Impact of rapid temperature fluctuations on acute stroke risk: a nationwide case-crossover study from 2001 to 2020

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Summary

Background Climate factors greatly affect cardiovascular health, with stroke ranking among serious global concerns. However, the impact of rapid temperature fluctuations on stroke risk remains underexplored. Given Taiwan's aging population and the intensifying effects of climate change, understanding influence of ambient temperatures on stroke risk is crucial for public health protection. This study aimed to explore the link between ambient temperature, sudden day-to-day temperature changes, and stroke onset in Taiwan, taking air pollutants into consideration.

Methods We conducted a time-stratified case-crossover study from 2001 to 2020 using Distributed Lag Nonlinear Models (DLNM) within conditional logistic regression to examine lagged associations between temperature parameters and stroke risk. We analyzed associations separately for total stroke, ischemic stroke, and hemorrhagic stroke to identify potential differences in risk patterns, using odds ratios (ORs) relative to the temperature associated with the lowest stroke risk. Data from the National Health Insurance Research Database (NHIRD) identified the study population, including 1,100,074 first-time stroke emergency events and self-matched with 2,200,148 non-stroke onset dates as controls. The primary exposure assessments included daily temperatures (mean, maximum, and minimum) and temperature fluctuations (diurnal temperature range (DTR), sudden day-to-day temperature increases (TDI), and sudden day-to-day temperature decrease (TDD)), adjusted for air pollutants ($PM_{2.5}$, O_3, SO_2, and NO_2), and rainfall. Lag periods up to 13 days prior to the corresponding event or control days were used to examine the lag effect of stroke risk.

Findings Through DLNM exposure-lag-response effect analysis after adjustment for $PM_{2.5}$, O_3, SO_2, NO_2, and rainfall, the study revealed that when TDI exceeded 6 °C, the risk of ischemic stroke more than doubled compared to the lowest risk temperature (OR: 2.173, 95% CI: 1.887, 2.501). The risk continued to rise until 9 °C, with a second peak observed when TDI exceeded 16 °C (OR: 2.096, 95% CI: 1.733, 2.535). Conversely, TDD exceeding 14 °C was linked to heightened hemorrhagic stroke risk (OR: 2.187, 95% CI: 2.055, 2.326). Additionally, daily maximum temperature exceeding 35 °C was associated with an increased stroke risk, primarily affecting ischemic stroke, while daily minimum temperature below 16 °C was strongly associated with a doubled risk of hemorrhagic stroke.

Interpretation Our findings indicate that sudden day-to-day temperature increases and decreases are significant predictors of stroke onset. These results emphasize a noteworthy relationship between temperature and stroke risk over consecutive days, supporting interventions aimed at reducing stroke incidence.

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Research in context

Evidence before this study

Climate change is one of the most pressing global issues in the 21st century, with significant implications for human health. Stroke has become an increasing burden on global health, and there is growing evidence that meteorological conditions, including temperature fluctuations, contribute to stroke risk. Many existing studies have focused on stroke mortality, which may not fully capture the factors that trigger stroke occurrence. Although temperature fluctuations have been associated with stroke risk, a deeper understanding of short-term temperature changes, including both increases and decreases in temperature, is crucial. These insights are essential for developing effective prevention strategies and mitigating stroke incidence attributed to climate change.

Added value of this study

This study contributes to the existing evidence by investigating the effect of temperature fluctuations on stroke incidence through developing sudden day-to-day temperature increase (TDI) and sudden day-to-day temperature decrease (TDD) parameters. Although several studies use diurnal temperature range (DTR) to assess daily temperature variations and their relationship to stroke risk, DTR alone may not sufficiently capture the short-term impacts of temperature fluctuations, particularly as abrupt temperature changes often last for more than a single day. Furthermore, DTR does not distinguish between temperature increases or decreases, which are linked to different types of extreme weather events, such as heatwaves or cold spells.

By incorporating TDI and TDD parameters, we found that sudden day-to-day temperature changes are significantly associate with stroke-related emergency department visits, even after adjusting for air pollution factors. Specifically, TDD was associated with an increased risk of hemorrhagic stroke, whereas TDI was linked to an elevated risk of ischemic stroke. Notably, a TDI exceeding 6 °C and with a second peak beyond 16 °C doubled the risk of ischemic stroke, while a TDD exceeding 14 °C doubled the risk of hemorrhagic stroke. These findings highlight the important role of short-term temperature fluctuations in stroke risk.

Implications of all the available evidence

The distinct patterns of stroke-related emergency department visits between TDI and TDD reflect their distinct physiological impacts. Our findings highlight the importance of gradual adaptation and effective extreme weather responses in prevention of stroke. This study provides a foundation for further exploration of the effects of short-term temperature fluctuations on stroke occurrence and offers supporting evidence for public health initiatives aimed at reducing climate-related stroke risk.

Introduction

Climate change is one of the most pressing global issues in the 21st century, impacting not only the environment but also posing a direct threat to human health. Among its various health implications, cardiovascular diseases stand out as one of the most prominent issues affected by climate change, including factors such as extreme temperature, air pollution, and extreme weather events.[1] According to the Global Burden of Disease (GBD) report in 2021, stroke ranks as the second-leading cause of death and the third-leading cause of disability-adjusted life year (DALYs) globally.[2] Moreover, there was an increase in incidence (70.0%), prevalence (85.0%), deaths (43.0%), and DALYs (32.0%) from 1990 to 2019.[2] Meteorological conditions have been confirmed as significant factors contributing to the occurrence of stroke.[3–7]

Previous studies have investigated the impact of climate change on cardiovascular diseases using various methods and data analyses. Research in Taiwan found that average daily temperature and cardiovascular disease mortality had an inverse relationship within a specific temperature range, 12.91 °C–26.36 °C.[8] Additionally, investigations have uncovered a nonlinear relationship between temperature variation and mortality rates, with both low and high temperatures associated with increased incidence and mortality rates of cardiovascular diseases.[9–12] Large-scale cohort studies in China showed that both low and high temperatures were associated with an increased risk of clinical visits for cardiovascular diseases.[13] Moreover, climate change involves alternations in weather patterns and temperature variability, potentially exacerbating health risks. A multi-country study, including Taiwan, assessed the impact of temperature variability on mortality and found a positive association between temperature variability and mortality across different countries/regions. This implicates the importance of assessing temperature variability in relation to health risks.[14]

Much of the existing research focuses on mortality as the primary outcome, which may be biased due to variations in environmental factors, such as access to hospitals and the quality of healthcare. Previous epidemiological research has indicated that rapid fluctuations in temperature within a single day pose an independent risk factor for human health,[15] with studies demonstrating an increase in hospital admissions and stroke mortality associated with diurnal temperature range (DTR).[16,17] Additionally, evidence also suggests that long-term temperature variability have the increased risk of mortality among stroke patients.[18] Temperature variability may influence CVD by activating thermoregulation, which stimulates the autonomic nervous system, leading to disruption of cardiac functions.[19,20] However, assessing the impact of sudden temperature drops or spikes, particularly those representing cold or heat waves, using only DTR may be insufficient. While long-term temperature variability has been associated with adverse health outcomes, short-term fluctuations may provide more actionable insights for preventing stroke incidence. A recent study have identified temperature variability over a three-day period is related to various cardiovascular outcomes, including stroke.[21] Further understanding of the relationship between short-term temperature variability and stroke onset is essential, particularly from a policy perspective, to inform preventive measures and reduce the incidence of stroke in the context of climate change.

Taiwan is gradually transitioning into a super-aged society, with the elderly population expected to surpass 20% by 2039 and reach 43.6% by 2070. Older adults are more sensitive to climate change. Statistics from the Ministry of Health and Welfare's 2021 report indicate a continuous increase in mortality rates from heart disease and hypertension, highlighting the impact of climate factors on cardiovascular diseases for the first time. Given ongoing global warming, population aging, and the increased vulnerability of patients with multiple risk factors for cardiovascular diseases, these trends are expected to worsen in the coming years. Therefore, we conduct a time-stratified case-crossover study to quantitatively evaluate the link between ambient daily temperature parameters, temperature fluctuation parameters, and stroke onset. Additionally, we apply lag patterns using Distributed Lag Nonlinear Models (DLNM) within conditional logistic regression to identify potential windows of exposure and to identify susceptible populations that may be particularly vulnerable to temperature-related stroke incidence.

Methods

Study population

The study utilized the National Health Insurance Research Database (NHIRD) to identify the study population in Taiwan. The NHIRD consists of claims data from the national health insurance beneficiaries, which covers approximately 99% of the population in Taiwan.[22,23] First, all patients (n = 1,781,712) with stroke-related emergency department visits diagnosed with ICD-9430 to 438 or ICD-10-CM code I60 to I69 for hemorrhagic stroke (430–432; I60–I62) and ischemic stroke (433–434; I63–I66) from January 1, 2001, to December 31, 2020, were identified. For patients with multiple stroke events, only the initial stroke occurrence was selected as a case to focus specifically on initial stroke events. Therefore, recurrent strokes (n = 661,917) were excluded. In addition, patients residing on outlying islands (n = 5321) were excluded due to the smaller sample size and different environmental factors comprising outlying islands compared to Taiwan's main island. Patients with missing insurance data (n = 9900) and those who failed to be matched with the two control days (n = 4500), often due to loss of insurance eligibility such as citizenship renunciation, relocation abroad, expiration of the alien resident certificate, or missing,[24] were also excluded (Supplementary Figure S1).

Finally, the study population comprised 1,100,074 stroke cases, self-matched with 2,200,148 non-stroke onset dates serving as controls. The present study protocol was approved by the Research Ethics Committee of the National Health Research Institutes (Approval Number: EC1110702-E). This study utilizes data from a legally authorized health insurance database that has been de-identified or cannot be used to identify specific individuals. As such, the Research Ethics Committee has determined that this project qualifies for an exemption from informed consent.

Study design

The study employed a case-crossover design to investigate the correlation between short-term meteorological parameters and stroke emergency department visits. In the case-crossover design, each subject serves as their own control, with each stroke-related emergency department visit categorized as a case.[25] This methodological approach helps mitigate time-invariant factors such as gender, age, and smoking habits,[26] allowing for an assessment of the impact of extreme temperatures on subgroups based on characteristics such as age, health status, or lifestyle factors.[27,28] Using a population with no history of stroke as controls would introduce biases not related to the potential risk factors interested in this study. This design ensures that the observed associations are more likely to reflect the impact of temperature parameters rather than differences in baseline characteristics between cases and controls. Two control days were matched to each case according to three and five weeks prior to the event of a stroke-related emergency department visit, considering the day of the week and season. This approach was chosen to avoid short-term temporal confounding such as day of the week and season and to ensure that each case and two control dates are sufficiently spaced without overlapping. This design minimizes potential biases that could arise after the events, such as disease recurrence following the stroke event. The hazard period of the case includes the event date (lag 0) and the 13 days preceding the event (lag 1 to lag 13), capturing the meteorological parameters such as daily mean temperature, daily maximum temperature, daily minimum temperature, DTR, sudden day-to-day temperature increase (TDI), and sudden day-to-day temperature decrease (TDD). These lags are used to evaluate the relationship between temperature parameters and stroke-related emergency visits. Each control period also includes the control day and the corresponding 13 preceding lag days. The lag duration was selected based on previous studies.[29,30]

Exposure data

Environmental exposure in this study focused on daily temperature parameters and temperature fluctuation parameters as primary variables. This study utilized gridded daily observational data from the Taiwan Climate Change Projection Information and Adaptation Knowledge Platform (TCCIP) from 2001 to 2020. The downscaling approach used for the TCCIP data involved integrating information from 953 meteorological stations across Taiwan, including the Central Weather Bureau, Agricultural Research and Extension Station, Taiwan Forestry Research Institute, Taiwan Agricultural Research Institute, Civil Aeronautics Administration, and Taiwan Power Company. This comprehensive data collection allowed for the creation of high-resolution temperature and rainfall grids at a 1 × 1 km spatial resolution, covering 120,701 grid points from 1960 to 2021, with a total of 22,646-time points across Taiwan.[31] To eliminate the possible issues with extreme values, variations in temporal scale, and spatial discrepancies inherent in the original station data, TCCIP conducted a cross-validation experiment to assess the uncertainties in generating gridded daily temperature data. While errors exceeded 4 °C in the central mountain range, they remained below 1 °C in most areas, indicating greater uncertainty in regions with lower station density. Since major populations in Taiwan are primarily located in flat areas, data reliability remains robust in these regions.

Regarding spatial resolution, patient locations were available at the township level (368 townships). We employed Geographic Information System (GIS) spatial statistics to integrate the TCCIP data. This process involved averaging the data within each 0.01-degree grid across each township, which enabled the aggregation of gridded daily climate data at the 368-township level, creating a comprehensive daily township-level climate database from 2001 to 2020. Among these townships, only 22 mountainous regions exceeded 250 km^2, while most flatland townships were smaller than 100 km^2, ensuring minimal temperature variation within each unit.

This study included the daily temperature parameters of daily mean temperature, daily maximum temperature, and daily minimum temperature. We also investigated short-term temperature fluctuation parameters, DTR, TDI, and TDD. The DTR signifies the difference between the daily maximum and minimum temperatures within a day, reflecting intraday variability. However, abrupt temperature changes often span more than one day. As a result, we developed two new indicators: TDI (Sudden day-to-day temperature increase) and TDD (sudden day-to-day temperature decrease). These indicators assess temperature fluctuations over consecutive days while remaining sensitive to rapid and acute temperature changes relevant for evaluating short-term effects on stroke-related emergency department visits. We first compare the mean temperatures of two consecutive days to determine the direction of temperature change. If today's mean temperature is higher than the previous day's, warming trend is identified, and TDI is calculated. If today's mean temperature is lower than the previous day's, cooling trend is identified, and TDD is calculated. The indicators are calculated as follows:

1. Sudden day-to-day temperature increase (TDI):

$$TDI = T_{\max,day\ n} - T_{\min,day(n-1)}$$

where $T_{\max,\ day\ n}$ represents the maximum temperature on day n, and $T_{\min,\ day\ (n-1)}$ represents the minimum temperature on the previous day (n–1).

2. Sudden day-to-day temperature decrease (TDD):

$$TDD = T_{\max,day\ (n-1)} - T_{\min,day\ n}$$

where $T_{\max,\ day\ (n-1)}$ represents the maximum temperature on the previous day (n–1), and $T_{\min,\ day\ n}$ represents the minimum temperature on day n.

Daily air pollutant data, including $PM_{2.5}$, O_3, SO_2, and NO_2 from 68 monitoring stations covering 2001 to 2020, were obtained from the Taiwan Ministry of Environment (https://data.moenv.gov.tw/). For each participant's address, daily levels of air pollutants and temperature parameters for case days and control days were recorded at the township level.

Statistical analysis

Conditional logistic regression models were employed to quantify the association between stroke emergency department visits and daily temperature parameters as well as temperature fluctuations. To explore the possible nonlinear and lagged associations of temperature and stroke, we incorporated the distributed lag nonlinear model (DLNM) into the conditional logistic regression models.[32] This DLNM model creates a flexible cross-basis function for daily temperature and its changes, allowing for nonlinear exposure–response relationships in each lag day and nonlinear lagged effects.[33] In this study, we used a natural cubic *B*-spline with four degrees of freedom (df) in the exposure-response curve in the cross-basis function to allow a smooth and flexible representation of the non-linear relationship between temperature parameters and stroke-related emergency department visits. We also modeled effects across different lag days with non-linear trends to balance model complexity and interpretability while capturing potential delayed effects. This approach provides sufficient flexibility in estimating short-term lag effects while avoiding overfitting.

Below is the formula of the main model in this study:

$$\text{logit}[\Pr(Y=1)] = \sum_s \alpha_s + f(T)$$

The function f is a bi-dimensional function describing the daily temperature (T) along lags. The parameter α_s is the intercept for strata. Y refers to the case or the control, and stratum is defined as the same days of the week in the same month and year for the same patient. We used a maximum lag of 13 days prior to stroke onset (lag 0–13 days) to fully explore the lag pattern of short-term temperature exposure and then used it for subsequent analyses.

Sensitivity analyses were conducted to assess the stroke risk curves for TDI, TDD, daily maximum temperature, daily minimum temperature, and DTR across four different scenarios; (A) Lag 0–6, non-adjusted model; (B) Lag 0–13, non-adjusted model; (C) Lag 0–6, adjusted model; (D) Lag 0–13, adjusted model. Adjusted models included $PM_{2.5}$, O_3, SO_2, NO_2, and rainfall. Among these, the lag 0–13 with adjusted model demonstrated the best model fit, as indicated by the lowest Akaike Information Criterion (AIC) value (Supplementary Figures S2–S16). Therefore, we selected this model for our final model.

We then plotted the overall cumulative exposure-lag-response relationship curves after truncating the temperature and its changes distribution. To better interpret our results, we selected the temperature corresponding to the lowest stroke risk in the exposure-response curve as a referent. The lowest stroke risk temperature was used as the reference temperature for TDI, TDD, daily maximum temperature, daily minimum temperature, DTR, and daily mean temperature. The findings were reported with odds ratio (OR) compared to the lowest stroke risk temperature, along with 95% confidence intervals (CIs) of stroke onset. We analyzed associations separately for total stroke, ischemic stroke, and hemorrhagic stroke to identify potential differences in risk patterns. All statistical analyses were performed in the R software (R package: dlnm, survival. version 3.4.4, R Foundation for Statistical Computing, Vienna, Austria) and SAS (SAS Institute Inc., Cary, North Carolina, U.S.A.). The statistical significance level was set at p-value <0.05.

Role of the funding source
The funders had no role in the research design, data collection and analysis, manuscript preparation, or publication decision.

Results
The study included 1,100,074 patients with stroke-related emergency department visits, comprising 647,129 (58.8%) males and 452,945 (41.2%) females. Most cases were individuals above middle age, 344,265 (31.3%) in 45–64 years old, 538,944 (49.0%) in 65–84 years old, and 113,932 (10.4%) above 85 years old. Across four seasons, the stroke-related emergency department visits were approximately equally distributed, with 283,033 patients (25.7%) in winter, 278,625 (25.3%) in spring, 270,045 (24.5%) in summer, and 268,371 (24.4%) in autumn. Hemorrhagic stroke accounted for 278,404 (25.3%) patients, while ischemic stroke comprised 482,034 (43.8%) patients (Supplementary Table S1).

Fig. 1 demonstrates the mean and standard deviation of temperature parameters, including daily mean temperature, daily maximum temperature, daily minimum temperature, DTR, TDI, and TDD, among cases and controls separated by seasons. Cases exhibited higher daily temperature values (mean, minimum, and maximum) than controls during spring and summer, whereas in autumn and winter, cases showed lower temperature values compared to controls. Regarding temperature fluctuation parameters (DTR, TDI, and TDD), cases showed higher temperature values than controls in winter but lower values in spring.

Figs. 2–6 illustrate the DLNM exposure-lag-response effect of TDI, TDD, daily maximum temperature, daily minimum temperature, and DTR, respectively, on stroke-related emergency department visits adjusted for $PM_{2.5}$, O_3, SO_2, NO_2, and rainfall. The figures present the ORs with 95% CIs, relative to the temperature associated with the lowest stroke risk. Regarding temperature fluctuation parameters, TDI was associated with an increased risk of overall stroke and ischemic stroke (Fig. 2). Particularly, the risk of ischemic stroke-related emergency department visits began to significantly rise two-fold when the TDI Δt exceeded 6 °C (OR: 2.173, 95% CI: 1.887, 2.501), and this trend continued until TDI Δt 9 °C. A second peak in ischemic stroke risk was observed when TDI Δt exceeded 16 °C with an OR of 2.096 (95% CI: 1.733, 2.535) (Fig. 2C). However, no significant risk was observed for hemorrhagic stroke (Fig. 2B). TDD followed a U-shaped relationship across all three stroke types, with the lowest risk observed at TDD around Δt 7 °C (Fig. 3). The risk of hemorrhagic stroke-related emergency department visits doubled when TDD Δt dropped by more than 14 °C (OR: 2.187, 95% CI: 2.055, 2.326) (Fig. 3B). DTR also showed a U-shaped relationship for all stroke types, with the lowest risk occurring at Δt between 5 and 7 °C (Fig. 6). However, even as DTR increased further, the associated risk did not exceed a twofold increase.

For daily temperature parameters, daily maximum temperature was associated with an increased risk of overall stroke and ischemic stroke (Fig. 4). The risk of overall stroke-related emergency department visits

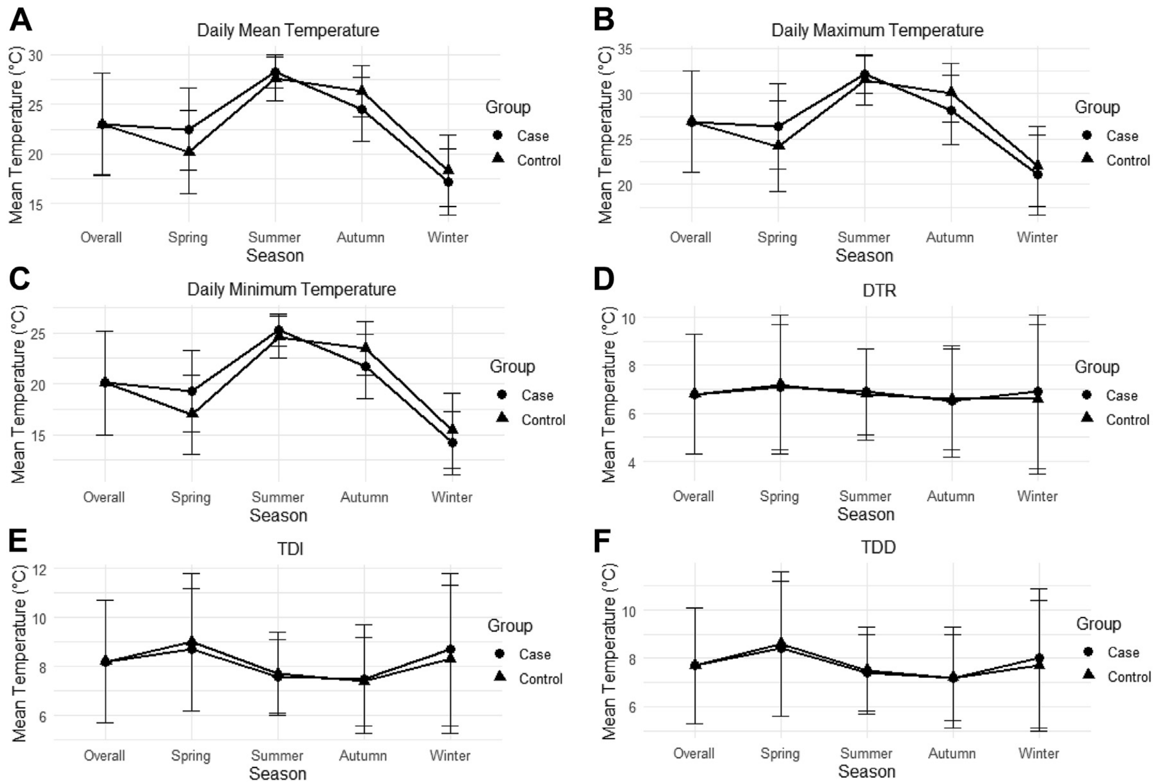

Fig. 1: Mean and standard deviation of temperature parameters in cases with stroke-related emergency department visits and controls. Abbreviations: DTR (Diurnal Temperature Range), TDI (Temperature Difference Increase, defined as the difference between the daily maximum temperature and the previous day's minimum temperature), and TDD (Temperature Difference Decrease, defined as the difference between the daily minimum temperature and the previous day's maximum temperature).

significantly increased when the maximum temperature was above 35 °C (OR: 1.028, 95% CI: 1.003, 1.055), reaching an OR of 1.134 (95% CI: 1.038, 1.238) at 40 °C (Fig. 4A). Additionally, the risk of ischemic stroke-related emergency department visits rose significantly when the maximum temperature was above 29 °C (OR: 1.018, 95% CI: 1.003, 1.033), reaching an OR of 1.281 (95% CI: 1.117, 1.469) at 40 °C (Fig. 4C). In contrast, the risk of hemorrhagic stroke gradually decreased with increased temperatures. Daily minimum temperature was associated with an increased risk of both hemorrhagic and ischemic stroke risk (Fig. 5). The risk of

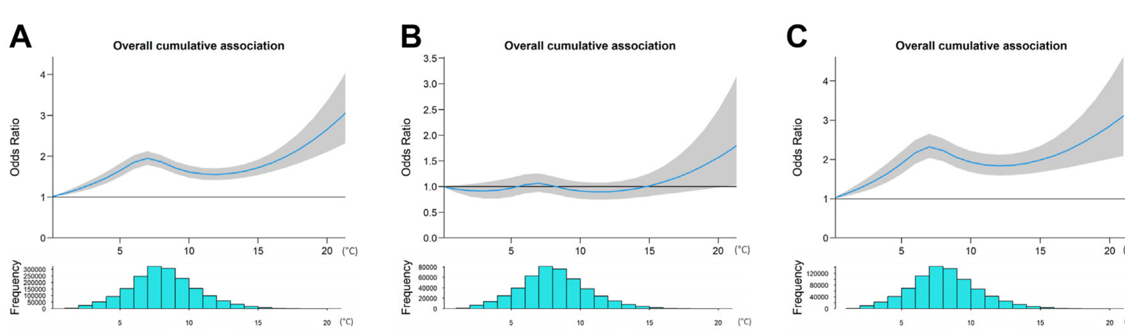

Fig. 2: Stroke risk curves across lag days 0–13 for TDI using the DLNM model: (A) Overall stroke risk, (B) Hemorrhagic stroke risk, (C) Ischemic stroke risk. Note: TDI represents the difference between the daily maximum temperature and the previous day's minimum temperature. Odds ratios were calculated based on the lowest stroke risk temperature, adjusted for $PM_{2.5}$, O_3, SO_2, NO_2, and rainfall.

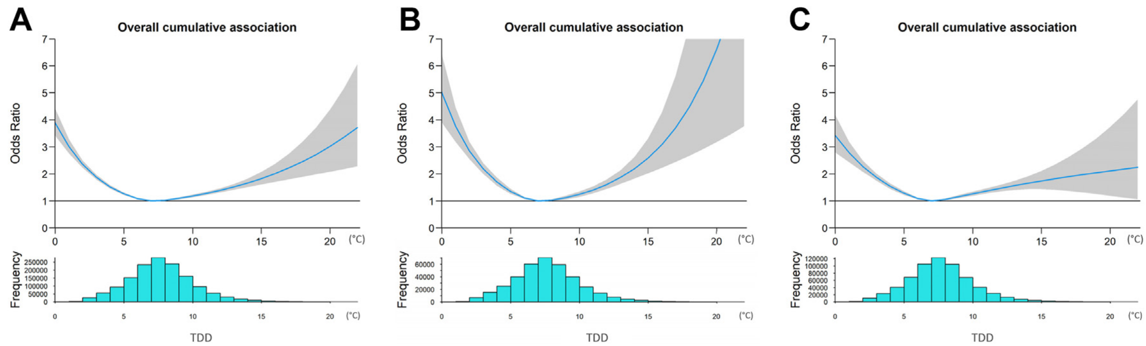

Fig. 3: Stroke risk curves across lag days 0–13 for TDD using the DLNM model: (A) Overall stroke risk, (B) Hemorrhagic stroke risk, (C) Ischemic stroke risk. Note: TDD represents the difference between the daily minimum temperature and the previous day's maximum temperature. Odds ratios were calculated based on the lowest stroke risk temperature, adjusted for $PM_{2.5}$, O_3, SO_2, NO_2, and rainfall.

hemorrhagic stroke-related emergency department visits significantly rose when the minimum temperature decreased below 30 °C (OR: 1.032, 95% CI: 1.006, 1.059), reaching doubled risk at 16 °C (OR: 2.051, 95% CI: 1.823, 2.307) (Fig. 5B). The risk of ischemic stroke-related emergency department visits significantly increased when the minimum temperature dropped below 13 °C (OR: 1.019, 95% CI: 1.002, 1.037), reaching an OR of 1.325 (95% CI: 1.150, 1.527) at 0 °C (Fig. 5C).

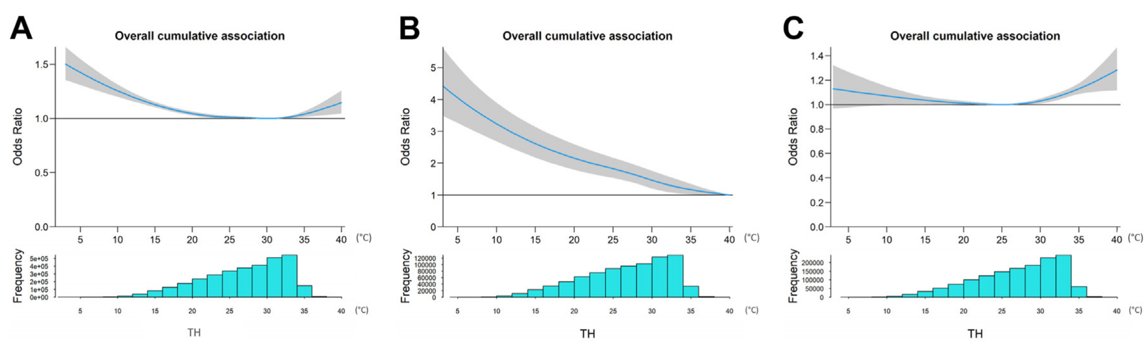

Fig. 4: Stroke risk curves across lag days 0–13 for daily maximum temperature using the DLNM model: (A) Overall stroke risk, (B) Hemorrhagic stroke risk, (C) Ischemic stroke risk. Note: TH represents the daily maximum temperature. Odds ratios were calculated based on the lowest stroke risk temperature, adjustment for $PM_{2.5}$, O_3, SO_2, NO_2, and rainfall.

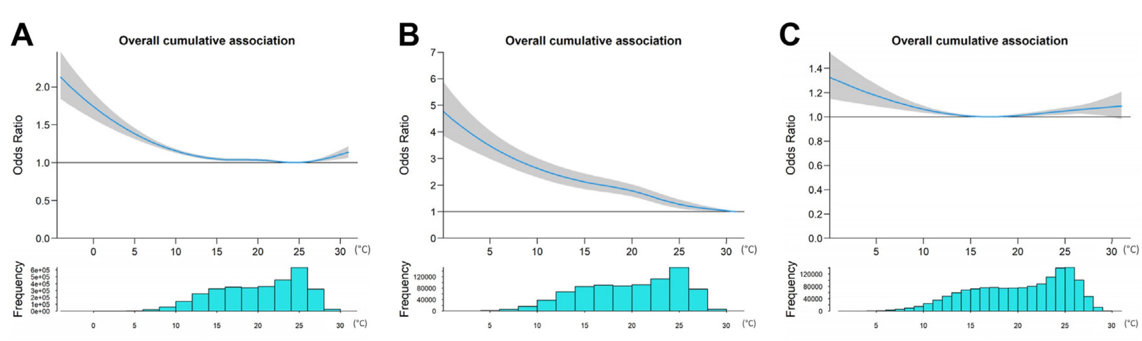

Fig. 5: Stroke risk curves across lag days 0–13 for daily minimum temperature using the DLNM model: (A) Overall stroke risk, (B) Hemorrhagic stroke risk, (C) Ischemic stroke risk. Note: TL represents the daily minimum temperature. Odds ratios were calculated based on the lowest stroke risk temperature, adjusted for $PM_{2.5}$, O_3, SO_2, NO_2, and rainfall.

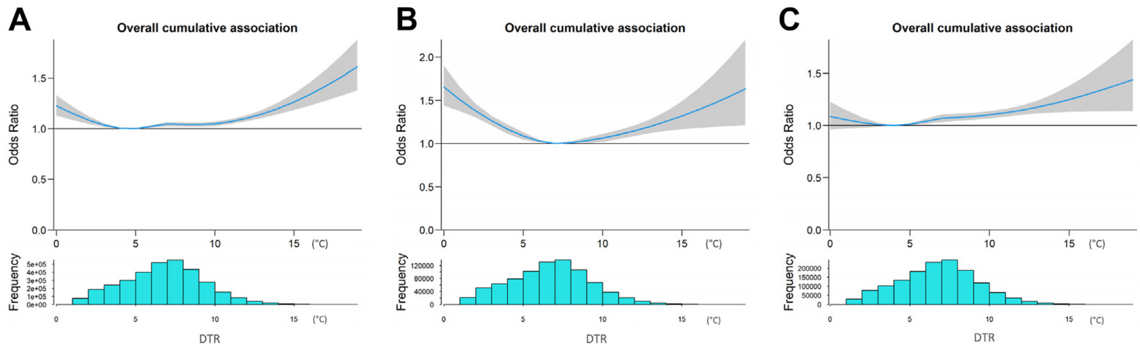

Fig. 6: Stroke risk curves across lag days 0–13 for DTR using the DLNM model: (A) Overall stroke risk, (B) Hemorrhagic stroke risk, (C) Ischemic stroke risk. Note: DTR represents diurnal temperature range. Odds ratios were calculated based on the lowest stroke risk temperature, adjusted for $PM_{2.5}$, O_3, SO_2, NO_2, and rainfall.

Further analysis using conditional logistic regression analysis examined the association between each temperature parameter and stroke-related emergency department visits across different regions of Taiwan, adjusting for $PM_{2.5}$, O_3, SO_2, and NO_2, and rainfall (Supplementary Table S3). TDI was positively associated with overall stroke (OR: 1.007, 95% CI: 1.005, 1.009). Stratified analyses revealed that in winter, the highest risk associated with TDI was observed in southern Taiwan (OR: 1.115, 95% CI: 1.110, 1.119). Meanwhile, TDD was most strongly associated with stroke risk in northern Taiwan during summer (OR: 1.079, 95% CI: 1.075, 1.083). The effect of TDI was more strongly associated with stroke risk in males and individuals aged >45 years. Supplementary Table S4 further indicates the impact of extreme temperature fluctuations on stroke risk. Specifically, TDI ≥6 °C was associated with a 6.7% higher risk of ischemic stroke and a 2.8% higher risk of hemorrhagic stroke compared to TDI <6 °C. Conversely, TDD ≥14 °C was linked to an 18.1% increased risk of hemorrhagic stroke compared to TDI <14 °C.

Discussion

In this study, we employed a time-stratified case-crossover design to examine the impact of ambient temperature parameters on stroke emergency department visits in Taiwan from 2001 to 2020. We found 1,100,074 first-time stroke emergency subjects and self-matched with 2,200,148 non-stroke onset dates as controls. Through DLNM exposure-lag-response effect analysis after adjustment for $PM_{2.5}$, O_3, SO_2, NO_2, and rainfall, the study identified a significant two-fold increase in ischemic stroke risk when TDI exceeded 6 °C (Δt >6 °C), continuing to rise until 9 °C, with a second peak observed beyond 16 °C (Δt >16 °C). Conversely, TDD exceeding 14 °C (Δt >14 °C) was linked to an increased two-fold risk of hemorrhagic stroke. Moreover, elevated daily maximum temperatures above 35 °C significantly increased the risk of overall stroke-related emergency department visits, particularly for ischemic stroke. Conversely, lower daily minimum temperatures below 16 °C was doubled associated with an increased risk of hemorrhagic stroke. Our findings offer supporting evidence for targeted interventions to reduce stroke risk associated with sudden temperature changes.

Temperature fluctuation parameters and risk of stroke in DLNM model

DTR has often been used as an indicator of temperature fluctuations to explore their impact on stroke incidence. In this study, a U-shaped relationship was observed between DTR and overall stroke risk, hemorrhagic stroke risk, and ischemic stroke risk, with the lowest risk occurring DTR at 5–7 °C. However, even as DTR increased further, the risk did not exceed a twofold increase. Notably, DTR does not differentiate whether the effect stems from temperature increases or decreases, such as those associated with cold spells or heat waves. This limitation suggests that DTR alone may be insufficient to fully capture the impact of sudden temperature fluctuations on stroke risk. Our study highlights the distinct association between temperature fluctuations and various stroke types, underscoring the significance of temperature dynamics in stroke risk. The sudden day-to-day temperature change parameters examined here may serve as a valuable indicator for stroke incidence, warranting further investigation into its impact on stroke risk.

While direct comparisons with similar studies are limited, our findings coincide with several existing studies demonstrating varying impacts of temperature parameters on specific stroke types. For instance, a study by Lim et al. in South Korea revealed an association between high ambient temperature and increased ischemic stroke mortality, while decreased risk was observed for intracerebral hemorrhage mortality.[34] Similarly, a study focusing on the ultra-short-term temperature impact found that higher temperatures

7 h before the event were associated with ischemic stroke risk, while lower temperatures 5 h before the event were associated with the risk of hemorrhagic stroke.[35] These findings across studies support our findings and suggest the effects of temperature fluctuations on different stroke types. However, conflicting results have also been reported. For example, a study by Vaičiulis et al. in Lithuania found that personal cold spells were associated with ischemic stroke but not hemorrhagic stroke.[36] Further examination of the effect of sudden temperature fluctuations on stroke types is required to better understand the relationship between temperature fluctuation and different stroke types.

Our results on the effect of TDI on stroke-related emergency department visits showed a gradual increase in stroke risk as TDI increased, with significantly positive associations for overall and ischemic strokes. However, we observed a slight decline in risk around 7–11 °C for both overall and ischemic strokes before the upward trend resumed, although the effect remained significantly positive. The first peak (Δt >6 °C–9 °C) suggests that some individuals, particularly those with pre-existing cardiovascular conditions, may be more sensitive to these sudden changes. The second peak (Δt >16 °C) indicates that more extreme temperature shifts may exacerbate dehydration, electrolyte imbalances, and blood pressure fluctuations, significantly increasing ischemic stroke risk. This extreme stress may overwhelm the body's adaptive mechanisms, leading to a second surge in stroke cases. While a two-peak pattern in the TDI-stroke relationship is plausible, further investigation is needed to confirm.

For TDD, we found a U-shaped relationship with stroke-related emergency department visits across overall, hemorrhagic, and ischemic strokes, with the lowest risk occurring when the temperatures decrease by approximately 7 °C. It is possible that moderate ambient temperature decreases the positive effect due to adaptive behaviors, such as adjusting clothing, utilizing warming equipment, staying indoors, and limiting outdoor activities. These behaviors may help maintain body temperature and prevent the activation of physiological cold-defense mechanisms, such as peripheral vasoconstriction to prevent excessive heat loss to the environment and redistribute warm blood to the core and vital organs.[37] However, excessive temperature fluctuations in both directions, increase or decrease, may overwhelm thermoregulatory mechanisms, particularly in older adults and individuals with chronic conditions, leading to increased stroke risk.

The distinct patterns of stroke-related emergency department visits between TDI and TDD reflect their distinct physiological effects. While sudden warming imposes increasing cardiovascular stress, leading to a relatively steady rise in stroke risk, a lower risk of stroke was observed with moderate cooling. This lower risk may be influenced by several factors, including adaptive behaviors. Our findings highlight the importance of gradual adaptation and effective extreme weather responses in stroke prevention.

Effect of daily temperature parameters and stroke

In DLNM analysis with conditional logistic regression, we observed that daily maximum temperature showed a risk of stroke, with the risk significantly rising when the temperature increased by over 35 °C. Daily minimum temperature was associated with a risk of hemorrhagic stroke, with the risk reaching double when the temperature decreased below 16 °C. Numerous existing studies corroborate the relationship between extreme temperature parameters and stroke. For example, a multinational study covering 15 cities in Northeast Asia (including three cities in Taiwan, six in South Korea, and six in Japan) investigated adverse reactions to extreme temperatures and their temporal change from 1972 to 2009. In Taiwan, the constant cold-related risk was observed over the study period with a slight increase in the late 2000s, while the heat-related risk demonstrated a slight decrease from the mid-1990s through the 2000s.[38] Another multinational study covering 567 cities in 27 countries across five continents found that both high and low temperatures are associated with increased risk of mortality from cardiovascular causes, ischemic heart disease, stroke, and heart failure, with 2 and 9 excess deaths per 1000 cardiovascular deaths attributed to extreme heat and cold weather, respectively.[39] Furthermore, a systematic review and meta-analysis of 20 studies concluded that both heat and cold temperatures are positively associated with stroke morbidity and mortality risk.[40]

There have been numerous studies with diverse results accumulated across the world. A case-crossover study in South Korea also observed the effect of decreased temperature on increasing ischemic stroke incidence, particularly in winter.[41] Research in the United States revealed that increased lower temperature and larger DTR are associated with an increased ischemic stroke hospitalization rate.[42] Conversely, a time-stratified crossover study in Israel linked high temperatures in summer to an elevated stroke risk.[43] Moreover, a case–control study in Germany found a significant increase in the risk of ischemic stroke with notable temperature fluctuations.[44] Studies in Japan demonstrated that climatic conditions affect the risk of stroke, both ischemic and hemorrhagic, in females.[45] Our study's findings regarding the relationship between daily temperature parameters and stroke contribute to existing evidence, suggesting a potential nonlinear association between temperature and different types of stroke risk.

Potential mechanisms between temperature parameters and stroke risk

Currently, the biological mechanism of temperature variability on stroke is still uncertain. Human core body temperature is usually maintained within a narrow range, and the body temperature of healthy individuals is maintained at 37 ± 0.5 °C.[46] It has been observed that ambient temperature fluctuations induce changes in distal skin temperature parallel to the change direction in ambient temperature.[47] Furthermore, existing evidence exhibits a range of physiological changes due to short-term ambient temperature variabilities, such as blood pressure, inflammation, stress level, and immune function.[47–49] Short-term temperature variabilities may contribute to a disturbance in human body thermoregulation, causing various physiological changes, and ultimately leading to serious health outcomes like stroke. To further explore the biological plausibility of our findings, we have included Supplementary Figures S20–S24, which present stroke risk curves for temperature-related indicators using a shorter lag of 0–3 days. While the overall trend remains consistent, the estimated risk values are generally lower, and the AIC values are higher compared to the 0–13 day lag. This suggests that while immediate temperature fluctuations may contribute to stroke risk, a slightly longer exposure window may better capture delayed physiological responses, such as inflammatory processes, coagulation changes, and cardiovascular stress, which could explain the stronger associations observed with the 0–13 day lag.

Exposure to high temperatures can induce vasodilation, increased peripheral circulation, and sweating, leading to dehydration.[50] However, induced hypercoagulability due to hemoconcentration and hyperviscosity may increase the risk of ischemic stroke.[50,51] On the other hand, exposure to low temperatures and decreases in temperature are associated with higher blood pressure, a common physiological response induced by sympathetic nervous system activation,[47,52] which may exacerbate aortic wall damage, thereby contributing to the increased risk of hemorrhagic stroke.[53]

Strengths and limitations

There are several strengths in this study. Employing a time-stratified case-crossover design and statistical analysis of DLNM in conditional logistic regression facilitated capturing exposure-lag-response effects, which enhanced the understanding of the relationship between ambient temperature and stroke risk. The case-crossover design has allowed the elimination of time-invariant confounding factors such as age and sex, and factors that are unlikely to change significantly within the short-term exposure window, such as smoking and socioeconomic status (SES). Another strength is that the inclusion of a large study population in Taiwan over a decade contributed to minimizing the random error and allowed further stratifying analysis by season and geographic regions. In addition, this study explored the temperature effect on different stroke types, hemorrhage and ischemic, which highlighted the varying temperature fluctuation effects on hemorrhage and ischemic stroke risks.

However, there are some limitations that should be acknowledged in the present study. First, exposure measurement errors are unavoidable. People's movements and daily activities may introduce inaccuracies in measuring their temperature exposure. While personal temperature exposure measurement would provide the most precise relationship between temperature and stroke risk, it was impractical to measure personal temperature exposure for all study participants due to the large population size. Second, although high-resolution temperature grids at a 1 × 1 km spatial resolution were utilized, the participant address data available to us was limited to the township level, which restricted our ability to fully leverage the high-resolution temperature data. Third, the DLNM model does not explicitly examine the causal pathway among temperature, air pollution, and stroke. To address this limitation, we adjusted for air pollution in our models and revealed that regardless of its inclusion, the temperature-related patterns and associations with stroke risk remained constant. Lastly, the potential omission of confounding variables in the analysis, such as exposure to greenness, short-term physical activity levels, psychosocial stressors, and access to healthcare. These confounding factors may vary within each time stratum, but they are unlikely to change significantly within a short-term window.

Conclusion

This study provides evidence suggesting that TDD is associated with a heightened risk of hemorrhagic stroke, whereas TDI is linked to an elevated risk of ischemic stroke. Our findings set the stage for further exploration of the effects of short-term temperature changes on stroke happened and offer supporting evidence for initiatives aimed at reducing stroke incidence.

Contributors

MK was responsible for data curation, visualization, and original draft preparation. WTW contributed to conceptualization, investigation, and writing–reviewing and editing, and was responsible for the decision to submit the manuscript. CPL handled formal analysis. YYC handled formal analysis and accessed and verified the data. YHY provided resources, conducted investigations, and supervised the project. CCL was involved in resources and investigation. PCC oversaw the supervision of the entire project and accessed and verified the data.

Data sharing statement

The data used in this study were obtained from the National Health Insurance Research Database (NHIRD) of Taiwan and are not publicly accessible. Access to these data requires approval from the Health and Welfare Data Science Center (HWDC) under the Ministry of Health and Welfare. Researchers may apply for access through the HWDC website (https://dep.mohw.gov.tw/DOS/).

Editor note

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Declaration of interests

The authors declare no conflict of interests for this article.

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Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2025.101546.

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