

HHS Public Access

Author manuscript

Hyg Environ Health Adv. Author manuscript; available in PMC 2025 June 13.

Published in final edited form as: *Hyg Environ Health Adv.* 2025 June ; 14: . doi:10.1016/j.heha.2025.100123.

The association between temperature variability, morbidity and mortality for specific categories of disease: A systematic review and meta-analysis

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Abstract

While research into temperature-related health outcomes has focused on absolute temperature exposure, an increasing number of studies have explored the distinct effect of temperature variability (TV). However, systematic reviews in this area have focused on a limited number of health outcomes and intra-day TV. A systematic review was therefore conducted for studies of intra- and/or inter-day TV and cardiovascular, respiratory, renal or mental illnesses through April 2023 (n = 38). There was a consistent relationship between cardiovascular disease (CVD) or respiratory disease (RD) morbidity, mortality and both diurnal temperature range (DTR) or short-term inter-day TV, particularly for the elderly. The effect of DTR and short-term inter-day TV were stronger on hot days and the warm season for CVD, but on cold days and cold season for RD. Meta-analysis for CVD or RD and DTR showed a significant 0.7 %/C° increase in CVD mortality, but not morbidity, respectively. Most studies focused on CVD, RD, DTR or short-term inter-day TV, while few studies explored renal, GU, or mental health outcomes aside from schizophrenia. Future studies are needed to assess non-linear relationships between TV and disease, and the modifying effect of socioeconomic status.

Keywords

Climate change; Health effects; Extreme weather; Health outcome threshold; Temperature variability; Diurnal temperature range; Mental health

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CRediT authorship contribution statement

Maxwell D. Weidmann: Writing – review & editing, Writing – original draft, Visualization, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

1. Introduction

From 2000 to 2019, non-optimal temperatures have been associated with more than 5 million, or about 9.4 % of all deaths globally (Zhao et al., 2021). Approximately 8.5 % of deaths were cold-related and 0.9 % were heat related, though cold-related deaths have decreased by 275,000 per year during this time while the heat-related deaths have increased by 113,000 per year, consistent with increased heat exposure due to Anthropogenic global warming (AGW¹) (Zhao et al., 2021; IPCC, Climate Change 2023). Numerous studies have demonstrated the effects of increased ambient temperatures on physical disease outcomes (Fletcher et al., 2012; Li et al., 2019; Lin and al., 2012; Lin et al., 2009; Qu et al., 2023; Zeng et al., 2017), including a meta-analyses demonstrating a particularly strong association of heat exposure with all-cause, cardiovascular, cerebrovascular and respiratory mortality (Song et al., 2017). In contrast, meta-analysis showed no significant effect of heat exposure with morbidity for these outcomes, which was only significant for metabolic (e.g. diabetes) or genitourinary diseases (Song et al., 2017). AGW has also been associated with increases in the severity and frequencies of extreme heat events (heatwaves) (IPCC, Climate Change 2023; Rossati, 2017), with heatwaves showing significant increases in all-cause, cardiovascular and respiratory mortality, as well as cardiovascular morbidity (Zhao et al., 2021). Additionally mental health outcomes have also been found to be influenced by heat exposure (Deng et al., 2022), with significant effects on both morbidity and mortality. The greatest mortality effects were found in substance-related mental disorders and organic mental disorders, with increases in morbidity for mood disorders, organic mental disorders, schizophrenia, neurotic and anxiety disorders (Liu et al., 2021).

AGW has typically been associated with changes in average temperature, or excessively high temperature, but its effects on temperature are not the same during the day as compared to night, over the land as compared to ocean, or during different seasons (Easterling et al., 1997; Vose et al., 2005). AGW has had a relatively large impact on daily minimum relative to daily mean or maximum temperatures, with a number of studies observing that minimum temperature has been increasing at approximately twice the rate of maximum temperatures since 1950 (Easterling et al., 1997; Vose et al., 2005; Alexander et al., 2006; Sun et al., 2019; Thorne et al., 2016). As expected, this has resulted in a decrease in the diurnal temperature range (DTR) observed globally, and particularly in the Northern Hemisphere, though the magnitude of these changes varies considerably by geographical location (Sun et al., 2019; Thorne et al., 2016). Indeed, some locations such as the Yangtze River basin and parts of India have been found to have increases in DTR over the late 20th century (Guan et al., 2015; Rai et al., 2012).

AGW has also been shown to affect temperature variability (TV) occurring across other time scales, which is typically measured as standard deviation in mean daily temperatures

¹**Key Terms:** Cardiovascular disease (CVD), diurnal temperature range (DTR), respiratory disease (RD), temperature variability (TV), mental health (MH), renal/genitourinary disease (GU), anthropogenic global warming (AGW), temperature change between neighboring days (TCN), relative risk (RR), excess risk (ER), confidence interval (CI), acute coronary syndrome (ACS), chronic obstructive pulmonary disease (COPD), distributed lag non-linear model (DLNM), day of the week (DOW), emergency department (ED), generalized additive model (GAM), generalized linear model (GLM), heart failure (HF), International Classification of Disease (ICD), lives lost per death (LLD), respiratory tract infection (RTI), socioeconomic status (SES), weekly temperature variability (WTV), years of life lost (YLL)

over a given time-period (Guo et al., 2021). In addition to diurnal temperature range (DTR), temperature variability has also been characterized as temperature changes between neighboring days (TCN), standard deviation within 3–7 days (synoptic-scale), intra-monthly, 30–90 days (sub-seasonal), seasonal, inter-annual or decadal time scales (Guo et al., 2021). The mechanisms by which AGW influences TV differs both by time scale and regional features (Guo et al., 2021). The Fifth Phase of the Coupled Model Intercomparison Project (CMIP5) projections demonstrate a decrease in TCN for both maximum and minimum temperatures over high latitudes in winter months, but an increase in TCN over the summer months in Europe (Guo et al., 2021). Likewise, over synoptic time scales TV has been found to decrease over the Northern hemisphere due to reduced temperature gradients with high latitudes, but increase over central and eastern Europe (Schneider et al., 2015). It is therefore likely that effects of both intra- and inter-day TV on specific health outcomes are modified by seasonal and climate-specific factors, which vary on a regional basis.

Despite the potential climate implications of inter-day temperature variability across a variety of time scales, there have been no systematic reviews on the effects of inter-day temperature variability of the week to annual timescale on morbidity and mortality related to cardiovascular disease (CVD), respiratory disease (RD), renal/genitourinary disease (GU) or mental health (MH). Only two systematic reviews assessed DTR, with one review focusing on CVD outcomes alone (Phung et al., 2016), to find a small but significant increase in CVD mortality (RR 1.007, 95 % CI 1.002–1.012), but larger increase in CVD morbidity (RR 1.022, 95 % CI 1.006–1.039), with increasing DTR via meta-analysis. The other systematic review included mainly studies assessing CVD, RD or all-cause mortality and only including studies up to 2013 (Cheng et al., 2014).

Therefore, the objectives of this systematic review include: 1) Systematically evaluate studies assessing the effect of exposure to either DTR or inter-day TV on morbidity and mortality related categories of cause-specific illness, such as cardiovascular disease, respiratory disease, renal/genitourinary disease and mental illness; 2) Compare the effects of intra- and inter-day TV exposures on different time scales to identify particularly vulnerable populations and the extent to which the effect of these TV indicators are modified by season and ambient temperature; and 3) Identify gaps and inconsistencies in the current literature that warrant further study.

2. Methods

2.1. Data sources

Searches were conducted on PubMed, Web of Science, EBSCO, and PsycINFO, which are commonly used sources for literature in the biomedical sciences, health and medical fields. The reference lists from selected articles and previous systemic reviews were also included as a data source.

2.2. Search criteria

A systematic literature review was conducted by searching for publications up to March 31st, 2023 containing the weather indicator keywords/terms: "temperature variability or

diurnal temperature range," as well as the health indicator keywords/terms: "cardiovascular disease or respiratory disease or renal disease or genitourinary disease or kidney disease or mental health or mental illness" (Table 1). Title and abstract review were used as an initial screen for the inclusion and exclusion criteria defined below. Full-text review of the remaining records was then conducted to confirm that methodologies were in accordance with these criteria.

2.3. Inclusion and exclusion criteria

Articles were then included if: 1) They used an explicit measure of DTR or inter-day temperature variability as an exposure, 2) They included cause-specific morbidity or mortality outcomes including at least one of the following: 3) evaluated outcomes in cardiovascular disease, 4) respiratory disease, 5) renal/genitourinary disease, or 6) mental illness. Studies were excluded if they: 1) Only assessed all-cause mortality or morbidity, 2) Did not include outcomes in one of the disease categories defined above, 3) Were methods studies that did not report on clinical outcomes, or 4) Were not peer-reviewed.

2.4. Meta-analysis

Studies assessing DTR as an exposure were included in a meta-analysis, though there were insufficient studies using uniform methodology to study other indicators of temperature variability for meta-analysis. Within studies assessing the effect of DTR on health outcomes, studies assessing renal/urogenital disease or mental health were not included due to the reduced number of studies and large heterogeneity of study methodology. Studies were also excluded if they assessed multi-day averages of DTR, such as monthly or annual timescales. A random-effects model was used to pool effect sizes of studies assessing the association between DTR and hospitalizations or mortality associated with cardiovascular or respiratory disease. The analysis was completed in R, using the 'meta' package, and the Dersimonian-Laird estimator was used to estimate between-study heterogeneity (DerSimonian and Laird, 1986).

3. Results

3.1. Description of study selection

As shown in Fig. 1, 1149 records were initially retrieved based on initial search criteria, and these were narrowed down to thirty-six records upon review of titles and abstracts for those that did not include the weather indicators of interest, did not include any of the specific outcomes or did not represent primary research (reviews or meta-analyses). Removal of duplicate records that matched into more than one category, records that represented methodological research, records that included disease-specific risk factors rather than outcomes, resulted in a list of twenty-three full-text articles, and review of the reference lists of these articles resulted in an additional fifteen studies included, for a total of thirty-eight studies reviewed.

3.2. Characteristics of the studies included

Key characteristics of the thirty-eight studies included in this review are summarized in Table 2. Twenty-five of the studies (66 %) included some form of cardiovascular disease

(CVD) as an outcome (Liang et al., 2008; Cao et al., 2009; Tam et al., 2009; Luo et al., 2013; Zheng et al., 2016; Tian et al., 2019; Phosri et al., 2020; Kang et al., 2021; Yu et al., 2021; Zha et al., 2021; Zhai et al., 2021; Rahman et al., 2022; Tang et al., 2022; Zhai et al., 2022; Qi et al., 2023; Lim et al., 2015; Lee et al., 2018; Gong et al., 2023; Wang et al., 2022; Kan et al., 2007; Lim et al., 2012; Wang et al., 2013; Qiu et al., 2013), although seven (28%) of these studies looked only at specific forms of CVD, rather than CVD as a general category of disease (Liang et al., 2008; Cao et al., 2009; Yu et al., 2021; Qiu et al., 2013). Eighteen of the studies (47 %) included respiratory disease (RD) as a health outcome (Luo et al., 2013; Phosri et al., 2020; Rahman et al., 2022; Qi et al., 2023; Lim et al., 2015; Lee et al., 2018; Gong et al., 2023; Wang et al., 2022; Kan et al., 2007; Lim et al., 2012; Wang et al., 2013; Sun et al., 2018; Pedder et al., 2021; Song et al., 2008; Liang et al., 2009; Ge et al., 2013; Xu et al., 2013; Li et al., 2014), but seven of these studies only looked at specific subsets of respiratory disease (Pedder et al., 2021; Song et al., 2008; Liang et al., 2009; Ge et al., 2013; Xu et al., 2013; Li et al., 2014; Chang and Ku, 2023). Only four studies (11 %) looked at renal system diseases as a health outcome (Lee et al., 2018; Wang et al., 2022; Wang et al., 2013; Li et al., 2022). Six studies (16 %) looked at mental health outcomes (Wang et al., 2022; Sung et al., 2011; Hiltunen et al., 2014; Zhao et al., 2016; Zhao et al., 2017; Xue et al., 2019), with four (66 %) of these studies looking at specific mental health outcomes (Sung et al., 2011; Hiltunen et al., 2014; Zhao et al., 2016; Zhao et al., 2017), and one study looking at mental health through self-assessment (17 %) (Xue et al., 2019).

Thirty-two of the studies (84 %) included time series analysis, with only nine studies (24 %) including either another method or a combination of study designs. Of these nine studies, there was one retrospective cohort study (Sung et al., 2011), three prospective cohort studies (Kang et al., 2021; Tang et al., 2022; Sun et al., 2018), two studies with a longitudinal design (one with difference-in-difference analysis) (Liang et al., 2009; Xue et al., 2019), and two studies using the case-crossover method in addition to time series (Cao et al., 2009; Lim et al., 2012). Regarding the location of study populations, twenty-nine of the included studies (74 %) were conducted in China or Taiwan, three (8 %) were conducted in other parts of East Asia, three (8 %) of studies were conducted on populations in the western hemisphere (Lim et al., 2015; Hiltunen et al., 2014; Magalhaes et al., 2011) and only two (6 %) studies conducted in the global south (Pedder et al., 2021).

3.3. Cardiovascular disease outcomes

Out of studies assessing CVD outcomes, twenty (80 %) assessed DTR (Liang et al., 2008; Cao et al., 2009; Tam et al., 2009; Luo et al., 2013; Zheng et al., 2016; Phosri et al., 2020; Zha et al., 2021; Zhai et al., 2021; Tang et al., 2022; Zhai et al., 2022; Qi et al., 2023; Lim et al., 2015; Lee et al., 2018; Wang et al., 2022; Kan et al., 2007; Lim et al., 2012; Wang et al., 2013; Qiu et al., 2013), with eighteen of these (90 %) assessing short-term DTR (single day or averages over a exposure days) (Liang et al., 2008; Cao et al., 2009; Tam et al., 2009; Luo et al., 2013; Zheng et al., 2016; Phosri et al., 2000; Zha et al., 2009; Tam et al., 2009; Luo et al., 2013; Zheng et al., 2015; Lee et al., 2018; Wang et al., 2022; Kan et al., 2007; Lim et al., 2012; Wang et al., 2013; Qiu et al., 2013) and two (10 %) assessing annually averaged DTR (Tang et al., 2022; Qi et al., 2023). Ten studies looked at the association of short-term DTR with CVD-associated ED or hospital admissions (Liang et al., 2008; Zheng et al., 2016; Zha

et al., 2021; Zhai et al., 2021; Zhai et al., 2022; Lee et al., 2018; Wang et al., 2022), and all but one study (Wang et al., 2022) showed an association between increased DTR and CVD admissions (or a subset of CVD, such as HF).

3.3.1. Cardiovascular disease morbidity and DTR: Three studies looking at the relationship between DTR and hospital admission in two rural areas, and one suburban area, of China found similarly shaped bimodal peaks in CVD incidence (Zha et al., 2021; Zhai et al., 2022). In two of these studies there was a higher increase in RR of CVD admission for the lower DTR peak (2.24, p < 0.05; 2.95, 95 %CI 1.605–5.425), at a DTR of approximately 6 °C, though both low and high DTR (~19 °C) peaks in RR of CVD admission were significant in these studies (Zha et al., 2021; Zhai et al., 2022). However, the other study from rural China found that only the higher DTR (17 °C) peak (RR 1.78, p < 0.05) had a significant effect, particularly for men (RR 1.94) and those <65 years (RR 2.23), while those >65 years were more sensitive to lower DTR, having a higher RR for the 6 °C DTR peak (2.55) (Zhai et al., 2021).

Five studies assessed the association of single-day DTR with morbidity due to subsets of CVD, as cerebrovascular events (strokes) (Magalhaes et al., 2011; Shaposhnikov et al., 2014), myocardial infarction (MI) (Shaposhnikov et al., 2014), acute coronary syndrome (ACS) (Liang et al., 2008), and heart failure (Lim et al., 2012; Qiu et al., 2013). Both studies assessing stroke risk found a significant relationship between DTR and either overall stroke (26 % increase per 10 °C increase from DTR of minimum risk) (Shaposhnikov et al., 2014), or hemorrhagic strokes only (12 % increase per °C) (Magalhaes et al., 2011). Heart failure was also significantly associated with DTR in both studies for which it was assessed, which found similar 3–4 % increase in risk of heart failure admission per 1 °C DTR increase (Lim et al., 2012; Qiu et al., 2013). In contrast, only one of the two studies assessing the effect of acute coronary CVD outcomes found a significant relationship with DTR (34.6 % increase in ACS admissions when DTR >9.6 °C, relative to <9.6 °C) (Liang et al., 2008).

There were mixed results for age stratification, with one study showing a greater association within either >65 or <65 year age groups relative to the overall population (Zhai et al., 2022). Three studies showed a greater association in those >75 years (Zheng et al., 2016; Wang et al., 2013; Qiu et al., 2013), while another study showed greater sensitivity for those <65 years (Zha et al., 2021). There were also mixed results by gender, with three studies from urban areas showing a greater effect of DTR in CVD admissions in women (Zheng et al., 2016; Wang et al., 2013; Qiu et al., 2013) while two studies in rural areas showed greater sensitivity to DTR in men (Zha et al., 2021; Zhai et al., 2021). Other studies showed different effects of DTR on men and women, with two studies in different rural districts of China showing that women were more sensitive to lower DTR (~6 °C), and especially extremely low DTR (<1 % tile), while men were more sensitive to higher DTR (Zhai et al., 2021; Zhai et al., 2022). Only two studies looked at the modifying effect of season on the DTR-CVD admission relationship with the first study in Hong Kong showing that, for heart failure specifically, there was only a significant increase in admissions during the cold season on individual lag days, and the overall effect at lag0-5 days was >6-fold higher in the cold season (Qiu et al., 2013). A later study in Bangkok, Thailand, found that the overall relationship between extremely high DTR (>11.6 °C) and CVD admissions 1.206 (95 % CI:

1.002–1.452), was higher in the winter, but not present in summer or rainy season (Phosri et al., 2020).

3.3.2. Cardiovascular disease mortality and DTR: There were also eight studies looking at the effect of DTR on CVD-related mortality (Cao et al., 2009; Tam et al., 2009; Luo et al., 2013; Tang et al., 2022; Qi et al., 2023; Lim et al., 2015; Lee et al., 2018; Kan et al., 2007), all of which showed a significant increase in CVD mortality with increasing DTR. There was significant variation in the magnitude of the effects seen for short and long-term DTR, however, with one study looking specifically at coronary heart disease finding up to a 3.6 % increase in mortality per 1 °C increase in short-term DTR (peaking at lag 3 days) using a unidirectional case-crossover design (Cao et al., 2009). In contrast, a time series analysis of data from Hong Kong found cumulative RR at lag0-3 and lag0-4 of 1.7 % per 1 °C increase in DTR (Tam et al., 2009), and a study spanning 95 communities in the US found only a 0.35 % increase in CVD mortality per 1 °C of DTR increase, with a nearly two-fold higher risk in the elderly (0.39 % vs 0.21 %, p < 0.05) (Lim et al., 2015). A Japanese-wide study using IQR intervals of DTR as a metric found that each IQR increase corresponded to 2 % increase in CVD mortality risk, and that this relationship stronger with increasing ambient temperature (p < 0.001) (Lee et al., 2018). Finally, a Chinese study looking at two urban districts found large increases in RR of mortality with extremely low DTR (<1 % tile) at longer lag times than assessed in the previous studies (lag0–13 and 0-20) while increases in CVD mortality due to extremely high DTR (>99 % tile) were only significant at shorter lags (0-6 and 0-13) (Luo et al., 2013). Studies looking at long-term DTR also found a large range of effect sizes on CVD mortality, with one country-wide time series study from China finding a small but significant 3 % increase in CVD mortality per 10 °C increase in DTR (annual), with the greatest effect at lower elevations (<500 m) (Qi et al., 2023). In contrast, a prospective cohort study spanning 14 Chinese provinces found a 12 % increase in risk for CVD mortality per 1 °C increase in annually averaged DTR, with a linear increase in risk with increasing DTR, while stroke risk increased by 9 % per 1 $^{\circ}$ C of DTR, but showed a logarithmic increase at DTRs >10 °C (Tang et al., 2022).

3.3.3. Cardiovascular disease and inter-day TV: There were eight studies assessing CVD outcomes and some form of inter-day temperature variability (TV) indicator, four included an indicator that combined intra-day and inter-day TV (Tian et al., 2019; Yu et al., 2021; Rahman et al., 2022; Gong et al., 2023), two included both DTR and inter-day TV indicators (Shaposhnikov et al., 2014; Wang et al., 2022), while the remaining two assessed only inter-day TV (Kang et al., 2021; Jin et al., 2022). These latter two studies used prospective cohort design to assess long-term TV, wherein the standard deviations of daily mean temperatures were averaged over the year prior to each survey (Kang et al., 2021; Jin et al., 2022). Kang et al., (2021) looked at overall CVD risk to find an overall 6 % increase per 1C increase in long-term TV and the greatest effect for those aged 35–65 years. One of two studies assessing the association of intra-day TV and stroke found significant associations (Tian et al., 2019; Shaposhnikov et al., 2014), finding that ischemic stroke had the greatest association (0.82 %/ °C increase in TV from day 0–1 prior) of all CVD categories assessed (Tian et al., 2019), while no significant association was found for TCN and overall stroke (Shaposhnikov et al., 2014). The former study also found significant

associations between inter-day TV and ischemic heart disease, heart failure and arrhythmia hospital admissions peaking for TV from 0–1 days prior to admission (Tian et al., 2019), while no significant association with inter-day TV from days 0–7 prior to admission was found for acute aortic dissection (Yu et al., 2021).

Of the four studies looking at short-term TV metrics that combined intra- and inter-day variability, those looking at risk of overall CVD hospital or ED admission found a more modest effect, with either a 0.44 % or 1 % increase in CVD risk per 1 ° C of TV, peaking at lag0–1 days (Tian et al., 2019; Rahman et al., 2022). A greater magnitude increase in CVD admissions per 1 °C TV increase was seen for men (0.51 %), those >75 years (0.81 %), those living in warmer regions (0.58 %), and for ischemic heart disease (0.82 %) amongst a Chinese urban population spanning 184 cities (Tian et al., 2019). Another study examining years of life lost (YLL) and life-lost per death (LLD) from CVD found most LLD attributable to short-term TV (lag0–1) was due to TV greater than 2.5 °C (96.6 %), and was greater for those <65 years, as well as warmer, humid, lower latitude and high altitude areas (Gong et al., 2023). In contrast, a study looking specifically at short-term TV effect on acute aortic dissection in Wuhan China found a protective or null effect of increased TV except for lag0–2 and 0–3 exposure days for women only (Yu et al., 2021).

3.4. Respiratory disease outcomes

Of the eighteen studies looking at RD outcomes, fifteen (83 %) assessed DTR as an indicator (Luo et al., 2013; Phosri et al., 2020; Qi et al., 2023; Lim et al., 2015; Lee et al., 2018; Wang et al., 2022; Kan et al., 2007; Lim et al., 2012; Wang et al., 2013; Pedder et al., 2021; Song et al., 2008; Liang et al., 2009; Ge et al., 2013; Xu et al., 2013; Li et al., 2014), with only one study looking at long-term DTR (Qi et al., 2023). The latter study, assessing annually averaged DTR across 266 cities in China, found a 4 % increase in RD mortality per 10 °C rise in DTR, only at elevations above 500 m (Qi et al., 2023). Of the remaining fourteen studies, four looked at the relationship between DTR and overall RD hospital admissions, with one study in Bangkok, Thailand finding no association between DTR and RD admissions (Phosri et al., 2020). Though another study spanning 20 sites in China found a 1.5 % increase in RD visits to the ED for each 1 °C increase in DTR only during the autumn (Wang et al., 2022). Wang et al. (2013) found a similar increase of ~ 2 % per 1C DTR increase, with a larger effect found in men (Wang et al., 2013), and Lim et al., (2012) used both case-crossover and time series designs to find a significant 1 % increase in RD hospital admissions per 1 °C DTR increase for both approaches. The latter study also found that COPD admissions had a more pronounced 2 % increase per 1 °C DTR increase by the time series analysis, while asthma had a more pronounced effect by case-crossover analysis (2 %/1 °C DTR), and particularly in those >75 years (4 %/1 °C DTR).

3.4.1. Respiratory disease morbidity and DTR: There were an additional five studies that assessed subsets of RD morbidity. One assessed the role of DTR in COPD morbidity, finding a roughly 3 % increase in COPD admissions to the ED per 1 °C increase in DTR (Liang et al., 2009). One study assessed the role of DTR in childhood asthma morbidity, finding an ~6 % increase in risk per 1 °C increase in DTR (from 10 °C to 15 °C), and this was only significant for male children, with a larger effect in children age

5–9 years (18 %/1 °C) (Xu et al., 2013). Two studies also looked at ED admissions for overall respiratory tract infection (RTI), with similar findings for the RTI morbidity-DTR association peaking at lag1 or lag2 days, with overall lag0–1 or lag0–2 effect of ~2 % increase in admissions for RTI per 1 °C DTR increase (Ge et al., 2013; Li et al., 2014). A study from one district of South Africa also found a significant association between DTR and pneumonia admissions only when DTR was greater than 21 °C, which occurred 12 days per year at this location (Pedder et al., 2021).

3.4.2. Respiratory disease mortality and DTR: Five studies assessed the relationship between RD mortality and short-term effect of DTR. Two studies found a similar ~1 % increase in RD mortality risk per 1 °C increase in DTR, one spanning all of Japan over a 43-year period found this effect peaking at lag 2 days for hot days (>75 % tile) and lag >8 days for cold days (<25 % tile) (Lee et al., 2018), while another large study in Shanghai found significant effects at lag0, lag1 and lag4 days, and the DTR effect was only significant on relatively cool days (<23 °C) (Kan et al., 2007). A third study of 95 communities across the US looking at DTR as a continuous variable found a smaller 0.3 % (95 % CI 0.2–0.4 %) increase in RD mortality per 1 °C increase in DTR at cumulative lag0-3 days, and was only significant for those >65 years by subgroup analysis (0.33 %, 95 % CI 0.22–0.44 %) (Lim et al., 2015). The fourth study in two districts of China looked only at DTR by percentile, and for longer lags up to 27 days, finding a 381 % increase in RD mortality cumulative excessive rate (annual) over the entire lag period for extremely low DTR (<1 % tile), and that both <1 % tile and >99 % tile DTR showed significantly increased risk of RD mortality during the cold season, with longer cumulative lag (0-20 and 0-27 days) (Luo et al., 2013). Finally, Song et al., (2008) looked exclusively at COPD deaths in Shanghai to find a 1.25 % increase per 1 °C DTR increase, but found a larger 1.57 % increase on cold days (<22 °C) (Song et al., 2008).

3.4.3. Respiratory disease and inter-day TV: Four studies assessed the relationship between RD outcomes and inter-day TV, with two studies looking at combined metrics of inter- and intra-day variability, one looking at short-term inter-day variability and the remaining looking at three-month (seasonal) inter-day variability (Rahman et al., 2022; Gong et al., 2023; Wang et al., 2022; Sun et al., 2018). Sun et al., (2018) was a prospective cohort study of Hong Kong residents >65 years looking at seasonal TV, and finding a 20 % increase in risk of RD hospital admission per 1 °C of increased TV during the winter, but not summer (Sun et al., 2018). Wang et al. (2022) also looked at RD visits to the ED at 20 sites spanning most of China, but looked at short-term temperature change on neighboring days (TCN) to find a significant increase of 4.8 % in visits for RD per 1 °C increase in TCN in winter (relative to 2 %/1 °C overall), while the effect for DTR was only 1.5 %/1 °C and specific for autumn (Wang et al., 2022). Studies looking at mixed short-term TV metrics found increased risk of RD admission the ED (2.1 %/1C increase in TV) at short lag periods (cumulative 0-1 and 0-7 days), with greater effect in those >50 years, during the hot/dry or monsoon seasons (Rahman et al., 2022). The only study assessing the effect of TV (lag 0-1days) on mortality found overall 0.54 LLD for RD, with highest levels of YLL at extremely low (<2 °C) or high TV (>10 °C), and greater overall association of TV on YLL in the elderly (>65 years), with mortality data from 5 Chinese provinces (Gong et al., 2023).

3.5. Renal/Genitourinary (GU) disease outcomes

Of the four studies that assessed either intra- or inter-day TV and renal disease, Wang et al. (2022) represents the largest study of GU outcomes, assessing both metrics to find an increase of 4 % in GU ED visits per 1 °C increase in TCN, which was attributed entirely to a summer season effect of 8.3 %/1 °C, with no significant change for the other seasons or with DTR (Wang et al., 2022). The other three studies assessed DTR only, with Wang et al. (2013) finding that there was a significant increase in GU morbidity peaking at lag0–5 of 1.81 % per 1 °C DTR increase, but was only significant for men and those >75 years (Wang et al., 2013). Li et al. (2022) found a significant increase in the RR of renal disease when DTR was either below 5 % tile or greater than 95 % tile at lag 0–7, lag0–14 and lag0–21, peaking at lag0–21 with RR of 6.96 (5 % tile) and 5.96 (95 % tile). Lee et al. (2018) assessed renal disease mortality, finding a 3–4 % increase per IQR increase in DTR (IQR = 4.6 °C overall), which was greater in warmer regions (4–5 %) and peaked with <2-day lag for extremely hot days (>99 % tile) and 3–4 day lag for extremely cool days (<1 % tile).

3.6. Mental health (MH) outcomes

Of the three studies assessing the role of TV in schizophrenia outcomes, two studies from the same Chinese province (Anhui) looked at the association between ED admissions and either DTR alone (Zhao et al., 2016) or both DTR and TCN (Zhao et al., 2017). For single lag days, the peak increase in ED admission risk for schizophrenia was at a 2.7 % increase for DTR of >95 % tile at lag0, and a 18.7 % increased risk for cumulative lag0-11 days, with greater risk for those aged 15–29, 50–64 and born in spring or autumn (Zhao et al., 2016). For both DTR and TCN, increase in RR peaked at lag3 and lag4 for those born in the spring at 95 % tile (DTR only) and 99 % tile (DTR and TCN). A retrospective cohort study across 21 of 25 districts in Taiwan also found that increasing DTR was associated with increased risk of schizophrenia hospital admission, beginning at 10-24 % tile and peaking at the highest DTRs (>99 % tile) with a 22 % increase (p < 0.01). One study looking at the association of suicide rates in Finland with DTR and short-term inter-day TV (from lag0-1 to lag0-5) found that only two of six sites had significant increases in suicide rates for men at lag0-1 and lag0-5 for men and lag0-5 at a third site for women (p = 0.02), while DTR was only significantly associated with suicide risk for women at one site at (2.4 %/1 °C, p =0.02).

Two studies looked at the relationship between TV and overall mental health outcomes, Wang et al. (2022) assessing 20 sites across China to find an 11.8 % (95 % CI 3.6–21.2) increase in risk of ED visit for mental illness per 1 °C increase in TCN in Spring only, and no significant effect for DTR (Wang et al., 2022). Xue et al. (2019) assessed annual TV relationship with "mental health score" (MHS) in a questionnaire-based longitudinal study spanning 25 provinces of China, and finding a 15 % decrease in MHS per 1 °C increase in TV, and more specifically that increasing TV was associated with reports of nervousness, upset, hopelessness and meaninglessness (Xue et al., 2019).

3.7. Confounding factors

Table 2 details confounding factors controlled for in each of the studies, with the most common being daily mean temperature (n = 29), relative humidity (n = 27), as well as some

form of air pollutant (such as (O₃, PM_{2.5}, PM₁₀, SO₂, CO, NO, or NO₂) (n = 22). Another prominent confounder noted in most studies, but only included in 24 % of studies (n = 9) was socioeconomic status (SES).

3.8. Limitations of included studies

The most common limitation, which was present in all studies assessed, was the dependence on ecologic methods of temperature assessment. While the resolution of temperature assessment varied greatly from 1 km (by interpolation) to >50 km for districts in which as few as a single were available, no study included data on local temperature exposure in the workplace or home setting. As access to indoor heating and cooling systems may greatly influence exposure to temperature variability, this is a major limitation. Twenty-seven (75 %) of the studies did not contain any metric of socio-economic status (SES), such as income or education level, in their model or stratified analysis, which may reduce confounding due to unknown indoor temperature exposure but does not serve as a proxy for such exposure data. Twenty-five (69 %) of the studies only covered one city or district, therefore representing only a narrow geographic area that may not be representative of other regions.

3.9. Meta-analysis

Due to methodological differences, only eight studies reviewed here were suitable for meta-analysis for an exposure of DTR (Figs. 2–3). The pooled effect of studies assessing the association between DTR and hospitalizations due to respiratory disease, but not cardiovascular disease, was found to be significant, with a 1.0 % increase in hospitalizations per degree Celsius (Fig. 2A–B). When both respiratory and cardiovascular hospitalizations were combined, there was also no significant pooled effect (Fig. 2C). In contrast, both cardiovascular and respiratory disease mortality produced a pooled effect that was significant, with an effect size was only 0.7 % per degree Celsius increase in DTR (Fig. 3A–B), and this was consistent with a significant pooled effect when both disease categories were combined across mortality outcomes (Fig. 3C). There was a high level of heterogeneity ($I^2 > 0.75$) for all groups and subgroups assessed, with the exception of hospital admissions due to respiratory disease.

4. Discussion

4.1. Overview

Here we have reviewed studies assessing a wide range of intra- and inter-day TV metrics. Our meta-analysis assessing the effect of intra-day TV (DTR) on CVD and RD showed a consistent association between increasing DTR and disease-specific mortality. However, the meta-analysis assessing the effect of DTR on hospital admissions only showed a significant effect for respiratory disease, with a non-significant trend towards increased risk with increasing DTR. Combined with a high degree of heterogeneity for all outcome and exposure groups assessed by meta-analysis, our review of the literature suggests that the associations between DTR and CVD or RD outcomes are not linear. Instead, it is likely that extremely low or high DTR impacts these outcomes in a manner influenced by regional climate and seasonality.

4.2. Diurnal temperature range, health outcomes and vulnerable groups

The effect of DTR on CVD morbidity showed an unexpectedly bimodal peak in studies assessing rural areas, with effects at both low and high DTR, but with effects diminishing at extremely low and high DTR. Overall, these studies suggest that the relationship between age and gender on vulnerability to the CVD risk cause by DTR are not always linear. Studies that only looked at linear relationships found mixed results, though there was consensus around greater effect of DTR on CVD morbidity for those >75 years or >65 years (Zheng et al., 2016; Lim et al., 2015; Wang et al., 2013; Qiu et al., 2013), while other found greater effect for <65 years (Zha et al., 2021). However, when one looks at low and high DTR peaks separately, the high DTR peak (~17 °C) was found to have a greater impact on CVD admissions for <65 years and men, while the opposite relationship for age and gender was found for the low DTR peak (6 °C). It is also possible that the bimodal peaks found in studies assessing rural areas of China, and farmers who have increased outdoor exposure, may represent a specific subpopulation, and further studies into such non-linear relationships across a large range of DTRs should be repeated in urban areas.

Studies assessing the relationship between DTR and CVD mortality found a strong relationship between CVD mortality risk and increasing DTR, albeit of a variety of magnitudes. However, many of these studies looked only at the linear relationship between DTR and CVD mortality. Only one study assessed the effects of extremely low DTR on CVD mortality, finding significant increases only at longer lag times than included for most studies, over a period of 2–3 weeks, while elevated DTR had a more immediate effect, within one week or less (Tam et al., 2009; Luo et al., 2013). Only one study assessed short-term DTR and CVD mortality stratified by age or gender, finding a far greater risk of mortality in the elderly (>65 years) per 1 °C increase in DTR, though there was still a significant increase for those <65 years (Lim et al., 2015). A large prospective cohort study assessing annually-averaged DTR found that there was no association between risk of CVD mortality and age, but gender stratification found that there was only a significant effect of increasing DTR in men (HR 1.21 vs 1.03; p = 0.063) (Tang et al., 2022).

For both RD morbidity and mortality, most studies assessed only the linear relationship between increasing DTR and health outcomes. However, the one study assessing both extremely low and high DTR found that only extremely low DTR (<1 % tile) had a significant effect on RD mortality over the full lag period assessed (27 days) (Luo et al., 2013). Only one study included a stratified analysis of overall RD morbidity and DTR by age and gender, finding no difference by age, but a larger effect in men, while COPD admissions specifically were more affected by DTR in those >75 (Wang et al., 2013). Two studies of asthma-related admissions also found a larger effect of DTR on male children, ages 5–9 years, and amongst adults those >75 years were more vulnerable (Lim et al., 2012; Xu et al., 2013). Only one study exploring the relationship between DTR and RD mortality conducted stratified analyses for age or gender, finding that increase in RD mortality associated with short-term DTR (lag0–3 days) was only significant in the elderly (>65 years) (Lim et al., 2015). However, this group did not assess the effect of DTR on RD morbidity.

Among studies assessing the effect of DTR on renal disease, only one study from Beijing stratified by age and gender, finding that there was only a significant effect of DTR on GU admissions in men or those >75 years (Wang et al., 2013). Among mental health outcomes, there was a consistent finding of significant increase in schizophrenia-related ED or hospital admission with increasing DTR, but only one study looked at gender and age differences, finding a greater effect for those <65 years and in men (Zhao et al., 2016).

4.3. Inter-day temperature variability and health outcomes and vulnerable groups

Interestingly, there were marked differences seen in the effects of intra-annual TV (longterm) versus TCN and synoptic time scales (short-term). Most studies assessing the association of inter-day TV and CVD risk looked only at morbidity, but the effect of intra-annual TV had the greatest effect on adults aged 35–65 years (with no difference by gender) (Kang et al., 2021), while the greatest effect of TV on CVD morbidity on the scale of days was found in those >75 years and men (Tian et al., 2019). Short-term TV was also more closely associated with RD morbidity in those >50, and >65 for RD mortality (Rahman et al., 2022; Gong et al., 2023). This is understandable as different mechanisms are likely to occur related to chronic exposure to higher TV relative to sharper swings in temperature on day to week time scales. As with increased ambient temperature, increased short-term TV had greatest effect with a short lag of 2–3 days or less, but since few studies adjusted for SES, not to mention employment, access to indoor cooling or outdoor exposure, further work needs to be done to determine whether increased influence of inter-annual TV on middle-aged adults is due to such a confounding variable.

None of the studies reviewed here that assessed inter-day TV and renal/GU outcomes performed a stratified analysis by age, gender or SES co-variates and specific outcomes. Though Wang et al. (2022) did find an increased effect of TCN in those aged <44 years, relative to those >45 years for all ED visits, there was no stratification by age or gender and cause-specific morbidity (Wang et al., 2022). Only one study reviewed here assessed the association between inter-day TV and MH status with analysis stratified by demographic and SES variables, finding no significant modifying effect by any of the variables assessed (including age, gender, education level, income, or urbanity of residence) (Xue et al., 2019).

For all TV time-scales, CVD morbidity was associated with increasing TV, however, the one study assessing CVD and RD mortality associations with short-term TV found that, while most LLD due to TV were for TV >2.5 °C, extremely low TV also produced a significant increase in both CVD and RD mortality (Gong et al., 2023). Interestingly, there was strong evidence from a prospective cohort study that was excluded from this review that a 1 °C increase in intra-annual TV was associated with an 8.3 % increase in dyslipidemia risk (Jin et al., 2022). Dyslipidemia has been found to represent a major risk factor for cardiovascular disease and suggests one potential etiology for the relationship observed between CVD risk and intra-annual TV found by Kang et al. 2021 (Kang et al., 2021; Jin et al., 2022).

4.4. The modifying effect of ambient temperature and season on TV-related health outcomes

Several studies demonstrated that the relationship between DTR and CVD mortality was significantly modified by day-to-day ambient temperature changes, while the effect of DTR on RD mortality was more influenced by seasonal effects and regional climate (Luo et al., 2013; Lee et al., 2018). The CVD mortality risk attributable to increasing DTR was greater for relatively hot compared to cold days across Japan, while RD mortality was more influenced by DTR in cooler regions (Lee et al., 2018; Kan et al., 2007), and during the cold season for extremely high or low DTR (Luo et al., 2013), but not for relatively hot or cool days. Interestingly, the effects of ambient temperature on the morbidity/DTR relationship were different, with extremely high DTR having a greater effect on CVD morbidity in the winter, while RD morbidity was more affected by DTR in the autumn (Phosri et al., 2020; Wang et al., 2022; Qiu et al., 2013). Overall, the effect of increasing DTR, as well as extremely high and low DTR, on RD appeared to have a longer lag relative to CVD, especially on relatively cold days and in the cold season, pointing to different mechanisms of influence on RD in the setting of high vs. low ambient temperature (Luo et al., 2013; Lee et al., 2018).

In contrast, CVD morbidity and mortality were more affected by short-term inter-day TV in warmer regions of China, with mortality also associated with more humid and lower latitude areas (Tian et al., 2019; Gong et al., 2023). The modifying effect of season was more similar for RD morbidity between DTR and short-term TV, with the latter having a greater effect during the winter in two of the three studies assessing seasonality (Wang et al., 2022; Sun et al., 2018), with the third being a time-series limited to a single city (Rahman et al., 2022).

Only one study assessed the effect of ambient temperature or seasonality on MH outcomes, finding that increasing TCN (short-term TV) only had a significant effect MH-related ED visits in the Spring, a transitional month (Wang et al., 2022). However, this study did not assess the effect of different types of mental illness. There was a consistently greater effect of increasing short-term inter-day TV or DTR on renal/-genitourinary disease morbidity and mortality in the summer season and in warmer regions, respectively (Lee et al., 2018; Wang et al., 2022). However, these trends for summer season in China and warmer regions of Japan represent only two studies, and with overlapping but different definitions of renal vs. genitourinary disease (Lee et al., 2018; Wang et al., 2022)

4.5. Biological plausibility

The physiological mechanisms explaining the vulnerability of the human body to TV has been studied to the greatest extent for DTR. Specifically for CVD, high intra-day variability in temperature has been found to increase cardiac load via relatively rapid changes in blood pressure, oxygen diffusion and heart rate (Liang et al., 2008; Imai et al., 1998). The relation of RD to increasing DTR and TV in studies reviewed here was found to be particularly large on colder days and in winter, which may related to a combination of reduced respiratory immunity and thickened secretions during cold periods, combined with increased risk of bronchospasm with sudden temperature increase (Diesel et al., 1991; Graudenz et al., 2006). Finally, the autonomic nervous system has been found to be influenced by short-term

changes in temperature (1-2 days) and seasonal differences, and the resulting dysregulation with increasing DTR or inter-day TV may be related to any of the health outcome categories assessed here (Cheng et al., 2014; Shinkawa et al., 1990; Mercer et al., 1999).

4.6. Key gaps and areas for future research

Overall, there was a particular paucity of research into renal disease and mental illness. Three of four studies assessing renal disease looked at morbidity only, and only one study assessed renal disease mortality and DTR. There were no studies assessing inter-day TV and renal disease mortality, and only one study assessing renal disease morbidity and inter-day TV. For mental health outcomes, only one study assessed overall mental illness and there were no studies in which the morbidity related to different types of mental illnesses were compared. Since mental health is a broad category of diverse neurophysiological and psychological processes, future studies assessing the effects of TV on related subgroups of mental illness is crucial. While one study assessed suicide rate, there were no studies assessing mood disorders, anxiety disorders, substance abuse disorders or "organic" mental health disorders (such as personality disorders or dementia) despite clear evidence of their relationship to heat exposure and similar biological plausibility as to the influence of temperature variability, particularly on the day-to-week timescale (Liu et al., 2021). Consequently, there were no stratified analyses by age, gender or other demographic variables to assess which groups were most vulnerable to mental illness related to intraor inter-day TV.

The only prospective cohort studies we found conducted for TV assessed CVD (Kang et al., 2021; Tang et al., 2022; Jin et al., 2022) or RD (Sun et al., 2018) outcomes only, with no prospective cohort studies for renal or mental health outcomes. For RD outcomes, only ED admissions were assessed by prospective cohort (Sun et al., 2018), there were only one such study each for overall CVD hospitalizations or mortality, and all of these were conducted in China (Kang et al., 2021; Tang et al., 2022). As the vast majority (74 %) of studies were conducted in China or Taiwan, future studies that represent a more diverse range of regional climates are necessary for generalizable evidence on the relationship between TV and each of the health outcomes reviewed here, as well as assessment of which trends are related to regional differences. While there has been increasing attention to the relationship between extreme heat or cold and specific health outcomes in the western hemisphere such as North America and Europe (Fletcher et al., 2012; Li et al., 2019; Lin and al., 2012; Lin et al., 2009; Qu et al., 2023; Song et al., 2017), the relationship between temperature variability and specific health outcomes has not been as frequently assessed in these areas (Phung et al., 2016; Cheng et al., 2014). There were also only three studies that focused on rural areas, and in particular subpopulations such as farmers who may have greater exposure to outdoor temperatures, with each finding a pronounced effect of lower DTR on CVD risk (Zha et al., 2021; Zhai et al., 2021; Zhai et al., 2022). Additional research is required to assess the modifying effect of such outdoor occupations, as well as SES markers that correlate with access to indoor temperature regulation, in order to prevent exposure misclassification for those who spend the majority of their time indoors.

Except for studies in CVD morbidity and DTR, there were relatively few studies looking at non-linear relationships in either intra- or inter-day TV and specific health outcomes. In particular, there was a paucity of publications assessing the effects of lower-than-average TV on respiratory, renal or mental health outcomes. This may be particularly significant for DTR, as climate change is projected to cause a decrease in DTR in many regions, and studies using non-linear models such as DLNM to study DTR have found a marked increase in risk of CVD morbidity for low DTR, peaking at 6C and with a larger effect for those >65 years. Further, only one study assessed the modifying effect of transitional seasons on the relationship between TV and health outcomes, and this study only assessed DTR and TCN (Wang et al., 2022), but found that some outcomes (MH and RD) only had significant effects during transitional seasons (Spring and Autumn, respectively). While a second study assessed TV on a seasonally averaged scale, it did not include transitional months (Sun et al., 2018). Therefore, future studies should address the modifying effect of transitional season on the association between TV and specific health outcomes, in particular at the month to seasonal timescales of TV.

None of the studies reviewed here controlled for the cumulative effect of heat or cold waves, which may introduce negative confounding if there is a significant inverse relationship between such periods and temperature variability. While most studies controlled for mean daily temperature, or the mean temperature during longer intervals of analysis (Tian et al., 2019; Rahman et al., 2022), this does not account for the cumulative effect of heat or cold waves over multiple days, or account for how duration of the event may impact health outcomes. There is an increasing number of studies showing that, in addition to heatwave intensity, heatwave duration represents a significant secondary effect that is not controlled for in studies of temperature variability (Anderson and Bell, 2011; Gasparrini and Armstrong, 2011). Particularly for studies assessing metrics of inter-day TV, controlling for contemporaneous heat wave or cold wave duration would reduce potential confounding from increased health effects of prolonged extreme temperatures.

Finally, only two studies reviewed here included modeling of future cause-specific mortality related to DTR based on prior trends, and these studies looked only at annually-averaged DTR (Tang et al., 2022; Qi et al., 2023). Future studies that model morbidity rates for each category of health outcomes addressed here should incorporate region-specific data on the effects of DTR and inter-day TV at shorter time scales.

4.7. Study strengths and limitations

This review represents the first attempt to systematically include both studies of intraday temperature variability (DTR) as well as inter-day variability at scales ranging from neighboring days to annually averaged TV. In addition, we are the first study to include a wide range of health outcomes, including MH and renal/GU outcomes, and including an increasing number of large-scale studies on this topic that have been published since the last similar review in 2014 (Cheng et al., 2014), which also did not include cohort studies that have since been conducted related to CVD and RD outcomes.

There are several limitations to the current review, including the lack of meta-analysis for inter-day TV, which is due in part to the variety of study designs included in the

studies reviewed here. Additionally, there were slightly different definitions of CVD used in several studies, some including stroke and non-cardiac related circulatory disease, while others only included those relating strictly to the cardiovascular system, and this made the interpretation of these findings challenging when subgroups were not included for those specific categories. Similarly, some studies used the category of renal disease, while others looked at GU or urinary disease. While there was some overlap here, our assessment of these terms together was largely due to the paucity of studies in this area, and further studies are needed in each category to determine if there are meaningful differences for each category's relationship to TV. Finally, our inclusion of a wide range of health outcomes prevented a more fine-grained analysis of disease subgroups for each health outcomes, though significant findings for each are included in Table 2. In particular, CVD and RD included enough studies such that more detailed disease subgroup analysis is warranted. The limited number of studies (n < 10) with compatible outcome metrics (cardiovascular vs. respiratory disease, morbidity vs. mortality) for comparison by meta-analysis prevented meaningful assessment of publication bias by funnel plot analysis. However, p-value contours of plots including all DTR metrics suggested that there was a bias against publication of small studies quantifying the relationship between DTR and CVD or RD with non-significant results (data not shown).

5. Conclusions

In summary, here we find strong evidence that both CVD and RD morbidity and mortality increase as DTR increases above mean values for a particular area and with increasing inter-day temperature variability on the scale of one week. There is also strong evidence that the elderly, particularly >75 years are more vulnerable to CVD morbidity and mortality at high DTR, with more limited evidence for this relationship at low DTR. However, additional studies including analyses stratified by age, gender and particularly SES are needed to identify vulnerable groups, particularly for RD, renal/GU disease and mental illness. While a significant relationship between increasing DTR or TCN and schizophrenia morbidity has been demonstrated, future study into the effects of TV on other types of mental illness must still be assessed.

Additional studies conducted in the global south and western hemisphere are necessary to generalize findings from studies in Asia, and particularly to assess TV effects on health during transitional seasons such as Spring and Fall in temperate regions. There has also been little investigation into the effects of extremely low DTR on health outcomes, but early findings indicate that it may have a particularly large effect on CVD morbidity and mortality, as well as RD mortality, particularly for vulnerable groups such as women and outdoor workers (e.g. farmers). Considering the global trend towards lower DTR due to climate change, the effects of low DTR on CVD and RD outcomes will be important to effectively model the overall impact of climate change on human health.

Acknowledgements

I would like to acknowledge Dr. Shao Lin for her encouragement in my undertaking and developing this project, as well as Dr. Dawn Gao for her guidance and shared experience in developing systematic reviews with meta-analysis. I'd also like to acknowledge Imran Mehta for his feedback on initial drafts of this manuscript.

Funding sources

This work was supported by Grant # 1R01AG070949-01A1 from the National Institutes of Health.

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Author	Year	Disease	Outcome	% inc. risk per °C	SE			% inc per	. risk °℃		% inc. ı per	°C	95%-CI	Weight
Wang et al.b Wang et al.a Lim et al.a Qui et al	2022 2013 2012 2013	Cardiovasc. Cardiovasc. Cardiovasc. Cardiovasc.	Hospital admission Hospital admission Hospital admission Hospital admission	-0.4200 0.7600 1.0000 3.7600	0.2755 0.3546 0.3061 0.2041			-	-	+	-0 0 1 - 3	.42 .76 .00 .76	[-0.96; 0.12] [0.07; 1.45] [0.40; 1.60] [3.36; 4.16]	25.0% 24.8% 24.9% 25.2%
Random effects model Heterogeneity: $I^2 = 98\%$, τ^2	² = 4.32	65, <i>p</i> < 0.01				-4	-2	()	 2	_ 1 4	.28	[-0.78; 3.34]	100.0%
Author	Year	Disease	Outcome	% inc. risk per °C	SE			% inc per	:. risk ∙°C		% inc. ı per	risk °C	95%-CI	Weight
Wang et al.b Lim et al.a Wang et al.a	2022 2012 2013	Respiratory Respiratory Respiratory	Hospital admission Hospital admission Hospital admission	0.4100 1.0000 2.0800	0.2653 0.4082 0.6148			-		-	0 1 — 2	0.41 .00 2.08	[-0.11; 0.93] [0.20; 1.80] [0.88; 3.28]	41.3% 34.1% 24.7%
Random effects model Heterogeneity: $l^2 = 70\%$, τ	² = 0.38	368, <i>p</i> = 0.04				-3	-2	-1 (2 :	1 3	.02	[0.17; 1.87]	100.0%
Random effects model Heterogeneity: $l^2 = 97\%$, τ^2	2 = 3.00	Combined <i>A</i> 30, <i>p</i> < 0.01	A+B			-4	-2	2	0	2	4	1.22	2 [-0.09; 2.53]	100.0%
	Author Wang et al.b Wang et al.a Lim et al.a Qui et al Random effects model Heterogeneity: $l^2 = 98\%$, τ^2 Author Wang et al.b Lim et al.a Wang et al.a Random effects model Heterogeneity: $l^2 = 70\%$, τ^2 Random effects model Heterogeneity: $l^2 = 97\%$, τ^2	AuthorYearWang et al.b2022Wang et al.a2013Lim et al.a2012Qui et al2013Random effects modelHeterogeneity: $l^2 = 98\%$, $\tau^2 = 4.32$ AuthorYearWang et al.b2022Lim et al.a2013Random effects modelHeterogeneity: $l^2 = 70\%$, $\tau^2 = 0.36$ Random effects modelHeterogeneity: $l^2 = 97\%$, $\tau^2 = 3.00$	AuthorYearDiseaseWang et al.b2022Cardiovasc.Wang et al.a2013Cardiovasc.Lim et al.a2012Cardiovasc.Qui et al2013Cardiovasc.Random effects modelCardiovasc.Heterogeneity: $l^2 = 98\%$, $\tau^2 = 4.3265$, $p < 0.01$ AuthorYearDiseaseWang et al.b2022RespiratoryLim et al.a2012RespiratoryWang et al.a2013RespiratoryRandom effects modelHeterogeneity: $l^2 = 70\%$, $\tau^2 = 0.3868$, $p = 0.04$ Random effects modelCombined AHeterogeneity: $l^2 = 97\%$, $\tau^2 = 3.0030$, $p < 0.01$	AuthorYearDiseaseOutcomeWang et al.b2022Cardiovasc.Hospital admissionWang et al.a2013Cardiovasc.Hospital admissionLim et al.a2012Cardiovasc.Hospital admissionQui et al2013Cardiovasc.Hospital admissionRandom effects modelCardiovasc.Hospital admissionHeterogeneity: $l^2 = 98\%$, $\tau^2 = 4.3265$, $p < 0.01$ AuthorYearVang et al.b2022RespiratoryHospital admissionLim et al.a2012RespiratoryHospital admissionWang et al.a2012RespiratoryHospital admissionWang et al.a2013RespiratoryHospital admissionRandom effects modelHeterogeneity: $l^2 = 70\%$, $\tau^2 = 0.3868$, $p = 0.04$ Random effects modelCombined A+BHeterogeneity: $l^2 = 97\%$, $\tau^2 = 3.0030$, $p < 0.01$	AuthorYearDiseaseOutcome% inc. risk per °CWang et al.b2022Cardiovasc.Hospital admission-0.4200Uang et al.a2013Cardiovasc.Hospital admission0.7600Lim et al.a2012Cardiovasc.Hospital admission1.0000Qui et al2013Cardiovasc.Hospital admission3.7600Random effects modelHeterogeneity: $l^2 = 98\%$, $\tau^2 = 4.3265$, $p < 0.01$ % inc. risk per °CWang et al.b2022RespiratoryHospital admissionLim et al.a2012RespiratoryHospital admissionUang et al.a2012RespiratoryHospital admission2013RespiratoryHospital admission0.4100Lim et al.a2013RespiratoryHospital admissionWang et al.a2013RespiratoryHospital admission2018Random effects model2.0800Random effects modelCombined A+BHeterogeneity: $l^2 = 70\%$, $\tau^2 = 3.0030$, $p < 0.01$	AuthorYearDiseaseOutcome% inc. risk per °CSEWang et al.b2022Cardiovasc. 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Fig. 2. The effect of Diurnal Temperature Range (DTR) on hospital admissions due to cardiovascular or respiratory disease.

Forest plots displaying the individual and pooled effect sizes of studies assessing the percent increase per degree Celsius of DTR for hospitalizations due to cardiovascular disease (A), respiratory disease (B) or the pooled effect of both exposures (C).

А	Author	Year	Disease	Outcome	% inc. risk per °C	SE		%	inc. ri per °C	sk		% inc. risk per °C	95%-CI	Weight
	Lim et al.b Lee et al. Tam et al. Kan et al Cao et al.	2015 2018 2009 2007 2009	Cardiovasc. Cardiovasc. Cardiovasc. Cardiovasc. Cardiovasc.	Mortality Mortality Mortality Mortality Mortality	0.3500 0.4300 1.7000 1.8600 3.6200	0.0230 0.0255 0.7143 0.2347 0.7806			+	• =		0.35 0.43 1.70 1.86 - 3.62	[0.31; 0.39] [0.38; 0.48] [0.30; 3.10] [1.40; 2.32] [2.09; 5.15]	39.8% 39.6% 2.6% 15.8% 2.2%
	Random effects mode Heterogeneity: $I^2 = 94\%$, a	l 2 ² = 0.03	53, <i>p</i> < 0.01				-4	-2	0	2	4	0.73	[0.49; 0.96]	100.0%
R	Author	Year	Disease	Outcome	% inc. risk per °C	SE		% i F	nc. ris oer °C	sk		% inc. risk per °C	95%-CI	Weight
U	Lim et al.b Lee et al. Kan et al	2015 2018 2007	Respiratory Respiratory Respiratory	Mortality Mortality Mortality	0.3000 0.8600 1.5700	0.0510 0.0714 0.5102			+		6	0.30 0.86 1.57	[0.20; 0.40] [0.72; 1.00] [0.57; 2.57]	42.1% 41.5% 16.4%
	Random effects mode Heterogeneity: $l^2 = 96\%$, τ	l ² = 0.16	26, <i>p</i> < 0.01				-2	-1	0	<u> </u>	2	0.74	[0.22; 1.26]	100.0%
С	Random effects model Heterogeneity: $I^2 = 94\%$, τ^2	² = 0.043	Combined (30, <i>p</i> < 0.01	A+B)			-4	-2	0	2	4	0.71	[0.52; 0.90]	100.0%

Fig. 3. The effect of Diurnal Temperature Range (DTR) on mortality due to cardiovascular or respiratory disease.

Forest plots displaying the individual and pooled effect sizes of studies assessing the

percent increase per degree Celsius of DTR for mortality due to cardiovascular disease

(A), respiratory disease (B) or the pooled effect of both exposures (C).

Table 1

Search strategy for articles.

Temperature variability indicator (Combined by 'OR') (a)	Health indicators (Combined by 'OR') (b)	Descriptor (Combined by 'OR') (c)
temperature variability	cardiovascular	disease
temperature variation	respiratory	disorder
diurnal temperature range	renal	illness
	genitourinary	
	kidney	
	mental	

Note: Boolean operator 'AND used to combine a, b, c groups.

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Summary of s	tudies reviewed.			Table 2			
Author/year*	Study design/ population	Objective	Exposure	Outcome	Models/Methods	Findings	
	Time Series/173,911 non-accidental deaths occurring from	Examine the	DTR as a continuous	Mortality due to CVD (ICD-9 200 460, ICD-10	GAM with log link and Poisson error with smoothing terms for trend on days, daily termp, relative humidity, DOW and oir collutante	-CVD mortality peaked on lag1 at $0.97\%/1^{\circ}$ C ($0.66-1.29$), was significant, from lag0- lag3, and lag0-2 peak cum. lag at $1.86\%/1^{\circ}$ C ($1.40-2.32$) -RD mortality peaked at lag0 at $0.83\%/1^{\circ}$ C ($0.19-1.47$), was	-
2007 2007	January 2001 to December 2004 in the nine urban districts of Shanghai, China	between DTR and mortality	variance, expressed at single day lag (0-5) or cumulative lag (0-1 to 0-5)	100-199) or RD 100-199) or RD (ICD-9 460-519; ICD-10 100-198)	O3, PM ₁₀ , SO ₂ , NO ₂); (O3, PM ₁₀ , SO ₂ , NO ₂); stratified analysis by age, gender and warm cold days (based on daily temp effect on mortality)	significant at lag0, lag1 and lag4, with lag 0-5 peak cum. lag at 1.57%/1°c (0.67-2.47) -CVD mortality significant inc. when daily temp >23°C or -23°C, but RD only significant inc when term >73°C (1.47%)	Ţ

age, gender or other demographic variables -Assessed only for -Focused only on CVD SES, comorbidities for COPD, age or gender data or stratify around Did not include SES -Did not include SES -Only looked at ED Study conducted in -Single monitoring -Single geographic institution assessed -Did not adjust for single urban area -Only one weather monitoring station station and single -Only addresses -Only assessed Limitations admissions mortality mortality mortality location data used ACS admissions increased 34.4% when DTR greater than $9.6^{\circ}C (p < 0.05)$ DTR 9.6°C relative to <6.6°C mortality on when daily mean admission risk by ~14% when directly correlated with DTR by month (r = 0.90) and increased by 0.8%/1°C DTR -1.25% (95%CI 0.35-2.15) increase in COPD mortality -0.51% inc. in COPD mortality when daily mean temp >22°C mean daily temp (r = -0.95) inc. at Lag 1, with greatest -Significant inc. in COPD indirectly correlated with -COPD admissions were -1.57% inc. in COPD RR of CVD mortality at lag0-2, 0.57-2.37) per 1°C inc. in DTR temp <22°C (p < 0.05)season, and air pollutant distribution, regressing daily mean temp above model using a Poisson GAM with smoothing relative humidity, and adjusting for DOW, SO_2 , NO_2 and O_3) and and below 22°C based the effects of holiday, for daily mean temp, stratified analysis for Generalized additive PM₁₀, SO₂, CO, NO, air pollution (PM10, PM₁₀, SO₂, CO, NO, model adjusting for on COPD risk from multivariate Poisson Poisson regression concentrations (O₃, adjusting for DOW concentrations (O₃, daily mean temp regression model and air pollutant Univariate and NO₂). N0,) (codes 490-496 in ICD9, and as codes J40-J47 in ICD10) ED Admission for ACS (ICD-9 codes 491-496) Daily COPD deaths codes 491-496), RR reported relative to lowest DTR Mortality from CVD (ICD-9 390for COPD (ICD-9 ED admissions expressed in %tile (40th, 60th, 80th and 90th %tiles) DTR as categorical DTR as continuous DTR as expressed as a 4-day moving Daily DTR variable variable average between DTR¹ and ED admissions for COPD in Taiwan events, average daily temperature and DTR between DTR and between DTR and mortality due to COPD in Shanghai relationship between ACS Determine the relationship relationship relationship Assess the Assess the Examine Shanghai, China from in Taichung City, Taiwan from January Time series/17,874 deaths due to COPD COPD admissions in hospital in Taichung 1st, 2001 to March 31st, 2003 in nine districts of Longitudinal/3,263 Time series/40,166 mortality in Hong a single university City, Taiwan from Time series/1020 patients admitted to ED for ACS January 2001 to January 2001 to December 2004 December 2002 cases of CVD Study desig population **Fime Series/17** occurring fre December 2004 nine urban distr Shanghai, Cł January 200 non-accidental Author/year* Song et al., 2008 Tam et al., 2009 Liang et al. Kan et al. Liang et al 2007 2009

Limitations	population > 65yrs -Single geographic location DTR not representative	-Assessed only CHD -Assessed only CHD -Single geographical location	-Single urban center assessed -Did not control or stratify analysis for SES or demographic factors	-Did not control for SES, demographic info aside from age and gender	-Did not control for SES variables or air pollutants aside from PM_{10} -Only included 4 cities covering ~37% of
Findings	cumulative RR at Lag 0-3 and 0-4, with 1.7%/1°C DTR inc. $(p < 0.05)$	-all three analyses methods had significant increase in daily CHD mortality for each 1°C increase in DTR for lag 2-4, peaking on lag 3. Time series -2.63%/1°C, unidirectional case crossover - 3.62%/1°C, bidirectional case crossover - 2.22%/1°C	-GAM showed significant increase in primary intracerebral hemorrhage (PICH) risk of 11.8% per 1°C1C inc. in DTR 24hrs prior No significant increase for ischemic stroke, but significant decrease of ~8% risk of partial circulation infarct per 1°C1C DTR inc. 24hrs prior	-Observed consistently increasing risk of schizophrenia admission with increasing DTR, beginning at 10-24 percentile, and peaking at 99percentile (1.22, p < 0.01), dose-response -no significant relationship found for schizoaffective	-Time-Series showed significant inc. in admissions for total CVD (~1%/1°C), RD (~1%/1°C), cardiac failure (~3%/1°C), asthma (~1%/1°C) and COPD (~2%/1°C) -CC showed significant inc. in
Models/Methods	for day of the week, daily mean temp and humidity, daily cone. of NO ₂ , SO ₂ , PM ₁₀ and O ₃ , smoothing for seasonal effects	Time series: GAM smoothed for DOW, daily mean temp, relative humidity PM10, SO2, NO2, and O3 Levels. Case-crossover: Unidirectional and bidirectional and bi	Poisson GAM including daily maximum, minimum temperature, DTR, atmospheric pressure, relative humidity and total precipitation as continuous variables over 24hr, 7-day or 14- day periods prior to stroke	Generalized Linear Model to categorize admissions as schizophrenia and non-schizophrenia, co- variates were season, age, gender, region and hospital	 Poisson GLM with splines for time trend, DOW, mean daily temp and PM₁₀, using distributed lag of 0-9 days, two stage by city
Outcome	459 or ICD-10 J00– 199)	Mortality due to coronary heart disease (ICD-9; 390–398 and 410– 429, and ICD-10; 100-109 and 120– 152)	Registry of all first- time stroke cases by active surveillance, based on WHO criteria, neurologist and radiological findings	Schizophrenia and Schizoaffective inpatient admission (ICD-9 codes: 295.0-295.9)	Hospital admissions for CVD (ICD-10: 100–199, G45, G46, M30, M31, R58, excluding G45.3, 167,3, 168.0, 188, 197,8, 198.0) and
Exposure		DTR as a continuous variable	DTR as a continuous variable	DTR was divided into 10 % tile groups from <1% tile to 99% tile	DTR as a continuous variable
Objective	CVD mortality for >65yrs	Determine whether intra-day temp variability is an independent risk factor for acute heart disease death	Determine the association between DTR, stroke and stroke subtypes	Examine the association between DTR and schizophrenia admissions amongst psychiatric inpatients	Investigate the risk of hospital admission for CVD and RD in four metropolitan areas in Korea
Study design/ population	Kong, China population >65yrs from 1997-2002	Time Series and Case Crossover/ 37,256 CVD-related deaths in the 9 urban districts of the Shanghai Municipal Center of Disease Control and Prevention (China) (SMCDCP) January 2001 to December 2004	Time Series/462 first- time stroke cases in the city of Porto, Portugal from October 1998 to September 2000	Retrospective Cohort/ 26,863 patients with schizophrenia inpatient admissions and 37,525 and 37,525 patients with non-schizophrenia inpatient admissions from 1996-2007 in 21 of 25 districts of Taiwan	Time Series and Case-Crossover (CC)/ Hospital admissions for CVD or RD in four of the largest cities in South Korea from 2003 to 2006
Author/year*		Cao et al., 2009	Magalhaes et al., 2011	Sung et al. 2011	Lim et al., 2012

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Limitations	nation, did not include suburbs or rural	-Data from single institution/ geographical region -Did not include SES or demographic data, such as age and gender	-Restricted to one geographic area -Coarse analysis of lag time (cumulative only) -Mortality only, rather than morbidity	-Limited to one urban center -could not separate first admission readmission -Did not include SES- related variables
Findings	risk for total RD (~1%/1°C), cardiac failure (~5%/1C), and asthma (~2%/1°C) -Asthma admission risk significantly higher in >75 (4% vs 1%/1°C)	-Inc. in RTI ED visits were significant at lag0 and lag1, peaking at lag1 at $1.72\%/1^{\circ}$ C inc. in DTR ($p < 0.05$) -Cumulative lag significant at lag0-1, 2.08%/1°C inc. in DTR ($p < 0.05$) -linear relationship between inc. DTR and RTI risk	-Overall (lag 0-27) both CV and respiratory disease showed significantly inc. cumulative excessive risk (250% and 381%) with <1% tile DTR -1% tile DTR causes significant Inc. risk of CVD mortality at shorter lags lag 0-13 and 0-20, and -99% tile with lag 0-6 and 0-13 significant inc. -<1% tile and >99% tile DTR show significant inc. of RD mortality at lag 0-20 and 0-27 for cold season	-Inc. in HF admissions was significant at all lags per 1°C DTR inc., peaking for lag1 at 0.89%/1°C (0.34-1.43), with lag0-5 = 3.76%/1°C -Significant inc. effect for women relative to men at lag0 (1.31%) and lag0-5 (4.41%) - 75 years had greatest inc. risk of HF admission with lag0-5 of 4.13%/1°C DTR, significantly higher than 65-74 or <65, peaking at lag1 -A significantly higher risk of HF admission seen in cool season for lag1, lag2 and lag0-5 (more than 6-fold higher at lag0-5)
Models/Methods	and then metanalysis 2) Matched case- crossover with 28-day window and matching of controls by daily mean temp. adjusted by same variables as GLM	GAM with log link and Poisson error with smoothing terms used for trend on days, temperature level, relative humidity, DOW and air pollutants (PM ₁₀ .SO ₂ , and NO ₂)	DLNM with log link and Poisson error, using linear regression for air pollution concentrations, and using time-smoothing to account for seasonal effects and day-of-week (DOW) signals	Poisson GAM with smoothing splines for seasonal effects, long- term trend, daily mean temp, relative humidity, DOW, holidays, influenza epidemics. Stratified analysis by warm or cool season, sex and age, sensitivity analysis for O ₃ , PM ₁₀ , SO ₂ , and NO ₂
Outcome	RD (ICD-10: J00- J98), as well as subgroups of each.	RTI diagnosis on ED visit as resp virus, pharyngitis, laryngitis, croup, viral ottis, bronchiolitis, & pneumonia	Mortality from CVD (ICD-10: 100– 199) and RD (ICD-10: 100–199)	ED admissions for heart failure (ICD-9: 487)
Exposure		DTR as a continuous variable, expressed at single day lag (0-5) or cumulative lag (0-1 to 0-5)	DTR categorized by percentile. >99% tile and <1% ile as extreme DTR	DTR as continuous variable, for daily lag0 to lag5 and cum lag0-5
Objective		Assess the association between RT1 morbidity and DTR	Examine relationship between DTR and mortality due to CV, respiratory, cerebrovascular disease or total non-accidental	Examine the association between HF and DTR, as well as effect modifiers age, sex and season
Study design/ population		Time Series/11,017 ED visits from January 2008 through June 2009 from Huashan Hospital in Shanghai, China	Time series/36,168 non-accidental deaths in Yue Xiu and Li Wan Districts of Guangzhou, China from January 1 st , 2006, to December 31 st , 2008	Time Series/95,897 ED admissions for HF across Hong Kong, China from January 2000 to December 2007
Author/year*		Ge et al., 2013	Luo et al., 2013	Qui et al., 2013

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Limitations	-Limited to two hospitals in one urban center -Did not control for SES-related or demographic variables	-Only used data from one weather station -Only assessed one urban area -did not include SES data	-Assessed only one urban center -Did not adjust for SES	-Low absolute numbers of suicide by gender at some sites -Lack of SES data availability
Findings	 -No significant relationship between MI or stroke and TCN -No significant relationship between DTR and MI -A 10°C increase in DTR from 4°C (minimum stroke risk) was associated with a 26% (2%-57%) increase in stroke admissions 	-CVD only significant inc. at lag0-1 and 0-2 (0.62% and 0.76%/1°C inc.) -RD significant inc. at lag0, lag3 and all cum. lag, peaking at lag0-7, 208%/1°CC -GU only significant inc. at cum. lag0-5, lag0-6 and lag0-7, peaking at lag0-5 (1.81%/1°C) -CVD has dec. risk at DTR <6°C, RD with inc. risk ×10°C, linear non-significant trend for GU -CVD only significant in women and >75 years, RD significant in men and both age groups, GU only significant in men and	-Significant inc. in asthma admission risk with DTR > 14°C, relative to mean of 10°C -RR at DTR 15C relative to 10C peaks for lag0-9 at 1.31 (1.11.1.58) -DTR effect only significant for children 5-9 years, at all lags, peaking at lag0-11 (RR 1.91) -Only significant for male children peaking at lag0-8 (RR 1.43)	-Significant inc. in suicide rate for men at two sites with decrease in daily mean temp. from previous day and 5 days prior, resp., and the latter for women at a third location
Models/Methods	Poisson general linearized model with continuous predictors of mean temperature, DTR, TCN, mean barometric pressure, 24h-index of geomagnetic activity, and categorical variables for days with geomagnetic storms, heat/cold waves and DOW	GAM with regression spline functions to control for long-term trend, seasonal patterns, DOW, public holidays, daily mean temp and relative humidity, and air pollutants (PM ₁₀ , SO ₂ , and NO ₂); stratified analyses by age, gender and season	DLNM using cubic splines to control for mean daily temp, relative humidity, seasonal patterns, long- term tend, DOW, influenza epidemics and air pollutants (PM ₁₀ , SO ₂ , and NO ₂)	Poisson regression model, initially run with 21 variables (including 6 related to temp. variability), then 6 models generated to
Outcome	Daily counts of hospital admissions for MI or stroke	ED admission for CVD (ICD10:100– 199), RD (ICD10:100–199), GI (ICD10:100–199), K93)and GU disease (ICD10:N00–N99).	ED admission for asthma (ICD-10: J45)	Daily suicide rate recorded in national database for each city
Exposure	DTR and TCN as continuous variables for lag up to 7 days, selecting lag of peak effect	DTR as a continuous variable, expressed at single day lag (0-7) or cumulative lag (0-1 to 0-7)	DTR as continuous variable and as a 5°C increase in DTR above mean (10°C vs. 15°C)	DTR (T_{d}), inter- day temp variability (from D0-D1, D0-D2, D0-D5, D0-D4 and D0-D5)
Objective	Examine the association between DTR or TCN and MI or stroke hospitalizations	Evaluate the short- term effect of DTR on ED admissions among elderly adults in Beijing.	Examine the relationship between DTR and childhood asthma	Determine association between ambient temperature, thermal season
Study design/ population	Time Series/2,833 MI and 1,096 stroke hospital admissions from two large hospitals Moscow, Russia from January 1992 to December 2005	Time Series/114,870 ED admissions of those >65 years from three large hospitals in Beijing, China from January 2021 December 2021	Time Series/13,324 ED admissions for asthma in children in Brisbane Australia from January 2009 December 2009	Ecological/10, 802 suicides from 1974-2010 at six population centers within Finland
Author/year*	Shaposhnikov et al. 2013	Wang et al., 2013	Xue et al., 2013	Hiltunen et al. 2014

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Author/year*	Study design/ population	Objective	Exposure	Outcome	Models/Methods	Findings	Limitations
		timing and suicide in Finland			cover subsets of the 21 variables	 -1.024 increase in rate ratio of suicide for women at one site with each degree of DTR increase 	
Li et al., 2014	Time Series/8237 ED visits for RTI in those >65 years from January 2010 to December 2012 from Sun Yat-Sen University hospital in Guangzhou, China	Assess relationship between RT1 and DTR in an elderly population	DTR as a continuous variable, expressed at single day lag (0-5) or cumulative lag (0-1 to 0-5)	RTI diagnosis on ED visit as resp virus, pharyngitis, laryngitis, croup, viral otitis, bronchiolitis, & pneumonia	Negative binomial model with sensitivity analysis for air pollutants (PM ₁₀ , SO ₂ , and NO ₂)	-Inc. in RTI ED visits peaked at lag2 at $1.56\%/1^{\circ}$ C inc. in DTR (p = 0.01) -Cumulative lag peaked at lag0-2, 2.07%/1^{\circ} inc. in DTR (p < 0.01)	-Single institution -Did not report covariates included in model aside from air pollutants -Published as letter without peer review
Lim et al., 2015	Time Series/US residents included in the National Morbidity Mortality Air Pollution Study (NMMAPS) in one of 95 communities for which air pollution data available, from 1987-2000	Examine the effects of DTR on non- accidental mortality (NAM), as well as cardiovascular and respiratory mortality, in the US	DTR as a continuous variable	Mortality from non-accidental (ICD-9 < 800), CVD (ICD-91: 390-459and RD (ICD-9, 490-496)	 Poisson generalized linear model, controlling for ambient temp, short and long term (seasonal) time ternds A generalized additive model was used to assess for non-linear relationships between DTR and mortality 	 -0.35% and 0.30% increase in mortality per 1°C increase in DTR for CVD and RD mortality, respectively (p < 0.05) -This increased mortality risk was seen largely for those >65yrs at death 	-Assessed only mortality -Did not consider many demographic or SES factors in model and analysis -air pollution data not available at all sites
Zheng et al., 2016	Time series/22,069 ED admissions in people >65 years from three large hospitals in the Haidian district of Beijing from January 2009 to December 2011	Examine the modifying effect of age, gender and season on the relationship between DTR and ED admission for CVD	DTR as a continuous variable	ED admissions associated with all CVD (ICD-10: 100- 199, G45-G46)	Poisson generalized additive model controlling for long term trends, seasonality, DOW, public holiday, relative humidity and mean daily temp, including PM ₁₀ , SO2 and NO2 as confounders. Separate analyses performed by gender, and age >75 or <75 yrs	-Larger magnitude effects on all CVD admissions seen for women, except for cerebrovascular disease, with 1.46%/1°C DTR increase for women at lag 0-1 and 0.2 ->75 years category had larger effects for all CVD types -larger cerebrovascular disease effects seen in warm season -women >75 show larger effect on all CVD admissions/1°C DTR in cold season, but men less	-Only covers one narrow geographical area - Weather data from one station -No SES data included
Zhao et al., 2016	Time series/36,607 ED admissions for schizophrenia from January 1, 2005 to November 30, 2014, in Anhui province, China	Examine association of DTR and schizophrenia ED admissions, how this relationship is influenced by age, gender, marital status	75 th and 95 th %tile of DTR relative to 50 th %tile	ED admission for schizophrenia (ICD-10 codes: F20-F29)	Poisson generalized linear regression combined with DLNM with mean temp, relative humidity, seasonality, long-term trend, DOW and public holiday included as confounders	-95% tile DTR exposure with significant 2.7% inc. risk of schizophrenia admission at lag 0 (max. effect), with cumulative effect), with cumulative effect peaking at lag 0-11 days (RR = 1.187) -authors found greater risk in those aged 15-29, 50-64, born in spring or autumn, male or married	-Data obtained from single city -SES and air pollution data not included as potential confounders
Zhao et al., 2017	Time series/18,417 ED admissions for schizophrenia from	Examine association of DTR and temp change	DTR and TCN at 75%tile, 95%tile and 99%tile	ED admission for schizophrenia	Poisson generalized linear regression combined with DLNM	-Significant inc. in RR for lag 2, 3, and 4 days in those born in Spring and exposed to DTR	-Data obtained from single city -SES and air pollution

Author/year*	Study design/ population	Objective	Exposure	Outcome	Models/Methods	Findings	Limitations
	January 1, 2005 to November 30, 2014, in Anhui province, China	btw neighboring days (TCN) with schizophrenia ED admissions and by birth season		(ICD-10 codes: F20-F29)	with mean temp, relative humidity, seasonality, and long- term trend controlled for using natural cubic splines	at 95% tile and 99% tile -Significant inc. in RR for lag 3, and 4 days in those born in Spring and exposed to TCN at 99% tile (inc. in temp)	data not included as potential confounders
Lee et al., 2018	Time Series/ 39,943,041 deaths from 1972 to 2015, inclusive, in all 47 prefectures of Japan	Determine whether temperature is an effect modifier on relationship between DTR and mortality	DTR and mean temp. over 3-day moving average, segregated into 5 % tile groups, or expressed as IQR (overall = 4.6C)	Mortality divided into twelve categories, including total CVD (ICD-8: 390-458, ICD-9: 390-458, ICD-9: 390-458, ICD-9: 100-199), total RD (ICD-8: 460-519, ICD-10: 100-199) and renal disease (ICD-8: 580-599, ICD-10: N00-N39)	Two-stage model with 1 st stage using distributed lag for time- series regression for each prefecture and then metanalysis of all prefectures, adjusting for relative humidity and DOW	2% inc. in total CVD, -4% inc. in RD and -4% inc. in renal disease mortality per IQR increase in DTR -CVD mortality % inc. per DTR IQR significanty inc. at higher relative mean daily for RD mortality for RD mortality CVD and RD mortality CVD and RD mortality inc. with DTR inc. peaks at lag2 days for extremely hot days, but on extremely hot days, but on extremely rol days for CVD and >8 days for RD	-only one weather monitoring station available per prefecture -air pollution, demographic, SES and other weather indicator data not included in analysis -temperature range studied not representative globally
Sun et al., 2018	Prospective cohort/ 66.820 Hong Kong residents >65 years enrolled from 1998 to 2001 and followed until 2010	Assess association of seasonal temperature variability with respiratory disease	Seasonal temp variability defined as standard deviation of daily mean temp in summer (June- Aug) or winter (Dec-Feb)	Emergency hospital admissions for respiratory diseases (ICD-9: 460:519)	Cox proportional hazards model controlling for age, sex, marital status, BMI, physical activity, housing type, educational attaimment, smoking status, and medication. Sensitivity analysis controlling for average daily temp, pre- existing resp disease and PM _{2.5}	-Hazard ratios (HRs) of 1.20 (95% CT 1.08-1.32), 1.15 (1.01-1.31) and 1.41 (1.15-1.71) for total respiratory diseases, pneunonia and COPD, respectively, per 1°C increase in TV during the winter -HR for summer were not significant	-No data on hospital admissions prior to enrollment -Enrollment was voluntary (selection bias) -Did not adjust for humidity and wind chill
Tian et al., 2019	Time series/8 million hospital admission for CVD in 184 Chinese cities from 2014 to 2017	Examine short-term associations between temperature variability and hospital admissions for CVD in urban China	Standard deviation of max and min daily temp for each day included in exposure interval from TV_{0-1} to TV_{0-7} (combined intra- and intra-day variability)	CVD admissions, including ischemic heart disease (ICD-10: 120- 125), heart failure (ICD-10: 150), arrhythmias (ICD-10: 147-149) and ischemic stroke (ICD-10: 163)	DLNM model used for each TV time range, with two stage analysis, first for each city, and then a city, and then a metanalysis combining cities into regions and antional, considering DOW, public holidays and long-term trend. Stratified analysis for age, sex and geographic region. PM _{2.5} , NO ₂ , and SO ₂ also added as confounders	-There was a 0.44% increase in CVD admissions per $1^{\circ}C$ of TV _{0.1} , the greatest for any lag interval, with ischemic stroke showing the greatest effect of subgroups at 0.82%/ $1^{\circ}C$ -Greater effects for CVD were seen for male gender (0.51%/ $1^{\circ}C$, for the elderly (0.81%/ $1^{\circ}C$ for >75), and for warmer regions (0.58%/ $1^{\circ}C$)	-Did not include children -Only included urban areas -Exposure metric does not distinguish between intra- and inter-day temp variability -did not incorporate relative humidity

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Limitations	-High risk of misclassification -low time-resolution of exposure	-Only one small geographical location considered -Admissions data did not include patient residence, so misclassification of exposure may occur for those living outside Bangkok -SES, air pollutants aside from ozone and PM ₁₀ not considered	-Pneumonia not confirmed radiologically or microbiologically -Did not include demographic data or air pollution into model -Single geographic location of weather data -Admission data not geocoded to ensure exposure was not misclassified	-Did not incorporate relative humidity
Findings	 - 15% decrease in MHS associated with 1°C inc. in temp variability - Inc. in temp variability associated with inc. in feeling nervous, upset, hopelessness and meaninglessness 	-Overall (lag 0-21) RR was significantly increased for CVD admissions at 99% tile DTR at 1.206 -No significant association for RD admissions show strong relationship to DTR in winter season, none in summer or rainy season	-Significant association between DTR and pneumonia admissions occurred only when DTR > 21°C, which was a rare event only occurring ~12 days/year at this location	-For a 1C increase in long- term TV, there was a 6% increase in CVD incidence -Exposure to the highest tertile of TV reduced disease-free years for those 35-65yrs by 2.11yrs, with a 72% higher risk of CVD for those in the highest tertile relative to lowest
Models/Methods	Logistic regression model adjusting for covariates PM _{2.5} , mean temperature and Normalized Difference Vegetation Index (NDVI)	Quasi-Poisson generalized Linear Regression combined with DLNM controlling for daily mean temp, relative humidity, DOW, public holiday, seasonal trend, long-term trend, ozone and PM ₁₀ .	DLNM model adjusting for seasonality and DOW, as well as mean daily temp and relative humidity when assessing DTR	Cox proportional hazards model used to measure association between TV and CVD incidence/mortality, adjusting for sex, age, BMI, alcohol, smoking use, education level, urbanity, hypertension, diabetes, dyslipidemia and annual mean temp
Outcome	Significant change in mental health score (MHS)	Hospital admissions due to CVD or RD (ICD-10: 100-199, and 100-100)	Hospital admission for pneumonia, based on recorded reason for admission (not ICD code)	CVD incidence obtained from interviews and health records including coronary heart disease (CHD), stroke, chronic heart failure, and death due to other CVD"
Exposure	Standard deviation of mean daily temperature within one calendar year	DTR derived as average from three monitoring sites in Bangkok, continuous variable and 99% tile relative to mean	Mean daily temperature, daily relative humidity and DTR as continuous variables	TV defined as standard deviation of daily mean temperatures for survey years derived from ERA5 global forecasting models
Objective	Estimate Estimate associations between environmental factors and self- assessed mental health	Examine the relationship between short-term DTR exposure and hospital admissions for CVD and RD in Bangkok, Thailand	Investigate the delayed effects of different temperature indicators and relative humidity on pneumonia hospital admissions	Estimate the effect of long-term temperature variability on cardiovascular disease in China
Study design/ population	Longitudinal study, Difference- in-difference/21,543 adults from 25 Chinese provinces who filled out the China Family Panel Studies (CFPS) questionnaire in both 2010 and 2014	Time Series/255,333 hospitalizations due to CVD, and 247,872 due to RD, from 2006 to 2014 in Bangkok, to 2014 in Bangkok,	Time Series/ 4062 Pneumonia hospitalizations from October 2015 in the Mopani district of South Africa	Prospective cohort study/30,036 subjects selected at random from Chinese Hypertension Survey participants from 16 cities and 17 counties in China and followed from 2017 to 2019, with 23,721 retained in final analysis
Author/year*	Xue at al., 2019	Phosri et al., 2020	Pedder et al., 2021	Kang et al., 2021

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Limitations	-Single geographical location -Outcomes data not linked to residence of patients -TV patients -TV metric does not differentiate between inter and intraday variability -Only one-fifth of patients were female, limiting subgroup sample analysis	-Single geographical location -Does not include data on air pollution -Only considers inpatient data -Narrow outcome definition by ICD-10 code, does not encompass all CVD	-Single geographical area studied (cannot generalize) -Did not include data on SES or comorbidities -Did not include air pollution data in model analysis	-Focused only on outpatients -Did not include age, SES or medical history -One climactic region included
Findings	 Overall cold exposure (0.5°C) or less was found to produce significant increase in AAD at lag 0 or 1 day TV only found to have a protective effect with -11% RR per 1°C TV increase at 0-2 and 0-3 exposure days, respectively for females only 	-Bi-modal peak seen in DTR effect on RR of CVD overall, with low DTR effect peaking at 6.1°C (RR 2.95) and high DTR at 19.1°C (RR 2.60), relative to mean DTR of 13°C -adults <65yrs and males were found more sensitive to DTR than women or the elderly	 Bimodal peak observed for increased RR with both low (6°C) and high (17°C) DTR, with high DTR peak significant (1.78) Both RR peaks higher and significant in men, 1.55 for low DTR and 1.94 for high DTR peak greater in >65 yrs. while extremely high DTR peak greater in <65 (2.23) extremely low DTR had greater fetct on women and >65 yrs. while extremely high DTR led to higher risk in men and <65 years 	-Overall, there were no significant effects of DTR on urinary disease RR at any lag -D Zhangye, both -5% tile and >95% tile produced significant increases in RR at 7, 14 and 21d lag, increasing to lag 21 (low 6.96, high 5.96)
Models/Methods	DLNM following quasi- Poisson regression, with relative humidity, atmospheric pressure, public holidays and DOW as confounders and including considering PM ₁₀ , NO ₂ and SO ₂	DLNM combined with quasi-Poisson GAM including terms for relative humidity, mean temperature, air velocity, sunshine, precepitation, and pressure, long-term trend, seasonality, DOW and public holidays	DLNM model including relative humidity, windspeed, mean daily temp, sunshine hours, long-term trend, DOW and public holidays as covariates	DLNM with quasi- Poisson distribution including average temp, relative humidity, PM _{2.5} , long-term trend, DOW and public holidays, sensitivity analyses accounted for
Outcome	AAD defined as dissection onset within 14 days of presentation and confirmed by review of medical records (not ICD code)	Hospital admission for coronary heart disease (ICD-10: 125.101), arrhythmia, myocardial infarction (ICD-10: 120.052), coronary atherosclerotic heart disease (ICD-10: 125.103), hypertension (ICD-10: ICD-10).	Hospital admission for: chronic rheumatic heart disease (ICD-10: 105– 109), hypertension (ICD-10: 10–115), ischemic heart disease (ICD-10: 120–125) and other types of heart disease (ICD-10: 130–152)	Outpatient visits for urinary disease (ICD-10: N00-N39)
Exposure	Standard deviation of max and min daily temp for each day included in exposure interval from $TV_{0,1}$ to $TV_{0,7}$ (combined intra- and inter-day variability)	DTR calculated from daily mean and maximum temp data obtained for district from China Meteorological Science Data Sharing Service	DTR calculated from daily mean and maximum temp data obtained for district from China Meteorological Science Data Sharing Service	Short-term DTR expressed as continuous variable and as extremely low (<5% percentile) high DTR (>95% tile)
Objective	Examine the relationship between AAD, daily mean temp and temp variability, as well as lag from exposures to outcomes	Examine relationship between DTR and CVD morbidity in suburban populations, identifying vulnerable subpopulations	Examine Erataionship between DTR and CVD morbidity in nural China	Analyze the effects of meteorological factors, including DTR, on unnary health in arid regions of western China
Study design/ population	Time series/2120 patients diagnosed with Acute Aortic Dissection (AAD) at Tongju hospital in Wuhan China from 2011 to 2018	Time series/Sub- urban farmers who were admitted for CVD in Qingyang, China from 2011 to 2015, recruited through New Rural Cooperative Medical Scheme (NRCMS)	Time series/24,940 hospital admission for CVD from 2015 to 2019 from 2015 city through New Rural Cooperative Medical Insurance of Gansu Province (NRCMI)'s health database	Time series/132,698 outpatient visits for urinary diseases in the three main cities of Ganshu province, China, from January 2014 to December 2016
Author/year*	Yu et al., 2021	Zha et al., 2021	Zhai et al., 2021	Li et al., 2022

Limitations		-Lack of SES data, smoking data, medications or comorbid conditions -single geographic location -unable to distinguish intra- from inter-day TV	-Length of follow-up only ~5 years -Only looked at mortality rather than morbidity effect	-Did not report associations over different lag periods -Did not include metrics of SES or medical history	-Single geographic site -Did not include metrics of SES or medical history -Did not include
Findings		-There were significant increases in CVD risk (1.0%/ 1° C) for TV ₀₋₁ only, but for both TV ₀₋₁ (2.1%/ 1° C) an TV ₀₋₇ there were significant inc. in RD risk -Larger effects were seen at 0-1 and 0-2 lags CVD by age stratification at 50 years, largest effect for <50 years in monsoon season -RD showed great effect in >50yr group for all lags, particularly in hot/dry season and monsoon season	-CVD and stroke mortality risk increased by 12% and 9%/1°C inc. in DTR, respectively (model 4) -Stroke mortality had U- shaped curve with exponential increase at DTR >10°C, while CVD showed more linear response	-Mental illness EDV inc. 11.8%/1°C inc. in TCN in Spring only -No significant association for -GU disease increased -GU disease increased 8.25%/1°C inc. in TCN in summer and 4.03%/1°C inc. in TCN overall -RD disease inc. 4.19%/1°C in TCN overall, and inc. 1.46%/1°C DTR for autumn,	-DTR had larger magnitude and more significant effect over 30-day lag period, with bimodal peaks at low DTR (6°C) and high DTR (20°C)
Models/Methods	effects of PM ₁₀ , NO ₂ , SO ₂ , CO, O ₃	quasi-Poisson time- series generalized regression model with a DLNM model used for non-linear components, including long-term trend, seasonaliy, DOW with stratified analysis for age > or <50yrs, season, as well as sensitivity analysis to measure effect of relative humidity and warm/cold waves	Multivariate Cox proportional hazards regression model levels including different covariates, model one including demographic and substance use, model 2 including co- motel 2 including co- pM2, S, NO ₂ and ambient temp, while model 4 included education and GDP	Quasi-Poisson regression with DLNM adjusting for mean temp., relative humidity, PM2_5, 02, atmospheric pressure, seasonal, DOW and long-term time trends	Poisson generalized linear regression modeling combined with distributed lag nonlinear modeling
Outcome		Cardiovascular or respiratory disease listed as reason for ED visit during initial screening (not by ICD code)	All-cause mortality, CVD diagnosis and mortality (ICD-10: 100-125; 127-188, and 195-99), stroke diagnosis and mortality (ICD codes not listed)	RD (ICD–10: J), circulatory disease (ICD–10: I), GU (ICD–10: N) or mental health ED visits ((ICD–10: F)	Hospital admission for: chronic rheumatic heart disease (ICD-10: 105–
Exposure		TV was calculated as standard deviation of min and max temperature on each exposure day, from 2.8 exposure days (TV ₀₋₁ to TV ₀₋₇)	Long-term DTR calculated as annual mean difference from daily min to max termp, interpolated from 2419 weather stations to 1km resolution	DTR and TCN (mean temperature change on neighboring days) as continuous variables	DTR calculated from mean daily max and min temp obtained from China
Objective		Assess the effect of short-term TV on cardiovascular and respiratory disease ED visits	Assess the longitudinal association of DTR with all-cause and CVD mortality in a nationwide prospective cohort, and predict future climate-change related DTR changes	Evaluate association between DTR or TCN and specific ED visit types, considering seasonal variation and vulnerable populations	Compare the effects of ambient temp and DTR on CVD incidence in rural China
Study design/ population		Time series/340,758 cardiovascular and 38,233 respiratory disease ED visits in Dhaka City, Bangladesh from January 2014 to December 2017	Prospective Cohort study/Baseline population of 22,702 recruited from China Hypertension Survey from 2012-2015 across 14 provinces and followed from 2018-2019	Time series/4.3 million ED visits from 2014 to 2018 at 20 sites spanning all 11 geo-meteorological regions of China	Time series/32,567 hospital admissions for CVD across 30 hospitals in Qingyang City, Gansu, China
Author/year*		Rahman et al., 2022	Tang et al., 2022	Wang et al., 2022	Zhai et al., 2022

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Limitations	episodes of CVD not resulting in hospitalization	-Data not evenly distributed across all regions of China -Weather indicator did not distinguish between intra- and
Findings	with greater overall RR as low DTR (2.24) -Women had a more pronounced peak RR at low DTR (2.49), but greater RR for men at high DTR peak (2.06) -Both >65yrs and <65 years had more pronounced RR at high DTR Rn whole pop, and low DTR RR peaked at lag 7	-The minimum YLL was at TV 2.5°C nationally, with a U- shaped curve -Most LLD attributable to TV was from TV greater than 2.5°C (96.6%), LLD was greater in those <65, and for CVD (0.654) relative to RD (0.54y) -Increased LLD from TV
Models/Methods	(DLNM) including mean temp, atmospheric pressure, relative humidity, wind speed, long-term trend, DOW and public holidays. Sensitivity analysis with PM _{2.5} , PM ₁₀ and SO ₂ found no difference	Two-stage analysis: 1 st with DLNM controlling for daily temp, relative humidity, DOW, long- term trend and PM ₁₀ for each county, then 2 nd a metanalysis
Outcome	 [09), hypertension (ICD-10: 110–115), ischemic heart disease (ICD-10: 120–125) and other types of heart disease (ICD-10: 130–152) 	YLL/100,000 population and years of life lost per death (LLD) calculated from province-specific mortality and life- expectancy data based on WHO

Sharing Service

Science Data

Meteorological

from January 2014 to

March 2017

Exposure

Objective

Study design/ population

Author/year*

ACS - acute coronary syndrome, cum. -cumulative DTR - diurnal Temperature Range, COPD - Chronic Obstructive Pulmonary Disease, CVD - cardiovascular disease, DLNM - distributed lag non-linear Classification of Disease, inc. - increase, LLD - lives lost per death, MH - mental health, RD - respiratory disease, RTI - respiratory tract infection, SES - socioeconomic status, TV - temperature model, DOW - day of the week, ED - emergency department, GAM - generalized additive model, GLM - generalized linear model, GU - genitourinary, HF - heart failure, ICD - International variability, YLL – years of life lost.

-SES, medical history, air pollution data not

-Did not assess morbidity, only mortality

by altitude, with only significant inc. at 4% for

season, four regions of China, age, gender and

disease (I20–I25),

and COPD (J41-

J4

education status

<500m

included

averaged over entire

mortality per 10°C increase in long term DTR, with slight

(<500m), and only significant -RD with far greater variation

below 1500m

increase at lower elevation

DOW, relative humidity.

trend, long term trend, mean temp with a 14 day lag and stratified analysis for altitude,

(ICD-10: I00-I99). RD (ICD-10: J00-

and minimum temp

for each city from

through China Meteorological

Data Service

DTR changes

Center

data obtained

morality to predict between DTR and

cause-specific

from 266 cities in the Disease Surveillance Points system across

Qi et al., 2023

specific mortality

Time Series/Cause-

future changes in mortality due to

China from 2013 to

2017

J98), including coronary artery stroke (160-169)

subgroups of

accidental, CVD

-Approx 3% increase in CVD

linear regression model

mortality by ICD-10 code: Non-

Annually averaged

DTR calculated from daily max

Examine the association

Cause specific

Two stage Poisson including seasonal Citv

-Temperature data

inter-day variability

was found for warmer, more humid, lower latitude, high altitude areas and for those

geographic subgroup analyses also performed data. Demographic and

(ICD-10: I00-I99), RD (ICD-10: J00-

J98)

methods; CVD

preceding two day

variability and years of life lost

between temp association

Investigate

(YLL) in China

provincial Centers for

for which mortality data available from

Gong et al., 2023

Chinese provinces over 2013 to 2017

counties from 5

Time Series/364

Disease Control and

Prevention

Hyg Environ Health Adv. Author manuscript; available in PMC 2025 June 13.

(combines intra

and inter-day

variability)

temperature from

max and min

deviation of the

Temp variability TV) as standard with low education

* Red = CVD outcome, yellow = RD outcome, orange = CVD and RD outcomes included, light gold = renal or GU outcomes included, dark gold = CVD, RD and renal/GU outcomes included, light blue = mental health outcome, dark blue = CVD, RD, renal/GU and MH outcomes included.