RESEARCH ARTICLE

The synergistic effects of atmospheric pollutants and meteorological factors on air pollution-sensitive diseases in typical cities of Beijing-Tianjin-Hebei, China

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Climate change poses a major global public health challenge. Despite significant air quality improvements from pollution control measures in the Beijing-Tianjin-Hebei region of China, the association mechanisms among air pollutants, meteorological factors, and population health risks remain a core scientific concern. Focusing on Zhangjiakou, a representative city within the Beijing-Tianjin-Hebei region, this study integrated semi-parametric generalized additive models (SGAM) with distributed lag non-linear models (DLNM) to systematically analyze health risks of air pollution-sensitive diseases from synergistic atmospheric pollution-meteorology interactions. The results demonstrated that, although Zhangjiakou is a low-pollution city, ambient pollutants still posed significant health risks with lagged health effects on pulmonary and cardiovascular diseases. Increasing pollutant concentrations elevated the relative risk (RR) for both disease categories, particularly for NO_2. Daily mean temperature exhibited a U-shaped nonlinear relationship with pulmonary outpatient visits and a reverse J-shaped relationship with cardiovascular diseases, identifying a minimum-risk threshold at 9.0°C where low-temperature exposure showed significantly higher RR than high-temperature exposure. Daily mean relative humidity displayed an inverted U-shaped relationship with both diseases, peaking at a maximum-risk threshold of 46% with dry conditions conferring higher risks than high humidity. Multi-factor interaction analysis confirmed statistically significant synergistic effects of temperature with SO_2, NO_2, and humidity on respiratory diseases risk ($P < 0.05$), temperature with SO_2 and humidity on cardiovascular outpatient visits ($P < 0.05$); and temperature with SO_2, NO_2, and humidity on cardiovascular hospitalizations ($P < 0.01$). Critically, even in low-pollution areas, compounded meteorology-pollutant effects remained key threats to public health.

Keywords: low ambient air pollution; meteorological factors; health risk; exposure-outcome interdependence; synergistic effects.

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Introduction

Climate change has emerged as a critical global public health challenge in the 21st century with its threats to human health becoming increasingly evident. Extreme temperature events, particularly heat exceeding physiological adaptation thresholds, can directly trigger vascular endothelial damage, significantly increasing the risk of severe acute conditions including cerebral hemorrhage, cerebrovascular rupture, myocardial infarction, and gastrointestinal hemorrhage. Concurrently, these events exacerbate the burden of respiratory and cardiovascular diseases, posing substantial threats to population health [1]. Extensive epidemiological studies demonstrate that the relationship between daily mean temperature and population mortality/morbidity rates typically exhibits non-linear "U"-, "V"-, or "J"-shaped patterns, indicating the existence of an optimal temperature range associated with minimal health risks [2]. Climate change significantly influences the generation and distribution of atmospheric pollutants [3]. Air pollution, stemming from economic growth and urbanization, has been increasingly acknowledged as a major urban challenge due to its pervasive health impacts [4]. Numerous domestic and international studies reveal direct associations between temperature/humidity and the incidence/mortality of various diseases. Changes in temperature or humidity exhibit non-linear relationships of "U", "V", or "J" shapes with disease outcomes and curve patterns varying across countries and regions [5, 6]. Furthermore, meteorological conditions and air pollution may exert synergistic effects on adverse population health outcomes [7].

Atmospheric pollutants and meteorological factors impact human health through multiple pathways. High temperatures can cause water-electrolyte imbalance and dehydration, while humid environments facilitate pathogen transmission, potentially expanding susceptible populations for respiratory diseases. Elevated concentrations of pollutants like NO_2, $PM_{2.5}$, PM_{10}, SO_2 directly irritate airways, induce inflammation, and further compromise cardiovascular function [8]. In northern China, exemplified by the similar air environments of Hohhot and Zhangjiakou, studies indicated significant correlations between major pollutant concentrations and meteorological factors. Meteorological conditions played a crucial role in pollutant dispersion and removal, thereby substantially influencing disease trends and severity such as pediatric asthma [9]. Epidemiological research has further deepened understanding of environmental risks. Evidence suggested that increases in concentrations of major air pollutants ($PM_{2.5}$, PM_{10}, SO_2, NO_2) were associated with rising disease incidence among residents, potentially exhibiting an approximately linear no-threshold pattern even at concentrations below current air quality standards [10, 11]. Studies employing advanced statistical models such as random forests identified $PM_{2.5}$, PM_{10}, and NO_2 as significant factors affecting respiratory disease mortality [12]. Research on elite athletes demonstrated that even minimal air pollution exposure and subtle meteorological variations might correlate with alterations in pulmonary function parameters and respiratory symptoms [13]. Regional studies provided robust evidence in Zagreb, Croatia, which both low and high temperatures significantly increased emergency medical demand for cardiovascular diseases, particularly myocardial infarction [14]. Existing research indicated that the peak health impact of pollutants might not occur on the exposure day, suggesting potential lag effects and cumulative effects [15]. In Japan, studies observed significant associations between hospital admissions for cardio-cerebrovascular diseases and preceding days of low temperature and falling barometric pressure [16]. Additionally, individual characteristics of age and gender may modify the health effects of meteorological factors and air pollution, though the nature and magnitude of these associations vary considerably across countries and cities [17]. China announced its climate goals in September 2020 to achieve carbon peak by 2030 and carbon neutrality by 2060 [18].

Zhangjiakou, a typical city with relatively low air pollution within the Beijing-Tianjin-Hebei region, features distinct meteorological characteristics including large annual/diurnal temperature ranges and significant interannual humidity variations. Investigating the synergistic effects of air pollution and meteorological factors on air pollution-sensitive diseases in populations of such cities holds significant guiding importance. This study employed Semi-parametric

Generalized Additive Model (SGAM) and Distributed Lag Non-linear Model (DLNM) to investigate whether air quality in Zhangjiakou posed health risks to residents [19, 20]. The structure of the SGAM was determined by the intrinsic relationships within the study data, enabling better characterization of the underlying relationship between the expected value of the response variable and the explanatory variables. Its linear component captured the overall trend of the dependent variable, allowing extrapolation and suitability for prediction. The non-linear component permitted local adjustments to the dependent variable, enabling more precise fitting of sample data, reducing misjudgment risks, and avoiding the "curse of dimensionality" [21]. By revealing the synergistic mechanism of atmospheric pollutants and meteorological factors on population health in Zhangjiakou, a lightly polluted city in the Beijing-Tianjin-Hebei region, this study provided a key scientific breakthrough, which not only deepened the understanding of health hazards from complex environmental exposures and promoted interdisciplinary integration and methodological innovation between environmental epidemiology and meteorology, but also directly supported the construction of a precise health risk early-warning system based on the "pollution-meteorology" dual-driver framework, which aided public health departments in formulating targeted protection strategies and optimizing medical resource allocation. Furthermore, the findings of this research provided critical scientific evidence for implementing differentiated pollution control measures under specific high-risk meteorological conditions, evaluating the health benefits of governance strategies, and addressing climate change-induced health risks in the Beijing-Tianjin-Hebei region and similar areas, which holds significant theoretical and practical value for advancing scientific decision-making and precise interventions in the environmental health domain.

Materials and methods

Data sources

This study utilized three core datasets from Zhangjiakou, a representative city in the Beijing-Tianjin-Hebei region, covering the period of 2019 to 2021. Air quality data were obtained from the China National Environmental Monitoring Centre (http://www.cnemc.cn/), comprising the Air Quality Index (AQI) and concentrations of six pollutants including $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3. Meteorological data originated from the Daily Surface Climate Dataset of China provided by the National Meteorological Science Data Center (http://data.cma.cn/) including daily mean temperature, relative humidity, and wind speed. Disease records were extracted from the anonymized registry of a provincial tertiary hospital in Zhangjiakou, Hebei, China, covering all age groups without gender restrictions. The dataset encompassed 83,605 respiratory diseases outpatient visits, 11,918 pulmonary hospitalizations, 106,175 cardiovascular outpatient visits, and 17,778 cardiovascular hospitalizations, all representing typical pollution-sensitive diseases. All procedures of this study were approved by the Medical Ethics Committee of Hebei North University (Zhangjiakou, Hebei, China).

Study methods

SGAM was used to establish a model for the interactive effects of daily average temperature and atmospheric pollutants, which incorporated factors including atmospheric pollution concentrations, time series, weekly variation effects, public holiday impacts, and atmospheric moisture to adjust for their impacts on the combined effects of daily average temperature and atmospheric pollutants. The calculation was shown below.

$$\log[E(Y_t)] = \beta \times X_t + s(PM_{2.5}, df) + s(PM_{10}, df) + s(SO_2, df) + s(NO_2, df) + s(CO, df) + s(O_3, df) + s(RH, df) + s(time, df) + DOW + holiday + \alpha \quad (1)$$

where $E(Y_t)$ was outpatient consultations on the t-th day. β was the regression coefficient. X_t was the average temperature (°C) on the t-th day. *s( )*

was a non-parametric spline smoothing function. *df* was the degrees of freedom. atmospheric pollutants signified the daily average concentrations of each atmospheric pollution on the t-th day with the degrees of freedom for each pollutant concentration being the optimal value selected by default in the system. *RH* was the daily average atmospheric moisture on the t-th day with a degree of freedom of 5. *time* was the date with a degree of freedom of 7. DOW accounted for the "day-of-the-week" effect, ranging from 1 to 7. *holiday* indicated whether it was a holiday with a value of 0 or 1. α was the residual error.

The distributed lag non-linear model (DLNM) was applied in epidemiology, using cross-basis to explain and transform variables, and elucidating the theory of distributed lag nonlinear models. The mathematical representation of the distributed lag non-linear models was as follows.

$$g(\mu_t) = \alpha + \sum_{j=1}^{J} f_j\left(x_{tj}; \beta_j\right) + \sum_{k=1}^{K} \gamma_k \mu_{tk} \qquad (2)$$

where t was time. $\mu_t \equiv E(Y)$. E[Y] was the expected value of the outcome variable Y at time t. g was the link function. Y followed various optional probability distributions such as poison, normal, gamma, *etc*. The term $f_j(\ )$ represented various basis functions for the predictor variable x_j, which captured the smooth relationship between x_j and the linear predictor. The notation (z_t) represented the linear predictor vector. Additionally, u_{tk} denoted the linear effect of other confounding factors with γ_k being the coefficients for these linear effects. The formula for the basis function was then given below.

$$f\left(x_t; \beta_j\right) = z_t^T \beta \qquad (3)$$

where zt represented a matrix, which was incorporated into formula (2) to estimate the values of the parameters that described the association between the regressor and the target variable.

A semi-parametric generalized additive model (SGAM) was employed in this study to elucidate the interaction effects between ambient temperature and air pollutants, while utilizing a distributed lag non-linear model (DLNM) to reveal lagged non-linear associations. Data statistical analysis was conducted using SPSS software (IBM, Armonk, New York, USA), whereas data visualization, supplementary analyses, and predictive modeling were implemented in R (https://www.r-project.org/).

Results and discussion

Characteristics of air pollution in Zhangjiakou city

The results showed that the overall air quality of Zhangjiakou city was at a good level or above. The daily average concentrations of $PM_{2.5}$, PM_{10}, SO_2, CO, NO_2, and O_3 were 26.89 μg/m³, 65.62 μg/m³, 10.75 μg/m³, 0.64 mg/m³, 19.92 μg/m³, and 75.28 μg/m³, respectively. However, extreme pollution occurred at very few individual time points. On March 15, 2021, the PM_{10} concentration reached 964 μg/m³ and the $PM_{2.5}$ concentration reached 276 μg/m³, while, on March 28, 2021, the PM_{10} concentration reached 1,971 μg/m³ and the $PM_{2.5}$ concentration reached 291 μg/m³, which were far exceeding China's current national environmental protection standard values. Seasonally, O_3 concentrations in the Zhangjiakou region exhibited higher levels in summer and lower levels in winter, while the concentrations of other atmospheric pollutants all showed higher levels in winter and spring and lower levels in summer and autumn. World Health Organization (WHO) states in its Air Quality Guidelines (AQGs) that, when atmospheric pollutant concentrations reaches the Interim Targets (IT-1, IT-2, IT-3, IT-4), pollutant exposure still poses varying degrees of health risks to the population, even when the guideline values are met, health hazards may still exist. The comparison of 2019 - 2021 daily average concentration values of various atmospheric pollutants in Zhangjiakou city with AQGs demonstrated that the concentration values of the various pollutants were mostly located between AQGs values and the IT-1 values

(Figure 1). Therefore, Zhangjiakou belongs to a low-pollution city.

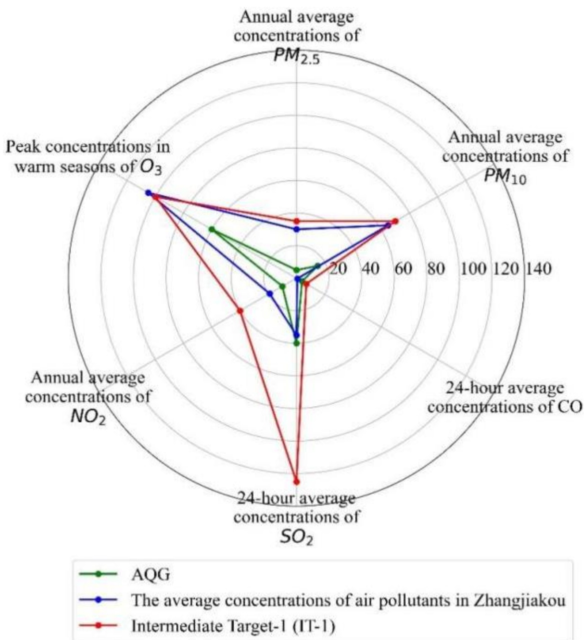


Figure 1. Comparison of concentrations of atmospheric pollutants in Zhangjiakou from 2019 to 2021 with WHO Air Quality Guideline values.

Distribution characteristics of air pollution-sensitive diseases

The average daily outpatient consultations and hospitalizations for respiratory diseases were 74 and 11, respectively, while for cardiovascular diseases, they were 105 and 17, respectively. When stratified by gender, the mean daily outpatient consultations for respiratory diseases was 37 for both males and females, while the mean daily hospitalizations for respiratory diseases was 8 for males and 3 for females. For cardiovascular diseases, the mean daily outpatient consultations were 50 for males and 55 for females, and the mean daily number of hospitalizations were 9 for males and 8 for females. When stratified by gender, the average daily outpatient consultations for respiratory diseases were 37 for both males and females, while the mean daily hospitalizations for respiratory diseases were 8 for males and 3 for females. For cardiovascular diseases, the mean daily number of outpatient consultations were 50 for males and 55 for females, and the average daily number of hospitalizations were 9 for males and 8 for females. When stratified by age into three groups of below 15 years old, 15 - 64 years old, and 65 and above years old, the average daily outpatient consultations for respiratory diseases were 1, 50, and 22 for each group, respectively, while the mean daily hospitalizations were 0, 5, and 6, respectively. For cardiovascular diseases, the average daily outpatient consultations were 1, 68, and 37, respectively, and the average daily number of hospitalizations were 0, 7, and 10, respectively (Table 1).

The time-series variations in daily hospital visits for respiratory and cardiovascular diseases in Zhangjiakou city from 2019 to 2021 showed that respiratory diseases visits exhibited periodic fluctuations with January consistently representing the peak period. Hospital admissions for these diseases generally demonstrated higher volumes during cooler months and lower volumes in warmer months. Cardiovascular disease visits, meanwhile, showed a distinct seasonal pattern of higher winter incidence and lower frequency in other seasons. Although no significant fluctuation pattern was observed in cardiovascular admissions, they similarly displayed an overall trend of higher frequency in cooler months and lower frequency in warmer months. It should be noted that, during the pandemic lockdown restrictions from February to April 2020, both outpatient visits and hospital admissions for the two disease categories showed marked declines (Figure 2).

Impact of temperature and atmospheric moisture on respiratory diseases

Based on air quality, meteorological factors, and respiratory diseases records from Zhangjiakou (2019-2021), equation (1) was employed to model the exposure-outcome interdependence between daily mean temperature and pulmonary outpatient visits/hospitalizations, quantifying their relative risks (RR). With daily temperature and atmospheric moisture as core independent

Table 1. Daily outpatient and hospitalization statistics for respiratory/cardiovascular diseases in Zhangjiakou city (2019 – 2021).

Diseases	Patient	Mean ± SD	Min	P25	P50	P75	Max
Outpatient consultations for respiratory diseases	Total number	74.05 ± 49.09	0	29	80	109	329
	Male	37.49 ± 25.46	0	14	40	55	176
	Women	36.56 ± 24.55	0	14	39	54	156
	≤ 14 yrs	0.70 ± 1.23	0	0	0	1	14
	15 – 64 yrs	50.78 ± 34.48	0	20	53	74.5	267
	≥ 65 yrs	22.57 ± 15.61	0	8	24	34	81
Hospitalizations for respiratory diseases	Total number	10.96 ± 6.94	0	5	11	15	38
	Male	8.19 ± 5.00	0	4	8	11	32
	Women	3.59 ± 2.38	0	1	3	5	15
	≤ 14 yrs	0 ± 0.03	0	0	0	0	1
	15 – 64 yrs	4.77 ± 3.43	0	2	4	7	19
	≥ 65 yrs	6.19 ± 4.30	0	3	6	9	24
Outpatient consultations for cardiovascular diseases	Total number	104.88 ± 73.10	0	39	108	155	392
	Male	49.88 ± 36.80	0	19	49	71	184
	Women	55.00 ± 38.09	0	19	58	83	208
	≤ 14 yrs	0.59 ± 1.01	0	0	0	1	8
	15 – 64 yrs	67.69 ± 47.03	0	26	71	102	300
	≥ 65 yrs	36.60 ± 27.49	0	13	36	54	140
Hospitalizations for cardiovascular diseases	Total number	17.06 ± 10.07	0	9	17	23	59
	Male	8.96 ± 5.45	0	5	9	12	31
	Women	8.10 ± 5.43	0	4	7	11	30
	≤ 14 yrs	0 ± 0.06	0	0	0	0	1
	15 – 64 yrs	7.40 ± 4.84	0	4	7	10	28
	≥ 65 yrs	9.65 ± 6.13	0	5	9	13	33

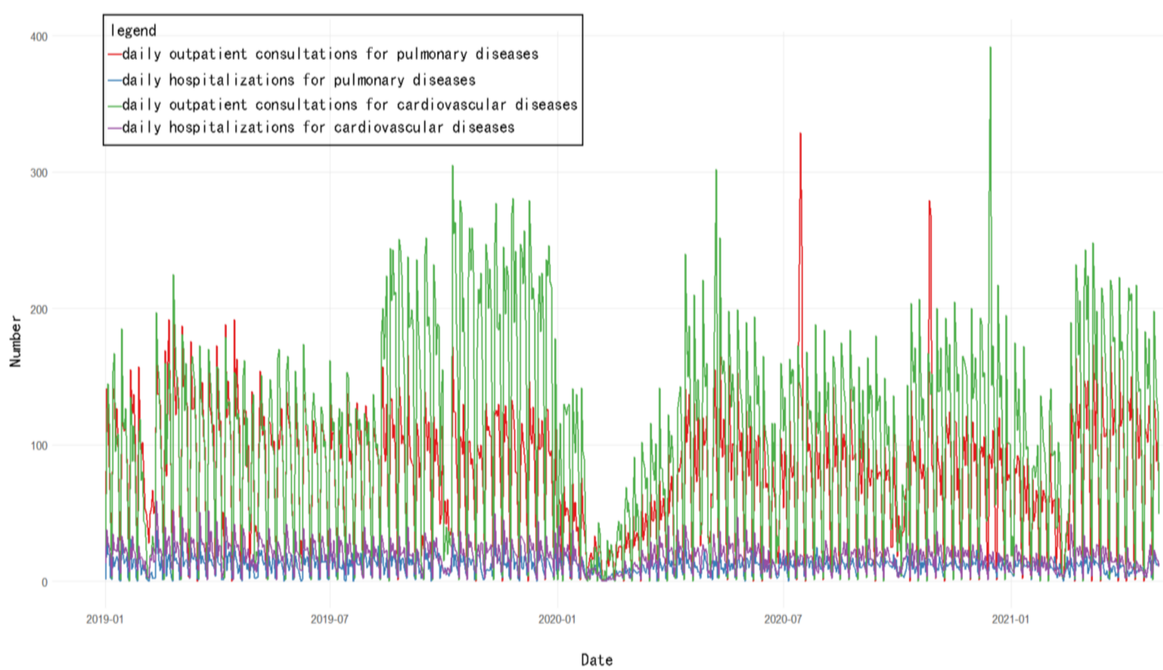
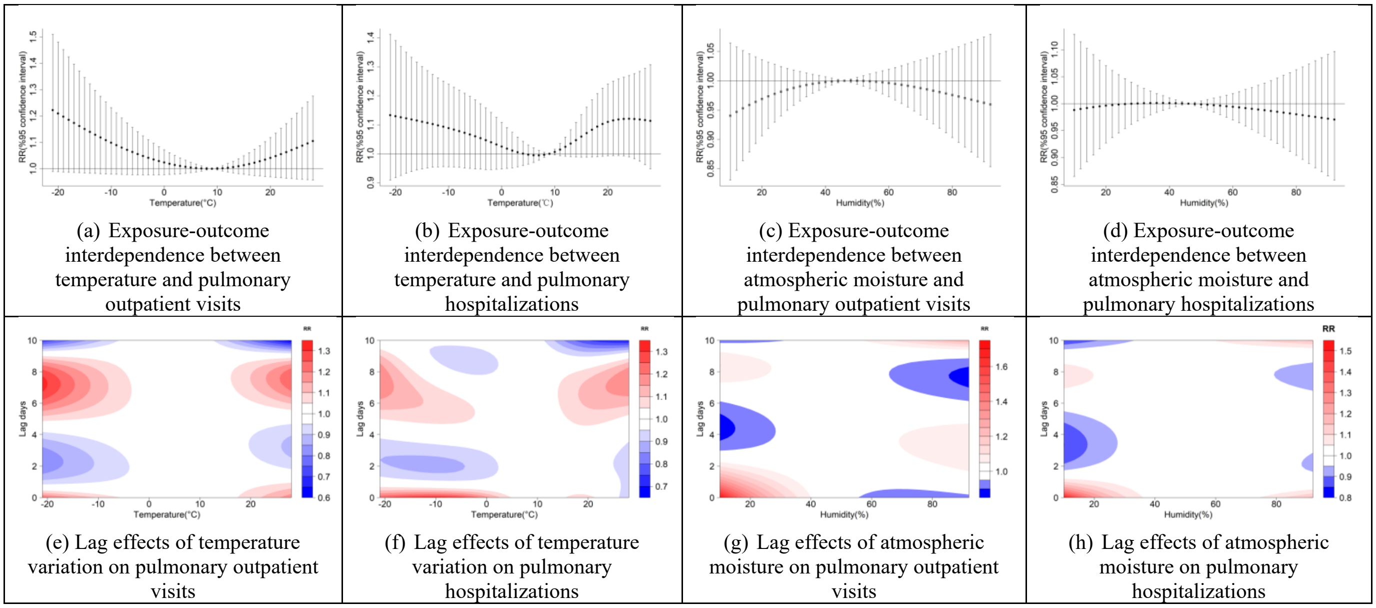


Figure 2. Time-series plot of daily cases counts for respiratory and cardiovascular diseases in Zhangjiakou city (2019-2021).



(a) Exposure-outcome interdependence between temperature and pulmonary outpatient visits

(b) Exposure-outcome interdependence between temperature and pulmonary hospitalizations

(c) Exposure-outcome interdependence between atmospheric moisture and pulmonary outpatient visits

(d) Exposure-outcome interdependence between atmospheric moisture and pulmonary hospitalizations

(e) Lag effects of temperature variation on pulmonary outpatient visits

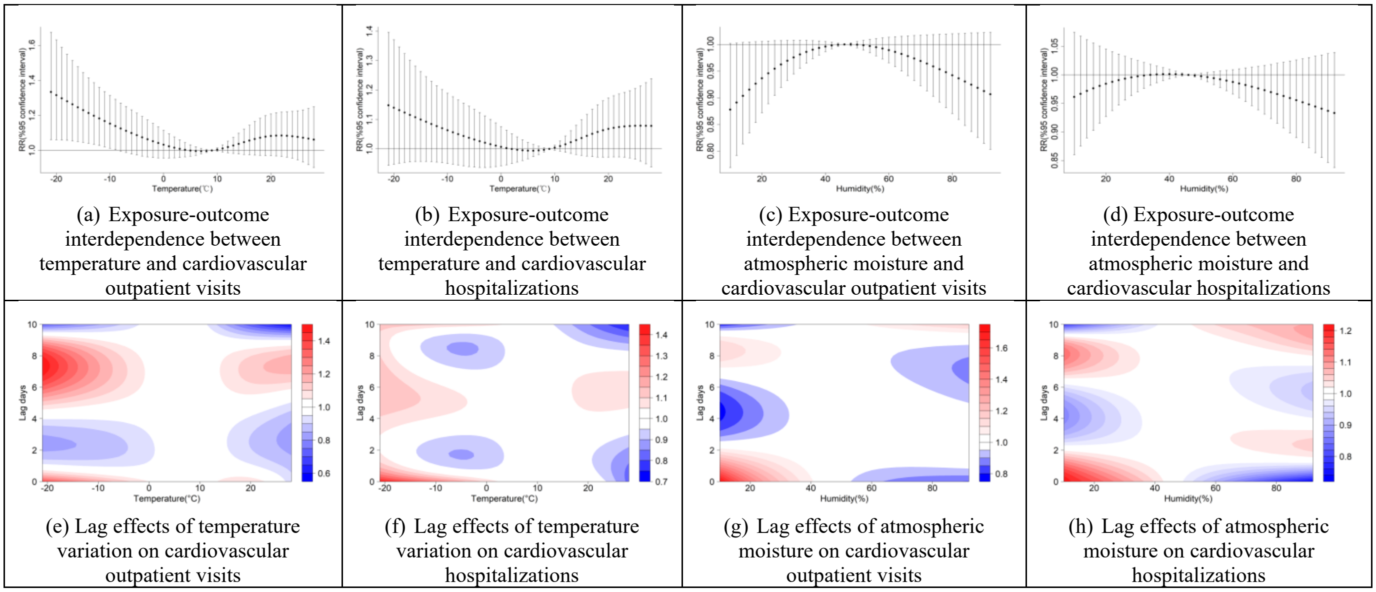
(f) Lag effects of temperature variation on pulmonary hospitalizations

(g) Lag effects of atmospheric moisture on pulmonary outpatient visits

(h) Lag effects of atmospheric moisture on pulmonary hospitalizations

Figure 3. Impact of temperature and atmospheric moisture on respiratory diseases in Zhangjiakou city.

variables and respiratory outpatient visits/hospitalizations as separate dependent variables, analytical models were constructed after controlling for temporal trends, day-of-week effects, and pollutant confounders. The results demonstrated that the temperature-exposure response curve exhibited a significant U-shaped nonlinear pattern ($P < 0.01$), identifying 9.0°C as the minimum-risk threshold (Figures 3a and 3b). Deviations from this threshold (T < 9.0°C or T > 9.0°C) significantly increased RR for both outpatient visits and hospitalizations with particularly pronounced RR elevations during cold exposure (T < 9.0°C). Conversely, the atmospheric moisture-exposure response curve revealed a significant inverted U-shaped relationship, peaking at a maximum-risk threshold of 46% daily average atmospheric moisture (RH) (Figures 3c and 3d). Atmospheric moisture deviations (RH < 46% or RH > 46%) significantly reduced health care utilization RR with more substantial declines under dry conditions (RH < 46%). This evidence indicated compounded health threats from cold-dry synergism on respiratory health. The minimum, 25th percentile, 75th percentile, and maximum daily average temperatures were taken as observation values to investigate the contribution of ambient temperature on respiratory diseases over lag times ranging from 0 to 10 days. Analysis of the data revealed that daily average temperatures of 8°C and 19°C posed no health risks to the respiratory system. However, daily minimum temperatures of -21°C and maximum temperatures of 28°C had a robust correlation with respiratory diseases in the population with low temperatures exhibiting a more significant impact than high temperatures. The higher values of the RR for outpatient consultations and hospitalizations due to respiratory diseases associated with daily minimum temperatures occurred on the same day (lag 0) with RR values of 1.19 (0.65 ~ 2.20) and 1.24 (0.68 ~ 2.26), respectively. The subsequent second peak appeared on the seventh day (lag 7) with RR values of 1.32 (1.05 ~ 1.66) and 1.19 (0.95 ~ 1.48), respectively. All results passed the significance test ($P < 0.05$), indicating statistical significance. The contribution of temperature changes on outpatient consultations and hospitalizations for respiratory diseases at different lag times (lag 0 ~ lag 10) was shown in Figures 3e and 3f. The RR for the association between atmospheric moisture



(a) Exposure-outcome interdependence between temperature and cardiovascular outpatient visits
(b) Exposure-outcome interdependence between temperature and cardiovascular hospitalizations
(c) Exposure-outcome interdependence between atmospheric moisture and cardiovascular outpatient visits
(d) Exposure-outcome interdependence between atmospheric moisture and cardiovascular hospitalizations
(e) Lag effects of temperature variation on cardiovascular outpatient visits
(f) Lag effects of temperature variation on cardiovascular hospitalizations
(g) Lag effects of atmospheric moisture on cardiovascular outpatient visits
(h) Lag effects of atmospheric moisture on cardiovascular hospitalizations

Figure 4. The impacts of temperature and atmospheric moisture on cardiovascular diseases in Zhangjiakou.

and respiratory diseases was fitted and showed that the hazardous effect of low atmospheric moisture on respiratory diseases was most significant at lag 0 day (lag 0) and continued to cause elevated risk during lag 7 - 9 days (lag 7 - 9). In contrast, the effect of high atmospheric moisture was concentrated in two time periods including lag 2 - 5 days (lag 2 - 5) and lag 9 - 10 days (lag 9 - 10). Data analysis indicated that the risk effect of extremely low humidity (10% RH) on respiratory diseases was significantly higher than that of high humidity (92% RH). At lag 0, the RR values for respiratory disease outpatient visits associated with 10% and 92% atmospheric moisture were 1.73 (0.57 - 5.23) and 0.94 (0.37 - 2.40), respectively. By lag 8, the RR values were 1.10 (0.94 - 1.26) and 0.88 (0.77 - 1.02), respectively. Hospital admission data showed a similar pattern that, at lag 0, the RR values for extremely low and high humidity were 1.53 (0.47 - 5.03) and 1.17 (0.44 - 3.10), respectively. By lag 8, they were 1.07 (0.92 - 1.25) and 0.93 (0.81 - 1.08), respectively (Figures 3g and 3h). All association results showed significant difference ($P < 0.05$). Notably, the outpatient RR (1.73) and hospitalization RR (1.53) for 10% low-humidity environment at lag 0 represented the highest risk levels, indicating that the immediate threat of dry conditions to respiratory health was statistically significant.

Impact of temperature and atmospheric moisture on cardiovascular diseases

The RR of temperature on cardiovascular diseases showed that, after adjusting for long-term temporal trends, day-of-week effects, and major air pollutants of $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, O_3, the exposure-outcome interdependence between daily average temperature and cardiovascular diseases related outpatient visits/admissions in Zhangjiakou city exhibited an approximately reverse J-shaped pattern (Figures 4a and 4b). The results indicated that 9.0°C served as the critical threshold temperature, at which the RR for both cardiovascular diseases outpatient visits and hospital admissions were minimized. When temperatures were below or higher than this threshold, both outpatient visits and hospital admissions demonstrated an increasing trend. Simultaneously, the exposure-outcome interdependence between relative humidity and cardiovascular diseases related outpatient visits/admissions in Zhangjiakou displayed an approximately inverted U-shaped distribution (Figures 4c and 4d). Analysis revealed that 46% relative humidity was the threshold for impact, where cardiovascular diseases risk was maximized at this humidity level. When relative humidity was either lower or higher than 46%, both outpatient visits and hospital admissions exhibited a decreasing trend. During the study period, the minimum, 25th percentile, 75th percentile, and maximum values of the daily average temperature in Zhangjiakou were -21°C, 8°C, 19°C, and 28°C, respectively. The results indicated that 8°C and 19°C were relatively comfortable temperatures for the population, associated with lower cardiovascular disease risk, while the daily minimum temperature of -21°C and daily maximum temperature of 28°C showed significant correlations with the number of cardiovascular diseases outpatient visits and hospital admissions. The peak RR for the impact of the daily minimum temperature on both outpatient visits and admissions occurred on the same day (lag 0) with RR values of 1.37 (0.75 - 2.50) and 1.42 (0.84 - 2.42), respectively. A second peak in outpatient visits appeared at lag 7 days, and for hospital admissions, it appeared at lag 6 days. Both results were statistically significant ($P < 0.05$). Using 9.0°C as the reference temperature, analysis of the impact of different temperatures and lag days (lag 0 - lag 10) on cardiovascular diseases outpatient visits and admissions revealed that, on the same day (lag 0) and at lags 6 - 8 days (lag 6 - 8), temperatures deviating from 9°C on both higher and lower sides gradually increased the risk of cardiovascular diseases outpatient visits (Figures 4e and 4f). Similarly, on the same day (lag 0), temperature deviations from 9°C on both higher and lower sides also gradually increased the risk of hospital admissions. Under extreme temperatures, the impact of the minimum temperature (-21°C) and maximum temperature (28°C) on outpatient visit risk manifested as that the highest risk occurred on the same day, subsequently decreased, reaching its lowest point at lag 2 days, then rose again to peak at lag 7 days before declining once more. The impact of the minimum temperature (-21°C) on hospital admission risk was characterized by the highest risk on the same day followed by a decline to its lowest point around lag 2 days, after which it exhibited mild fluctuations. Conversely, the impact of the maximum temperature (28°C) on hospital admission risk showed an initial increase followed by a decrease with increasing lag time, peaking at lag 6 days. Analysis of the impact of different atmospheric moisture levels and lag days (lag 0 ~ lag 10) on cardiovascular diseases outpatient visits and hospital admissions showed that, for outpatient visits, the risk associated with low humidity was the highest on the same day (lag 0). Low humidity also posed a risk at lags 7 - 9 days (lag 7 - 9), while high humidity posed a risk at lag 10 days (lag 10). For hospital admissions, the risk associated with low humidity was significant on the same day (lag 0) and at lag 8 days (lag 8), whereas the risk associated with high humidity appeared at lags 2 - 3 days (lag 2 - 3) and lags 8 - 10 days (lag 8 - 10). Overall, the risk of low humidity on hospital admissions was higher than that of high humidity, indicating that a dry environment poses a greater cardiovascular health risk to the Zhangjiakou population than a highly humid environment. As the lag time extended, both extremely low (10%) and extremely high (92%) atmospheric moisture levels presented a stable risk profile with low-amplitude fluctuations. Specifically, on the same day (lag 0), the RR for outpatient visits and hospital admissions at 10% humidity were 1.73 (0.55 - 5.46) and 1.21 (0.45 -3.29), respectively. At 92% humidity, they were 0.85 (0.32 - 2.24) and 0.73 (0.31 - 1.72), respectively. At lag 8 days, the RR for outpatient visits and hospital admissions at 10% humidity were 1.13 (0.97 - 1.32) and 1.13 (0.99 - 1.30), respectively, while, at 92% humidity, they were 0.90 (0.78 - 1.04) and 1.02 (0.90 - 1.15), respectively (Figures 4g and 4h). All the results were statistically significant ($P < 0.05$).

Synergistic effects of meteorological factors and atmospheric pollutants on population health risks

Spearman correlation analysis was employed to calculate correlation coefficients between six air pollutants ($PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, O_3) and the Air Quality Index (AQI) with daily average temperature and atmospheric moisture in Zhangjiakou from 2019 to 2021. The results

Table 2. Mutual effects of temperature, atmospheric moisture, and atmospheric pollutants on respiratory diseases in Zhangjiakou (2019 - 2021).

Respiratory diseases	Synergistic effects	Estimate	Std. Error	t value	Pr (>|t|)
Outpatient consultations	Main effect of average temperature	4.98	0.66	7.56	1.16e-13***
	Synergistic effect of $PM_{2.5}$	0.06	1.06	0.06	0.96
	Synergistic effect of PM_{10}	-1.23	1.46	-0.83	0.40
	Synergistic effect of SO_2	-1.09	0.47	-2.32	0.02058*
	Synergistic effect of NO_2	1.26	0.62	2.04	0.04177*
	Synergistic effect of CO	-0.06	0.64	-0.08	0.92
	Synergistic effect of O_3	-0.25	0.37	-0.71	0.47
	Synergistic effect of average atmospheric moisture	-0.12	0.19	-0.64	0.04474*
Hospitalizations	Main effect of average temperature	-0.30	0.33	-0.97	9.74e-07***
	Synergistic effect of $PM_{2.5}$	0.15	1.16	0.13	0.90
	Synergistic effect of PM_{10}	-1.05	1.61	-0.66	0.51
	Synergistic effect of SO_2	-1.19	0.47	-2.57	0.00986**
	Synergistic effect of NO_2	1.75	0.63	2.8	0.00571**
	Synergistic effect of CO	-0.68	0.66	-1.04	0.29
	Synergistic effect of O_3	0.30	0.38	0.80	0.42
	Synergistic effect of average atmospheric moisture	-0.28	0.20	-1.52	0.03116*

Note: *: a significant impact at the 0.05 level. **: a significant impact at the 0.01 level. ***: a significant impact at the 0.001 level.

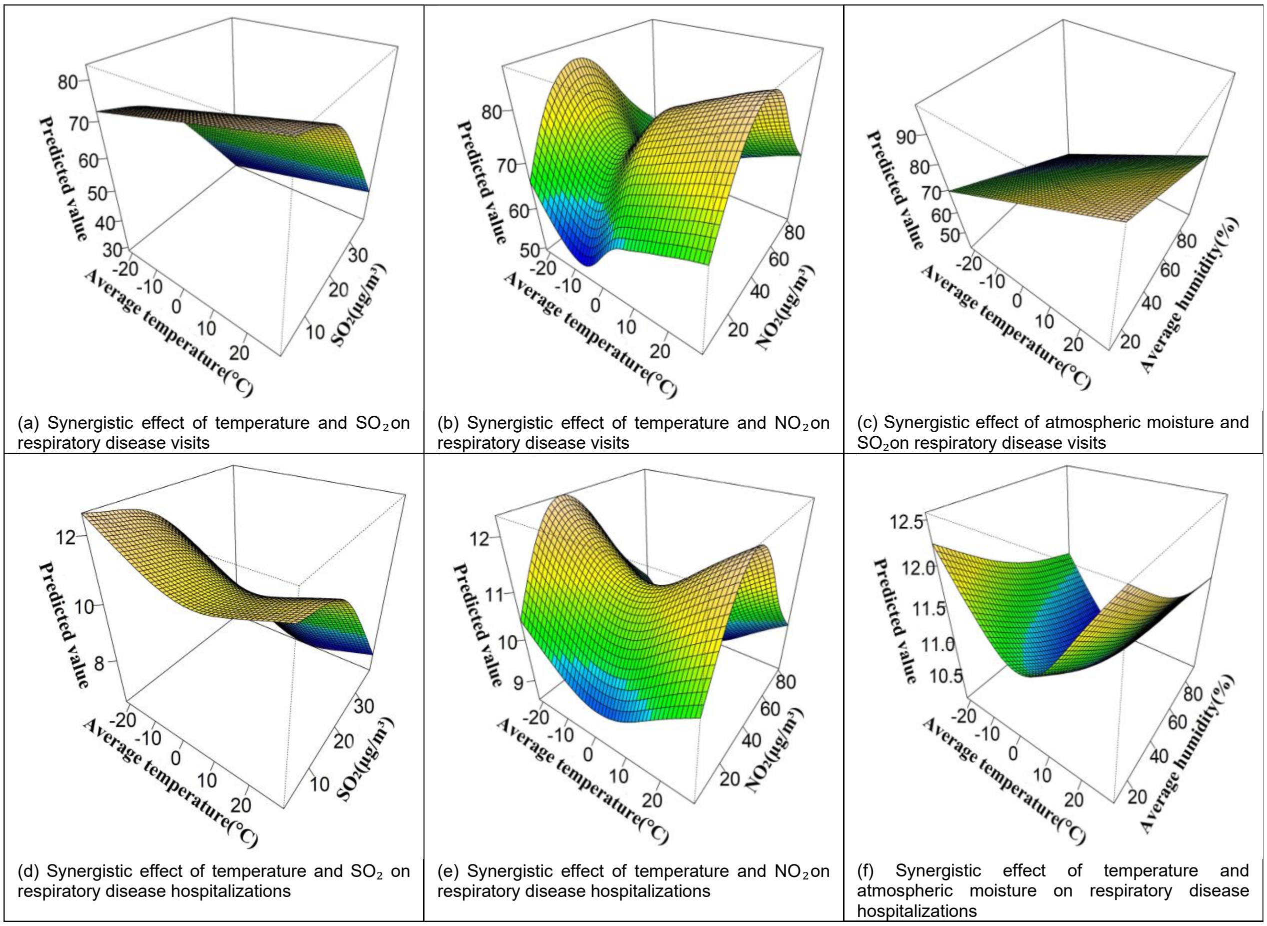
demonstrated that daily temperature showed statistically significant positive correlations with atmospheric moisture, AQI, and O_3, but negative correlations with all other pollutants except PM_{10}. Atmospheric moisture exhibited negative correlations with AQI and PM_{10}, yet positive correlations with the other four pollutants. AQI maintained significant positive correlations with all pollutants. Notably, PM_{10}, $PM_{2.5}$, SO_2, NO_2, and CO all displayed negative correlations with O_3, while these five pollutants showed statistically significant positive correlations with one another. These findings suggested that there were complex interactions between meteorological factors and atmospheric pollutants in Zhangjiakou city, and these correlations might have important implications for public health and environmental management. Understanding these relationships was crucial for developing effective Initiatives to curb the damaging effects of atmospheric pollution on human health.

(1) Mutual effect of ambient temperature, atmospheric pollutants, and atmospheric moisture on respiratory diseases

The results showed that the mutual effect of temperature with SO_2, NO_2, and atmospheric moisture on respiratory diseases outpatient consultations and hospitalizations was statistically significant, while the synergistic effect with other atmospheric pollutants was not. Analysis revealed that the impact of atmospheric pollutants in combination with temperature on respiratory diseases differed from that of individual pollutants. SO_2 as a single pollutant had no statistically significant impact on respiratory diseases outpatient consultations, but its synergistic effect with temperature did have statistical significance, which suggested that the risk of atmospheric pollutants to human health varied under different meteorological conditions. Therefore, analyzing the health risk of atmospheric pollutants to humans in conjunction with meteorological factors provided a more objective result (Table 2).

(2) The association of the interactive effects of ambient temperature, particulate matter and gases, and atmospheric moisture with respiratory diseases numbers

The RR of daily temperature and SO_2 interaction on respiratory disease outpatient visits in Zhangjiakou showed that, under constant temperature, increasing SO_2 concentrations correlated with decreasing visit risk, whereas, at



(a) Synergistic effect of temperature and SO_2 on respiratory disease visits

(b) Synergistic effect of temperature and NO_2 on respiratory disease visits

(c) Synergistic effect of atmospheric moisture and SO_2 on respiratory disease visits

(d) Synergistic effect of temperature and SO_2 on respiratory disease hospitalizations

(e) Synergistic effect of temperature and NO_2 on respiratory disease hospitalizations

(f) Synergistic effect of temperature and atmospheric moisture on respiratory disease hospitalizations

Figure 5. Synergistic effects of temperature, air pollutants, and relative humidity on respiratory diseases in Zhangjiakou.

fixed SO_2 levels, rising temperature significantly exacerbated risk. Peak risk occurred at the combined exposure scenario of 28.9°C and 2μg/m³ SO_2 (Figure 5a). Isothermal conditions showed NO_2 elevation driving respiratory visit/hospitalization risks along a unimodal curve as increase followed by decrease. Under fixed NO_2 concentrations, temperature increase generated a V-shaped risk response for visits (decrease then increase), confirming the dual-pathway damage mechanism of temperature extremes. Peak visit risk emerged under high-temperature/moderate-NO_2 conditions as 28.9°C/32 μg/m³ (Figure 5b), while hospitalization risk peaked under low-temperature/moderate-NO_2 exposure of -21.5°C/28.86 μg/m³ (Figure 5e). The temperature-humidity interaction on the RR of respiratory visits indicated that increasing humidity under constant temperature conditions suppressed the risk of visits, whereas increasing temperature under constant humidity conditions exacerbated the risk, confirming the synergistic hazards in dry-hot environments. Maximum risk concentration occurred at the extreme combination of 28.9°C and 10% humidity (Figure 5c). The differential impacts of SO_2-temperature interaction on respiratory hospitalizations in Zhangjiakou showed that, under isothermal conditions, SO_2 concentration increase exhibited negative correlation with hospitalization rates. At fixed SO_2 levels, temperature elevation drove hospitalization rates along a J-shaped curve (initial decrease followed by increase) with particularly pronounced risk escalation in low-temperature zones. Peak hospitalization risk manifested at the combined exposure of -21.5°C and 2 μg/m³ SO_2 (Figure 5d). Synergistic effects of

Table 3. Interactive effect of ambient temperature, atmospheric moisture, and atmospheric pollutants on cardiovascular diseases in Zhangjiakou (2019 - 2021).

Cardiovascular diseases	Synergistic effects	Estimate	Std. Error	t value	Pr (>|t|)
Outpatient consultations	Main effect of average temperature	5.125	0.730	7.021	4.74e-12***
	Synergistic effect of $PM_{2.5}$	0.153	1.096	0.139	0.889
	Synergistic effect of PM_{10}	-1.634	1.554	-1.051	0.294
	Synergistic effect of SO_2	-0.97	0.478	-2.028	0.04295*
	Synergistic effect of NO_2	0.934	0.637	1.466	0.143
	Synergistic effect of CO	0.229	0.672	0.340	0.734
	Synergistic effect of O_3	-0.164	0.398	-0.412	0.681
	Synergistic effect of average atmospheric moisture	-0.395	0.193	-2.048	0.04084 *
Hospitalizations	Main effect of average temperature	4.226	0.573	7.380	4.03e-13***
	Synergistic effect of $PM_{2.5}$	-0.494	0.997	-0.495	0.621
	Synergistic effect of PM_{10}	-0.232	1.345	-0.172	0.863
	Synergistic effect of SO_2	-1.258	0.412	-3.049	0.002370**
	Synergistic effect of NO_2	1.973	0.543	3.630	0.000302***
	Synergistic effect of CO	-0.414	0.572	-0.725	0.469
	Synergistic effect of O_3	0.335	0.327	1.026	0.305
	Synergistic effect of average atmospheric moisture	-0.497	0.161	-3.082	0.002110**

Note: *: a significant impact at the 0.05 level. **: a significant impact at the 0.01 level. ***: a significant impact at the 0.001 level.

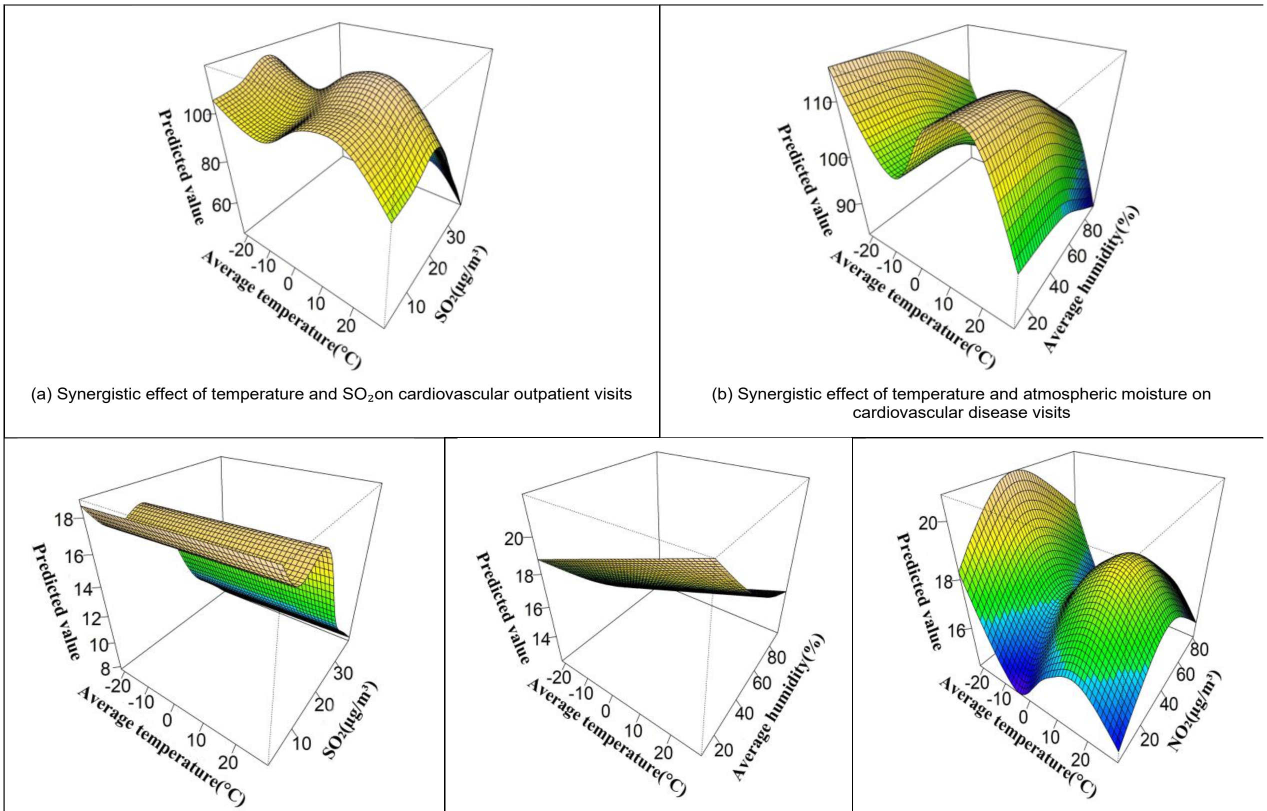
temperature and atmospheric moisture on respiratory hospitalization risk indicated minimal humidity impact under constant temperature, whereas fixed humidity conditions showed temperature increase driving a U-shaped risk response with both extreme heat and cold significantly elevating risk. Hot-dry and cold-dry environments exhibited the strongest synergistic effects with the 28.9°C/10% RH combination showing the most pronounced risk peak (Figure 5f).

(3) Interactive effect of temperature, air contaminants, and atmospheric moisture on cardiovascular diseases

The combined effects of mean daily temperature, atmospheric moisture, and concurrent particulate matter and gases on cardiovascular disease outpatient consultations and hospitalizations in Zhangjiakou from 2019 to 2021 showed that the interactive effect of ambient temperature, SO_2, and atmospheric moisture on cardiovascular disease outpatient consultations was significant. Similarly, the synergistic effect of temperature, SO_2, NO_2, and atmospheric moisture on cardiovascular disease hospitalizations was also significant (Table 3). However, the synergistic effect with other atmospheric pollutants was not statistically significant.

(4) Contribution of the interactive effect of ambient temperature, atmospheric pollutants, and moisture on cardiovascular disease cases

The three-dimensional distribution of RR for cardiovascular outpatient visits under temperature-SO_2 interaction showed that, under constant temperature conditions, visit risk followed a unimodal pattern as initial increase then decrease with rising SO_2 concentrations. At fixed SO_2 levels, low temperatures significantly increased visit risk. Peak risk occurred at the combined exposure of 13.8°C and 15 μg/m³ SO_2 (Figure 6a). The RR of temperature-humidity interaction on cardiovascular visits indicated that higher humidity reduced outpatient visit risk under constant temperature, while elevated temperatures showed minimal impact at fixed humidity. Maximum RR manifested in hot-dry conditions (21.5°C/10% RH) (Figure 6b). The impact mechanism of SO_2-temperature interaction on cardiovascular hospitalizations showed that constant temperature conditions reduced hospitalization risk with decreasing SO_2



(a) Synergistic effect of temperature and SO_2on cardiovascular outpatient visits

(b) Synergistic effect of temperature and atmospheric moisture on cardiovascular disease visits

(c) Synergistic effect of temperature and SO_2 on cardiovascular disease hospitalizations

(d) Synergistic effect of temperature and atmospheric moisture on cardiovascular disease hospitalizations

(e) Synergistic effect of temperature and NO_2 on cardiovascular disease hospitalizations

Figure 6. Synergistic effects of temperature, air pollutants, and atmospheric moisture on cardiovascular diseases in Zhangjiakou.

concentrations. At fixed SO_2 levels, temperature variations demonstrated non-significant risk effects. The hospitalization risk maximum occurred at 13.8°C with 2 $\mu g/m^3$ SO_2 (Figure 6c). The synergistic effects of temperature-humidity interaction on hospitalization risk showed that higher humidity suppressed risk under constant temperature, while low temperatures exhibited limited impact at fixed humidity. Peak risk was observed under hot-dry conditions at 28.9°C/10% RH (Figure 6d). The RR of temperature-NO_2 interaction on cardiovascular hospitalizations revealed that, at constant temperature, rising NO_2 concentrations drove hospitalization risk along an inverted U-shaped curve. Fixed NO_2 conditions showed significantly increased risk at low temperatures. The maximum relative risk occurred at the extreme exposure combination of -21.5°C and 38 $\mu g/m^3$ NO_2 (Figure 6e).

Conclusion

Based on the analysis of atmospheric pollution concentrations, Zhangjiakou, a typical city in the Beijing-Tianjin-Hebei region, was classified as a city with light air pollution. The analysis revealed that, even though the concentrations of atmospheric pollutants in Zhangjiakou were below the current national secondary standards, there were still certain risks to human health. The relative risk of NO_2 was particularly evident for respiratory and cardiovascular diseases among the population. The concentrations of $PM_{2.5}$, PM_{10}, and NO_2 posed a higher relative risk for cardiovascular diseases than for respiratory diseases in Zhangjiakou. The cooperative effects of atmospheric conditions of temperature and moisture combined with atmospheric pollutants had a complex impact on respiratory and cardiovascular diseases in Zhangjiakou. These effects were influenced by multiple factors and differed for different diseases. The findings of this study indicated that high moisture environments posed a higher health risk to the population than dry environments. The synergistic effects of temperature with SO_2 and NO_2 had statistical significance in influencing outpatient consultations and hospitalizations for respiratory diseases, but not with other atmospheric pollutants. The synergistic effect of temperature and SO_2 had statistical significance for both outpatient consultations and hospitalizations related to cardiovascular diseases. Additionally, the synergistic effect of temperature and NO_2 had statistical significance for cardiovascular hospitalizations. The synergistic effects of temperature and moisture also had statistical significance for both respiratory and cardiovascular diseases.

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