# An Effect of 24-hour Temperature Change on Outpatient and Emergency and Inpatient Visits for Cardiovascular Diseases in Northwest China

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# Abstract

**Background:** Some studies suggested 24-hour temperature change (TC24) was one of the potential risk factors for human health. However, evidence of the short-term effect of TC24 on outpatient and emergency department (O&ED) visits and hospitalizations for cause-specific cardiovascular diseases (CVDs) is still limited.

**Objective:** To explore the short-term effects of TC24 on O&ED visits and hospitalizations for CVDs in northwest China which is an area with large temperature variation.

**Method**: The O&ED visits records for CVDs of 3 general hospitals and the inpatient records for CVDs of 4 general hospitals were collected from January 1, 2013 to December 31, 2016, in Jinchang City, northwest China. Meteorological and air pollution data were also obtained during the same study period from local meteorological monitoring stations and environmental monitoring station, respectively. A generalized additive model (GAM) with Poisson regression was employed to analyze the effects of TC24 on O&ED visits and hospitalizations for CVDs.

**Results:** V-shaped relationship were found between TC24 and O&ED visits and hospitalizations for CVDs including total CVD, hypertension, coronary heart disease (CHD) and stroke. Stratified analysis showed that men and patients over 65 years old were more susceptible to temperature changes. Whether heating may modify the effects of TC24 on O&ED visits and hospitalizations for CVDs.

**Conclusion:** TC24 can affect the O&ED visits and hospitalizations for CVDs in this study. This study provides useful data for policy makers to better prepare local responses to the impact of changes in temperatures on population health.


# 1. Background

Cardiovascular diseases (CVDs) are the most common non-communicable diseases and the leading cause of global mortality (Moazzeni et al. 2021). According to the latest research (Roth et al. 2020) about the Global Burden of Disease (GBD) showed that the cases of total CVD nearly doubled from 271 million in 1990 to 523 million in 2019, and the number of CVD deaths steadily increased from 12.1 million in 1990, reaching 18.6 million in 2019. So, there is an urgent need to focus on implementing existing cost-effective policies and interventions.

24-hour temperature change (TC24), a meteorological indicator reflecting changes in daytime temperature, is calculated by the current day's mean temperature minus the previous day's mean temperature. As the increased weather variability and climate instability, the frequency, intensity and duration of TC24 have shown an increasing trend(Epstein 2005; Xu et al. 2016). Previous studies(Goldberg et al. 2011; Guo et al. 2011) have shown that daytime temperature sudden changes can significantly increase the risk of diseases and death among population, which also indicated that TC24 can be a parameters reflecting the effect of changes in meteorological environment on human health(Cheng et al. 2014b; Goldberg et al. 2011; Kim et al. 2016; Lin et al. 2013).

Previous epidemiological studies have found significant evidence that TC24 was positively correlated to the non-accidental mortality, CVDs and respiratory disease mortality(Cheng et al. 2014b; Li et al. 2020; Lin et al. 2013). For instance, Guo et al. (Guo et al. 2011) found that non-accidental mortality increased by 15.7% (95%CI:2.4%, 30.7%) for per 3℃ decrease in negative TC24, CVDs mortality increased by 35.3% (95%CI:3.3%, 77.2%) for per 3℃increase in positive TC24, and people aged under 65 years were more vulnerable in Brisbane, Australia; CVDs mortality increased by 25.2% (95%CI:13.3%, 38.6%) for per 3℃ decrease of negative TC24, and people aged 75 years and older were more vulnerable in Los Angeles, USA. Another study(Zhan et al. 2017) in 106 communities of United States found that TC24 was associated with non-accidental, CVDs and respiratory disease mortality, but negative temperature change showed a protective factor for death, which is inconsistent with other results, the relative risk of extreme negative temperature change was 0.41–0.63. In addition, there was a study showed a significant association between diurnal temperature range and emergency department visits in Charlottesville(Davis et al. 2020), exposure to temperature variability has been found the association with increased risk of hospitalization for ischemic heart disease(Zhao et al. 2019b). However, the study on the relationship between TC24 and CVDs morbidity was relatively limited. Existing research mainly focuses on the relationship between TC24 and death for c CVDs. Meanwhile, most studies only analyze the total CVDs deaths, there are not many studies involving cause-specific CVDs. In terms of the types of diseases, no study considered the association between both outpatient and emergency department(O&ED) visits and hospitalizations for CVDs and TC24 in one study.

In this context, in order to explore the underlying effect of temperature variability on human health, a time series analysis was conducted to analyze the association between TC24 and both O&ED visits and hospitalizations for total CVD, hypertension, coronary heart disease (CHD) and stroke in an area with large temperature differences in northwest China.

## 2. Materials And Methods

# 2.1 O&ED visits and hospitalizations data

The O&ED visits records for CVDs of 3 general hospitals and the inpatient records for CVDs of 4 general hospitals were collected, from January 1, 2013 to December 31, 2016, in Jinchang City, northwest China. The information about each patient's date of O&ED visits or hospitalizations, medical treatment number, sex, age, and principal diagnosis were extracted. All CVDs were identified based on the primary diagnosis according to the International Classification of Diseases codes (10th Revision, ICD-10), including total cardiovascular disease (ICD-10: I00-I99, total CVD), hypertension (ICD-10: I10-I15), coronary heart disease (ICD-10: I20-I25, CHD), and stroke (ICD-10: I60-I65).

# 2.2 Meteorological and air pollution data

The meteorological data, including daily minimum, mean and maximum temperature, atmospheric pressure, relative humidity and mean wind speed, were derived between January 1, 2013 and December 31, 2016 from Jinchang Meteorological Bureau. The air pollution data during the same period were obtained from Jinchang Environmental Monitoring Station, mainly including particulate matter less than 10μm in aerodynamic diameter ($PM_{10}$), sulfur dioxide ($SO_2$), and nitrogen dioxide ($NO_2$). The meteorological data and pollutant data used in this manuscript were the average value of Jinchang City. The location distribution of Environmental Monitoring Stations and the hospitals in Jinchang City is shown in the Fig. 1.

TC24 refers to the difference between the average temperature of the day and the average temperature of the previous day. The TC24 was divided into two parts: negative temperature change and positive temperature change, a negative difference is a negative temperature change, which means that the temperature decreases and the temperature change is less than zero, a positive difference is a positive temperature change, which means that the temperature increases and the temperature change is greater than zero.

## 2.3 Statistical methods

A generalized additive model (GAM) based on a quasi-poisson regression was used to analyze the associations between TC24 and O&ED visits and hospitalizations. The smooth spline function was applied to control the potential effect of long-term trends and nonlinear confounding effects of weather conditions (temperature, relative humidity, air pressure, and wind speed). Day of the week (DOW) and holidays as the variable factors were controlled due to the possible variations in admission events during the week and on holidays. According to the actual heating time, a year can be divided into non-heating months (from April to October) and heating months (from November to March of the following year). The season was added in the model as a dummy variable. $PM_{10}$, $SO_2$ and $NO_2$ were directly introduced into model control as linear variables. The basic model was as follows:

$$\begin{aligned}\mathrm{Log}[\mathrm{E}(\mathrm{Yt}|\mathrm{X})] = {} & s(\mathrm{Time}, df_1) + as.factor(\mathrm{Dow}) + \mathrm{Holiday} + \mathrm{Season} \\ & + s(\mathrm{Temp}, df_2) + s(\mathrm{Rh}, df_3) + s(\mathrm{Windsp}, df_4) \\ & + s(\mathrm{Pressure}, df_5) + \mathrm{PM}_{10} + \mathrm{SO}_2 + \mathrm{NO}_2 \qquad (1)\end{aligned}$$

Where Yt|X is daily counts of the O&ED visits and hospitalizations for CVDs; E(Yt|X) is the expected number of the O&ED visits and hospitalizations; s() is smoothing spline function. Time represents long-term trend. Temp represents temperature. Rh represents relative humidity. Windsp represents wind speed. Pressure represents atmospheric pressure. Dow represents day of the week. $df_{1\text{-}5}$ is the degree of freedom for each index, which is determined by the minimum principle of Akaike Information Criterion (AIC)(Deng et al. 2020; Phosri et al. 2020).

Then TC24 was introduced into the model (1), according to the minimum principle of AIC, the optimal fitting model was selected to draw the exposure response curve of TC24 with the O&ED visits and hospital admissions for CVDs. Considering that the cumulative lag effect of TC24 has been counterbalanced(Zhai et al. 2021), only the single lag effect (Lag0-Lag7) is analyzed. Then the maximum effect estimate was selected for subsequent analysis study. In addition, using distributed lag non-linear model (DLNM)(Gasparrini 2014) to capture the complete lag-response curve of TC24 on CVDs verified and compared the results obtained by GAM. Then the single day lag influence was calculated to effectively depict the characteristics of the association between negative TC24 and positive TC24 and CVDs, and the optimal fitting models were applied to investigate the impact of TC24 on subgroups according to gender (male and female) and age groups (< 65, 65–74 and ≥ 75) (Park et al. 2021; Varano et al. 2021). At the same time, we also conduct a stratified analysis of heating and non-heating months.

Sensitivity analyses were conducted in non-heating months, removing the confounding effects of heating months, and compare with the effect of the whole year. In addition, considering that the effect of outdoor average temperature and $PM_{10}$ on O&ED visits and hospitalizations also has a significant lag effect, the same lag days of TC24 were used for sensitivity analysis according to the results reported in China(Madaniyazi et al. 2016) and the United States(Halonen et al. 2011) to further clarity the TC24 impact on O&ED visits and hospitalizations in this study.

The excess risk (ER, with 95% confidence intervals (CIs)) was used to reflect the estimates of the TC24 effect on the O&ED visits and hospitalizations for CVDs at specific lag days with a 1℃ change in TC24. All statistical analyses were performed using “mgcv” package in R statistical software version 3.6.2. Statistically significant level was defined as *P*-values less than 0.05 (2-sided).

# 3. Results

## 3.1 Description Statistics

Table 1 shows the distribution characteristics of the O&ED visits and hospitalizations for CVDs, meteorological and environmental factors from 2013 to 2016 in Jinchang. A total of 138,367 O&ED visits were collected, the average daily counts of O&ED visits was 95 cases. 78,229 cases were admitted as hypertension, 24,175 cases were admitted as CHD and 8,106 cases were admitted as stroke. A total of 34,699 hospitalizations for CVDs were obtained, the average daily counts of hospitalizations was 24 cases. Of the total number of cases, 9,253 cases were admitted as hypertension, 8,688 were admitted as CHD and 5,310 were admitted as stroke. During the study period, the average of TC24, negative temperature change and positive temperature change were 0.003℃, -2.05℃ and 1.84℃, respectively. The mean temperature, relative humidity, wind speed and atmospheric pressure in Jinchang were 9.95℃, 39.57%, 1.78m/s and 848.88hpa, respectively. The maximum daily temperature reached 25.30℃. The average concentrations of $PM_{10}$, $SO_2$ and $NO_2$ were 104.82ug/m$^3$, 48.72ug/m$^3$ and 20.07ug/m$^3$, respectively.

Table 1
Descriptive statistics of OEVs, hospitalizations, meteorological factors and pollutants in Jinchang from 2013 to 2016

| Variables | Number | Mean ± SD | Min. | $P_{25}$ | $P_{50}$ | $P_{75}$ | Max. |
|---|---|---|---|---|---|---|---|
| O&ED visits | | | | | | | |
| Total CVD | 138367 | 94.71 ± 58.23 | 3.00 | 54.00 | 94.00 | 119.00 | 347.00 |
| Hypertension | 78229 | 53.54 ± 40.04 | 1.00 | 27.00 | 48.00 | 67.00 | 216.00 |
| CHD | 24175 | 16.55 ± 10.22 | 0.00 | 9.00 | 16.00 | 21.00 | 78.00 |
| Stroke | 8106 | 5.55 ± 4.04 | 0.00 | 3.00 | 5.00 | 8.00 | 28.00 |
| Hospitalizations | | | | | | | |
| Total CVD | 34699 | 23.75 ± 11.19 | 1.00 | 15.00 | 23.00 | 31.00 | 67.00 |
| Hypertension | 9253 | 6.33 ± 4.35 | 0.00 | 3.00 | 6.00 | 9.00 | 39.00 |
| CHD | 8688 | 5.95 ± 3.19 | 0.00 | 4.00 | 6.00 | 8.00 | 19.00 |
| Stroke | 5310 | 3.63 ± 2.22 | 0.00 | 2.00 | 3.00 | 5.00 | 14.00 |
| Meteorological factors | | | | | | | |
| TC24 (°C) | | 0.003 ± 2.512 | -12.60 | -1.40 | 0.20 | 1.60 | 7.10 |
| Negative TC24 (°C) | | -2.05 ± 1.92 | -12.60 | -2.70 | -1.60 | -0.70 | -0.02 |
| Positive TC24 (°C) | | 1.84 ± 1.30 | 0.10 | 0.80 | 1.60 | 2.60 | 7.10 |
| Mean temperature (°C) | | 9.95 ± 10.97 | -16.40 | 0.20 | 11.40 | 19.30 | 29.60 |
| Relative humidity (%) | | 39.57 ± 16.90 | 2.00 | 26.00 | 38.00 | 50.00 | 96.00 |
| Wind speed (m/s) | | 1.78 ± 0.81 | 0.30 | 1.20 | 1.60 | 2.20 | 5.30 |
| Atmospheric pressure (hpa) | | 848.88 ± 5.49 | 833.80 | 844.90 | 848.70 | 852.70 | 868.30 |
| Air pollutant concentrations | | | | | | | |

Note: SD: standard deviation. $P_{25}$ = 25th percentile. $P_{50}$ = 50th percentile. $P_{75}$ = 75th percentile. Min: Minimum. Max: Maximum.

| Variables | Number | Mean ± SD | Min. | $P_{25}$ | $P_{50}$ | $P_{75}$ | Max. |
|---|---|---|---|---|---|---|---|
| $PM_{10}$ (μg /$m^3$) | | 104.82 ± 104.02 | 10.00 | 55.00 | 80.00 | 119.33 | 1783.33 |
| $SO_2$ (μg /$m^3$) | | 48.72 ± 39.70 | 2.00 | 20.33 | 39.67 | 64.00 | 281.00 |
| $NO_2$(μg /$m^3$) | | 20.07 ± 8.84 | 3.33 | 13.33 | 19.00 | 25.67 | 62.00 |

Note: SD: standard deviation. $P_{25}$ = 25th percentile. $P_{50}$ = 50th percentile. $P_{75}$ = 75th percentile. Min: Minimum. Max: Maximum.

## 3.2 Relationship between TC24 and O&ED visits and hospitalizations for CVDs

A Spearman correlation analysis showed that there is no serious collinearity between meteorological factors, which does not affect the fitting of the model (Table S1). Figure 2 shows the exposure-response relationship between TC24 and O&ED visits and inpatients for cause-specific CVD at the optimal lag days. It can be seen from the figure that there are roughly V-shaped curves between TC24 and the O&ED visits and hospitalizations for total CVD, hypertension, CHD and stroke. There is a lowest point near 0°C, which is lower or higher than 0°C, the number of O&ED visits and hospitalized patients showed an increasing trend. In addition, lag-response curve of TC24 on CVDs captured by DLNM is shown in the supplementary materials (Figure S1 and Figure S2). Both the trend of 3D graph and single lag exposure response curve are consistent with the shape of GAM fitting.

Table 2 shows the effects of TC24 on O&ED visits and hospitalizations for total CVD, hypertension, CHD, stroke at optimal lag days in Jinchang during 2013–2016. The results showed that negative and positive TC24 both had significant effects on OEVs for total CVD, hypertension, and CHD, while no significant effect on stroke. The largest estimates of negative TC24 effect on the O&ED visits for total CVD, hypertension and CHD were − 1.86% (95%CI: -2.26%, -1.47%), -2.12% (95%CI: -2.64%, -1.59%) and − 1.41% (95%CI: -2.40%, -0.40%), respectively. And the estimates of positive TC24 effect were 3.01% (95%CI: 2.41%, 3.62%), 3.90% (95%CI: 3.09%, 4.71%) and 2.66% (95%CI: 1.23%, 4.12%).

Simultaneously, the significant association between the negative TC24 and the hospitalizations for the total CVD, hypertension, and stroke was found, while only total CVD hospitalization was found to be statistically significant with TC24. The largest effect estimates of negative TC24 on hospitalizations for total CVD, hypertension and stroke were − 1.18% (95%CI: -1.97%, -0.38%), -2.23% (95%CI: -3.72%, -0.71%) and − 2.19% (95%CI: -4.16%, -0.17%), respectively.

Table 2
The ER and 95%CI for the association between TC24 and the O&ED visits and hospitalizations for cause-specific CVD

| | Lag days | Negative TC24 | | Positive TC24 | |
|---|---|---|---|---|---|
| | | ER (%) | 95% CI | ER (%) | 95% CI |
| O&ED visits | | | | | |
| Total CVD | Lag0 | -1.17* | (-1.68, -0.65) | 1.14* | (0.54, 1.76) |
| | Lag1 | -1.43* | (-1.90, -0.96) | 0.51 | (-0.11, 1.13) |
| | Lag2 | -1.08* | (-1.51, -0.65) | 3.01* | (2.41, 3.62) |
| | Lag3 | -0.28 | (-0.72, 0.15) | 1.24* | (0.66, 1.83) |
| | Lag4 | -0.79* | (-1.21, -0.37) | 1.53* | (0.92, 2.14) |
| | Lag5 | -1.86* | (-2.26, -1.47) | 0.93* | (0.31, 1.55) |
| | Lag6 | -1.05* | (-1.46, -0.64) | 2.28* | (1.68, 2.88) |
| | Lag7 | -1.00* | (-1.42, -0.57) | 0.39 | (-0.21, 0.99) |
| Hypertension | Lag0 | -1.68* | (-2.35, -1.00) | 1.55* | (0.74, 2.37) |
| | Lag1 | -1.87* | (-2.49, -1.24) | 1.57* | (0.75, 2.40) |
| | Lag2 | -1.67* | (-2.23, -1.11) | 3.90* | (3.09, 4.71) |
| | Lag3 | -0.82* | (-1.38, -0.25) | 1.88* | (1.10, 2.66) |
| | Lag4 | -1.30* | (-1.85, -0.75) | 1.64* | (0.83, 2.45) |
| | Lag5 | -2.12* | (-2.64, -1.59) | 1.68* | (0.85, 2.52) |
| | Lag6 | -1.34* | (-1.88, -0.80) | 2.48* | (1.69, 3.28) |
| | Lag7 | -1.30* | (-1.86, -0.74) | 0.92* | (0.13, 1.73) |
| CHD | Lag0 | -0.62 | (-1.86, 0.64) | 0.29 | (-1.12, 1.71) |
| | Lag1 | -1.22* | (-2.35, -0.09) | -1.33 | (-2.75, 0.10) |
| | Lag2 | -0.83 | (-1.85, 0.21) | 2.66* | (1.23, 4.12) |
| | Lag3 | 0.22 | (-0.84, 1.29) | 0.20 | (-1.17, 1.59) |

Note: *: $P < 0.05$

| | Lag days | Negative TC24 | | Positive TC24 | |
|---|---|---|---|---|---|
| | | ER (%) | 95% CI | ER (%) | 95% CI |
| | Lag4 | -0.12 | (-1.13, 0.91) | 0.35 | (-1.08, 1.80) |
| | Lag5 | -1.35* | (-2.29, -0.40) | 0.30 | (-1.18, 1.81) |
| | Lag6 | -1.04* | (-2.02, 0.05) | 2.45* | (1.02, 3.89) |
| | Lag7 | -1.41* | (-2.40, -0.40) | -0.95 | (-2.35, 0.47) |
| Stroke | Lag0 | -0.01 | (-2.14, 2.17) | 0.53 | (-1.94, 3.07) |
| | Lag1 | -1.52 | (-3.42, 0.41) | -0.28 | (-2.77, 2.27) |
| | Lag2 | 0.12 | (-1.68, 1.95) | 1.98 | (-0.42, 5.09) |
| | Lag3 | -0.15 | (-1.87, 1.60) | -0.61 | (-2.99, 4.44) |
| | Lag4 | -0.06 | (-1.80, 1.71) | 2.21 | (-0.27, 4.76) |
| | Lag5 | -0.01 | (-1.68, 1.69) | 1.47 | (-1.08, 4.08) |
| | Lag6 | -0.98 | (-2.61, 0.69) | 0.71 | (-1.71, 3.19) |
| | Lag7 | -0.55 | (-2.30, 1.23) | -1.46 | (-3.83, 0.97) |
| Hospitalizations | | | | | |
| Total CVD | Lag0 | 0.48 | (-0.50, 1.46) | -1.38 | (-2.54, -0.21) |
| | Lag1 | 0.33 | (-0.61, 1.27) | -0.90 | (-2.06, 0.27) |
| | Lag2 | -0.58 | (-1.40, 0.25) | 0.85 | (-0.32, 2.03) |
| | Lag3 | -0.53 | (-1.35, 0.29) | 0.30 | (-0.84, 1.46) |
| | Lag4 | -0.42 | (-1.24, 0.40) | 1.95* | (0.76, 3.14) |
| | Lag5 | -1.04* | (-1.83, -0.25) | 0.78 | (-0.41, 1.98) |
| | Lag6 | -1.15* | (-1.94, -0.36) | 0.25 | (-0.91, 1.42) |
| | Lag7 | -0.62 | (-1.44, 0.20) | 0.22 | (-0.94, 1.39) |
| Hypertension | Lag0 | 1.52 | (-0.50, 3.58) | -0.16 | (-2.39, 2.12) |
| | Lag1 | -0.16 | (-1.93, 1.64) | -0.65 | (-2.93, 1.69) |
| | Lag2 | -1.24 | (-2.78, 0.33) | 0.28 | (-1.99, 2.60) |
| | Lag3 | -0.49 | (-2.07, 1.12) | -1.26 | (-3.44, 0.97) |

Note: *: $P < 0.05$

| | Lag days | Negative TC24 | | Positive TC24 | |
|---|---|---|---|---|---|
| | | ER (%) | 95% CI | ER (%) | 95% CI |
| | Lag4 | -0.76 | (-2.34, 0.85) | 0.83 | (-1.44, 3.15) |
| | Lag5 | -0.49 | (-2.03, 1.08) | 1.30 | (-0.96, 3.61) |
| | Lag6 | -2.23* | (-3.72, -0.71) | 2.13 | (-0.11, 4.42) |
| | Lag7 | -1.49 | (-3.03, 0.09) | 1.04 | (-1.21, 3.33) |
| CHD | Lag0 | 0.10 | (-1.82, 2.05) | -1.74 | (-4.02, 0.60) |
| | Lag1 | 0.77 | (-1.05, 2.62) | -0.16 | (-2.46, 2.19) |
| | Lag2 | -0.47 | (-2.10, 1.19) | 1.11 | (-1.18, 3.45) |
| | Lag3 | -0.12 | (-1.75, 1.53) | 0.89 | (-1.39, 3.23) |
| | Lag4 | -0.26 | (-1.91, 1.41) | 1.70 | (-0.58, 4.03) |
| | Lag5 | -0.85 | (-2.42, 0.73) | 1.79 | (-0.55, 4.18) |
| | Lag6 | -0.09 | (-1.70, 1.54) | 0.07 | (-2.23, 2.42) |
| | Lag7 | -0.15 | (-1.79, 1.51) | -1.73 | (-3.98, 0.56) |
| Stroke | Lag0 | 1.25 | (-1.28, 3.84) | -1.22 | (-4.08, 1.72) |
| | Lag1 | -0.73 | (-2.96, 1.55) | -2.27 | (-5.15, 0.70) |
| | Lag2 | -0.64 | (-2.68, 1.44) | -0.18 | (-3.06, 2.79) |
| | Lag3 | -2.19* | (-4.16, -0.17) | 2.28 | (-0.59, 5.23) |
| | Lag4 | 0.22 | (-1.87, 2.36) | 1.23 | (-1.73, 4.28) |
| | Lag5 | -1.18 | (-3.15, 0.83) | 0.05 | (-2.93, 3.12) |
| | Lag6 | -1.27 | (-3.28, 0.79) | -0.15 | (-3.04, 2.83) |
| | Lag7 | -0.88 | (-2.93, 1.21) | 2.80 | (-0.16, 5.85) |

Note: *: $P < 0.05$

## 3.3 Stratified analysis

The results of stratified analysis showed that the negative and positive TC24 both have a greater impact on males on the O&ED visits for all CVDs. Except for stroke O&ED visits, the effect estimates of TC24 were greater in people over 65 years of age than people under 65 years of age. For the hospitalizations, the significant association was found between the negative TC24 and admissions for total CVD and hypertension, and the effect estimates were the greatest in patients over 75 years old. More statistical significance of positive TC24 was found in hospitalized patients over 65 years of age for total CVD, CHD and stroke (Fig. 3). The effects of TC24 on CVDs in non-heating months are stronger than heating months, the ER of cause-specific cardiovascular diseases exposure to TC24 in non-heating months and heating months are shown in supplementary materials (Table S2 and Table S3).

## 3.4 Sensitivity analysis

Figure 4 and Fig. 5 show the effects of negative and positive TC24 on the O&ED visits and hospitalizations for cause-specific CVDs in full year and non-heating months, respectively. Compared with the effect of TC24 in full year, the effect of both negative and positive TC24 was stronger in the non-heating months on both O&ED visits and hospitalizations for CVDs.

Figure S3 shows the effect of TC24 on total CVDs after considering the lag effect of temperature and $PM_{10}$, the trend of the exposure response curve is consistent with the result of core model.

# 4. Discussion

This study examined the effect of TC24 on the O&ED visits and hospital admissions for cause-specific CVDs in Jinchang of northwest China, which found that the exposure-response relationship showed V-shaped. Both negative and positive TC24 have an impact on the admissions for CVDs. With the decrease of negative TC24 and the increase of positive TC24, the number of patients with total CVD, hypertension, CHD and stroke shows an increasing trend. Additionally, the effect of TC24 on men and patients over 65 years of age was greater than that of women and patients under 65 years of age. Indoor heating in winter may have a modifying effect on the TC24 effect.

Many researchers have described U-, V- or J-shaped associations between temperature and cardiovascular mortality or admission(Aklilu et al. 2020; McMichael et al. 2008; Turner et al. 2012). Similarly, this study found a "V" type relationship between TC24 and O&ED visits and hospital admissions for cause-specific CVDs, which showed an increased risk of admissions for CVDs with changes in both negative and positive TC24. A 1°C decrease of negative TC24 corresponded to 0.79%-2.12% increase in O&ED visits, and 1.04%-2.23% increase in hospital admissions. A 1°C increase of positive TC24 corresponded to 0.92%-3.90% increase in O&ED visits, and 1.95% increase in hospital admissions. Some previous research results were consistent with our study. Guo et al.(Guo et al. 2011) found that there was a "U" shaped curve between TC24 and the deaths for CVDs, and an increase of more than 3°C was associated with RR of 1.353 (95%CI: 1.033, 1.772) for cardiovascular mortality in Brisbane, Australia. Zhan et al.(Zhan et al. 2017) analyzed the correlation between the number of deaths and TC24 in 106 communities in the United States, and found that TC24 could significantly increase the risk of death for CVDs, the relative risk was 1.52(95%CI: 1.40, 1.65)for extremely positive TC24 (99th percentile) on CVDs mortality. Due to the limited research on the impact of TC24 on cardiovascular diseases, it cannot be directly compared with these studies. However, previous studies on the relationship between temperature changes and the number of emergency and hospitalizations for cardiovascular diseases have showed the similar results. For instance, a case-crossover study design suggested that emergency department visits for CVDs were related to a large decrease in temperature with significant odds ratio (OR): 1.29 (95%CI:1.1, 1.52)(Ostendorf et al. 2020). In addition, the OR of hospitalization for cardiac arrhythmia per 1°C increase in temperature variability was 1.012 (95% CI: 1.010, 1.015)(Zhao et al. 2019a). Kyobutungi et al.(Kyobutungi et al. 2005) conducted a case-crossover study of 303 patients with DTR and found that large changes in temperature (> 5°C) were associated with an increased risk of acute ischemic stroke regardless of whether the change was negative or positive, The OR for DTR > 5°C compared to no change in temperature was 2.0 (95% CI: 0.7, 5.9). In addition, the results of this study show that the effect of TC24 on O&ED visits was stronger than that on hospitalizations. These small absolute health effects in relation to exposures are biologically expected, for individuals, the impact is not so great that they are directly hospitalized, and yet the associations remain highly important from a public health standpoint since these small risks impact millions of people in a continuous manner (Brook and Kousha 2015). O&ED visits are a good indicator of the acute effects of temperature change, comparing with direct hospitalization, because when people in China with cardiovascular disease feel uncomfortable, the first choice they usually make is to visit the hospital emergency department(Guo et al. 2010).

The underlying mechanism of the effects of TC24 on CVDs in the population is still unclear. But as far as the current research results are concerned, TC24 will have adverse effects on patients with CVDs. With a large change in temperature, people's automatic thermoregulation system may not well adapt to sudden temperature change, particularly for people with certain disease conditions. Some studies showed that sudden changes in temperature would increase the blood cholesterol levels, blood pressure, plasma fibrinogen concentrations, peripheral vasoconstriction, heart rate, platelet viscosity, and reduce the immune system's resistance (Guo et al. 2011; Schneider et al. 2008). In addition, several studies have speculated that the relationship may, in part, be due to disruption of the autonomic nervous system and activation of the inflammation-coagulation cascade(Čulić 2014; Franciosi et al. 2017). The rapid cooling of ambient temperature may trigger sympathetic hyperactivity, which disturbs cardiac electrical activity(Franciosi et al. 2017), which may cause some adverse outcome. And temperature-induced damage is thought to be related to enhance sympathetic reactivity followed by activation of the sympathetic nervous system, renin-angiotensin system, as well as dehydration and a systemic inflammatory response(Liu et al. 2015). Studies on the underlying mechanism by which temperature challenge induces pathophysiological response and CVD await profound and lasting investigation.

Gender has been observed to be an effect modifier of the association between temperature variability and health outcomes. Some studies found that men or women were more susceptible while other studies indicated that there was no significant gender difference(Cheng et al. 2014a; Yang et al. 2018; Zhao et al. 2019a).This study found that men were more sensitive to the change of temperature than women. Lin et al.(Lin et al. 2013) found that increased daytime temperature in Guangzhou could significantly increase the risk of death in men, but the effect on women was not statistically significant. Another time series study(Cheng et al. 2016b) in Ma'anshan City, China also found that men were sensitive to daytime temperature changes. These are consistent with the results of this study. The inconsistency among these studies may be due to regional or population factors(Liu et al. 2015). For instance, maybe more opportunities for occupational exposure could partially explain that males were reported to be more affected by weather exposures(Baker et al. 2014). And males and females have different physiological structure, living habits and heat stress during work(Wang et al. 2020). The biological mechanism of gender as an effect modifier in the field of temperature-related epidemiology still needs more research to verify.

In addition, several studies(Ebi et al. 2004; Schneider et al. 2008) have suggested that the elderly were susceptible to temperature change, such as Cheng et al.(Cheng et al. 2014b) found that people over 65 years of age were more sensitive to TC24. And the association between temperature change and non-external mortality by age group, in Brisbane, people under 65 years of age were vulnerable to a sharp increase in temperature, while those aged 65–74 years were sensitive to a sudden drop in temperature, in Los Angeles, both people aged 65–74 and over 75 years were vulnerable to a sudden temperature drop, while no significant effects of temperature change were found for those under 65 years of age(Guo et al. 2011). Moreover, people over 75 years of age were identified as a particularly vulnerable population to TC24(Zhan et al. 2017). These results were not consistent. This study concluded that TC24 had a more obvious impact on people over 65 years of age. It maybe because as their ability to regulate body temperature is poor, and their adaptability to temperature changes decreases. Temperature changes may induce the increase in heart rate in the elderly(Zhao et al. 2019a), Moreover, The geriatrics people usually suffer from preexisting medical illness and have physiological changes in thermoregulation which make them more vulnerable to temperature change(Aklilu et al. 2020). Therefore, a rapid change of daily temperature may cause a sudden change in the circulation and heart rate of elderly, which may trigger the occurrence of cardiopulmonary and other diseases, and lead to fatal consequence.

The article conducted an analysis of non-heating months for sensitivity, and found that TC24 in non-heating months had a more significant impact on the number of patients with CVDs. Cheng et al.(Cheng et al. 2016a) found that positive TC24 would significantly increase the number of ambulance dispatches, and the risk of ambulance dispatch was higher in summer and autumn (June-November). Also, a study of multiple Korean cities by Lim reported that people were more sensitive to short-term temperature change in summer and autumn(Lim et al. 2012). These results were similar to this article. The possible reason could be that the mean temperature of warm season is larger than that of cold season, and people are more likely to spend more time outside(Xerxes et al. 2015), which increases their exposure to outdoor temperature change and thus results in greater health risk. On the other hand, In the heating months, the indoor temperature is relatively stable, and people stay indoors for longer, reducing the exposure time to outdoor with large temperature changes. After removing the heating months data, the impact was greater than that of the whole year. Therefore, it can be suggested that the overall effect may underestimate the cardiovascular health effect on the population.

It is worth mentioning that this study was conducted based on data of O&ED visits and hospitalizations to analyze the exposure-response relationship curves while adjusting for numerous potential factors. Nonetheless, this study has some limitations. First, this research was an ecological study as with many studies, there may be an ecological fallacy. However, based on previous evidence of the association between temperature changes and risk of illness of people, this bias could be greatly reduced. Second, temperature changes data on individual exposure were not available, the data on temperature change in this study came from local weather monitoring stations which is obtained in the same way in this field. There may be some measurement bias. Third, personal characteristics such as, marital status, education level, and socio-economic status may affect the short-term effects of TC24 on CVDs, this research only involves gender, age and seasons, which could not accurately estimate the effect of TC24 in different groups.

In conclusion, we found there were adverse effects due to TC24 on O&ED visits and hospital admissions in CVDs patients, particularly for males and people aged 65 years in this study. These increased risks of medical visits and admissions during periods of temperature fluctuations highlight the importance of not only considering hot absolute temperatures in relation to human health, but also sudden changes in temperature, particularly for a relatively large temperature change. These results may have significant implication in enhancing our knowledge of climate change-related health impact and allocating local public health resource more efficiently.

# Declarations

**Ethics approval and consent to participate:** The study was approved by the Ethics Committee of Lanzhou University School of Public Health and research subjects signed an informed consent.

**Consent for publication:** Not applicable.

**Availability of data and materials:** The datasets used during the current study are available from the corresponding author on reasonable request.

**Competing interests:** The authors declare that they have no competing interests.

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**Authors' contributions:** Conceptualization: Shan Zheng, Minzhen Wang and Yufeng Wang; Methodology: Xingfu Wei, Qin Shi, Xiangyan Meng, and Wenzhi Zhu; Formal analysis and investigation: Yanli Liu, Xingfu Wei and Qin Shi; Writing - original draft preparation: Qin Shi and Yanli Liu; Writing - review and editing: Shan Zheng, Yana Bai, Yonghong Nie and Feng Kang; Funding acquisition: Shan Zheng.

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# Figures

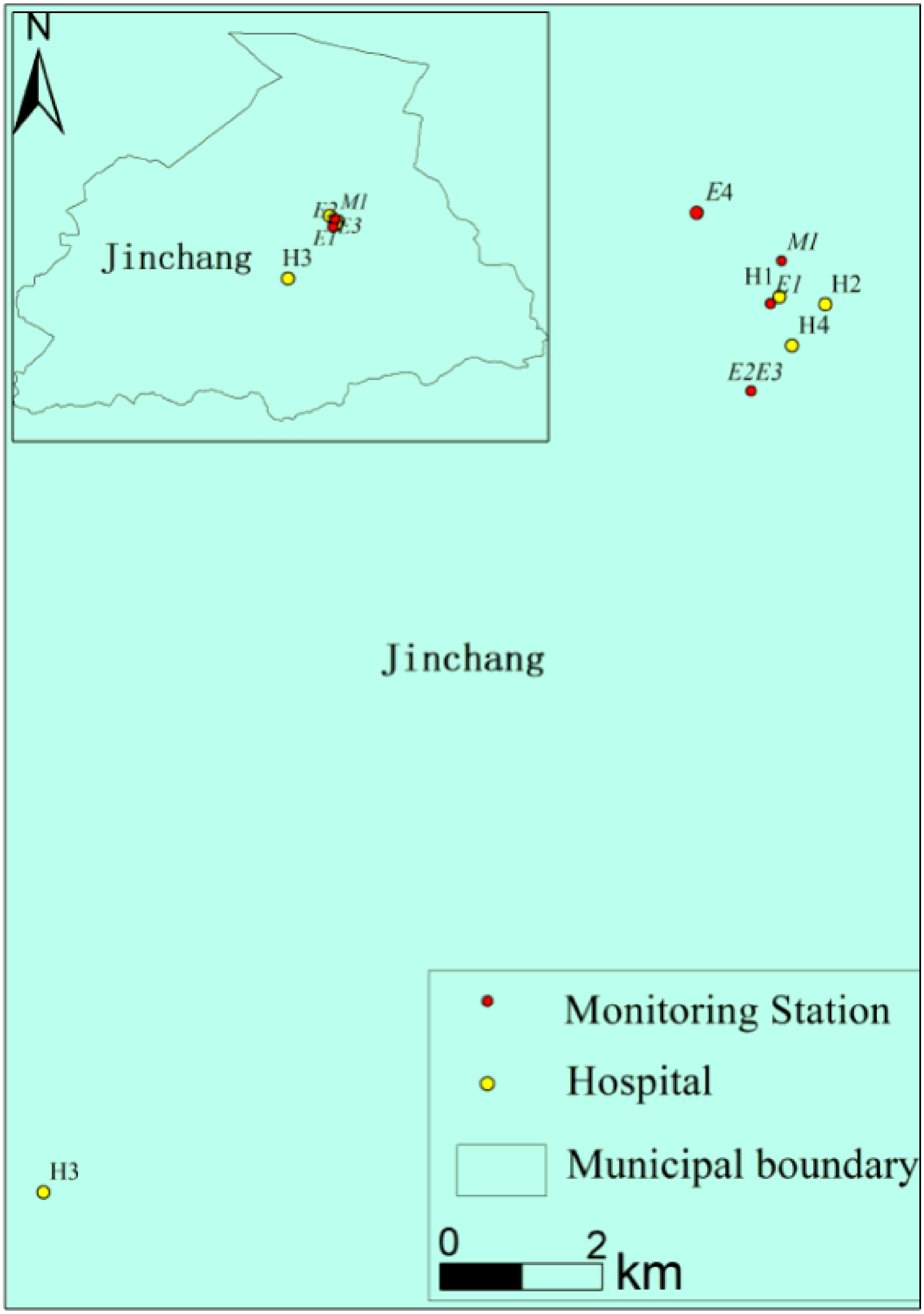
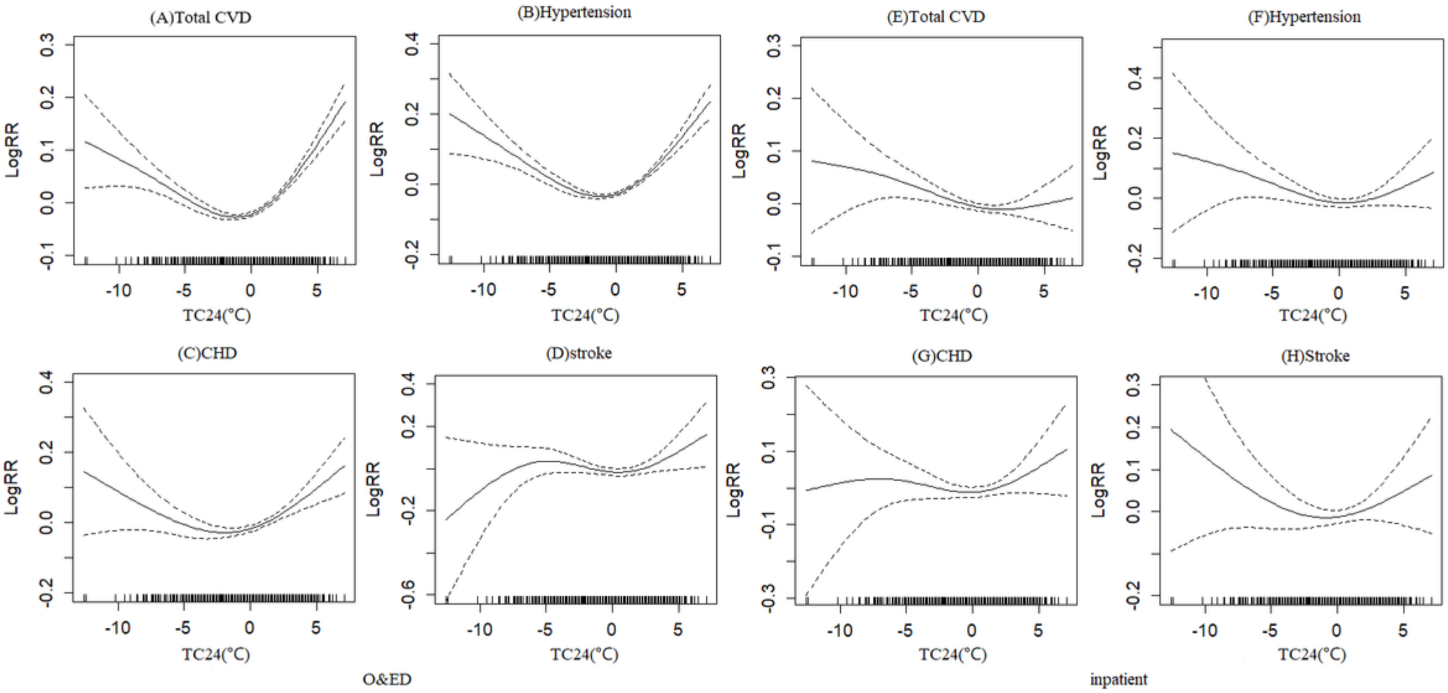


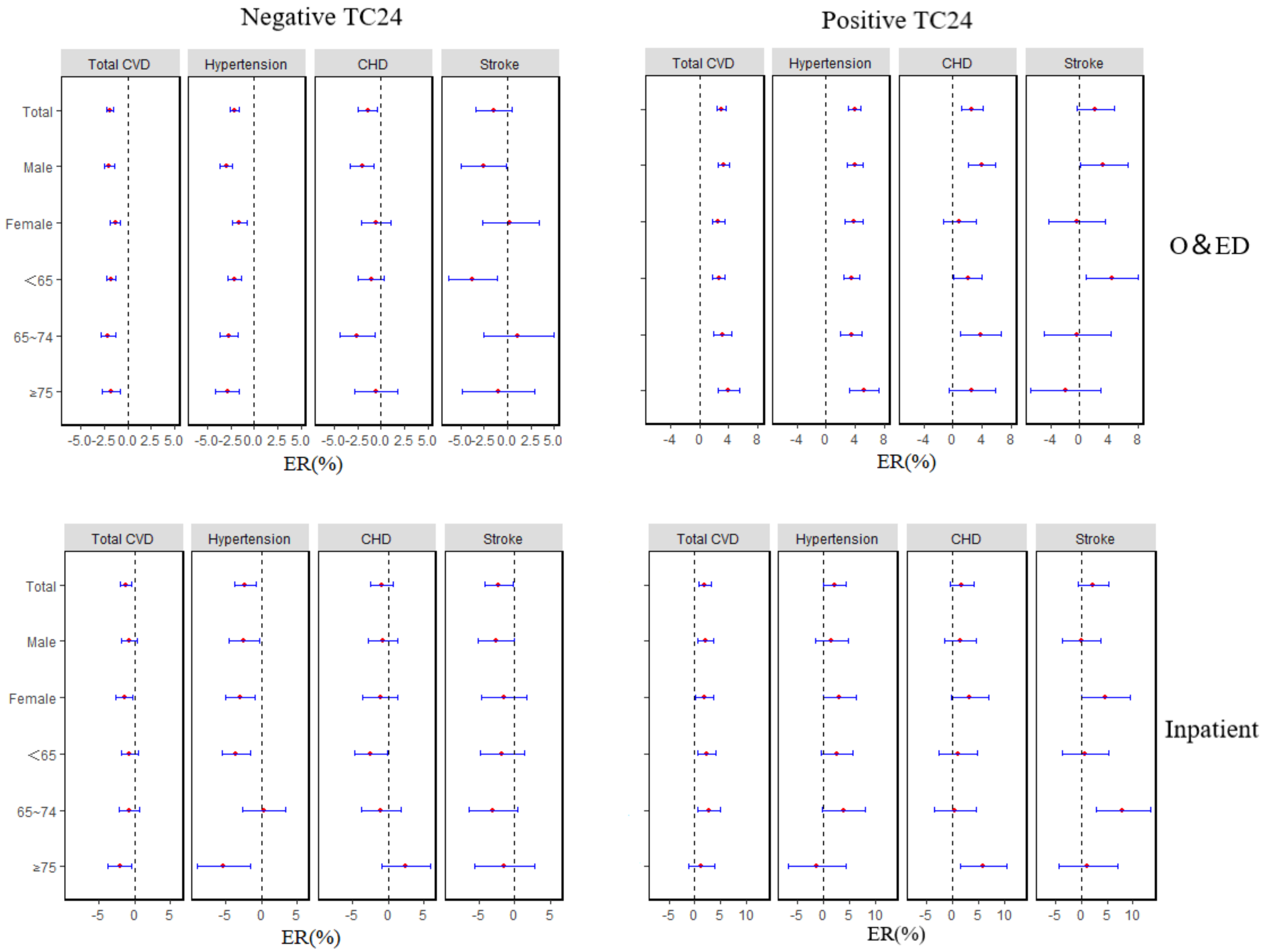

**Figure 1**

Spatial distribution of the Environmental Monitoring Station and the hospitals in Jinchang, China. The solid red circles denote the meteorological station(M1) and 4 environmental monitoring stations (E1, E2, E3, E4). Solid yellow circles indicate the hospitals (H1, H2, H3, H4). Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.



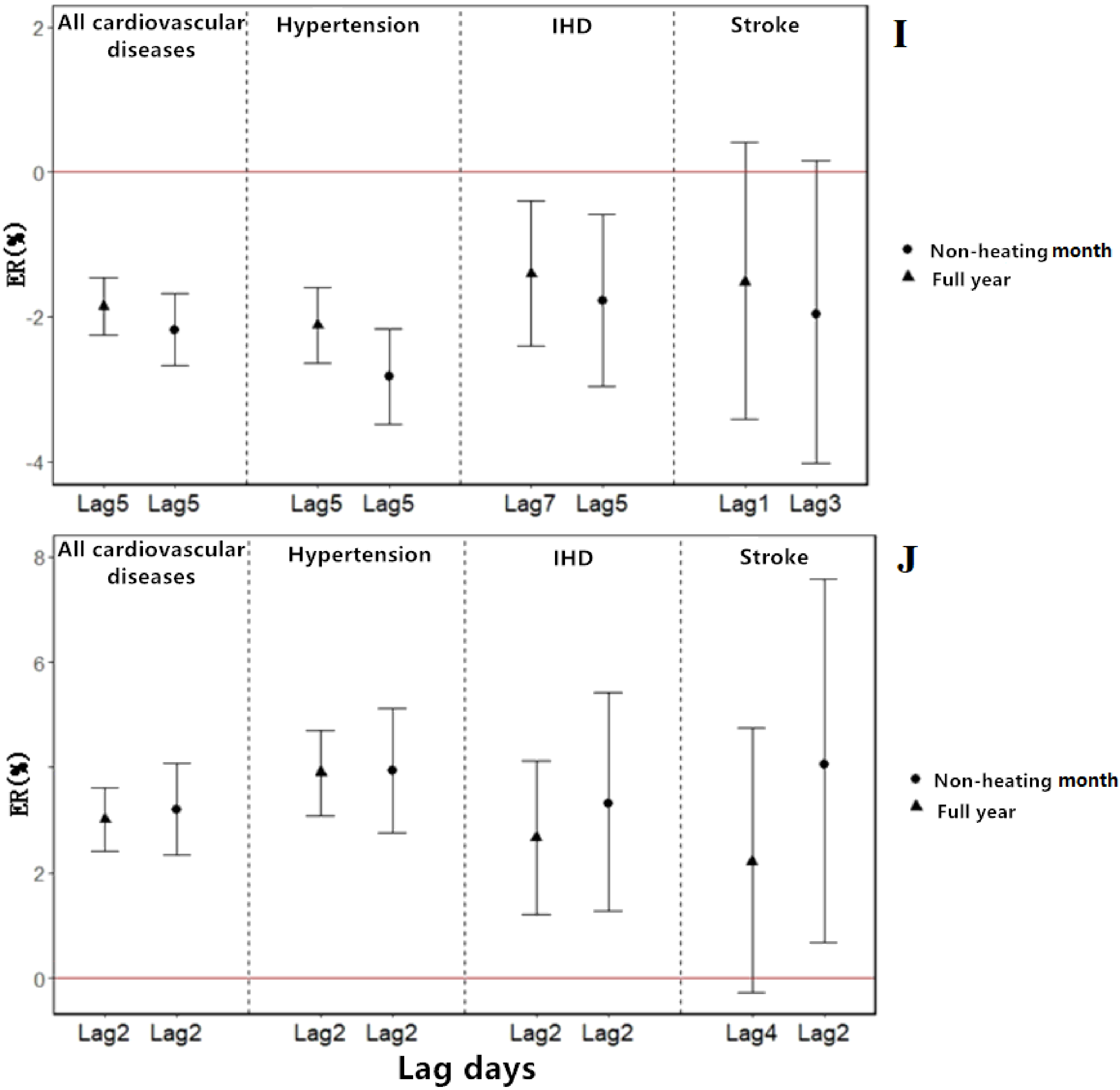

## Figure 2

Exposure-response curve of TC24 on O&ED visits and hospitalizations for total CVD, hypertension, CHD, stroke. A to D shows the association between TC24 and the O&ED visits for CVDs. E to H shows the association between TC24 and hospitalizations for CVDs. The optimal lag days were used for A (Lag2 day), B (Lag2 day), C (Lag2 day), D (Lag4 day), E (Lag6 day), F (Lag6 day), G (Lag5 day), and H (Lag3 day), respectively.




## Figure 3

Effects of TC24 on the O&ED visits and hospitalizations for cause-specific CVDs by gender and age.




## Figure 4

Effects of negative (I) and positive (J) TC24 on O&ED visits for cause-specific CVDs in full year and non-heating months.

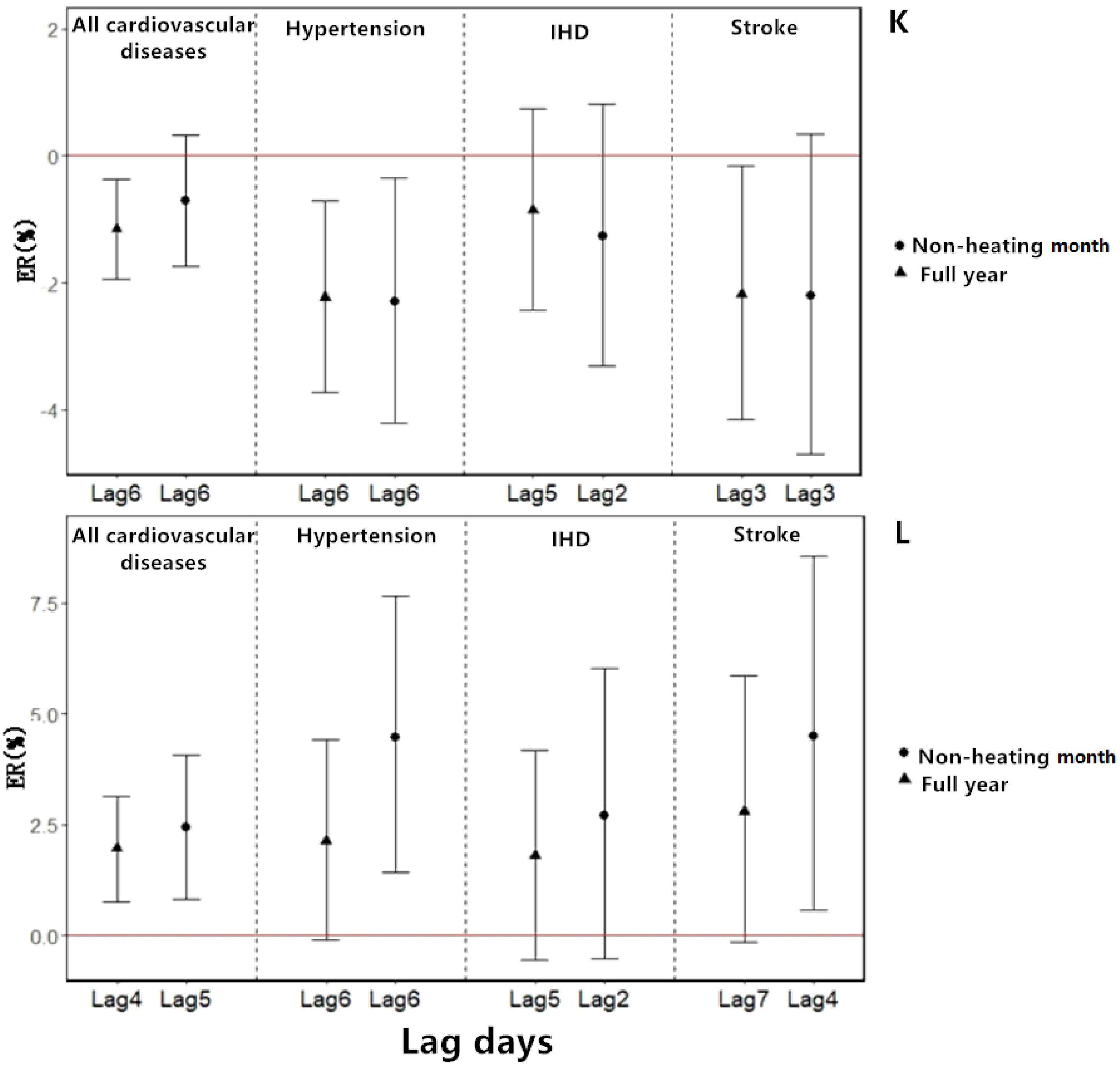



**Figure 5**

Effects of negative (K) and positive (L) TC24 on the hospitalizations for cause-specific CVDs in full year and non-heating months.

## Supplementary Files

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- SupplementaryMaterials.docx