Wu et al. BMC Pulmonary Medicine (2025) 25:145
https://doi.org/10.1186/s12890-025-03605-0

RESEARCH

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The short-term effects of different cold spell definitions on asthma outpatient visits in Lanzhou, China

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Abstract

Background With global warming, most studies have focused on the health impacts of heat waves, while the health effects of cold spells, especially in developing countries, still need to be explored. Additionally, existing research on temperature extremes and asthma primarily targets severe asthma cases requiring hospitalization or emergency care, neglecting outpatients with mild symptoms. This study aimed to identify the optimal definition of cold spells in Lanzhou, China, and examine their association with outpatient asthma visits, identifying potentially vulnerable populations.

Methods This study collected daily asthma outpatient records, along with meteorological and air pollutant data, from January 1, 2017, to December 31, 2020, in Lanzhou, Gansu Province. Twenty-four cold spell definitions were developed using four temperature indices (daily mean, daily minimum, daily mean apparent, and daily minimum apparent temperatures), two thresholds (P_{10} and P_5), and three durations (2, 3, and 4 days). A time-series fitted poisson generalized linear model (PGLM) and distributed lag nonlinear model (DLNM) were applied to estimate the short-term effects of cold seasons (November to March) on outpatient asthma visits, controlling for confounding factors such as humidity, air pollutants, time trends, holidays, and weekdays. Stratified analyses by sex and age were conducted to identify vulnerable populations and examine the influence of cold spell duration on asthma clinic visits.

Results Various definitions of cold spells influenced asthma outpatient visits, with similar trends observed. The model fit was best when the daily minimum apparent temperature was below the 10th percentile, and the duration was more significant than or equal to 4 days. Based on this optimal definition, for the total population, the main effect of the cold spell on asthma occurred at Lag0, Lag1, Lag6, and Lag7, with Lag7 producing the most significant effect ($RR = 1.208$, 95% CI: 1.052 ± 1.388). In the subgroup analyses, the cumulative effect of lag 0–7 days (Lag0-7) was higher for females and those in the 0–18 age group than for males and other age groups, respectively. In addition, the longer the duration of the cold spell from lag 3 days (Lag3) onwards, the greater its effect.

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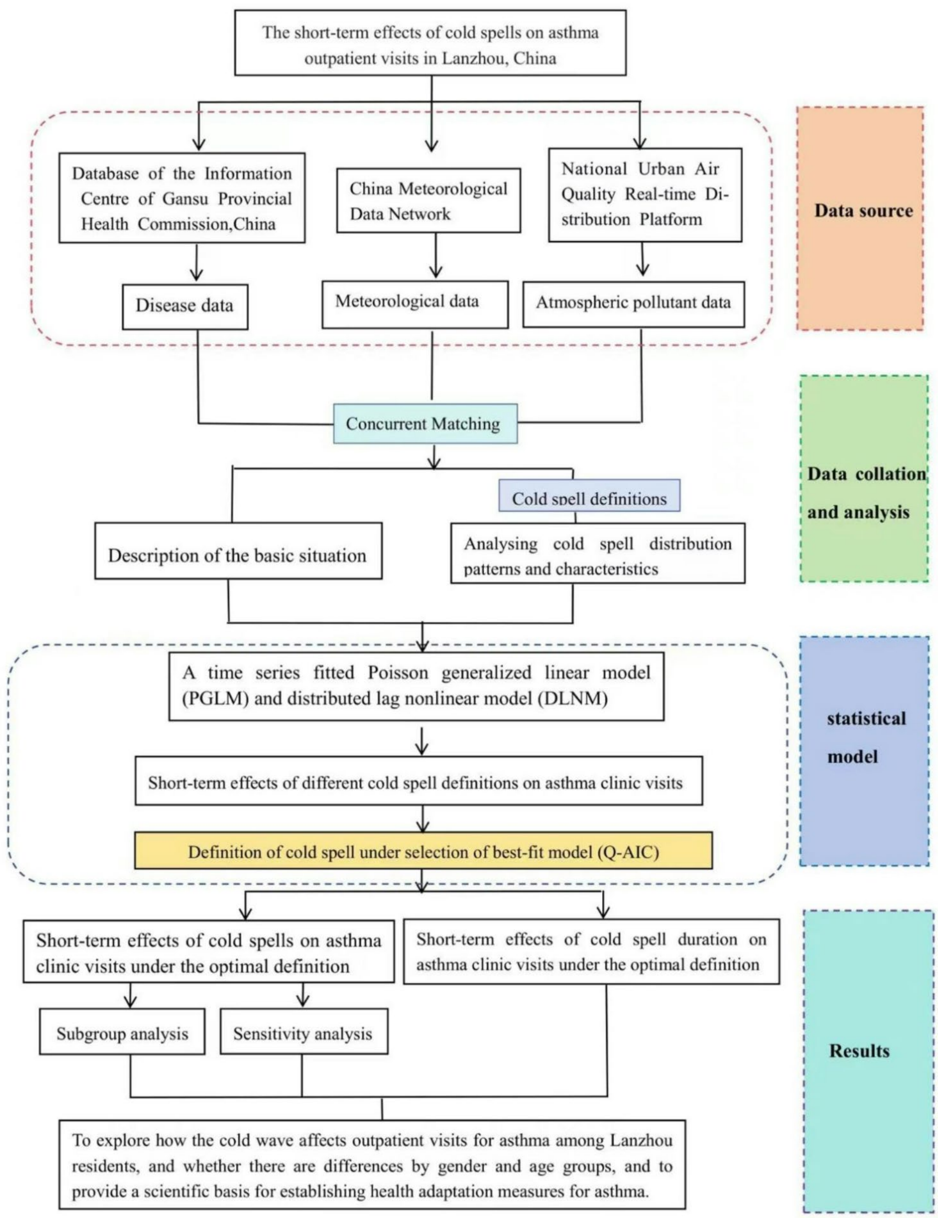
Conclusion Cold spells in Lanzhou City can notably increase asthma outpatient visits, with females and individuals aged 0–18 particularly affected. Moreover, the longer a cold spell persists, the greater its impact, especially in the latter days of the event.

Graphical Abstract



Keywords Cold spell, Asthma, Outpatient visits, Risk factors, Distributional lag nonlinear model, Poisson generalized liner model

Patient or public contribution In this study, the contributions of patients, healthcare providers, and the public were crucial in both the data collection and research design phases. Patients and service users shared their personal experiences of how cold weather affects their asthma, helping to shape the research focus. Healthcare providers supported patient follow-ups and ensured the accuracy of the data collected. During the writing phase, we also incorporated feedback from patients to ensure the results accurately reflect their needs and experiences.

Overall, the involvement of patients and relevant stakeholders provided valuable insights and support for this research.

Introduction

According to the *2023 Lancet Countdown: China's Health and Climate Change Report*, the impacts of climate change on human health are intensifying and are gradually attracting the attention of health practitioners and policymakers [1, 2]. Climate change affects human health by altering extreme weather events' frequency, intensity, and geographic distribution, resulting in human injury, illness, and death [3–9]. However, when assessing the health impacts of climate change, more attention is paid to extreme high temperatures, often underestimating the health risks associated with extreme low temperatures [6, 10]. In recent years, a growing body of research has shown that cold spells can significantly increase the incidence of a wide range of adverse health outcomes, such as death, cardiovascular disease, and respiratory disease [11–13]. Most previous studies have focused on the health effects of cold spells in developed countries while neglecting developing countries more vulnerable to extreme weather events [14, 15]. Therefore, an in-depth understanding of the synergistic effects of cold spells and environmental and individual vulnerability on health in developing countries and their underlying pathophysiological mechanisms is essential to understand and shape targeted public health prevention strategies fully.

The United Nations Intergovernmental Panel on Climate Change (IPCC) recognizes that climate change directly threatens respiratory health, including asthma, in its Sixth Assessment Report released in 2022. Asthma, a highly prevalent chronic respiratory disease characterized by recurrent episodes of shortness of breath, chest tightness, and wheezing, has become a severe public health problem [16]. Asthma prevalence is high globally, with an average prevalence of greater than 20% in developed countries and 3–5% in developing countries [17]. However, asthma is often underdiagnosed and underreported in developing countries, more so than in developed countries, due to limitations in medical resources, awareness and diagnostic capacity in these countries. As the world's most densely populated developing country, China faces a heavy asthma burden. The overall prevalence of asthma among Chinese adults (aged ≥ 20 years) is 4.2%, according to data from the national cross-sectional study of China's lung health (CPH) conducted between 2012 and 2015 [18]. In addition, the Global Burden of Disease (GBD) study further predicts that by 2025, the number of people living with asthma worldwide will increase to 400 million [19]. Obviously, with the rapid development of global industrialization and urbanization, as well as changes in the ecological environment, the prevalence of asthma will continue to rise [20], causing a relatively heavy burden of disease for patients and society.

Asthma onset is mainly influenced by individual and environmental factors [21–23]. Although several previous studies have identified several risk factors associated with the development of asthma, such as genetics, pollen, dust mites, air pollutants, weather extremes (dust storms, hurricanes, floods, heatwaves, cold spells), and behavioral lifestyles [24–27], a large body of literature has demonstrated the increasingly significant impact of environmental factors on asthma. Low ambient temperatures, as one of the major environmental factors, play an essential role in exacerbating chronic respiratory diseases [28], and asthma is more susceptible to extreme low temperatures [29]. Epidemiological studies in different regions have also shown that lower temperatures are significantly associated with a higher risk of outpatient visits or hospitalizations for people with asthma [30, 31]. In addition, most of the available research on temperature extremes and asthma has focused on severe asthma attacks requiring hospitalization or emergency room visits [32], excluding outpatients with mild asthma symptoms. However, as outpatient visits are likely to be the primary mode of healthcare seeking for people with mild asthma [33, 34], this would underestimate the actual burden of asthma. Outpatient visits usually include both scheduled and unscheduled visits. In China, the majority of outpatient visits for asthma patients are unscheduled, although regular follow-ups do occur, but in a smaller proportion. Most of these visits result from acute exacerbations of symptoms. Therefore, exploring the short-term impact of cold spells on asthma outpatient visits can help to identify asthma risk, reduce its epidemiological and socio-economic impact, and provide a practical reference for asthma diagnosis, prevention, and improvement of patient's quality of life.

There has been no uniform definition of cold spells worldwide due to differences in population adaptation to climate and regional variations [11, 15]. Early studies have mostly focused on temperature indices (e.g., daily maximum, daily minimum, or daily average temperature), temperature thresholds (either relative or absolute thresholds), and the severity and duration of cold days [35, 36]. However, studies have shown that different definitions of cold spells, both in terms of the choice of temperature thresholds and the setting of duration, may significantly affect the assessment of mortality or disease incidence risk [37]. A single definition does not accurately reflect the actual impact of cold spells on human health across different regions, potentially leading to overestimations or underestimations of cold-related mortality risks. Therefore, it is particularly important to select the most appropriate definition of cold wave warning based on the minimum quasi-poisson akaike information criterion (Q-AIC) in statistical methods, maximization of relative risk, and incorporation of local epidemiological studies. Based on the above background, the main objectives of this study were: (1) to define 24 cold spells based on different temperature indices, temperature thresholds, and duration days, aiming to establish a feasible definition of cold spells for the city of Lanzhou, Gansu Province, in order to assess the health effects of cold spells more accurately and to provide a unified standard for cold spells in other cities with similar climates; (2) the short-term and lagged effects of the cold season (November to March) on residential asthma outpatient visits in Lanzhou City were assessed by controlling for potential confounders using a time-series fitted poisson generalized linear model (PGLM) and a distributional lag nonlinear model (DLNM); (3) by understanding the relationship between cold spells and outpatient visits to asthma hospitals, it may be possible to explore better the different effects of cold wave characteristics and individual characteristics, identify potentially susceptible populations, and mitigate the adverse effects of cold waves on population health. The study's results may provide supportive evidence for future cold wave surveillance and asthma prevention and control in developing countries.

Materials and methods

Study area and demographic data

Lanzhou (36°06'N, 103°40'E) is located in the centre of Gansu Province, in the interior of northwest China, with a typical temperate continental climate. The city has a total of five districts and three counties, and precipitation is scarce, with an average annual precipitation of less than 400 mm and a dry climate. The average annual temperature is about 10℃, the average annual winter temperature is about −2℃, the average annual summer temperature is about 25℃, and the annual temperature difference between summer-winter is about 27℃. The seasons change significantly, winters are long and colder, and summers are short and hotter. According to the communiqué of the seventh national census of Gansu Province in 2020, the resident population of Lanzhou City was 4,359,400, of which 51.38% were male and 48.62% were female.

Data collection

Disease data

In this study, we collected outpatient morbidity information of asthma patients in Lanzhou City, Gansu Province, from 1 January 2017 to 31 December 2020, and the data were obtained from the database of the Information Centre of Gansu Provincial Health and Health Commission. Asthma diagnosis was based on the International Classification of Diseases, tenth revision (ICD-10), and patients with a confirmed diagnosis of asthma (J45) were finally screened. Specific variables included the hospital of consultation (i.e., hospitals where asthma patients typically receive outpatient care), date of consultation, current address, age, and gender. As all records were anonymized with no individually identifiable information, the study was exempt from a full ethical review. The information center performed uniform standardization, logical error checking, and disease code proofreading to ensure the completeness and accuracy of the data, as well as the hospital of consultation, date of consultation, current address, age, and gender.

Meteorological data

Daily meteorological data obtained from the China Meteorological Data Network (http://data.cma.cn/). There are three meteorological observation sites in Lanzhou City, located in Yuzhong County, Gaolan County and Yongdeng County (Fig. 1). These meteorological data reflect weather conditions near the study participants' place of residence or hospital to ensure that the data accurately represent the participants' exposure. Since there are a small number of non-continuous missing values in the raw meteorological data, this study selects the data before and after 5 days of missing data, calculates the average value of these 10 days, and fills in the missing values by using the neighbour interpolation method. The study data including daily maximum, minimum, and average temperatures (℃), relative humidity (%), pressure (hPa), wind speed (m/s), rainfall (mm) and sunshine hours (h). Apparent temperature (AT), also known as body temperature, refers to the actual temperature felt by the human body, which is usually affected by humidity, wind speed, and other factors and is usually calculated from the above conventional meteorological indicators [38], with the following formula:

$$\mathrm{AT} = \mathrm{MT} + 0.33 * \alpha - 0.70 * \mathrm{WS} - 4.00$$

$$\alpha = \mathrm{RH}/100 * 6105 * \exp[17.27 * \mathrm{MT}/(237.7 + \mathrm{MT})]$$

Where, AT—apparent temperature, ℃; MT—mean temperature,℃; α —vapour pressure, hpa; WS—wind speed, m/s; RH—relative humidity, %.

Atmospheric pollutant data

The daily air pollutant data are obtained from the National Urban Air Quality Real-time Distribution Platform (https://air.cnemc.cn:18007/) and include hourly concentrations of sulfur dioxide (SO_2), nitrogen dioxide (NO_2), respirable particulate matter (PM_{10} and $PM_{2.5}$) and ozone (O_3) and more. The daily average concentration of each air pollutant is calculated based on the hourly concentrations. In this study, daily monitoring

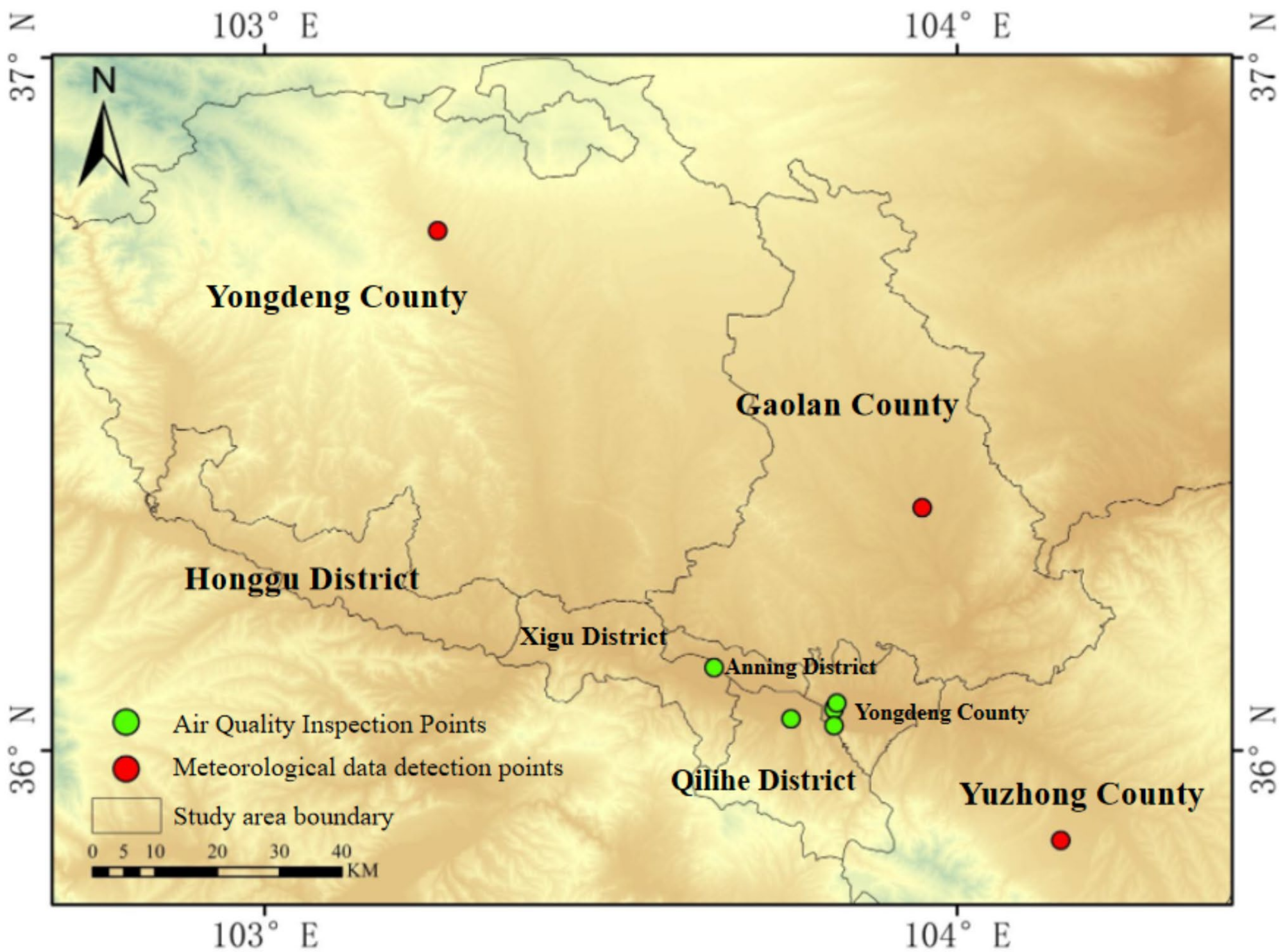


Fig. 1 Geographic location of Lanzhou City administrative districts and air quality and meteorological data monitoring sites

data from five air quality monitoring sites in Lanzhou City were used, and the average of these five sites was used as a representative exposure level for pollutants in the area (Fig. 1). For missing data, neighbourhood value interpolation was used to fill in the pairs. The data were matched by the date of the event (date of hospital visit) as well as the geographical location of the patient's residence.

Cold spell definitions

There are currently numerous ways to define cold waves globally [39–41]. Since different climate zones may be affected by cold waves in other ways, China, as a country with diverse climates, has not yet established a unified standard for defining cold waves. Based on previous studies [13, 42], this study was restricted to the cold season (November to March), considering that cold waves usually occur during the year's colder months. In addition, previous studies have shown that the definition of a cold wave with two or more consecutive days provides more accurate statistical estimates [43]. Therefore, 24 cold waves were defined in this study by combining different temperature indices (daily mean temperature, daily minimum temperature, daily mean AT, daily minimum AT), temperature thresholds (P_{10}, P_5), and number of days of duration (2, 3, 4 days). The study did not include the remaining higher or lower temperature thresholds because they corresponded to few cold wave events, would affect model stability, and would be of little significance for health warnings.

Statistical analysis

Considering that the number of daily outpatient visits for asthma is a small probability event that approximately obeys a Poisson distribution, the study used the number of daily outpatient visits for asthma as the dependent variable and the presence or absence of a cold spell event (non-cold spells day versus cold spells day) and the duration of the cold spells (non-cold spells day, cold spells duration of 2 days, cold spells duration of 3 days, and cold spells 4 days or more) as the independent variables. The relationship between cold spell events and asthma clinic attendance was analyzed using a poisson generalized linear model (PGLM) fitted to the time series, adjusting for potential confounders such as relative humidity, air pollutants, temporal trends, holiday effects and day of the week effects. A distributed lag nonlinear model (DLNM) was also used to investigate further the lagged and nonlinear effects of the cold spell on asthma outpatient visits by calculating single-day relative risk (*RR*) and cumulative relative risk (*CRR*).

The PGLM can identify the direct relationship between cold spell events and daily asthma clinic visits, revealing the immediate impact of cold spells on asthma clinic visits. In contrast, the DLNM not only analyses the lagged effects of cold spell events after they occur, revealing the long-term trends of cold spells on asthma clinic visits, but also identifies the nonlinear features of the cold spell effect, i.e., the different impacts of the duration and intensity of cold spells on asthma clinic visits. By combining the two, it is possible to consider both the immediate and lagged effects of the cold spell on asthma clinic visits, thus providing a complete picture of the cold spell's overall effect on asthma clinic morbidity. Therefore, by analyzing the model results under different cold spell definitions, we can better find the cold spell definitions that are closely related to the changes in asthma outpatient visits and thus optimize the selection of the 24 cold spell definitions to ensure that the selected definitions can truly reflect the multidimensional impact of cold spells on public health. The model established is as follows:

$$\begin{aligned} &\mathrm{Log\,E}\left(\mathrm{Y_t}\right) = \alpha\ + \mathrm{cb}\left(\mathrm{CS_t}, \mathrm{lag}\right) + \mathrm{ns}\left(\mathrm{Temp_t}, \mathrm{d}f = 2\right) \\ &+\mathrm{ns}\left(\mathrm{RH}, \mathrm{d}f = 3\right)\mathrm{ns} + \mathrm{ns}\left(\mathrm{PM_{2.5}}, \mathrm{d}f = 2\right) \\ &+\mathrm{ns}\left(\mathrm{NO_2}, \mathrm{d}f = 2\right)\ + \mathrm{ns}\left(\mathrm{O_3}, \mathrm{d}f = 3\right) \\ &+\mathrm{ns}\left(\mathrm{time_t}, \mathrm{d}f = 4\right) + \gamma\,\mathrm{DOW} + \eta\,\mathrm{Holiday} \end{aligned} \tag{1}$$

$$\begin{aligned} &\mathrm{Log\,E}\left(\mathrm{Y_t}\right) = \alpha\ + \mathrm{cb}\left(\mathrm{CSD_t}, \mathrm{lag}\right) + \mathrm{ns}\left(\mathrm{Temp_t}, \mathrm{d}f = 2\right) \\ &+\mathrm{ns}\left(\mathrm{RH}, \mathrm{d}f = 3\right)\mathrm{ns} + \mathrm{ns}\left(\mathrm{PM_{2.5}}, \mathrm{d}f = 2\right) \\ &+\mathrm{ns}\left(\mathrm{NO_2}, \mathrm{d}f = 2\right)\ + \mathrm{ns}\left(\mathrm{O_3}, \mathrm{d}f = 3\right) \\ &+\mathrm{ns}\left(\mathrm{time_t}, \mathrm{d}f = 4\right) + \gamma\,\mathrm{DOW} + \eta\,\mathrm{Holiday} \end{aligned} \tag{2}$$

Where, $E(Y_t)$—number of asthma outpatient visits on day t; α —intercept of the model; cb—crossbase matrix based on DLNM; CS—cold spell on day t (0 = non-cold spell day, 1 = cold spell day), as a binary variable, its relationship with exposure-response and lag-response was established through the natural cubic spline function; CSD—duration of cold spell on day t (0 = non-cold spell day, 1 = cold spell lasts for 2 days, 2 = cold spell lasts for 3 days, and 3 = cold spell lasts for 4 or more days), as an ordered categorical variable, CSD was similarly modeled in DLNM by the natural cubic spline function to explore its relationship with exposure-response and lag-response; ns—natural cubic spline function with knots positions determined based on data characteristics and Q-AIC criteria to ensure smoothness and validity of the relationship; lag—number of lagged days according to the Q-AIC criterion to fit a lag structure of up to 7 days; df—degrees of freedom, the Q-AIC criterion was used to determine the optimal degrees of freedom of the confounding factors; Temp—defining cold wave temperature index, which is a metric for identifying and assessing cold spell events based on specific temperature metrics, includingdaily mean temperature, daily minimum temperature, daily mean apparent temperature, and daily minimum apparent temperature; relative humidity was included in meteorological factors; $PM_{2.5}$, NO_2, and O_3 were included in pollutants; time—time trend variable; week effect (DOW) and holiday effect (Holiday) were controlled as categorical variables in the model.

Subgroups and sensitivity analysis

To further identify possible potentially susceptible populations, gender (male and female) and different age groups (0–18, 19–64, and ≥ 65 years) were analyzed in various subgroups. Sensitivity analyses were performed by adjusting the presence or absence of air pollutants $PM_{2.5}$, NO_2, and O_3 in the model and varying the degrees of freedom of time trend (4–5 df), relative humidity (3–4 df), and air pollutants (3–4 df) in the model to test the robustness of the findings.

This study was done in R 4.0.3, with the DLNM constructed in the 'dlnm' package, the natural spline function (ns) by loading the 'splines' package, and the Q-AIC calculation by loading the 'MuMIn' package. Air pollutants, meteorological factors, and outpatient visits were analyzed descriptively using a skewed distribution, with means, standard deviations, minimums, medians, interquartile ranges (IQRs), and maximums calculated. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

Results

Data description

A total of 106,636 asthma cases were collected in Lanzhou city during the study period, of which 40,974 cases (38.42%) were outpatient visits during the cold season, 50,644 cases (52.51%) were males, and 62,214 cases (58.34%) were in the 19-64-year-old group (Table 1). The mean daily apparent temperature, minimum daily apparent temperature, mean daily temperature, minimum daily temperature, relative humidity, mean wind speed, sunshine hours, rainfall, and atmospheric pressure were 1.21 ± 11.00 °C, -5.28 ± 10.63 °C, 7.72 ± 9.85 °C, 1.90 ± 9.82 °C, 58.73 ± 15.65%, 7.28 ± 1.62 m/s, 6.60 ± 3.49 h, 0.63 ± 1.97 mm, and 1017.03 ± 11.72 hPa. The mean concentrations of$PM_{2.5}$, NO_2, SO_2, O_3, and CO during the study period were 35.4 μg/m^3, 2.80 μg/m^3, 22.88 μg/m^3, 104.49 μg/m^3, and 0.91 μg/m^3, respectively (Table 2).

Figure 2 illustrates the time series distribution of total cases, minimum temperature, mean temperature, minimum AT, and mean AT for Lanzhou City from 2017 to

Table 1 Descriptive statistics of outpatient visits for asthma among residents of Lanzhou City, China, 2017–2020

Variables	Sum	Mean(SD)	Min	P_{25}	P_{50}	P_{75}	Max
Total	106,636	73.0(57.9)	0	21	66	116	267
Female	55,992	38.3(30.8)	0	10	34	63	145
Male	50,644	34.7(27.8)	0	11	31	54	137
0–18 years old	18,427	12.6(11.7)	0	3	10	19	75
19–64 years old	62,214	42.6(34.7)	0	12	38	69	215
≥65 years old	25,995	17.8(15.3)	0	4	15	29	79

Table 2 Descriptive statistics of meteorological variables and pollutant variables in Lanzhou City, China, 2017–2020

Variables	Mean(SD)	Min	P_{25}	P_{50}	P_{75}	Max
Mean AT(℃)	1.21(11.00)	-23.0	-9.3	1.5	11.0	22.7
Minimum AT(℃)	-5.28(10.63)	-27.0	-15.0	-5.00	4.2	15.7
Mean temperature (°C)	7.72(9.85)	-13.1	-1.2	8.7	16.6	26.4
Minimun temperature(°C)	1.90(9.82)	-19.8	-6.6	2.9	10.7	20.8
Relative humidity(%)	58.73(15.65)	17.0	47.0	60.0	70.0	96.0
Wind speed(m/s)	7.28(1.62)	3.8	6.1	7.0	8.0	16.0
Duration of sunlight(h)	6.60(3.49)	0	4.0	7.4	9.2	12.9
Rainfall(mm)	0.63(1.97)	0	0	0	0.2	19.7
Atmospheric pressure(hPa)	1017.03(11.72)	992.0	1007.0	1017.0	1026.0	1046.0
$PM_{2.5}$ (μg/m^3)	35.4±17.7	12.4	22.8	31.8	44.5	243.1
NO_2 (μg/m^3)	2.80(1.01)	1.0	2.0	3.0	3.0	7.0
SO_2 (μg/m^3)	22.88(11.53)	7.9	14.5	18.4	28.0	65.9
O_3 (μg/m^3)	104.49(26.52)	55.6	81.0	104.4	125.4	165.8
CO (μg/m^3)	0.91(0.34)	0.5	0.7	0.8	1.1	2.3

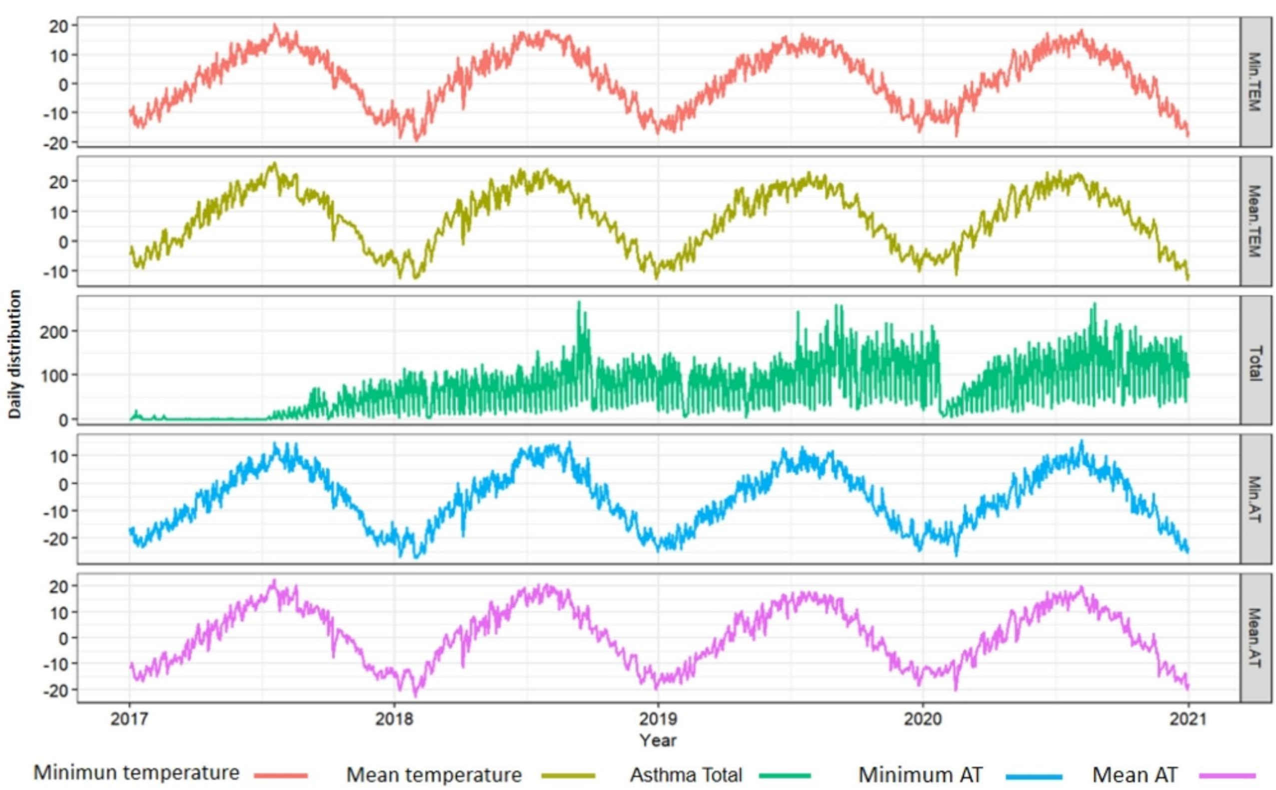


Fig. 2 Time series plot of daily total asthma cases and meteorological variables in Lanzhou City, China, 2017–2020

2020. These variables show similar temporal patterns where AT is always lower than the mean temperature. Studies have shown that AT is influenced by factors other than air temperature, such as humidity, wind speed, and solar radiation. Changes in these factors directly affect temperature perception and comfort. Therefore, AT can be a more appropriate indicator when assessing human comfort and formulating relevant policies.

Short-term effects of different cold spell definitions on asthma clinic visits

Figure 3 shows the RRs of a 0–7 day lag in asthma outpatient visits for the total population under 24 different definitions of cold spells.The effect of cold spells on asthma varied considerably across definitions, and the confidence intervals for effect estimates became wider as definitions became more stringent, with the effect of cold spells defined in terms of minimum AT on asthma outpatient visits being more significant. Among the 24 cold spell definitions, the Q-AIC value of the cold spell defined by the 10th percentile of the daily minimum AT as the threshold and greater than or equal to 4 days was the smallest, 5275.76, and based on the Q-AIC minimum criterion, the model fit was the best at this time (Table 3). The total number of days of cold spells in Lanzhou City from 2017 to 2020 under this definition was 9 days. In summary, the cold spell (CS21) under the definition of minimum daily AT below the 10th percentile and duration greater than or equal to 4 days was selected for this study's most suitable cold spell definition.

Short-term effects of the optimal cold spell definition on asthma clinic visits

The relationship between cold spells and asthma was further analyzed based on the optimal cold spell definition (CS21) obtained from the above analysis. Figure 4 shows the single-day lagged effect and the cumulative lagged effect of the cold spell on asthma outpatient visits in the total population and each subgroup of the study under the optimal cold spell definition. It was observed that there were some lagged effects of the cold spell on the total population and each subgroup, and the lagged trends were similar. For the total population, the main effect of cold wave on asthma was observed in Lag0,

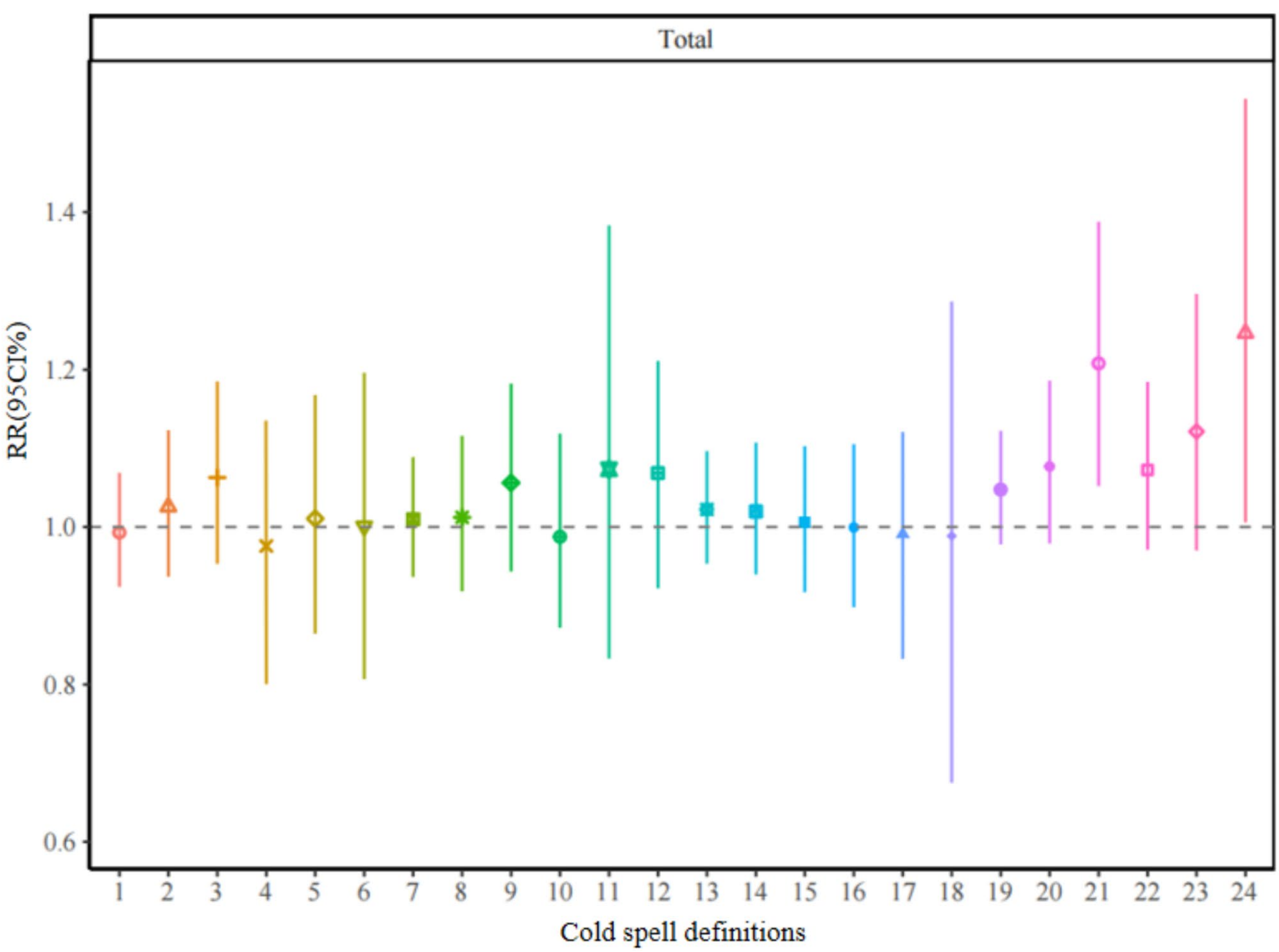


Fig. 3 Cumulative effect of lag 0–7 for total population under 24 definitions of cold spells

Table 3 Definition, distribution of days, and Q-AIC values for 24 cold spell definitions

Cold spells	Temperature indexes	Threshold	Durations	Number of cold spells	Q-AIC
cs1	Daily mean temperature	10th	2	29	5353.191
cs2	Daily mean temperature	10th	3	19	5353.892
cs3	Daily mean temperature	10th	4	12	5350.328
cs4	Daily mean temperature	5th	2	10	5330.23
cs5	Daily mean temperature	5th	3	4	5309.14
cs6	Daily mean temperature	5th	4	2	5286.314
cs7	Daily min temperature	10th	2	25	5351.996
cs8	Daily min temperature	10th	3	14	5349.188
cs9	Daily min temperature	10th	4	9	5336.546
cs10	Daily min temperature	5th	2	9	5352.721
cs11	Daily min temperature	5th	3	3	5350.975
cs12	Daily min temperature	5th	4	1	5356.410
cs13	Daily mean apparent temperature	10th	2	29	5339.827
cs14	Daily mean apparent temperature	10th	3	19	5349.434
cs15	Daily mean apparent temperature	10th	4	13	5354.423
cs16	Daily mean apparent temperature	5th	2	11	5338.004
cs17	Daily mean apparent temperature	5th	3	5	5304.629
cs18	Daily mean apparent temperature	5th	4	1	5279.931
cs19	Daily min apparent temperature	10th	2	28	5349.545
cs20	Daily min apparent temperature	10th	3	15	5323.742
cs21	Daily min apparent temperature	10th	4	9	5275.76
cs22	Daily min apparent temperature	5th	2	11	5342.179
cs23	Daily min apparent temperature	5th	3	5	5336.643
cs24	Daily min apparent temperature	5th	4	2	5329.780

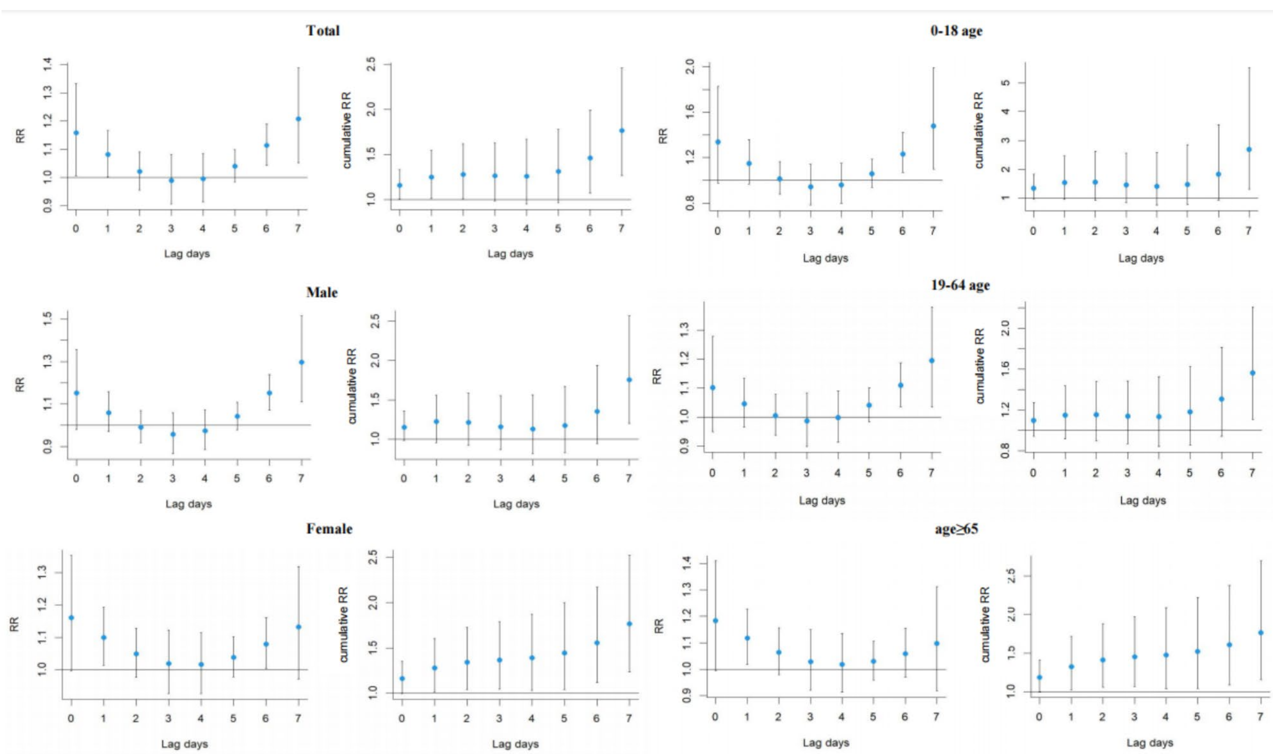


Fig. 4 Single-day and cumulative lagged effect values for the total population and each subgroup under the optimal cold spell definition

Lag1, Lag6, and Lag7, with Lag7 producing the most significant effect (*RR* = 1.208, 95% *CI*: 1.052 ± 1.388). In addition, the cumulative lag effect of asthma on the total population was significant and increased with lag time, with the highest cumulative effect occurring at lags 0–7 days (*CRR* = 1.766, 95% *CI*: 1.270 ± 2.459).

The study further explored the effect of cold spells on asthma clinic visits in various subgroups. The main effects of the optimal cold spell definition on asthma clinic visits in males were Lag6 (*RR* = 1.152, 95% *CI*: 1.071 ± 1.240), Lag7 (*RR* = 1.297, 95% *CI*: 1.111 ± 1.514), and for asthma clinic visits in females were Lag1 (*RR* = 1.100, 95% *CI*: 1.013 ± 1.193), and Lag6 (*RR* = 1.080, 95% *CI*: 1.004 ± 1.161), with the cumulative effect of lag 0–7 being slightly higher in females (*CRR* = 1.764, 95% *CI*: 1.236 ± 2.519) than in males (*CRR* = 1.756, 95% *CI*: 1.201 ± 2.568), but was not significantly different. In addition, the 0–18 years age group was significantly more affected by the cold spell than the 19–64 years age group and the ≥65 years age group, with cumulative effects lagged 0–7 days off (*CRR* = 2.697, 95% *CI*: 1.317 ± 5.527), (*CRR* = 1.565, 95% *CI*: 1.108 ± 2.210) and (*CRR* = 1.766, 95% *CI*: 1.156 ± 2.696) (Supplementary Tables 1 and 2).

Short-term effects of cold spell duration on asthma clinic visits under the optimal definition

The study categorized cold spell duration into four categorical variables (non-cold spell day, cold spell lasting 2 days, cold spell lasting 3 days, and cold spell lasting 4 days or more). CSD represents the cold spell duration (CSD1 = non-cold spell day, CSD1 = cold spell duration of 2 days, CSD3 = cold spell duration of 3 days, CSD4 = cold spell duration of 4 days or more).

Figure 5 shows that the longer the cold wave duration from lag 3 days onwards, the greater the effect. In lag 6, the effects of CSD 1, CSD 2, CSD 3, and CSD 4 were (*RR* = 1.040, 95% *CI*: 1.008 ± 1.074), (*RR* = 1.082, 95% *CI*: 1.016 ± 1.154), (*RR* = 1.172, 95% *CI*: 1.032 ± 1.331) and (*RR* = 1.268. 95% *CI*: 1.048 ± 1.535) (Supplementary Table 3).

Sensitivity analyses

By adjusting the presence or absence of air pollutants $PM_{2.5}$, NO_2, and O_3 in the model and changing the degrees of freedom of the confounding variables such as time trend (4–5 d*f*), relative humidity (3–4 d*f*), and air pollutants (3–4 d*f*) in the model, the changes in RR values of the risk of cold spells for outpatient asthma visits in the population were small. The main results of the study were relatively stable (Supplementary Table 4).

Discussion

Asthma is a multifactorial disease with genetic and environmental influences [44]. Previous studies have identified some of the risk factors associated with the pathogenesis of asthma; however, in recent years, asthma as a respiratory disease has become more susceptible to extreme temperature events due to global climate change, particularly the frequency of extreme weather, and is increasingly attracting widespread attention.It has been suggested that a combination of environmental and genetic factors is associated with the development of asthma. However, the rapid increase in the incidence of asthma over a short period is difficult to explain by changes in human genetics alone, and the role of environmental factors may be more prominent.In contrast to high temperatures, more attention has been paid to the effects of low temperatures on respiratory diseases, with some clinical, epidemiological, and biological evidence suggesting that cold air affects respiratory symptoms [28, 45]. The possible mechanisms by which hypothermia contributes to the development and exacerbation of asthma are as follows: (1) hypothermia directly induces bronchoconstriction, respiratory inflammation, and mucus hypersecretion, which collectively trigger respiratory hyperresponsiveness and lead to a decrease in lung function; [46] (2) cold conditions favor the survival and spread of influenza viruses and respiratory syncytial viruses, which may damage respiratory epithelial cells, thereby increasing sensitivity to allergens or irritants; [47] (3) the most likely mechanism for asthma exacerbations involves the transient receptor potential (TRP) channel. This sensor provides important information about ambient temperature, allowing the body to respond rapidly to temperature-induced respiratory changes, including deleterious responses to heat and cold [48].

There are many ways to define cold spells worldwide, for example, based on different thresholds of daily maximum, minimum, or average temperatures. However, such definitions based on absolute thresholds are challenging to apply nationally due to the differences in climatic patterns and adaptations of populations in different regions. So far, there has yet to be a unified definition in China. This study used four temperature indicators, combined with two temperature thresholds and three durations, to define 24 types of cold wave weather for the Lanzhou region.In most cases, the impact of the cold spell is enhanced as the temperature threshold decreases and the duration of the cold spell increases. In addition, the best-fitting model was obtained when the cold spell was defined as a daily minimum AT below the 10th percentile and a duration greater than or equal to 4 days.Temperature thresholds may vary depending on the climate of the study population and region, so the finding can only be extrapolated to areas with similar climatic and

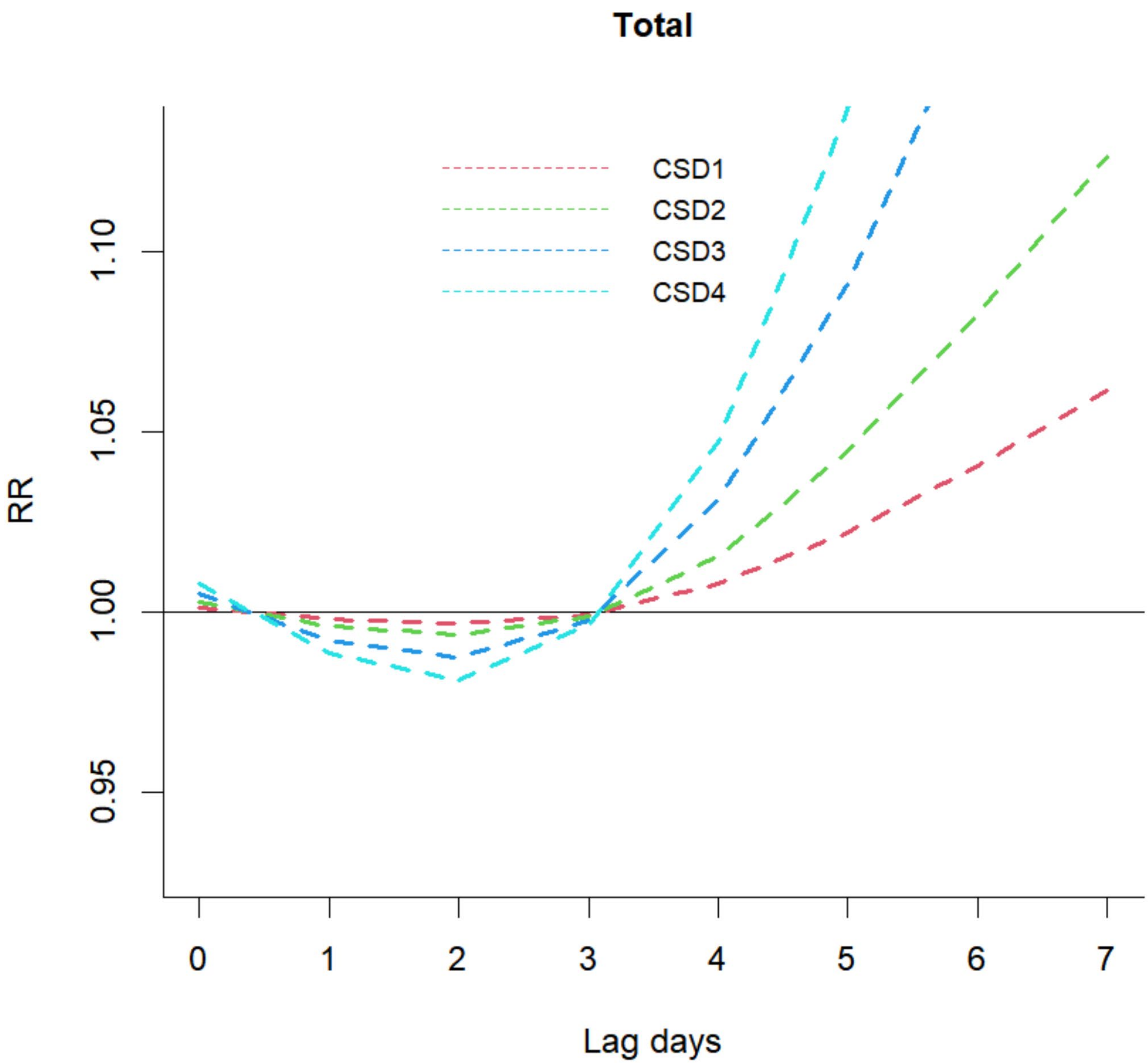


Fig. 5 Single-day lagged effect of different cold spell durations under the optimal cold spell definition

socio-economic conditions to Lanzhou City.In contrast to previous studies, the AT was chosen as the temperature indicator in this study, which has been applied in some studies to assess the impact of extreme temperature effects [49, 50]. AT considers a combination of ambient temperature, relative humidity, and wind speed, which can significantly influence the perception of ambient temperature.In addition, there is evidence that humidity also has a significant effect on the development of asthma [51, 52]. Therefore, when these factors coexist, there may be a superimposed effect on the impact of asthma.

Stratified analyses showed that the cold spell had an impact on the number of asthma outpatient attendances in different gender groups and that females were more sensitive than males.Extreme weather events are strongly associated with the risk of asthma emergency department visits, especially in women [53]. One study confirmed that males and females have different sensitivities to cold temperatures [54]. Specifically, female patients were more sensitive to hypothermy after exposure to cold spell events compared to male patients and, therefore, tended to seek early medical attention.A study in northern Finland showed that women report more cold weather-related symptoms than men when their asthma is more severe and uncontrolled compared to patients with mild and well-controlled asthma [55]. Similarly, a study in Beijing, China, found a U-shaped association between ambient temperature and the risk of hospitalization for asthma in adults, with females and younger patients being more susceptible to temperature extremes [56], both of which are similar to the results of this study.However, there are some inconsistent findings. For example, an Australian study examined the relationship between diurnal temperature range (DTR) and acute asthma hospitalizations in children and found that males and children aged 5–9 years with asthma were the most susceptible to temperature changes [57]. A Shenyang, China study also found that asthma visits increased with decreasing mean daily temperatures and were more pronounced in men [58]. Studies have shown that sex hormones, genetics, epigenetic variation, socio-environmental factors, and response to asthma treatment are important factors contributing to gender differences in asthma incidence, prevalence, and severity. Of these, sex hormones are key mediators of the variation in asthma prevalence between males and females [59]. In females, fluctuations in sex hormone levels during puberty, the menstrual cycle, and pregnancy have been linked to the pathogenesis of asthma [54]. This may be due to the DNA methylation in regions regulating sex hormones, specifically at *cytosine-phosphate-guanine (CpG)* sites during puberty, being influenced by extreme environmental exposures associated with asthma susceptibility [60, 61]. Another gender-related difference in response to cold may lie in the variation in body fat content between males and females. Women typically have a higher body fat percentage than men, which may allow them to maintain body temperature better when exposed to cold environments.

Regarding age, cold spells were significantly associated with outpatient asthma visits in children aged 0–18 years, with a much higher impact than in other age groups. This result is consistent with three studies in Chinese populations.Guo conducted a time-series study in Shanghai and showed a significant effect of cold spells on outpatient asthma visits in children [62]. Liu and colleagues found that the occurrence of cold spells was significantly associated with asthma hospitalization in children in Hefei City [63]. Chen investigated the effect of cold spells on the number of asthma hospital admissions in Beijing, and the results showed that young people were more sensitive to cold spells than middle-aged and older adults [8]. Similarly, a study from eight Korean cities found a stronger correlation between hypothermia and asthma hospitalization, with the younger age groups (0–14 and 15–64 years) being more closely associated than the older age groups (65–74 and ≥75 years) [64]. Possible explanations for this phenomenon are that children are more active, spend relatively more time outdoors, and have more exposure to cold weather. Secondly, children's respiratory systems still need to be fully developed, and they lack self-care skills. Therefore, identifying which subgroups are more susceptible to cold spells could help develop targeted asthma prevention measures, which will need to be validated in the future in a larger population.

The study further found that during the same cold spell event on multiple consecutive days, the impact of the cold spell on asthma was not constant but increased with duration. Specifically, if the cold spell lasted for four days, the effect on the residents on the fourth day could be much more significant than on the previous days. This result is consistent with previous studies [48]. As such, relevant organizations and departments need to attach great importance to the duration of cold spells, and when it is predicted that cold spells may persist for an extended period, more comprehensive and adequate protective measures can be taken to mitigate the excessive risk of prolonged cold spells to the health of the population.

This study has some limitations: (1) only a single region, Lanzhou City, China, was analyzed, making it difficult to generalize the results to other regions with different climatic and socio-economic conditions; (2) monitoring data on temperature and pollutants were obtained from outdoor fixed environmental monitoring stations, and exposure was estimated at the population level, which does not accurately represent individual exposure, making ecological bias unavoidable; (3) more detailed subgroup analyses for children aged 0–18 years were not conducted.

Conclusions

To gain insight into the impact of cold spells on the health of China's population, this study systematically analyzed 106,636 asthma cases reported in Lanzhou City, China, during 2017–2020. In Lanzhou, a cold spell, defined as a daily minimum AT below the 10th percentile and with a duration greater than or equal to 4 days, had the best model fit. The study results showed that cold spells were significantly associated with an increased risk of asthma outpatient visits and were more prevalent in females and the 0–18 year age group. In addition, if a cold spell lasted several days, the effect of the cold spell was more pronounced on the latter days. These findings provide an important basis for developing targeted health interventions to help reduce the adverse effects of cold spells on the population's health and provide a scientific basis for developing comprehensive asthma prevention and control strategies and measures by the relevant authorities.

Supplementary information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-025-03605-0.

Supplementary Tables

Acknowledgements
The authors thank the School of Public Health, Gansu University of Traditional Chinese Medicine, China, and the Information Centre of Gansu Health Commission for providing technical assistance for this study.

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Funding
This study was supported by the Gansu Provincial Joint Research Fund for Major Projects (Project No. 24JRRA876).

Data availability
The data that support the findings of this study are available from Statistical Information Centre of Gansu Provincial Health Commission but restrictions apply to the availability of these data, which were used under licence for thecurrent study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Statistical Information Centre of Gansu Provincial Health Commission.

Declarations

Ethics approval
This study was granted exemption by the ethics committee of University of Traditional Chinese Medicine (approval no.23/460–3131). We certify that the study was performed in accordance with the 1964 declaration of HELSIINKI and later amendments.

Consent to participate
Written informed consent was obtained from all the participants prior to the enrollment (or for the publication) of this study.

Consent for publication
All authors have read and approved the final manuscript and consent to its publication in BMC PULM MED. We confirm there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

Competing interests
The authors declare no competing interests.

Clinical trial number
Not applicable.

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Received: 29 December 2024 / Accepted: 17 March 2025
Published online: 31 March 2025

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