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Research article

Associations of ambient temperature with the CO poisoning risk in China

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ABSTRACT

Although studies have explored the relationship between temperature and CO poisoning, the results are not consistent, and there is still a lack of early warning criteria of temperature related to CO poisoning. In order to comprehensively study the exposure-response relationship between daily average temperature and CO poisoning, and to further explore the early warning criteria of temperature related to CO poisoning, we used daily cases of CO poisoning in 31 National Injury Surveillance System (NISS) surveillance sites in seven administrative geographical regions of China and daily meteorological data obtained from the China Meteorological Science Data Sharing Service Platform from 2009 to 2019 to do the analysis. Daily meteorological data of 698 weather stations across China were interpolated at a $0.01^\circ \times 0.01^\circ$spatial resolution, which were then applied to extract the daily meteorological data of all included NISS sites. The Distributed Lag Non-linear Model (DLNM) model was applied to estimate the exposure-response associations (relative risk, RR) of daily mean temperature with CO poisoning, which was then further used to identify early warning criteria of temperature related to CO poisoning.

A total of 10,618 CO poisoning cases were included in this study, with an average of 0.4 cases per day. There was generally a reverse J-shaped association between temperature and CO poisoning risk, indicating that both low and high temperature may increase the risk of CO poisoning, but low temperature usually has a longer lagged effects than high temperature. Spatialy, the exposure-response associations between temperatue and CO poisoning largely varied among regions, with greater effects of low temperatures in Southern China than in Northern China. The cumulative effects (RR, lag0-6 days) of 10 % percentile temperature ranged from 1.13 (95%CI: 1.01,1.26) in East China to 1.73 (95%CI:1.63,1.83) in South China. We also observed significant spatial variations in the early warning criteria of temperature related to CO poisoning across China. However, the patterns of high temperature effects on CO poisoning and the warning criteria of high temperature were mixed across China. In conclusions, both low temperature and high temperature may increase the risk of CO poisoning in China, and the effect of low temperature is more obvious, especially in South China, Northeast China, and North China. In addition, there is an urgent need to establish air temperature early warning and grading criteria for CO poisoning in different areas of China.

1. Introduction

Globaly, carbon monoxide (CO) poisoning is one of the most common types of fatal poisoning [1]. It has been reported that there are nearly one million cases of CO poisoning worldwide every year, resulting in about 40000 deaths [2]. In recent years, with the strengthening of public health education and the improvement of treatment measures, studies have shown that the overall global mortality rate of CO poisoning decreased by an average of 1.83 % per year from 1990 to 2017, but it is still one of the major public

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health problems in the world, especially in developing countries with uneven economic development [1]. According to global burden of disease study in 2019, the incidence of CO poisoning in China showed an upward trend from 1990 to 2019, and by 2019, the incidence of CO poisoning was 21.82 per 100000, which still caused a serious disease burden [3].

The risk factors related to CO poisoning mainly include fire, gas equipment failure, improper heating, and meteorological factors [4,5]. In recent years, some studies have paid more attention to the effects of meteorological factors, especially air temperature, on CO poisoning [4,6,7]. For example, a study found that air temperature was negatively correlated with CO poisoning, and for every 1 °C increase, the incidence of acute CO poisoning may be reduced by 10 % [7]. Studies from Jinan and Guangdong in China, also showed that cold waves were associated with an increased risk of CO poisoning and the influence had lag effect [6]·[8]. This may be because low temperatures may cause increased indoor heating and limited airflow, resulting in the accumulation of CO, thereby increasing the risk of CO poisoning [4]. However, the effect of high temperatures on CO poisoning is not clear and needs to be explored in further studies.

It is worth noting that in recent years, the Chinese government has formulated some recommended national standards related to CO poisoning and recommended standards for the meteorological industry [9,10], which have made great contributions to the prevention and reduction of CO poisoning. Meanwhile, some studies have also carried out the analysis and early warning and prediction of the relationship between ambient temperature and the risk of CO poisoning [4,6,7,11]. However, there are still some shortcomings: 1) Some related standards [9,10] only specify the grades and standards of non-occupational CO meteorological conditions during winter heating in northern China, which are limited in time and space and are not enough to tackle the challenges of the current epidemic situation and characteristics of CO poisoning deaths in China. 2) The data used in most previous studies come from CO poisoning events (single poisoning $\geq$3 people) that occurred in single or several cities, while CO poisoning reaching the event level, whether fatal or non-fatal poisoning, is only a small part of the overall CO poisoning [4,11], and does not fully reflect the relationship between temperature and CO poisoning. 3) Although some studies showed the effect of low temperatures on CO poisoning, there is still a lack of research on the effect of high temperatures [6,7]. Therefore, a comprehensive understanding of the relationship between temperature and CO poisoning, and the establishment of regional early warning standards will help to prevent and reduce the risk of CO poisoning, in line with the current challenges and needs to deal with the main epidemic characteristics of CO poisoning in China.

To fill in above research gaps, we conducted a time series study that included CO poisoning data from 31 National Injury Surveillance System (NISS) surveillance sites in seven administrative geographic regions of China from 2009 to 2019. We aimed to estimate the region-specific exposure-response relationship between daily temperature and CO poisoning risks, and further identify the warning grading criteria of temperature associated with CO poisoning.

2. Methods

2.1. Study setting and study objects

A total of 31 National Injury Surveillance System (NISS) monitoring sites (counties/districts) were selected in this study, and these NISS sites were distributed in seven administrative regions [North China (5), Northeast China (4), East China (7), Central China (3), South China (3), Northwest (5), and Southwest (4)] (Supplementary Table 1).

2.2. Data collection

Daily CO poisoning data in each NISS site from January 1, 2009 to December 31, 2019 were obtained from the NISS administrated by Chinese Center for Disease Control and Prevention. Considering the small number of daily CO poisoning cases in a single NISS monitoring site, we therefore combined the daily data of all sites in a single administrative region to enlarge the sample size and statistical efficacy, as did in a previous study [12].

The daily meteorological data of 698 meteorological stations in China from 2009 to 2019 were obtained from the China Meteorological Science Data Sharing Service Platform (http://data.cma.cn/), including average temperature (°C), relative humidity (%), wind speed (m/s), and so on. Because the meteorological stations do not cover all the study areas (counties), we use the meteorological spatial interpolation method Anusplin to interpolate the daily mean temperature and relative humidity to get the national raster data, and then extract the daily mean temperature and relative humidity of each selected NISS site. The daily wind speed data of the study areas come from the nearest meteorological monitoring station. The principle of the meteorological spatial interpolation method Anusplin is based on the thin plate spline function theory, introducing longitude and latitude as independent variables and altitude as covariable to carry out spatial interpolation of meteorological elements [13]. In this study, the raster data of the national daily mean temperature at the resolution of 0.01° × 0.01° are obtained by interpolation using the daily mean temperature data of 698 meteorological stations in China. The formula of the model is as follows:

$$Temp_i = f(lat_i, lon_i) + b \times alt_i + e_i \tag{1}$$

In formula (1), $Temp_i$ represents the daily mean temperature of the meteorological station, $f()$ represents the thin plate spline function, lat_i, lon_i, and alt_i represent the latitude, longitude, and altitude of the meteorological station, b represents the regression coefficient, and e_i represents the error term. The accuracy of the interpolation results is verified by the ten-fold crossover method. The results show that the R^2 of the interpolation model of daily mean temperature is 0.96, and the root mean square error (RMSE) is 2.37 °C. Using the same method to obtain the daily relative humidity of each study areas, the R^2 of the relative humidity interpolation model is 0.81, and the RMSE is 7.7 %. Finally, the daily average temperature and daily relative humidity of each NISS monitoring point in each region are extracted from the daily national raster data, while the daily wind speed data of the monitoring point are derived from the nearest meteorological station, and this method has been applied in other studies [14,15].

2.3. Statistical analysis

2.3.1. Assessing the exposure-response relationships between temperature and CO poisoning cases

Considering the lag effect of meteorological data on human health [16], the Distributed Lag Non-linear Model (DLNM) model was used in this study to evaluate the exposure-response relationship between daily temperature and CO poisoning cases. DLNM model is not only suitable for different types of distributed variables but also one of the most commonly used model methods for time series research by establishing two-dimensional cross-basis functions to consider the expose-response relationship and exposure lag effect at the same time [17]. Therefore, we used the time series data of seven NISS regions (31 monitoring sites) from 2009 to 2019 and applied the DLNM model to connect the quasi-Poisson distribution function (due to excessive discretization of CO poisoning cases) to fit the relationship between air temperature and CO poisoning cases in each region respectively. In the DLNM model, we controlled for confounding factors such as time trend, day of week effect, and daily average wind speed in the model, and set the maximum lag of temperature to 6 days. The formula of the DLNM model is as follows:

$$\mathrm{P}_t = cb(\mathrm{TM}, \mathrm{lag}) + ns(\mathrm{time}, \mathrm{e} * df) + \mathrm{DOW} + ns(\mathrm{ws}, 3) + ns(\mathrm{rh}, 3) \tag{2}$$

In formula (2), P_t represents the number of CO poisoning on the day t. $cb()$ indicates that the "cross basis" function of exposure effect and lag effect is constructed by the natural spline function, which is used to analyze the cumulative effect of exposure on poisoning cases in the past few days or the effect of exposure to different lag times. TM refers to air temperature, lag is the number of days of lag, and the degree of freedom of the natural spline function of temperature lag is 3. $ns()$ represents the natural smoothing spline function, and time is the time variable corresponding to the day t to control the long-term trend. e is the number of years, which is 11 (2009–2019) in this study. df represents the degree of freedom, determined according to the principle of AIC minimization, this study uses $df = 5$/year. AIC is often used to evaluate the index of goodness of fit of the model, the smaller the AIC value, the higher the goodness of fit of the model. The prediction accuracy of different models can be evaluated by the AIC of the model, and the appropriate model can be determined [18,19]. DOW is a classified variable that controls the "day of the week effect", ws refers to daily wind speed, rh refers to daily average relative humidity, and the degree of freedom is set to 3 [20].

In addition, after reducing the dimension of the model, the coefficient and covariance matrix of the cumulative 6-day exposure effect can be obtained. In the cumulative exposure-response relationship, the minimum poisoning temperature (MPT) was obtained as the reference value to divide the cold effect and heat effect, and the exposure-response curve of the relationship between temperature and the risk of poisoning cases was obtained. and the corresponding relative risk (RR) and 95 % confidence interval (95%CI) for each temperature were reported. In this study, in addition to reporting the nonlinear curve between air temperature and poisoning cases in each region, it is also reported that the RR value corresponding to 90 % quantile temperature in each region is taken as the representative value of high temperature; similarly, the RR value corresponding to 10 % quantile temperature in each region is reported as the representative value of low temperature.

2.3.2. Early warning criteria of temperature reated to CO poisoning

Bsed on above exposure-response relationship, we classified the temperature-related risk of CO poisoning (RR) estimated by the DLNM model. Referring to the previous research, the temperature range corresponding to the temperature effect without statistical significance was defined as the optimal temperature range, and then the temperature that caused the statistically significant effect (95%CI of RR does not include 1) was defined as the cold and heat effect threshold temperature. Then, the hot RR and cold RR above the threshold were equally divided into low, medium, and high levels, which were defined as low, medium, and high risk in turn, and the temperature ranges corresponding to different risk levels was set as the poisoning temperature early warning criteria. Finally, according to the risk levels of different regions, the early warning days of different levels and the average daily number of cases during the early warning period were calculated, and the number of excess cases relative to the threshold temperature of different risk levels was evaluated with the number of excess cases. The calculation formula is as follows:

$$\mathrm{AF} = (\mathrm{RR} - 1)/\mathrm{RR} \tag{3}$$

In which, the AF indicates the fraction of CO poisoning cases attributable to exposure to hot and cold temperatuers. The RR values were the associations between hot and cold temperatures and CO poisoning risks, which were obtained from equation (2).

$$E = N_t \times AF \tag{4}$$

In formula (4), E represents the number of excess cases, N_t represents the daily average number of cases in the risk region, and AF is estimated in equation (3).

2.3.3. Sensitivity analyses

We conducted sensitivity analyses to test the robustness of our findings. By changing the lag days (5, 6, 7 days) in the DLNM model of air temperature and CO poisoning, we compared the cumulative effect of the exposure-response relationship between air temperature and CO poisoning in each region under different lag days. Meantime, the degree of freedom (4, 5, 6/year) of the time trend in the model is also changed.

In this study, all analyses were performed using R software (V4.1.1, R Development Core Team), and the DLNM model was constructed using the 'dlnm' package. The results of the statistical tests were two-sided with values of $P < 0.05$ as statistical significance.

2.4. *Ethics statement*

The data utilization of the NISS had been reviewed and approved by the Ethical Review Committee of the National Center for Chronic and Noncommunicable Disease Control and Prevention, China CDC (number: 201502). Data were analyzed without including private information and no participants were contacted.

3. Results

3.1. *The general characteristics of the study population*

This study included a total of 10618 cases of CO poisoning that occurred in 31 NISS surveillance sites in seven administrative regions of China from 2009 to 2019, with an average of 0.4 cases of CO poisoning per day. There were more cases of CO poisoning in North China and Northeast China, with 4142 (39.0 %) and 1999 (18.8 %) cases respectively (Table 1). During the study period, the national average daily temperature was 14.5 °C, and the national average daily relative humidity is 67.4 % (Table 1).

3.2. *The exposure-response relationships between temperature and CO poisoning case*

Fig. 1 shows the exposure-response relationship between daily mean temperature and CO poisoning cases in seven admisnistrative regions in China. Genearlly, we observed an inverse J-shaped exposure-response relationship between air temperature and CO poisoning across all regions, indicating that both low and high temperature will increase the risk of CO poisoning, but the effect of low temperature is more obvious than high temperature.

The cumulative RRs of CO poisoning for 10 % percentile of temperature during lag0-6 days, compared with the reference temperature (MPT), ranged from the 1.13 (95%CI: 1.01,1.26) in East China to 1.73 (95%CI: 1.63,1.83) in South China. However, we did not find a significant association between the 10 % percentile of temperature and CO poisoning in Northwest China. By contrast, we found a weaker effects of high temperature on the risk of CO poisoning. We observed significant cumulative association of 90 % percentile of temperature during lag0-6 days only in South China and Southwest China, and the cumulative RRs were 1.17 (95%CI 1.05 1.20) and 1.10 (95%CI 1.01 1.20), respectively (Table 2).

Table 1
General characteristics of the study subjects.

Region	Variables	Mean ± SD	Minimum	25 % percentile	Median	75 % percentile	Maximum
North China	CO poisoning cases	1.0 ± 2.3	0.0	0.0	0.0	1.0	54.0
	Average temperature (°C)	12.8 ± 11.3	−14.4	1.8	14.4	23.3	32.0
	Relative humidity (%)	58.1 ± 17.5	14.2	44.6	59.4	72.2	95.0
	Wind speed (m/s)	2.1 ± 0.7	0.8	1.6	2.0	2.5	5.9
Northeast China	CO poisoning cases	0.5 ± 1.5	0.0	0.0	0.0	0.0	34.0
	Average temperature (°C)	6.6 ± 13.9	−24.7	−6.5	8.9	19.5	28.4
	Relative humidity (%)	65.1 ± 13.4	25.5	56.3	66.0	75.5	96.5
	Wind speed (m/s)	2.8 ± 1.0	0.8	2.0	2.6	3.4	7.7
East China	CO poisoning cases	0.3 ± 1.0	0.0	0.0	0.0	0.0	42.0
	Average temperature (°C)	17.3 ± 9.0	−5.6	9.3	18.5	24.8	35.0
	Relative humidity (%)	72.5 ± 12.4	26.3	64.1	73.4	82.0	97.9
	Wind speed (m/s)	2.4 ± 0.8	0.9	1.8	2.3	2.8	7.7
Central China	CO poisoning cases	0.2 ± 0.6	0.0	0.0	0.0	0.0	10.0
	Average temperature (°C)	17.6 ± 9.0	−3.4	9.6	18.7	25.4	33.8
	Relative humidity (%)	74.1 ± 11.9	29.3	66.3	75.0	83.0	98.0
	Wind speed (m/s)	2.0 ± 0.7	0.6	1.5	1.8	2.3	5.9
South China	CO poisoning cases	0.3 ± 0.8	0.0	0.0	0.0	0.0	10.0
	Average temperature (°C)	22.9 ± 5.7	3.7	18.7	24.3	27.8	32.2
	Relative humidity (%)	77.1 ± 11.8	26.0	71.7	78.7	85.3	98.3
	Wind speed (m/s)	2.3 ± 0.7	0.6	1.8	2.2	2.6	8.4
Northwest China	CO poisoning cases	0.3 ± 0.9	0.0	0.0	0.0	0.0	15.0
	Average temperature (°C)	8.3 ± 10.3	−14.7	−1.1	9.9	17.7	27.5
	Relative humidity (%)	55.6 ± 11.8	17.0	47.4	56.4	64.4	89.2
	Wind speed (m/s)	2.0 ± 0.5	0.9	1.6	1.9	2.3	5.2
Southwest China	CO poisoning cases	0.1 ± 0.5	0.0	0.0	0.0	0.0	10.0
	Average temperature (°C)	15.7 ± 5.2	−0.7	11.2	16.5	20.4	25.1
	Relative humidity (%)	69.1 ± 11.2	28.0	61.3	71.3	77.8	92.8
	Wind speed (m/s)	2.2 ± 0.7	0.8	1.7	2.1	2.6	5.4

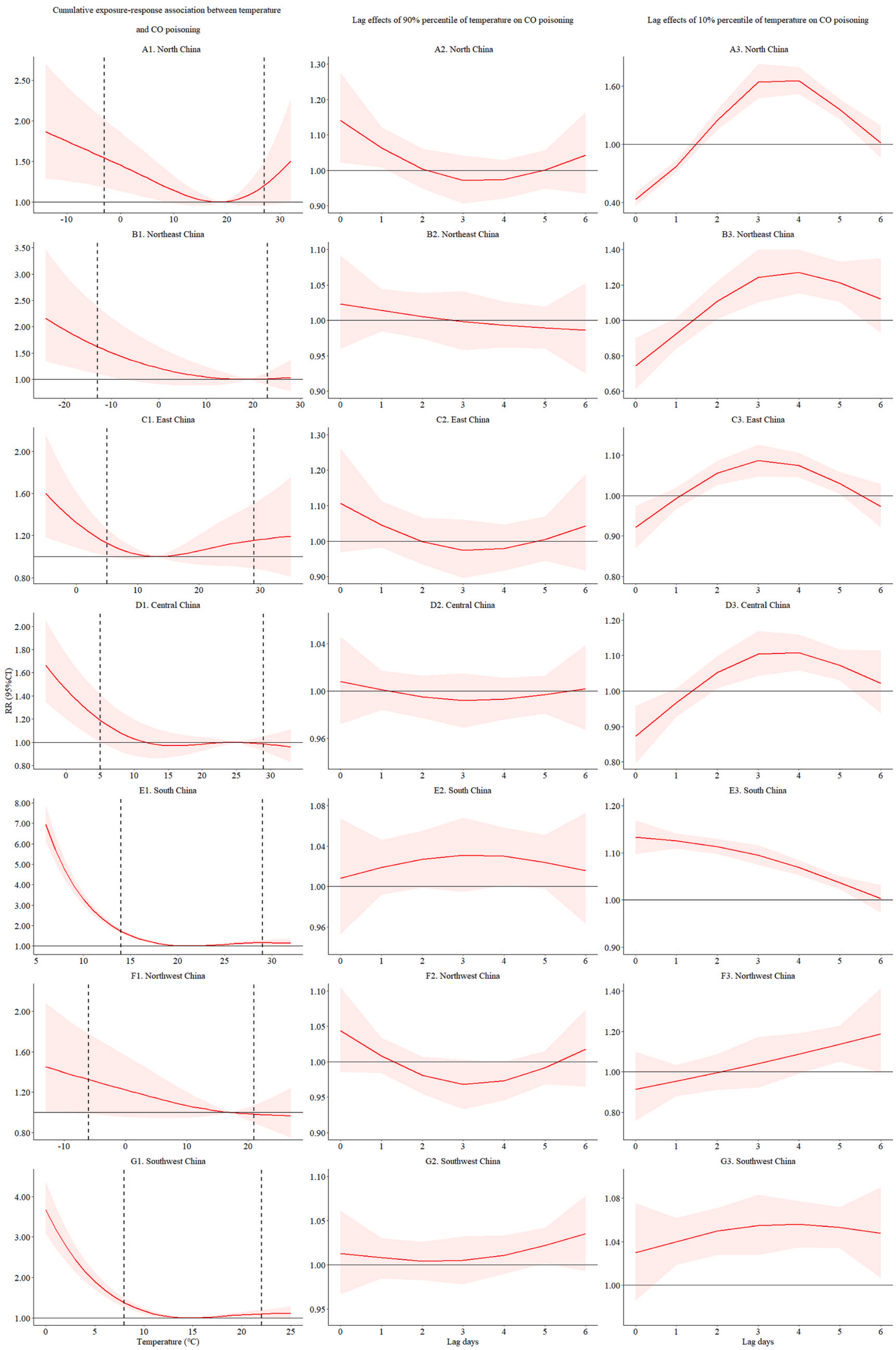

Fig. 1. The exposure-response associations of temperature with CO poisoning in different regions of China.

We observed different patterns of lag effects of low and high temperatures on CO poisoning (Fig. 1). The lagged effects of 90 % percentile of temperature was a U-shaped trend along lag 0–6 days. For example, the RR reducted from 1.14 (95%CI: 1.02, 1.27) at lag 0 day to non-significance at lag 2 day in North China. In contrast, the lagged effect of 10 % percentile of temperature was generally an inverted U-shaped trend along lag 0–6 days. For instance, the RRs increased and reached the peak at lag 4 day in North China (RR = 1.65, 95%CI: 1.52, 1.50), Northeast China (RR = 1.27, 95%CI: 1.15, 1.40), Central China (RR = 1.11, 95 % CI: 1.06, 1.16), and Southwest China (RR = 1.06, 95 % CI: 1.04, 1.08), and than decreased. However, the patterns of lagged effects were slightly different in South China, East China and Northwest China, with a monotonically dreasing trend, monotonically dreasing trend, and a flatten pattern, respectively (Fig. 1).

3.3. *Early warning criteria of temperature related to CO poisoning*

Table 3 shows the risk classification of CO poisoning related to the daily mean temperature. The threholds of temperatures with high risk of CO poisoning in North China, Northeast China, East China, Central China, South China, Northwest China, and Southwest China were −8 °C, −20 °C, −3 °C, −2 °C, 7 °C, −12 °C, and 1 °C, respectively. Correspondingly, the ranges of temperatures with medium risk were −7 °C–0 °C, −19 °C ~ -14 °C, −2 °C–0 °C, −1 °C–1 °C, 8 °C–11 °C, −11 °C ~ −10 °C and 2 °C–4 °C, respectively. Moreover, the ranges of temperatures with low risk were 1 °C–8 °C, −13 °C–8 °C, 1 °C–5 °C, 2 °C–5 °C, 12 °C–20 °C, −9 °C–8 °C and 5 °C–12 °C, respectively. It is worth noting that temperatures equal to or over 24 °C and 19 °C in South China and Southwest China were also defined as low risks.

Table 3 also shows the number of days, number of daily poisoning cases, and number of excess poisoning cases corresponding to different early warning grades. Genearlly, we observed a positive correlation between the daily number of poisoning cases and daily excess poisoning cases with the grade of early warning in all regions. For example, the average of daily excess poisoning cases corresponding to low-, medium, and high-risk in North China increased from 0.6 to 1.7.

3.4. *Sensitivity analyses*

We changed the lag days (5, 6, and 7 days) in the DLNM model, and the results of the model did not change significantly (Supplementary Fig. 1). In addition, we also changed the *df* of the time trend in the DLNM model (5, 6, and 7 per year), and the results show that the model is robust (Supplementary Fig. 2).

4. Discussion

In this study, based on CO poisoning data from 31 NISS monitoring sites in seven administrative regions of China from 2009 to 2019, we estimated the exposure-response associations between daily temperature and CO poisoning cases, and also identified the early warning criteria of temperature reated to CO poisoning based on the exposure-response associations. The results showed that temperature is an important environmental factor for CO poisoning, both low and high temperatures may increase the risk of CO poisoning, and the risk of poisoning varies greatly among regions. In addition, the development of early warning criteria for CO poisoning in different regions may allow us to accurately implement the corresponding preventive work, thus reducing the risk of CO poisoning. These findings deepen our understanding of the relationship between temperature and CO poisoning and have important

Table 2
Cumulative effects (RR, 95%CI) of the 10 % and 90 % percentile of temperature on CO poisoning in each region of China.

Region	Temperature (°C)		RR (95%CI)
North China	Reference	19	1
	10 % percentile	−3	1.54 (1.18,2.02)
	90 % percentile	27	1.20 (0.96,1.51)
Northeast China	Reference	19	1
	10 % percentile	−13	1.62 (1.11,2.34)
	90 % percentile	23	1.01 (0.90,1.13)
East China	Reference	13	1
	10 % percentile	5	1.13 (1.01,1.26)
	90 % percentile	29	1.16 (0.89,1.50)
Central China	Reference	25	1
	10 % percentile	5	1.19 (1.01,1.41)
	90 % percentile	29	0.99 (0.93,1.05)
South China	Reference	21	1
	10 % percentile	14	1.73 (1.63,1.83)
	90 % percentile	29	1.17 (1.05,1.30)
Northwest China	Reference	17	1
	10 % percentile	−6	1.32 (0.99,1.78)
	90 % percentile	21	0.98 (0.90,1.07)
Southwest China	Reference	15	1
	10 % percentile	8	1.38 (1.28,1.50)
	90 % percentile	22	1.10 (1.01,1.20)

Table 3
Risk classification of CO poisoning and early warning criteria of temperature in different regions of China.

Region	Type of effect	Risk Level	RRs	Early warning criteria (°C)	Early warning days (n, %)	Daily CO poisoning cases	Daily excess CO poisoning cases
North China	Cold effect	High	1.67 ~ 1.87	≤-8	44 (1.1)	3.7	1.7
		Medium	1.43 ~ 1.66	−7 ~ 0	728 (18.1)	2.6	1.0
		Low	1.20 ~ 1.42	1 ~ 8	718 (17.9)	1.9	0.6
	Optimal	–	1.00	–	2527 (62.9)	0.3	–
Northeast China	Cold effect	High	1.90 ~ 2.16	≤ −20	36 (0.9)	2.1	1.1
		Medium	1.63 ~ 1.89	−19 ~ -14	298 (7.4)	1.0	0.5
		Low	1.44 ~ 1.62	−13 ~ -8	561 (14.0)	1.0	0.4
	Optimal	–	1.00	–	3122 (77.7)	0.3	–
East China	Cold effect	High	1.43 ~ 1.60	≤ −3	1 (0.0)	2.0	0.8
		Medium	1.29 ~ 1.42	−2 ~ 0	38 (1.0)	0.7	0.2
		Low	1.13 ~ 1.28	1 ~ 5	394 (9.8)	0.6	0.1
	Optimal	–	1.00	–	3584 (89.2)	0.2	–
Central China	Cold effect	High	1.53 ~ 1.67	≤ −2	4 (0.1)	2.0	0.8
		Medium	1.35 ~ 1.52	−1 ~ 1	72 (1.8)	0.5	0.2
		Low	1.19 ~ 1.34	2 ~ 5	328 (8.2)	0.5	0.1
	Optimal	–	1.00	–	3613 (89.9)	0.1	–
South China	Cold effect	High	4.73 ~ 6.93	≤7	13 (0.3)	2.8	2.4
		Medium	2.34 ~ 4.72	8 ~ 11	105 (2.6)	1.9	1.5
		Low	1.02 ~ 2.33	12 ~ 20	1119 (27.9)	0.6	0.3
	Optimal	–	1.00	–	548 (13.6)	0.1	–
	Heat effect	Low	1.05 ~ 1.17	≥24	2232 (55.6)	0.1	<0.1
Northwest China	Cold effect	High	1.42 ~ 1.45	≤ −12	22 (0.6)	0.9	0.3
		Medium	1.40 ~ 1.41	−11 ~ -10	53 (1.3)	0.9	0.3
		Low	1.36 ~ 1.39	−9 ~ -8	146 (3.6)	0.9	0.3
	Optimal	–	1.00	–	3796 (94.5)	0.3	–
Southwest China	Cold effect	High	2.80 ~ 3.67	≤1	2 (0.1)	2.0	1.5
		Medium	1.91 ~ 2.79	2 ~ 4	26 (0.6)	0.5	0.3
		Low	1.05 ~ 1.90	5 ~ 12	1128 (28.1)	0.2	0.1
	Optimal	–	1.00	–	1153 (28.7)	0.1	–
	Heat effect	Low	1.06 ~ 1.11	≥19	1708 (42.5)	0.1	<0.1

public health implications for the primary prevention of CO poisoning.

In this study, we found that the exposure-response relationship between temperature and CO poisoning cases showed an inverse J-shaped type, that is, both low temperature and high temperature could increase the risk of CO poisoning, and the effect of low temperature was obvious, while that of high temperature was weak, which was not completely consistent with some previous studies [21–30]. For example, studies on non-occupational CO poisoning in Shanghai, Shanxi, Hebei, Guangxi, Guangdong, Changchun, and Jinan have shown a negative correlation between temperature and CO poisoning but did not report the effect of high temperature on CO poisoning [21–24,27–30]. However, this study found that high temperatures may also increase the risk of CO poisoning in South and Southwest China, and although the risk level was low, the duration was longer. To some extent, this indicates that attention should also be paid to the effect of high temperatures on CO poisoning. In addition, Hu et al. [25] and Liu et al. [26] found that the number of cases of non-occupational poisoning has increased in summer in recent years, and it is easy to be misdiagnosed because of atypical symptoms and seasonal factors, which suggests that special attention should be paid to the occurrence of CO poisoning in summer.

We also found that there were great regional variations in the risk of CO poisoning caused by temperature. In this study, the cumulative risk values of CO poisoning caused by low temperatures were observed in South China, Northeast China, North China, Southwest China, Central China, and East China, while the risk caused by high temperature was observed only in South and Southwest China. These differences my be related to the regional differences in the causes of CO poisoning and the different mechanisms of temperature-related CO poisoning. The causes of CO poisoning mainly include fire, gas leakage, improper installation and use of gas water heater, improper heating, or incomplete charcoal combustion, etc. However, China has a vast territory, and has different degrees of economic development, and different living habits among different regions. Hence, the causes of CO poisoning are also different in different regions. According to studies from North China [29,31,32], improper heating was the main cause of CO poisoning (84%–95 %), including coal-fired heating and gas-fired heating. Studies in Northeast China [30,33,34] showed that the main cause of CO poisoning was improper heating by household coal or charcoal fire, followed by improper use of carbon fire or gas in catering and other service places, gas leakage, etc. Studies in East China [21,24,35,36] showed that the main cause of CO poisoning was the improper installation and use of gas stoves and gas water heaters, while the improper use of gas water heaters in South China [28] was also led by the improper use of gas water heaters (70%–93 %), followed by the indoor use of carbon stoves, gas pipe leakage, etc. Relatively few studies have been conducted in central and southwest China, with a study in Xiangtan [37] showing that improper use of gas water heaters was the main cause of CO poisoning, and small sample studies in Sichuan and Tibet [38,39] suggested that improper use of gas water heaters and improper indoor coal heating may be the main causes. Therefore, in summary, improper heating may be the main cause of CO poisoning in North China and Northeast China, while improper installation or use of gas water heaters is the main cause of CO poisoning in South and Southwest China. In addition, it is worth noting that the indoor charcoal fire diet was suggested as a cause of CO poisoning in different regions, which needs to be explored in further studies.

The mechanism of temperature effect on CO poisoning may come from two levels. First, the temperature change may lead to the emergence or increase of some behavior patterns, which may lead to the emergence or increase of CO exposure. For example, in low-temperature days, the emergence or increase of demand behaviors such as heating, use of hot water, closed doors and windows, and corresponding improper operation may lead to exposure and an increase in the risk of CO poisoning [7]. In high-temperature weather, behaviors such as "air conditioner + hot pot" and "air conditioner + gas stove" (using air conditioner with closed doors and windows and using charcoal fire or gas for indoor diet) and corresponding improper operation may also cause exposure and increase the risk of CO poisoning [40]. Second, temperature and other meteorological factors synergize to make indoor CO less likely to be emitted. For example, warmer temperatures reduce the heat release rate, which is not conducive to smoke uplift, and in concert with other meteorological conditions that are not conducive to CO diffusion or emission, may increase the risk of CO poisoning [41].

In addition, according to the Haddon principle of injury prevention, preventing the emergence and formation of danger is the first prevention strategy [42]. We found that temperature is an important environmental factor of CO poisoning, and it is of great public health significance to provide early warning service for the risk of CO poisoning based on air temperature, to move forward the primary prevention of CO poisoning, and to start or strengthen prevention work and public warning of relevant institutions before the occurrence of CO poisoning. However, the existing meteorological condition early warning and prediction research and standard formulation of CO poisoning focus on the impact of other meteorological conditions (such as humidity, and wind speed) on CO diffusion, ignoring the important impact of temperature on CO exposure behavior. In this study, we found that the average number of daily poisoning cases and daily excess poisoning cases in most geographical regions of China increased with the increase of CO poisoning risk level related to daily average temperature. This suggests that it is necessary to establish temperature-related CO poisoning risk early warning standards by region, which also needs to be further verified in future research.

This study has several advantages. First, this study used the hospital outpatient or emergency CO poisoning data collected by the NISS system, which is representative of national medical institutions, breaking through the limitations of previous studies only using poisoning event data or local case data, thus comprehensively and accurately reflecting the dose-effect relationship between temperature and the occurrence of CO poisoning cases. Second, we used the DLNM model to evaluate the exposure-response relationship between daily temperature and CO poisoning cases, fully considering the non-linear relationship and lag effect between air temperature and CO poisoning. Third, it is found for the first time that both low temperature and high temperature have effects on CO poisoning, which is in line with the characteristics of the current changes in the causes of CO poisoning, and has guiding significance for future prevention work. Finally, this study proposed the risk classification of temperature-related CO poisoning in different regions and establishes the temperature early warning standards of high, medium, and low risk, which meets the urgent need to deal with the rising mortality of CO poisoning in the south, central, eastern and western regions of China, and has important public health significance and strong practical value.

This study also has several limitations. First, we did not examine the association of temperature with CO poisoning based on the surveillance site, but based on the administrative region data, and this may lead to bias to the results. Second, it is possible that some cases of CO poisoning result in fatalities without being included in hospital outpatient or emergency records. Third, due to the relatively lower frequency of CO poisoning cases in the study regions, a case-crossover study design based on individual information may be a better approach to estimate the association between ambient temperature and CO poisoning risks. However, because of the privacy reason, the individual information of each CO poisoning case was not available yet. In the future, we hope to conduct such analyses using a case-crossover study design. Finally, the findings of this study were based on the premise that other factors affecting the occurrence of CO poisoning remain unchanged, and thus the temperature early warning criteria we derived were only informative if there is no significant change in the lifestyle, behavioral habits, social policies and environmental support of the population. We hope to further incorporate meteorological factors and multiple factors affecting poisoning into the study in the future, to comprehensively evaluate the relationship between temperature and CO poisoning, and then get a more accurate temperature early warning standard. Additionally, meteorological warning for CO poisoning required not only the development of criteria for meteorological conditions for warning but also the development of defense recommendations corresponding to each level of warning. This study only proposed the temperature early warning classification and did not study the relevant early warning and defense suggestions, especially the response measures of the relevant government departments. Therefore, we suggest that the follow-up research can be further explored on this basis.

5. Conclusion

The nationwide study in China provides a comprehensive picture of the relationship between ambient temperature and CO poisoning. We observed that the exposure-response relationship between ambient temperature and CO poisoning showed an inverse J-shaped type, that is, both low temperature and high temperature could increase the risk of CO poisoning, while the effect of low temperature was more obvious, especially in the South, Northeast and North China, and of high temperature could be seen in South and Southwest China. In addition, based on the above exposure-response relationship, the temperature early warning classification of CO poisoning in different areas of China can be established. These findings can provide a reference for the prevention of CO poisoning based on temperature and have important public health significance and strong practical value.

The first column shows the cumulative exposure-response associations (RR, 95%CI for lag 0–6 days) of temperature with CO poisoning in each ragion of China, with the dotted line on the left representing the 10 % percentile of temperature and the dotted line on the right representing the 90 % percentile of temperature. The second column shows the lag effects of 90 % percentile of temperature on CO poisoning in each region, and the third column shows lag effects of 10 % percentile of temperature on CO poisoning in each region.

Data availability statement

The CO poisoning data from NISS are available upon reasonable request from the corresponding author (duanleilei@ncncd.chinacdc.cn). It is not publicly available because the information that could compromise the personal privacy.

CRediT authorship contribution statement

Xiao Deng: Conceptualization, Data curation, Formal analysis, Methodology, Validation, Writing – original draft, Writing – review & editing. **Ye Jin:** Formal analysis, Methodology. **Yuan Yuan:** Conceptualization, Writing – review & editing. **Yuan Wang:** Investigation, Data curation. **Pengpeng Ye:** Software, Investigation. **Chengye Sun:** Writing – review & editing, Supervision, Project administration, Conceptualization. **Leilei Duan:** Validation, Supervision, Resources, Project administration, Data curation.

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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e29147.

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