherence, experimental evidence, and analogy (Rothman et al., 2008). Our findings may meet five out of nine causal criteria, including strength of the association, consistency of findings, temporality, biological plausibility, and coherence. Among the selected studies, we observed a 4.5% increase from the pooled analysis in excess risk of diabetes due to excessive heat exposure (the highest RR = 1.69 and more than eight-tenths of the associations having the RR/OR ≥ 1), and Moon (2021) (Moon, 2021) found a 10% increase in such a risk, indicating that the strength of the association is relatively strong among environmental exposures. Our pooled overall positive finding for the excessive heat-diabetes association was consistently observed not only in those studies with different exposure definitions in different study designs but also among different populations from different countries in over ten years of studies. In terms of temporality, our findings also fulfill the requirement for this principle, which refers to the necessity that exposure precedes outcome in time. In this review, our results were obtained exclusively from the studies that employed the case-crossover or time-series study design. The nature of these study designs ensures that the exposure precedes the outcome. Thus, the excessive heat exposure preceded the diabetes-related hospital admissions/ED visits in our review. Additionally, the individual level of inherited characteristics (age, gender, race/ethnicity, family history and genetic background) is automatically controlled in the case-crossover studies by pairing cases to themselves, whereas the time trends and other time-related variables are adjusted in the time-series studies. It indicates that the temporal relationship between excessive heat exposure and diabetes-related hospital admissions/ED visits is valid. Finally, for the biological plausibility and coherence criteria, several studies proposed the potential biological and physical mechanisms to address why diabetic people are vulnerable to heat extremes (Li et al., 2016, Tien et al., 2016, Kenny et al., 2016, Vallianou et al., 2021, Centers for Disease Control and Prevention 2021). We discussed more details in the biological plausibility for the association of interest in the section below. Moreover, we did not find any current knowledge against the association of interest. Taken together, the evidence from our review and other studies suggests that the relationship between excessive heat exposure and diabetes is likely to be causal.

Vulnerable population

We found older age was a risk factor for the diabetes-related hospital admissions/ED visits due to excessive heat exposures among all socio-demographic factors evaluated in the selected studies. The pooled effect of the RR/OR for the association of interest assessed based on the studies using different extreme heat definitions clearly indicated that older diabetic adults (≥ 65 years of age) were more vulnerable to temperature extreme. This finding is consistent with a previous review performed by Song et al. (2021) (Song et al., 2021). Based on a meta-analysis, they found that diabetes patients aged 60 years or older were more vulnerable to heat effects (Song et al., 2021). Older adults generally have poorer health, diminished mobility, and cannot adjust well to extreme heat stress (Song et al., 2021). Because of reduced thermo-regulatory capacity, the aging population has increased susceptibility to temperature changes and thus higher rates of mortality and cardio-respiratory morbidity than younger populations during and after an extreme weather event (Al-Rousan et al., 2014, Gronlund et al., 2014, Gronlund et al., 2016). Most importantly, this subpopulation has a high prevalence of multiple comorbidities or baseline diseases, such as cardio-respiratory diseases, mental health disorders, kidney failure, and frailty, which complicates their ability to prepare for and react to extreme weather (Tillett, 2013).

The vulnerable populations were mainly observed in the studies conducted in the USA. The finding may indicate that differences in healthcare systems across the world, such as insurance systems, healthcare access, physician-and hospital bed-population ratios may also play a role in this matter. We did not identify other vulnerable populations to heat extremes.

Different heat exposure definitions and temperature indicators on diabetes

Unlike the outcome definition that is exclusively based on ICD code for diabetes, exposure definitions varied from study to study. In our review, the exposures defined with different heat definitions were consistently associated with a significantly/borderline significantly pooled effect of the associations of interest. It seems that the exposures defined as comparing the temperature above vs. below a heat threshold and measuring the temperature as a continuous variable were more sensitive for detecting a significant heat-diabetes association compared to the exposures defined as comparing hot days vs. references or duration of a heat exposure. However, since the 95% CIs for the associations of interest were overlapping among the different heat definitions, the detection ability among the different heat definitions was not statistically different.

The variation in the heat-diabetes association also occurred while using different heat indicators, including temperature increment units, reference or thresholds, and duration. When the heat exposure was measured as per unit increase, most of the associations examined were significantly and positively related to per 10°F (5.6°C) increase rather than per 1°C increase. One study showed a dramatically increased risk for diabetes-related out-patient visits with per 1°C increase beyond a threshold set as 29°C (Pudpong and Hajat, 2011). Since it was the only study focused on out-patient visits, we do not have other studies with which to compare this finding. In addition, in this study, the authors could not separate elective visits from unexpected visits. Therefore, we should interpret this finding with caution. Using above vs. below a heat threshold as the exposure indicator, we found that the pooled effect was stronger when the heat threshold was set as the 99th compared to 95th percentile. Song et al (2021) (Song et al., 2021) reported that a significant or a borderline significant association of interest was found with the heat threshold defined using the 99th or 95th percentile, respectively. On the other hand, we found significant, pooled heat-diabetes associations using both the 95th and 99th percentiles as the heat threshold indicators for the duration of exposure. Although the pooled effect was not significant for the 97th percentile as a heat threshold, we did observe a strong association of interest when the duration of the heat exposure was evaluated. We did not observe any significant, positive associations of interest when the 90th or 98th percentile was used as the heat indicator in the exposure. However, this finding should be interpreted with caution because the heat-diabetes association corresponding to the 90th percentile threshold was obtained from one association of interest in a single study. Although the pooled association related to the 98th percentile threshold was obtained from six associations of interest, they were all from a single study. Based on the associations tested in current review, our findings suggest that the threshold effect on diabetes was not linear and the 99th percentile threshold was most sensitive to capture the association of interest. It is no surprise that the highest threshold was more likely related to a positive association. However, the 99th percentile threshold setting may relate to a small sample size issue for the exposure if the study population is small. Therefore, when selecting a heat threshold for exposure, we should consider the size of the study population and the intensity and frequency of the heat extremes in the study location.

In terms of the temperature indicators, three times more of the associations examined employed temperature indicators than apparent temperature indicators. Specifically, Tmean was the most commonly used exposure indicator, followed by Tmax, ATmean, and the other three indicators (ATmax, ATmin, and Tmin) were tied for the least commonly used. In general, our review suggested that temperature indicators were more sensitive for the excessive heat-diabetes association compared to apparent temperature indicators, but the difference was not significant. More specifically, Tmean was the most sensitive exposure indicator for the associations tested, followed by Tmax and ATmean based on the pooled effect for each indicator. On the other hand, very few selected studies used ATmax, ATmin, or Tmin as an exposure indicator in their studies. However, even with a small sample size, we were able to obtain significant/borderline significant associations related to exposures using ATmax or ATmin but not Tmin as a temperature indicator. We do not have any existing results with which to compare above findings.

Among the examined heat-diabetes associations, we found that heat exposure duration (i.e., heatwaves) was a less sensitive indicator to capture a significant association of interest compared to those heat exposures measured as per unit increase or above vs. below a heat threshold. This finding is comparable with the result reported by Song et al. (2021) (Song et al., 2021) based on a systematic review and meta-analysis. A couple of reasons may explain why a longer excessive heat exposure did not show a stronger impact on diabetes. The prevalence of air-conditioning could play a role on the duration of excessive heat exposure in relation to diabetes. One study that contributed six associations of interest in our analysis was conducted in the Atlanta metropolitan area. It has been reported that the prevalence of air-conditioning was 94% in the Atlanta metropolitan area (Chen et al., 2017). Therefore, the excessive heat exposure may have less effects on health outcomes in the Atlanta metropolitan area compared to those areas with a lower prevalence of air-conditioning (Chen et al., 2017). Thus, the six null observations may weaken the overall association of interest. It is also possible that the duration of heat exposure may be less effective for diabetes-related hospital admissions/ED visits (Sherbakov et al., 2018). Furthermore, we did not observe a clear dose-response of the excessive heat exposure on diabetes related to an increase of duration of exposure. One possible reason could be due to the duration of heat exposure was defined too broad. Most of studies used the duration indicator as at least two consecutive days. This type of duration definition may be useful for detecting an aggregated duration effect but not sensitive to capture a dose-response, which may require a precise interval for grouping the duration of exposure. Qu et al. (2022) (Qu et al., 2022) found a dose-response effect related to the duration of extreme heat exposure on ED visits for renal diseases. Exposure of excessive heat for three, four, or five days significantly increased the renal disease-related ED visits with a peak at five days of excessive heat exposure. However, they did not find any significant increase for kidney disease related to one or two days of excessive heat exposure. Among the included studies, less than half of them tested lagged effects of excessive heat exposure on diabetes, and most of them focused on the single-day lags 0–3. We did not observe any consistently lagged effects in this review. It may be because the three-day lag was not long enough to capture such effect. Thus, our finding was not conclusive, and we lack evidence with which to compare this finding.

Biological plausibility for the association of interest

Biologically, the heat-diabetes association is plausible. Human studies suggest that people with diabetes are sensitive to thermal stress (Li et al., 2016, Tien et al., 2016, Kenny et al., 2016, Vallianou et al., 2021). People living with diabetes have a reduced ability to maintain a core temperature during heat stress (Kenny et al., 2016). They cannot appropriately increase skin blood flow and sweat during heat stress, resulting in greater increases in mean body temperature during heat stress (Kenny et al., 2016). The increased core temperature can lead to life-threatening complications (Kenny et al., 2016). Although the biological mechanism of how extreme temperature affects diabetes is not totally clear, one possible explanation could be that diabetes can damage blood vessels and nerves, such as the nerves in the sweat glands. Therefore, patients with diabetes may not be able to effectively cool their bodies during heat stress (Centers for Disease Control and Prevention 2021).

Strengths and Limitations

This review is one of the few comprehensive reviews evaluating extreme heat's effect on diabetes. Only articles from peer-reviewed journals over 10 years from different countries were included to assure the quality of the studies and their representativeness. We treated each excessive heat-diabetes association equally to calculate the overall percentage of significant association of interest. We also conducted meta-analysis to evaluate the pooled effect of association of interest. In addition, we focused on review of confounders and limitations in those selected articles.

Understanding the strengths and limitations of the previous studies could help us identify the research gaps and challenges and understand the future research directions in this area. The limitations of prior studies include: 1) selection bias; 2) the potential misclassification of exposures and outcomes; 3) lack of controls of some important factors, such as AC use, air pollutants, activity patterns, humidity, and green space, which are either the known risk factors of diabetes or are confounders; 4) an understudy of the association between heat exposure and diabetes-related ED visits since ED visits may be a more sensitive indicator of diabetes than hospital admissions; and 5) generalizability limitations due to selection bias.

Selection bias such as including elective admissions in the study may affect the association of interest because elective admissions are arranged admissions. This type of admissions is not likely related with heat exposure. Therefore, this bias may drive the association of interest towards the null if extreme ambiance temperature exposure is indeed associated with diabetes-related hospital admissions/ED visits. In addition, because different countries may have different definitions and policies for hospital admissions and ED visits, in some studies, diabetes-related hospital admissions may include diabetes-related ED visits, which could create a bias, although it is unclear if it would magnify or weaken the association between extreme heat and diabetes-related hospital admissions/ED visits. Finally, the selection of samples largely from a city with high AC usage may bias the association of interest towards the null. The case selection bias may affect the generalizability of this review’s findings, and therefore, we should interpret our findings with caution.

Information bias, specifically misclassification, existed in the reviewed studies. In general, misclassification of exposure and disease will bias the estimates of the association of interest towards or away from the null. However, it is more likely to be non-differential misclassification in those studies because the misclassification was equally distributed in the comparison groups. This type of misclassification will bias the estimates of the association of interest towards the null.

The majority of the reviewed studies used existing datasets. Some socio-demographic factors may be confounders for the association of interest, but data are not collected on those factors in those studies. However, studies that employ a case-crossover design will automatically control for this type of confounders because cases serve as their own controls. On the other hand, time-variant confounding factors should be appropriately adjusted. Failure to do so may bias the association of interest towards or away from the null. Potential confounders such as air pollutants, relative humidity, and holidays should be verified and controlled in the statistical models in those studies for testing the association between extreme ambient temperature exposure and health outcomes.

Public health impact and future steps

In this review, we found that extreme ambient heat exposure was related to a 4.5% increase in excess risk of diabetes and a 10% increase among older adults. In addition, the evidence from this review supports a potential causal relationship between extreme heat exposure and diabetes-related hospital admissions/ED visits. Considering that there are about 34.2 million diabetic people that compose 10.5% of the US population (Centers for Disease Control and Prevention, National Diabetes Statistics Report 2020), the public health impact due to extreme heat exposure on diabetes will be large. Theoretically all weather-related adverse health outcomes are preventable. The findings from this review will be useful for developing evidence-based interventions to reduce the impact of extreme heat exposure on diabetes, identifying the target population for the interventions (i.e., older adults), and supporting public health initiatives for public education to increase public awareness of the risk of extreme ambient heat exposure on diabetes.

In future studies, we may apply simulated weather data for study regions to minimize the misclassification of exposure. Extreme heat effects on diabetes-related ED visits should be further investigated because more prior studies were focused on extreme heat effects on diabetes-related hospital admissions. A heat-humidity index (heat index) measures what the weather “feels like ” at various temperatures and relative humidity may be used. The U.S. National Weather Service has linked heat index values to environmental health threats, both of which are used to generate excessive heat warnings. Therefore, this indicator may be more acceptable to the public than the apparent temperatures. For future study planning, we should also consider evaluating extreme heat exposure on diabetes-related ED visits and hospital admissions using heat index as an indicator to assess exposure while controlling for confounding factors. Furthermore, we should evaluate a longer lagged effect of excessive heat on diabetes not only for single-day lags, but also for multiple-day lags.

Conclusions

The results of this review demonstrated that extreme heat exposure is associated with diabetes-related hospital admissions/ED visits. Older adults with diabetes are the key population vulnerable to heat temperature extremes. Future studies should consider controlling for various biases and confounders.

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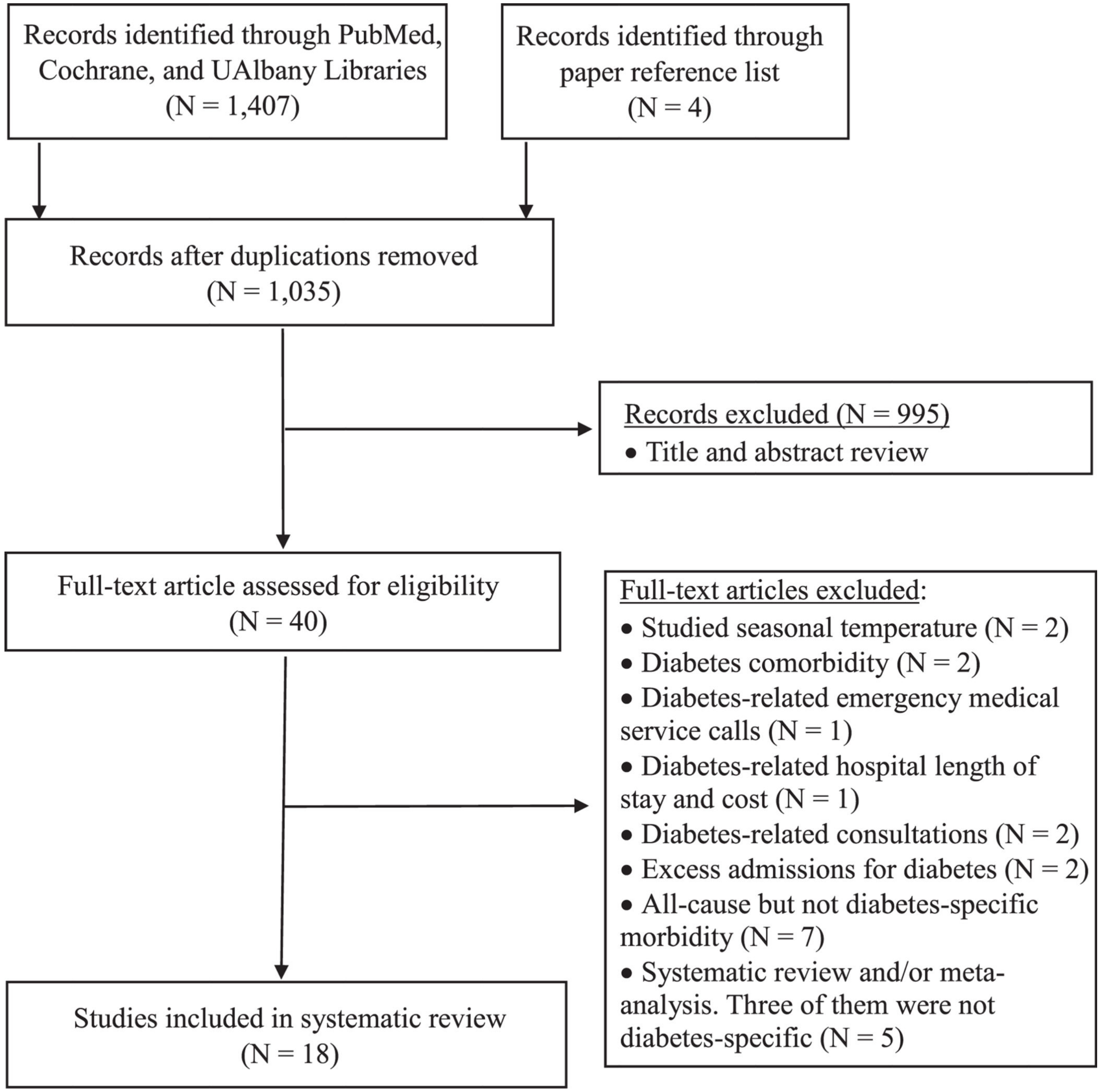
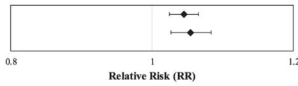


Fig. 1.
Eligible study selection process

Overall exposure

		RR (95% CI)
Overall Pooled Effect for Exposure Groups 1 to 4	**Heterogeneity**: $I^2 = 66.8\%$, $\tau^2 = 0.002$, $p < 0.0001$	1.045 (1.024, 1.066)
Overall Pooled Effect for Exposure Groups 1 to 3	**Heterogeneity**: $I^2 = 75.4\%$, $\tau^2 = 0.003$, $p < 0.0001$	1.054 (1.027, 1.083)

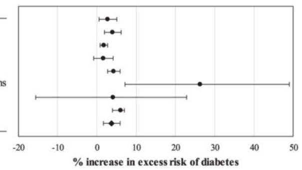


Exposure group 1*

Authors	Exposure group	Exposure indicator	Exposure definition	Outcome	% increase (95% CI)
Green et al. (2010)	Group 1	ATmean	per 10°F (5.6°C) increase	Hospital admissions	2.8 (0.6, 5.1)
Ostro et al. (2010)	Group 1	ATmean	per 10°F (5.6°C) increase	Hospital admissions	4.0 (1.9, 6.2)
Ostro et al. (2010)	Group 1	ATmax	per 10°F (5.6°C) increase	Hospital admissions	1.8 (0.9, 2.8)
Ostro et al. (2010)	Group 1	ATmin	per 10°F (5.6°C) increase	Hospital admissions	1.7 (-0.8, 4.2)
Basu et al. (2012)	Group 1	ATmean	per 10°F (5.6°C) increase	ED/Hospital admissions	4.3 (2.8, 5.9)
Pudpong and Hajat (2011)	Group 1	Tmean	per 1°C increase above 29°C	Outpatient visits	26.3 (7.1, 49)
Pudpong and Hajat (2011)	Group 1	Tmean	per 1°C increase linear	Hospital admissions	4.2 (-15.6, 22.9)
Xu R. et al. (2019)	Group 1	Tmean	per 5°C increase	Hospital admissions	6.0 (4.0, 7.0)
Pooled Effect (Random effects model)					**3.76 (1.64, 5.91)**

Heterogeneity: $I^2 = 77.8\%$, $\tau^2 = 0.0006$, $p < 0.0001$

*Exposure was measured as a continuous variable for per unit increase of an exposure indicator.

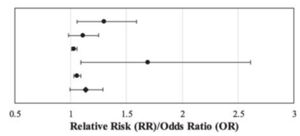


Exposure group 2*

Authors	Exposure group	Exposure indicator	Exposure definition	Outcome	RR/OR (95% CI)
Bai et al. (2016)	Group 2	Tmean	99th vs. 11th percentile	Hospital admissions	1.30 (1.06, 1.58)
Bai et al. (2016)	Group 2	Tmean	99th vs. 75th percentile	Hospital admissions	1.11 (0.98, 1.25)
Winquist et al. (2016)	Group 2	Tmax	75th vs. 25th percentile	ED visits	1.03 (1.01, 1.05)
Wang and Lin (2014)	Group 2	Tmean	32°C vs. 18°C	ED visits	1.69 (1.09, 2.61)
Sherbakov et al. (2018)	Group 2	Tmean	26°C vs. 20°C	Hospital admissions	1.06 (1.03, 1.09)
Pooled Effect (Random effects model)					**1.134 (0.996, 1.292)**

Heterogeneity: $I^2 = 67.7\%$, $\tau^2 = 0.016$, $p = 0.015$

*Exposure was assessed as a comparison between categorized hot and reference days.

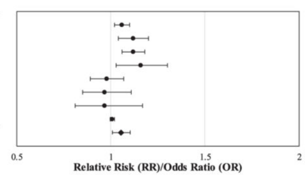


Exposure group 3*

Authors	Exposure group	Exposure indicator	Exposure definition	Outcome	RR/OR (95% CI)
Vaneckova and Barmbrick (2013)	Group 3	Tmean	≥95th vs. <95th percentile	Hospital admissions	1.06 (1.02, 1.10)
Vaneckova and Barmbrick (2013)	Group 3	Tmean	≥99th vs. <99th percentile	Hospital admissions	1.12 (1.04, 1.20)
Wilson et al. (2013)	Group 3	Tmax	>95th vs. ≤95th percentile	Hospital admissions	1.12 (1.06, 1.18)
Wilson et al. (2013)	Group 3	Tmax	>99th vs. ≤99th percentile	Hospital admissions	1.16 (1.03, 1.30)
Ogbomo et al. (2017)	Group 3	Tmean	>95th vs. ≤95th percentile	Hospital admissions	0.98 (0.89, 1.07)
Ogbomo et al. (2017)	Group 3	Tmean	>97th vs. ≤97th percentile	Hospital admissions	0.97 (0.85, 1.11)
Ogbomo et al. (2017)	Group 3	Tmean	>99th vs. ≤99th percentile	Hospital admissions	0.97 (0.81, 1.17)
Jiang et al. (2021)	Group 3	Tmin	>95th vs. ≤95th percentile	ED visits	1.01 (1.00, 1.02)
Pooled Effect (Random effects model)					**1.054 (1.008, 1.103)**

Heterogeneity: $I^2 = 77.7\%$, $\tau^2 = 0.003$, $p < 0.0001$

*Exposure was tested as the ambient temperature above vs. below a heat threshold.



Exposure group 4*

Authors	Exposure group	Exposure indicator	Exposure definition	Outcome	RR/OR (95% CI)
Wang et al. (2012)	Group 4	Tmax	≥37°C for >2 days	Hospital admissions	1.20 (0.67, 2.15)
Wilson et al. (2013)	Group 4	Tmax	>95th percentile for 3 days	Hospital admissions	1.07 (1.01, 1.14)
Wilson et al. (2013)	Group 4	Tmax	>99th percentile for 3 days	Hospital admissions	1.14 (1.01, 1.29)
Bobb et al. (2014)	Group 4	Tmean	>99th percentile for ≥2 days	Hospital admissions	1.05 (0.96, 1.14)
Chen et al. (2017)	Group 4	ATmean	>98th percentile for ≥2 days	ED visits	1.01 (0.95, 1.07)
Chen et al. (2017)	Group 4	ATmax	>98th percentile for ≥2 days	ED visits	0.99 (0.93, 1.05)
Chen et al. (2017)	Group 4	ATmin	>98th percentile for ≥2 days	ED visits	1.04 (0.98, 1.10)
Chen et al. (2017)	Group 4	Tmean	>98th percentile for ≥2 days	ED visits	0.99 (0.93, 1.04)
Chen et al. (2017)	Group 4	Tmax	>98th percentile for ≥2 days	ED visits	0.96 (0.90, 1.03)
Chen et al. (2017)	Group 4	Tmin	>98th percentile for ≥2 days	ED visits	0.97 (0.94, 1.01)
Ogbomo et al. (2017)	Group 4	Tmean	>97th percentile for 2 days	Hospital admissions	1.00 (0.80, 1.20)
Ogbomo et al. (2017)	Group 4	Tmean	>97th percentile for 3 days	Hospital admissions	1.00 (0.75, 1.30)
Ogbomo et al. (2017)	Group 4	Tmean	>97th percentile for 4 days	Hospital admissions	0.98 (0.65, 1.40)
Sherbakov et al. (2018)	Group 4	Tmean	>95th percentile for ≥2 days	Hospital admissions	1.03 (0.97, 1.09)
Campbell et al. (2019)	Group 4	EHF index	>95th percentile for 3 days	ED visits	1.57 (0.82, 3.01)
Xu Z. et al. (2019)	Group 4	Tmean	≥90th percentile for ≥2 days	Hospital admissions	1.04 (0.93, 1.18)
Xu Z. et al. (2019)	Group 4	Tmean	≥95th percentile for ≥2 days	Hospital admissions	1.18 (1.01, 1.39)
Xu Z. et al. (2019)	Group 4	Tmean	≥97th percentile for ≥2 days	Hospital admissions	1.37 (1.11, 1.69)
Xu Z. et al. (2019)	Group 4	Tmean	≥99th percentile for ≥2 days	Hospital admissions	1.28 (0.79, 2.07)
Pooled Effect (Random effects model)					**1.029 (0.997, 1.062)**

Heterogeneity: $I^2 = 44.4\%$, $\tau^2 = 0.002$, $p = 0.020$

*Exposure was defined as above a heat threshold for at least two consecutive days.

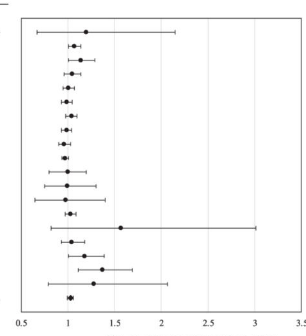


Fig. 2.

Impact of extreme ambient heat exposure on diabetes-related outcomes

Notes: ED, emergency department; Tmean, daily ambient mean temperature; Tmax, daily ambient maximum temperature; Tmin, daily ambient minimum temperature; ATmean, daily mean apparent temperature; ATmax, daily maximum apparent temperature; ATmin, daily minimum apparent temperature; EHF, Excess Heat Factor. Apparent temperature (AT) was calculated as AT (°C) = −2.653 + (0.994* temperature (°C)) + (0.0153* (dew point temperature (°C))^2) (Green et al., 2010, Ostro et al., 2010, Basu et al., 2012) or AT (°C) = −1.3 + (0.92* temperature (°C)) + (2.2* water vapor pressure (kPa)) (Chen et al., 2017).

Authors	Age group	Exposure group*	Exposure indicator	Outcome	RR/OR (95% CI)
Basu et al. (2012)	65 years or older	Group 1	ATmean, per 10°F (5.6°C) increase	ED/Hospital admission	1.07 (1.03,1.11)
Xu R. et al. (2019)	80 years or older	Group 1	Tmean, per 5°C increase	Hospital admissions	1.18 (1.13, 1.23)
Winquist et al. (2016)	65 years or older	Group 2	Tmax, 75th vs. 25th percentile	ED visits	1.05 (1.01, 1.10)
Wilson et al. (2013)	65 years or older	Group 3	Tmax, >95th vs. ≤95th percentile	Hospital admissions	1.12 (1.03, 1.21)
Wilson et al. (2013)	65 years or older	Group 3	Tmax, >99th vs. ≤99th percentile	Hospital admissions	1.18 (0.99, 1.39)
Ogbomo et al. (2017)	65 years or older	Group 3	Tmean, >97th vs. ≤97th percentile	Hospital admissions	1.09 (0.85, 1.39)
Wang et al. (2012)	65-74 years older	Group 4	Tmax, ≥37°C for >2 days	Hospital admissions	1.35 (0.25, 7.46)
Wang et al. (2012)	75 years or older	Group 4	Tmax, ≥37°C for >2 days	Hospital admissions	1.23 (0.47, 3.22)
Wilson et al. (2013)	65 years or older	Group 4	Tmax, >95th percentile for 3 days	Hospital admissions	1.06 (0.97, 1.15)
Wilson et al. (2013)	65 years or older	Group 4	Tmax, >99th percentile for 3 days	Hospital admissions	1.15 (0.95, 1.37)
Pooled Effect (Random effects model)					**1.100 (1.067, 1.135)**

Heterogeneity: $I^2 = 52.4\%$, $\tau^2 = 0.001$, $p = 0.026$

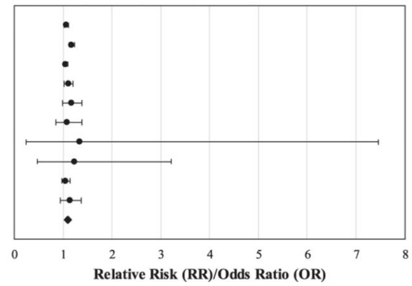


Fig. 3.

Heat-diabetes association among older adults

* Exposure group 1: exposure was measured as a continuous variable for per unit increase of an exposure indicator; group 2: exposure was assessed as a comparison between categorized hot and reference days; group 3: exposure was tested as the ambient temperature above vs. below a heat threshold; and group 4: exposure was defined as above a heat threshold for at least two consecutive days.

Notes: ED, emergency department; Tmean, daily ambient mean temperature; Tmax, daily ambient maximum temperature; Tmin, daily ambient minimum temperature; ATmean, daily mean apparent temperature. Apparent temperature (AT) was calculated as AT (°C) = −2.653 + (0.994* temperature (°C)) + (0.0153* (dew point temperature (°C))^2).

Table 1

Characteristics of the included studies

Author/year	Study Title	Study Design	Study Population	Exposure	Outcome	Results	Limitations and strategies to minimize
Green et al. 2010 (Green et al., 2010)	The effect of temperature on hospital admissions in nine California counties	Time-stratified case-crossover	50,282 patients obtained from the Office of Statewide Health Planning and Development, Patient Discharge Data (OSHPD PDD) with restricted to those whose residential zip codes was within 10 kilometers (km) of a temperature monitor in nine California counties, USA from 1999–2005	Heat, Daily mean apparent temperature (ATmean)	Diabetes-related hospital admissions Diabetes ascertainment was based on the *International Classification of Disease, 9th Revision* (ICD-9) code 250.	• A 10°F (5.6°C) increase in unlagged ATmean was corresponded to 2.8% (95% confidence interval (CI): 0.6-5.1%) increase of risk for diabetes- related hospital admissions adjusted for $PM_{2.5}$ and matched on O_3. • Significant increase of risk for diabetes- related hospital admissions per 10°F (5.6°C) increase was observed among patients who were ≥19 y of age • No gender or ethnicity effects were observed.	• Exposure assignment based on zip code rather than residence may lead to misclassification of exposure • Lack of information on air conditioning • Lack of information about patients' activity patterns Strategies used : • Restricted to those patients whose residential zip codes was within 10 kilometers (km) of a temperature monitor • Many costal homes don't have AC, AC usage may be less of a confounder in this study. • Evidence showed potential exposure misclassification was more likely to be non-differential, the association of interest was underestimated.
Ostro et al. 2010 (Ostro et al., 2010)	The effects of temperature and use of air conditioning on hospitalizations	Time-stratified case-crossover	98,476 patients obtained from the OSHPD with restricted to those whose residential zip code was within 25 km of a temperature monitor in California, USA from 19992005 AC ownership and use were obtained from the 2004 California Residential Appliance Saturation Survey (RASS)	Heat, ATmean/ daily minimum apparent temperature (ATmin) / daily maximum apparent temperature (ATmax)	Diabetes-related hospital admissions Diabetes ascertainment was based on the ICD-9 code 250.	• A 10°F (5.6°C) increase in unlagged ATmean or ATmax was corresponded to 4% (95% CI: 1.9-6.2%) or 1.8% (0.9-2.8%) increase, respectively, of risk for diabetes-related hospital admissions. • Ownership and usage of ACs significantly reduced the effects of temperature on adverse health outcomes.	• AC may be correlated with other factors that modify heat-diabetes association. Strategies used : • Conducted more analyses to test AC-income and AC-SES relationships, finding low or no relationships. • Utilized AC prevalence and use data were collected at local level.
Pudpong and Hajat 2011 (Pudpong and Hajat, 2011)	High temperature effects on out-patient visits and hospital admissions in Chiang Mai, Thailand	Time series	46,169 patients acquired from the Chiang Mai provincial health office (out-patient), the National Health Security Office (hospital admission data) in Chiang Mai, Thailand from 2002-2006	Heat, Daily mean temperature (Tmean)	Diabetes- related out-patient visits and hospital admissions Diabetes ascertainment was based on the International Classification of Disease, 10 th Revision (ICD-10) codes E10-E14.	• Per 1°C increase above an identified threshold of Tmean (29°C) was corresponded to 26.3% (95% CI: 7.1–49.0%) increase of risk for diabetes-related out-patient visits adjusted for between-month variation, day of the week, holidays, influenza, autoregressive term, humidity and rain, and air pollutants (SO_2 and O_3). • No positive association was found between heat and diabetes- related	• Data couldn't separate elective and emergency visits/admissions. • Used secondary data, with missing values for some variables. • Potential misclassification of outcome Strategies used : • Missing records were assumed to occur completely at random. • Used ICD code to categorize health outcomes across several health centers and hospitals.

Author/year	Study Title	Study Design	Study Population	Exposure	Outcome	Results	Limitations and strategies to minimize
						hospital admissions adjusted for above listed confounders.	
Wang et al. 2012 (Wang et al., 2012)	The impact of heatwaves on mortality and emergency hospital admissions from non-external causes in Brisbane, Australia	Time-stratified case-crossover	Patients (sample size was not available) obtained from the Health Information Center of Queensland Health in Brisbane, Australia from 1996–2005, specifically, during December 27th, 1999 - January 24th, 2000, December 24th, 2001 - January 21st, 2002, and February 16th, 2004 - March 15th, 2004.	Heatwave, Tmax	Diabetes-related emergency hospital admissions Diabetes ascertainment was based on the ICD-9 code 250 and ICD-10 codes E10-E14.	The odds ratio (OR) was 1.20 (95% CI: 0.67-2.15) for the association between diabetes-related emergency hospital admissions and exposure to heatwave events defined as Tmax ≥37°C for ≥2 consecutive days adjusted for RH, PM_{10}, NO_2, and O_3. • The adjusted OR of interest was not significant among older adults (age 65 + years).	• Limited generalization of the findings due to a one-city study • Potential exposure misclassification • Sample size was small because the study was focused on three extreme heatwave events. Strategies used/suggested: • No clear strategies were documented to minimize the limitations. • Authors observed many significant associations even using a greatly reduced dataset, indicating it may be worthwhile to further investigate the areas.
Basu et al. 2012 (Basu et al., 2012)	The effect of high ambient temperature on emergency room visits	Time-stratified case-crossover	80,769 patients obtained from the OSHPD with restricted to those whose residential zip code was within 10 km of a temperature monitor in California, USA from 2005–2008	Heat, ATmean	Diabetes- related hospital admissions originating with an emergency department (ED) visit at the same day Diabetes ascertainment was based on the ICD-9 code 250.	• A 10°F (5.6°C) increase in unlagged ATmean was corresponded to 4.3% (95% CI: 2.8-5.9%) increase of risk for diabetes- related hospital admissions adjusted for O_3, CO, NO_2, SO_2 and $PM_{2.5}$. • Compared to those 19-64 years of age, adults 65 years and older showed a stronger association of interest (7.0%, 95% CI: 2.9-11.3%). • Compared to Whites, Asians showed a greater association of interest (7.6%, 95% CI: −0.1–17.0%).	• Ecologic data for exposure • 7-day interval for selecting controls may be not applicable for studying heat waves lasting >6 days, causing control and case periods overlap. Strategies used : • Restricted to those patients whose residential zip code was within 10 km of a temperature monitor.
Vaneckova and Bambrick 2013 (Vaneckova and Bambrick, 2013)	Cause-specific hospital admissions on hot days in Sydney, Australia	Time-stratified case-crossover	97,418 patients obtained from all private and public hospitals located on Sydney, Australia from 1991–2009	Heat, Tmean	Diabetes-related hospital admissions Diabetes ascertainment was based on the ICD-9 code 250 and ICD-10 codes E10-E14.	• The OR of diabetes- related hospital admissions was 1.06 (95% CI: 1.02-1.10) in comparing exposures to extreme hot days (95 th percentile) vs. control days adjusted for relative humidity (RH) and air pollutants (O_3, PM_{10}). • The adjusted OR was 1.12 (95% CI: 1.04-1.20) for the association of interest with extreme hot days defined as 99th percentile.	• Also included planned admissions in the analysis • Didn't count the spatial variation in temperature within the region Strategies used : • Authors expected to observe a stronger association if it was possible to use a reliable set of unplanned admissions • Planned to address it in a future study
Wilson et al. 2013 (Wilson et al., 2013)	The impact of heat on mortality and morbidity in the greater metropolitan Sydney region: a case crossover analysis	Time-stratified case-crossover	Patients (sample size was not available) obtained from the New South Wales (NSW) Department of Health in Sydney, Australia from 1997–2010	Heat/ Heatwave, Tmax	Diabetes-related hospital admissions Diabetes ascertainment was based on the ICD-10 codes E10-E14.9.	• The OR of diabetes- related hospital admissions was 1.12 (95% CI: 1.06–1.18) or 1.16 (95% CI: 1.03–1.30) at lag 0 in comparing exposures to Tmax >95th vs. ≤95th or Tmax >99th vs. ≤99th percentiles, respectively, adjusted for daily influenza admissions, holidays,	• Potential exposure misclassification • Lack of data for usage of air conditioning during heat events • Potential issues of multiple comparisons Strategies used : • Employed case-crossover design to control for the effects of unmeasured

Author/year	Study Title	Study Design	Study Population	Exposure	Outcome	Results	Limitations and strategies to minimize
						dewpoint Tmax, PM_{10}, $PM_{2.5}$, NO_2, and O_3. • The adjusted OR was 1.07 (95% CI: 1.01–1.14) or 1.14 (95% CI: 1.01–1.29) for the association between diabetes-related hospital admissions and exposure to heatwave events defined as Tmax >95th or >99th percentiles for 3 consecutive days, respectively. • The adjusted OR of interest among older adults (age 65 + years) was 1.12 (95% CI: 1.03–1.21) at lag 0 in comparing exposures to Tmax >95th vs. ≤95th percentiles.	confounders that don't change over time. • Applied stricter p-values for multiple comparison testing.
Bobb et al. 2014 (Bobb et al., 2014)	Cause-specific risk of hospital admission related to extreme heat in older adults	Time series	Patients (admissions in heatwave days=5077 and in matched non-heatwave days=4836) obtained from the Medicare inpatient claim data in 1943 counties, USA from 1999–2010	Heatwave, Tmean	Hospital admissions for diabetes mellitus with complications Diabetes ascertainment was based on the validated Clinical Classifications Software (CCS) algorithm code 50 derived from the ICD-9 codes 249 and 250.	• The RR of diabetes-related hospital admissions was 1.05 (95% CI: 0.96–1.14) in comparing exposures to heatwave days (Tmean >99th percentiles for ≥2 consecutive days) vs. matched non-heatwave days. • The RR of interest remained unchanged adjusted for long-term trends and day of the week.	• Couldn't capture the diseases coded as secondary diagnoses because authors only used the primary diagnosis to identify diseases for admissions. • The CCS algorithm may define some of disease groups more heterogeneous than others. • Potential Confounding bias Strategies used : • Used matched time series analysis to control for confounding • Used the Bonferroni-Holm approach to reduce the potential false-positive results due to multiple comparison
Wang and Lin 2014 (Wang and Lin, 2014)	Association between temperature and emergency room visits for cardiorespiratory diseases, metabolic syndrome-related diseases, and accidents in metropolitan Taipei	Time series	3,573 patients obtained from the Taiwan National Health Research Institute in Taipei, China from 2000–2009	Heat, Tmean	Diabetes-related ED visits Diabetes ascertainment was based on the ICD-9-CM code 250.	• The RR of diabetes- related ED visits was 1.69 (95% CI: 1.09–2.61) at lag 0 in comparing exposures to hot days (32°C) vs. reference days (18°C) adjusted for air pollutants (PM_{10}, NOx, and O_3), RH, wind speed (WS), daily ED visits for pneumonia and influenza, holidays, day of the week, and long-term trends. • The adjusted cumulative 4-day RR of diabetes- related ED visits was not significant.	• Couldn't assess the comorbidity effect on the temperature-diabetes association. • Didn't evaluate other factors, such as availability of transportation, willingness to go to hospital, usage of air conditioning, marital status, and personal oncome for the association of interest. Strategies used/suggested : • No clear strategies were documented to minimize the limitations. • Authors suggested further studies may be focused on assessing physiological mechanisms associated extreme temperatures by region and disease.
Bai et al. 2016 (Bai et al., 2016)	Hospitalizations from hypertensive diseases, diabetes, and arrhythmia in	Time series	324,034 patients obtained from the Canadian Institute for Health Information in	Heat, Tmean	Diabetes-related hospital admissions Diabetes ascertainment was	• The RR of diabetes- related hospital admissions was 1.30 (95% CI: 1.06–1.58) or 1.11 (95% CI: 0.98–1.25) comparing exposures to	• Potential exposure misclassification • May underestimate the burden of hospital admissions for diabetes because authors employed primary

Author/year	Study Title	Study Design	Study Population	Exposure	Outcome	Results	Limitations and strategies to minimize
	relation to low and high temperatures: population-based study		Ontario, Canada from 1996–2013		based on the ICD-9 code 250 and ICD-10 codes E10-E14.	Tmean 99th vs. 11th or Tmean 99th vs. 75th percentiles, respectively, adjusted for NO_2, O_3, RH, daily influenza admissions, holidays, day of the week, seasonality, and long-term trends. • Compared to the reference group, the RRs of diabetes- related hospital admissions were significantly higher among diabetic patients who had cancer (RR = 1.42, 95% CI: 1.11–1.82) and among diabetic older adults who regularly took diuretics (RR = 1.27, 95% CI: 1.04–1.55).	diagnosis only to identify patients. • Didn't study diabetes-related ED visits, thus may miss the heat effect on diabetic patients who had more acute but less severe medical conditions. • Didn't control for $PM_{2.5}$ due to data missingness. Strategies used : • Based on the findings from a previous study and the nature of the spatially derived exposure, authors suggested that the potential exposure misclassification could be nondifferential. • Conducted sensitivity analysis using the data with available $PM_{2.5}$ and found the risk estimates were not altered.
Winquist et al. 2016 (Winquist et al., 2016)	Warm season temperatures and emergency department visits in Atlanta, Georgia	Time series	70,076 patients obtained from individual hospitals and from the Georgia Hospital Association with restricted to those whose zip code was at least partially within one of the 20 counties in the Atlanta metropolitan area, USA from 1993–2012	Heat, Tmax	Diabetes- related ED visits Diabetes ascertainment was based on the ICD-9 codes 249 and 250.	• The RR of diabetes- related ED visits was 1.03 (95% CI: 1.01–1.05) in comparing exposures to Tmax 75th vs. 25th percentiles adjusted for dewpoint T, day of the week, holidays, time trends, and periods of hospital participation. • The strongest association of interest was found in the ≥65 years of age group (RR = 1.05, 95% CI: 1.01–1.10).	• It is difficult to compare the magnitude of association in this study to others because different method was used to model and quantify heat effects. • Not controlled for air pollutants. Strategies used : • Modeled temperature effects using linear, quadratic, and cubic terms. • Conducted sensitivity analysis to verify air pollutant effects and decided not controlling air pollutants in the model.
Chen et al. 2017 (Chen et al., 2017)	Time-series analysis of heat waves and emergency department visits in Atlanta, 1993 to 2012	Time series	70,076 patients obtained from hospitals in the 20-county Atlanta metropolitan area, USA from 1993–2012	Heatwave, Tmax/ Minimum temperature (Tmin)/ Tmean ATmax/ ATmin/ ATmean	Diabetes- related ED visits Diabetes ascertainment was based on the ICD-9 codes 249 and 250.	• No statistically significant association was observed between 6 indicators of temperature metrics and diabetesrelated ED visits adjusted for dewpoint T, day of the week, holidays, and time trends.	• The results might not apply to other areas since Atlanta metropolitan area had high air-conditioning prevalence (94%). • Might not fully controlled temperature effect if the temperature metrics were different as the heatwave temperature metric and had independent health impacts. • Didn't control for air pollutants. Strategies used/suggested : • Authors suggested that high prevalence did not necessary lead to high utilization rate, affected by economic constrains. • No strategies were proposed to address temperature effects. • Assumed air pollutants were mediators in the association of interest.

Author/year	Study Title	Study Design	Study Population	Exposure	Outcome	Results	Limitations and strategies to minimize
Ogbomo et al. 2017 (Ogbomo et al., 2017)	Vulnerability to extreme-heat-associated hospitalization in three counties in Michigan, USA, 2000–2009	Time stratified case-crossover	26,363 patients obtained from Michigan Inpatient Database with restricted to those lived within 55 km of a temperature monitor in three Michigan counties, USA from 2000–2009	Heat/ Heatwave, Tmean	Diabetes-related hospital admissions Diabetes ascertainment was based on the ICD-9 code 250.	• No associations were observed between extreme heat/heatwave exposure and diabetes- related hospital admissions adjusted for O_3. • The null associations of interest were also found in strata for age, sex, race, payer, and county.	• Studied hospitalization only, ED visits may be a more sensitive indicator of the association • Ecologic exposure • Lack of sensitivity test to compare using AT or heat index Strategies used : • Authors agreed that ED may be more sensitive to heat effects but didn't propose methods to address • Restricted to those patients whose residential zip code was within 55 km of a temperature monitor • Limited ability because humidity or dewpoint was not measured
Sherbakov et al. 2018 (Sherbakov et al., 2018)	Ambient temperature and added heat wave effects on hospitalizations in California from 1999–2009	Time series	230,993 patients obtained from the OSHPD PDD with restricted to those lived within 12 km of a temperature monitor in California, USA from 1999–2009	Heat/ Heatwave, Tmean	Diabetes-related hospital admissions Diabetes ascertainment was based on the ICD-9 code 250.	• The RR of diabetes- related hospital admissions was 1.06 (95% CI: 1.03–1.09) in comparing exposures to hot days (26°C) vs. mild days (20°C) adjusted for time trend, air pollutants (CO, NO_2, SO_2, O_3, $PM_{2.5}$) and RH • The adjusted RR was 1.03 (95% CI: 0.97–1.09) for both	• Heat wave exposure was not at individual level. • Limited information about social demographic for patients because of nature of data Strategies used : • Restricted to those lived within 12 km of a temperature monitor • Used race/ethnic group as a substitute
Campbell et al. 2019 (Campbell et al., 2019)	The value of local heatwave impact assessment: a case-crossover analysis of hospital emergency department presentations in Tasmania, Australia	Time stratified case-crossover	1994 patients in the two most populous regions of Tasmania, Australia from 2008–2016	Heatwave, defined by using the Extreme Heat Factor index based on Tmean	Diabetes- related ED visits Diabetes ascertainment was based on the ICD-10 codes E10-E11 and E13-E14.	• The odds of ED visits were increased by 5% (OR = 1.05, 95% CI: 1.01–1.09) across the whole population. • The OR was 1.57 (95% CI: 0.82–3.01) for the association between exposure to heatwave events and diabetesrelated ED visits adjusted for public holidays and $PM_{2.5}$.	• Relatively small sample size for a 9-year study and the 95% CI is wide. Strategies used : • Combined all available data during study period
Xu Z. et al. 2019 (Xu et al., 2019)	Heatwaves and diabetes in Brisbane, Australia: a population-based retrospective cohort study	Time-stratified case-crossover and case-only	10,542 patients from the five biggest public and private hospitals in Brisbane, Australia from 2005–2013	Heatwave, Tmean	Diabetes-related hospital admissions Diabetes ascertainment was based on ICD-10 codes E10-E11 and E13-E14.	• The OR was 1.18 (95% CI: 1.01–1.39) or 1.37 (95% CI: 1.11–1.69) at lag 1 for the association between diabetesrelated hospital admissions and exposure to heatwave events defined as Tmean ≥95th or ≥97th percentiles for ≥2 consecutive days, respectively, adjusted for PM_{10}, NO_2, and RH. • The adjusted OR of interest was not significant when heatwave intensity was 90th or 99th percentiles. • Compared to adults (15-64 years of age), children (0-14 years of age) were vulnerable to heatwave effects. • Authors did not observe any	• Limited generalization of the findings due to a one-city study • Some patient level information was not available in the data. • Exposure measurement was conducted at population rather than individual level. Strategy used: • Conducted sensitivity analysis using satellite remote sensing data for exposure.

Author/year	Study Title	Study Design	Study Population	Exposure	Outcome	Results	Limitations and strategies to minimize
						significant modification effect of Socio-economic Indexes for areas (SEIFA) or normalized difference vegetation index (NDVI) on the association of interest.	
Xu R. et al. 2019 (Xu et al., 2019)	Association between heat exposure and hospitalization for diabetes in Brazil during 2000–2015: A nationwide case-crossover study	Time-stratified case-crossover	553,351 patients from 1,814 cities in Brazil from 2000–2015	Heat, Tmean	Diabetes-related hospital admissions Diabetes ascertainment was based on the ICD-10 codes E10-E14.	• A 5°C increase in Tmean was corresponded to 6% increase of risk for diabetes- related hospital admissions adjusted for public holidays (OR = 1.06, 95% CI: 1.04–1.07). • A 7.3% increase (95% CI: 3.5–10.9%) of risk for diabetes-related all hospital admissions was found in the hot season. • The heat-diabetes association was greatest in those who were ≥80 years of age (OR = 1.18, 95% CI: 1.13–1.23).	• Only had access to grid city-level temperature data, which might cause underestimate the association. of interest • Due to lack of financial incentive to hospitals, the specific subtypes of diabetes were limited. • No data for adjustment of RH Strategies used : • Conducted sensitivity analyses to verify, but no statistically significant findings were observed.
Jiang et al. 2021 (Jiang et al., 2021)	Using logic regression to characterize extreme heat exposures and their health associations: a time-series study of emergency department visits in Atlanta	Time series	Daily mean ED visits were 215 (total about 657,900 patients) from hospitals in the 20-county, Atlanta metropolitan area, USA during May to September from 1993–2012	Heat, Tmin	Diabetes- related ED visits Diabetes ascertainment was based on the ICD-9 codes 249 and 250.	The RR of diabetes- related ED visits was 1.009 (95% CI: 0.996–1.021) comparing exposures to Tmin >95th vs. ≤95th percentiles adjusted for non-extreme continuous same-day T, average T over the last 3 days, dewpoint T, day of the week, holidays, long-term temporal trend, seasonal variation, and hospital participation.	Logic regression can be stuck in a local minimum when many binary predictors are involved in estimation. The sample size in current study limited selection of all possible highly correlated heat exposure indicators using logic regression. The current approach could not estimate uncertainty associated with the extreme heat metrics. Strategies used/suggested: Used smaller number of binary predictors than the typical association studies. To conduct further penalization within logic regression. To integrate pseudolikelihood to the current approach.

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Table 2

Pooled effect of the excessive heat-diabetes association by various factors

Category	Relative risk (95% CI)	Number of associations examined
Temperature indicators		
Apparent temperature *	1.028 (1.017–1.038)	8
Temperature	1.059 (1.030–1.089)	32
Daily mean apparent temperature	1.038 (1.027–1.049)	4
Daily maximum apparent temperature	1.017 (1.008–1.027)	2
Daily minimum apparent temperature	1.021 (0.998–1.044)	2
Daily mean temperature	1.069 (1.030–1.110)	23
Daily maximum temperature	1.067 (1.014–1.122)	7
Daily minimum temperature	0.993 (0.956–1.031)	2
Heat threshold		
95th percentile in group 3 **	1.044 (0.989–1.102)	4
97th percentile in group 3	0.97 (0.85–1.11)	1
99th percentile in group 3	1.106 (1.017–1.203)	3
90th percentile in group 4 ***	1.04 (0.93–1.18)	1
95th percentile in group 4	1.096 (1.017–1.182)	5
97th percentile in group 4	1.097 (0.928–1.298)	4
98th percentile in group 4	0.990 (0.968–1.012)	6
99th percentile in group 4	1.083 (1.010–1.161)	3
90th percentile in groups 3 and 4	1.04 (0.93–1.18)	1
95th percentile in groups 3 and 4	1.064 (1.018–1.112)	9
97th percentile in groups 3 and 4	1.057 (0.925–1.207)	5
98th percentile in groups 3 and 4	0.990 (0.968–1.012)	6
99th percentile in groups 3 and 4	1.101 (1.053–1.151)	6
Study design		
Case-crossover	1.056 (1.032–1.080)	24
Time-series	1.036 (0.996–1.077)	16
Study location		
Australia	1.105 (1.069–1.142)	12

Category	Relative risk (95% CI)	Number of associations examined
Brazil	1.06 (1.04–1.07)	1
Canada	1.176 (1.013–1.364)	2
China	1.69 (1.09–2.61)	1
Thailand	1.153 (0.955–1.393)	2
USA	1.021 (1.011–1.032)	22

* Apparent temperature (AT) was calculated as AT (°C) = −2.653 + (0.994* temperature (°C)) + (0.0153* (dew point temperature (°C))^2) (Green et al., 2010, Ostro et al., 2010, Basu et al., 2012) or AT (°C) = −1.3 + (0.92* temperature (°C)) + (2.2* water vapor pressure (kPa)) (Chen et al., 2017).

** Exposure was tested as the ambient temperature above vs. below a heat threshold.

*** Exposure was defined as above a heat threshold for at least two consecutive days.