

# **GeoHealth**

## **RESEARCH ARTICLE**

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#### **Special Collection:**

One Health, Microbes, and Climate Change

#### **Key Points:**

- · Temperature had an inverted U-shape with respiratory syncytial virus infections, while relative humidity was positively correlated
- The risk effects of extreme climatic factors were observed on the concurrent day and persisted over extended lag periods
- The attributable burden of respiratory syncytial virus infections associated with cold was higher than that related to humid conditions

#### **Supporting Information:**

Supporting Information may be found in the online version of this article.

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# **Association of Ambient Temperature and Relative Humidity** With Respiratory Syncytial Virus Infections Among Hospitalized Children in Suzhou, Eastern China: A Time-**Series Analysis**

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**Abstract** Respiratory syncytial virus (RSV) is the leading cause of clinical pneumonia in children. We aimed to investigate the associations between ambient temperature, relative humidity, and pediatric RSV infections, and to assess the disease burden attributable to cold or humid conditions. Daily data on RSV hospitalizations among children aged ≤5 years, mean temperature, and relative humidity in Suzhou, China, from January 2016 to December 2019 were collected. A distributed lag nonlinear model with quasi-Poisson regression was employed to assess the exposure-lag-response associations. Attributable risks were calculated to quantify the disease burden due to climatic factors. We found an inverted U-shaped relationship between temperature and RSV infections, with the cumulative risk of RSV peaking at 7.5°C (RR = 4.30, 95% CI: 3.08– 6.02). The exposure-response curves for relative humidity exhibited a generally positive trend, peaking at 100.0% (RR = 3.14, 95% CI: 1.84–5.34). Using median values as references, the highest risk effects of extremely low (RR = 1.14, 95% CI: 1.04-1.25) and low (RR = 1.22, 95% CI: 1.12-1.32) temperatures, as well as high (RR = 1.09, 95% CI: 1.04–1.13) and extremely high (RR = 1.16, 95% CI: 1.07–1.27) relative humidity, occurred on the day of exposure and persisted for extended periods. The attributable fraction of RSV infections associated with cold or humid conditions was 55.23% (95% CI: 50.01%-64.03%) and 12.02% (95% CI: 9.36%-20.24%), respectively. The risk effect of high relative humidity was stronger in children aged 1-5 years. Our findings suggest nonlinear, lagged associations between climatic factors and pediatric RSV infections, which may inform future healthcare planning and RSV immunization strategies.

Plain Language Summary Respiratory syncytial virus (RSV) is the leading pathogen responsible for clinical pneumonia in infants and young children. RSV epidemics typically occur during the winter in temperate and subtropical climates, whereas in tropical climates, peak activity is observed during the rainy season. Climatic variables play a key role in shaping RSV seasonality, and understanding these drivers is essential for enhancing epidemic forecasting, informing healthcare planning, and developing effective prevention strategies. In this study, we used a distributed lag non-linear model to investigate the exposure-lag-response associations between ambient temperature and relative humidity and pediatric RSV infections in Suzhou, Eastern China. From 2016 to 2019, a total of 5,008 hospitalized cases of RSV infections among children aged ≤5 years were included in this analysis. We observed an inverted U-shaped relationship between ambient temperature and RSV infections, while relative humidity exhibited a generally positive correlation. The risk effects associated with extreme conditions of low temperature and high relative humidity were observed on the day of exposure and extended over prolonged lag periods. Besides, cold or humid conditions could account for a substantial proportion of pediatric RSV infections. These findings will enhance early warning systems for RSV epidemics and inform healthcare planning.

## 1. Introduction

Respiratory syncytial virus (RSV) is the leading pathogen responsible for acute lower respiratory infections in infants and young children, with RSV infections ranking as the second most frequent cause of infant mortality globally (Lozano et al., 2012; Terstappen et al., 2024). Serological surveys have indicated that nearly every child is likely to be infected at least once with RSV before reaching 5 years of age (T. T. Lam et al., 2019). RSV imposes a significant burden on healthcare systems. Globally, it is estimated to lead to approximately 3.6 million hospital

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Visualization: Yingfeng Lu Writing – original draft: Yingfeng Lu Writing – review & editing: Xuejun Shao, Genming Zhao admissions for acute lower respiratory infections and 101,400 associated deaths each year among children under the age of five (Li, Wang, Blau, et al., 2022). In 2017, the global cost of managing inpatient and outpatient RSV infections among young children was estimated to be  $\epsilon$ 4.82 billion (S. Zhang et al., 2020).

RSV demonstrates annual seasonal epidemics across most regions worldwide (Obando-Pacheco et al., 2018). In temperate and subtropical climates, RSV epidemics typically occur during winter, whereas in tropical climates, peak activity is observed during the rainy season (Darniot et al., 2018). It is well documented that meteorological variables, such as temperature and relative humidity, exert a substantial influence on hosts, airborne pathogens, and their environmental interactions, thereby modulating the seasonal patterns of RSV (He et al., 2023). Understanding the meteorological drivers of RSV activity is crucial for improving early predictions of RSV epidemics, facilitating healthcare planning, and informing the development of effective disease prevention and control strategies, including immunization programs. Growing evidence further highlights the significant role of temperature and humidity in shaping RSV seasonality (Radhakrishnan et al., 2020; Tang & Loh, 2014). For instance, a global study has indicated that increased RSV activity tends to occur in conditions of lower temperatures and higher relative humidity (Li et al., 2019). However, the relationship between climatic variability and disease dynamics is complex, nonlinear, and often characterized by multiple delayed events (Xiao et al., 2017). Currently, evidence on the exposure-lag-response relationship between RSV activity and climatic conditions, which could improve epidemic predictions, optimize healthcare resource allocation, and inform targeted prevention strategies, remains limited, particularly in subtropical regions. In addition, no investigations have attempted to quantify the attributable disease burden of RSV infections due to meteorological factors, either in terms of relative excess (fractions) or absolute excess (case counts), which better reflected the overall disease burden and disease prevention effectiveness.

Therefore, this study aimed to investigate the associations between ambient temperature and relative humidity and pediatric RSV infections in subtropical Suzhou, China, while also quantifying the disease burden attributable to climatic factors within the context of their complex exposure-lag-response relationships. The findings can be expected to support the development of targeted RSV prevention and control strategies, including immunization programs, thereby mitigating the overall burden of RSV infections.

# 2. Methods

## 2.1. Study Site

The study was conducted in Suzhou (30°47′ to 32°02′N, 119°55′ to 121°20′E), a major city in eastern China, encompassing an estimated area of 8,657 km² and a population of approximately 12 million. Suzhou has a humid subtropical monsoon climate with four distinct seasons. Soochow University Affiliated Children's Hospital (SCH) is the only tertiary children's hospital in Suzhou, with a capacity of 1,306 beds. It provides medical care to approximately 2.3 million outpatients and 70,000 inpatients annually. According to our Healthcare Admission Survey (HAS), SCH accounted for 65.2% of all pediatric admissions in downtown Suzhou (Shan et al., 2018).

### 2.2. Data Collection

Data on laboratory-confirmed RSV hospitalizations, including gender, age, and hospitalization date, were collected from the Laboratory Information System (LIS) at SCH from 1 January 2016 to 31 December 2019. Nasopharyngeal secretions were collected within 24 hr of admission from pediatric respiratory patients, with RSV detection routinely conducted via direct fluorescence antibody testing. A laboratory-confirmed RSV infections case was defined as a positive result in laboratory testing. Hospitalized children aged ≤5 years were included in the study. Daily counts of RSV hospitalizations were compiled to construct a database for further analysis.

Daily meteorological data for Suzhou (observation site code: 58439), including mean temperature (°C), relative humidity (%), wind speed (m/s) and sunshine duration (hr) for the study period were retrieved from China Meteorological Data Network (http://data.cma.cn/). The daily mean temperature (°C), relative humidity (%) and wind speed (m/s) were calculated as the average of the four readings at 0200, 0800, 1400, and 2000 every day (China Meteorological Data Service Center, 2025a, 2025b, 2025c).

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## 2.3. Statistical Analysis

Descriptive analyses were conducted for daily hospitalized cases of RSV infections, mean temperature, relative humidity, wind speed and sunshine duration. The time series diagram for the focused variables was plotted to show their temporal trends. Additionally, the correlation between different meteorological factors was evaluated using Spearman rank analysis, and meteorological factor pairs were included in subsequent analyses if the correlation coefficient was <0.7 to avoid multicollinearity.

To better estimate the nonlinear and lagged effects of mean temperature and relative humidity on RSV infections among children, we developed a distributed lag non-linear model (DLNM) for each meteorological factor and combined it with a quasi-Poisson regression model to account for overdispersion in count data (Gasparrini, 2014). DLNM can provide a flexible cross-basis function, enabling the modeling of complex, nonlinear exposure-response relationships across lag days and cumulative lagged effects for both mean temperature and relative humidity (Gasparrini et al., 2015). The model was formulated as follows:

$$Log[E(Y_t)] = \alpha + cb(M, lag) + \sum ns(X_i, df) + year + month + DOW + holiday$$

where  $E(Y_t)$  denotes the expected daily count of RSV infections; cb(M, lag) indicates the cross-basis function for the primary meteorological variable of interest (e.g., mean temperature or relative humidity); ns() represents the natural cubic spline function; Xi denotes the confounding meteorological variables that should be controlled. To adjust seasonality and long-term trend, we used year and month as categorical variables in the model (He et al., 2021; Li et al., 2020; Z. Xu et al., 2019). Besides, DOW represents the categorical variable for day of week and holiday denotes the binomial variable to control public holidays.

The exposure-outcome relationships were modeled using a natural cubic spline with specified degrees of freedom (df). Knots for meteorological variables were placed at equally spaced quantiles, while knots for the lag structure were set at equally spaced intervals on the log scale of lag days. We empirically selected a maximum of up to 14 lag days according to previous studies (Li, Wang, Broberg, et al., 2022; Wagatsuma et al., 2023). The optimal df for the natural cubic spline functions were determined primarily based on the Quasi-Akaike Information Criterion. The final df selected for the meteorological factors and their corresponding lags were 4 and 3 for mean temperature, and 3 and 3 for relative humidity, respectively. We defined the median values of daily mean temperature and relative humidity as the reference levels to model the exposure-response relationship and estimate relative risks (RRs) with corresponding 95% confidence intervals (CIs), based on previous studies (Lam et al., 2018; Yang et al., 2024). The effects of extreme weather conditions were explored by comparing extremely low (1st percentile) and low (10th percentile) values, as well as high (90th percentile) and extremely high (99th percentile) values of mean temperature and relative humidity, with their respective medians. We also conducted subgroup analyses stratified by gender (male and female) and age (<1 year and 1–5 years). Z-test was used to identify statistical differences between stratum-specific estimates (Altman & Bland, 2003).

As our analysis observed an increased risk of RSV infections under cold or humid conditions, we calculated the attributable number (AN) and attributable fraction (AF) of RSV infections due to cold or humid conditions. We followed the forward approach provided by Gasparrini and Leone, which estimated the future burden caused by the current exposure (Gasparrini & Leone, 2014). The total AN of RSV infections due to cold or humid conditions was calculated as the sum of contributions from days with mean temperatures lower than the median or relative humidity higher than the median, respectively. The total AF was given by dividing the total AN by the total number of RSV infections cases. Further we separated the total AN and AF into contributions from extremely and moderately cold or humid conditions. Extremely cold or humid conditions were defined as ranges with mean temperatures below the 1st percentile and relative humidity above the 99th percentile, respectively, while moderately cold or humid conditions were defined as ranges between the median and these respective cutoffs. Empirical confidence intervals for AN and AF were estimated using Monte Carlo simulations with 5,000 random samples, assuming a multivariate normal distribution of the best linear unbiased predictions of the reduced coefficients.

The predicted versus observed RSV plot was used to assess the model's predictive performance (Figure S1 in Supporting Information S1). Partial autocorrelation function (PACF) plots were used to evaluate the extent of residual autocorrelation (Figure S2 in Supporting Information S1). The model was considered adequate if the

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Table 1
Descriptive Statistics for Daily RSV Infections Cases and Meteorological Factors in Suzhou, 2016–2019

					Percentile		
Variables	Mean	SD	Minimum	25th	50th	75th	Maximum
Daily RSV cases							
Total	3.5	5.0	0	0	1	5	28
Age group (year)							
<1	2.4	3.5	0	0	1	4	19
1–5	1.1	1.9	0	0	0	1	15
Gender							
Male	2.2	3.2	0	1	1	3	18
Female	1.3	2.1	0	1	0	2	14
Meteorological variables							
Mean temperature (°C)	17.8	8.9	-5.7	10.1	18.4	25.0	35.3
Relative humidity (%)	75.3	13.1	31.0	67.0	76.0	85.0	100.0
Wind speed (m/s)	2.3	0.9	0.7	1.7	2.2	2.8	6.7
Sunshine duration (hr)	4.9	4.1	0	0.2	5.1	8.7	12.8

Note. SD, standard deviation.

absolute values of the PACF for the first two lag days were less than 0.1 (Kan et al., 2008). Sensitivity analyses were performed to determine the selected model and specified parameters. We conducted the sensitivity analysis to evaluate the robustness of the model as follows: (a) The df (3–5) for mean temperature and relative humidity, and df (3–5) for lag space were adjusted. (b) The maximum lag days (10–17 days) for mean temperature and relative humidity were changed. (c) The number and placement of knots in the natural cubic spline functions for mean temperature and relative humidity were adjusted (at the 10th and 90th percentiles or at the 10th, 75th, and 90th percentiles).

The "dlnm" package in R (version:4.1.2) was utilized for data processing and statistical analysis. The AN and AF were calculated by the function "attrdl" provided by Gasparrini and colleagues (Gasparrini & Leone, 2014). A two-sided *p*-value <0.05 was set as the level of statistical significance.

## 3. Results

### 3.1. Data Description

From 2016 to 2019, a total of 5,008 hospitalized cases of RSV infections among children aged ≤5 years were included in this analysis. Table 1 presents the statistical characteristics of daily RSV infections cases and climatic variables. The average daily number of RSV cases was 3.5, with a male-to-female ratio of 1.7:1. On average, the daily mean temperature and relative humidity were 17.8°C (SD: 8.9) and 75.3% (SD: 13.1), respectively. Additionally, the seasonal pattern of daily RSV cases, as shown in Figure 1, indicates that RSV infections exhibited annual winter/spring peaks and were rarely observed during the hot summer.

The Spearman correlation analysis indicated that the correlation coefficients (r) between mean temperature and other meteorological variables, including relative humidity, wind speed, and sunshine duration, were less than 0.7 (Table S1 in Supporting Information S1). As no multicollinearity was detected, all other meteorological variables were included as control variables when examining the effect of mean temperature. Given that the correlation coefficient (r) between relative humidity and sunshine duration exceeded 0.7, only mean temperature and wind speed were included in the multivariable model when assessing the effect of relative humidity.

## 3.2. Nonlinear and Lagged Effect of Meteorological Factors on RSV Infections

Figure 2 presents the cumulative exposure-response curves for the relationship between mean temperature, relative humidity, and RSV infections across a 0–14 days lag period, using median values as references. The

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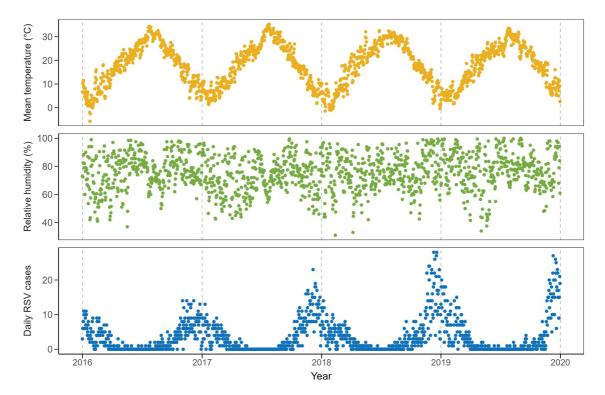


Figure 1. The time series distributions of daily meteorological factors and counts of RSV infections cases in Suzhou, China, 2016–2019.

effects of meteorological factors on the RSV infections were nonlinear. We observed an inverted U-shaped relationship between temperature and RSV infections, with the cumulative risk of RSV infections peaking at  $7.5^{\circ}$ C (RR = 4.30, 95% CI: 3.08–6.02). In contrast, the cumulative exposure-response curves for relative humidity on the risk of RSV infections showed a generally positive trend. The cumulative risk of RSV infections increased within the ranges of 31.0%–50.0% and 86.0%–100.0%, peaking at 100.0% (RR = 3.14, 95% CI: 1.84–5.34). Figure 3 shows the three-dimensional relationship between mean temperature, relative humidity, and RSV infections over a lag of 14 days, using median values as references. The largest separate effects of temperature and

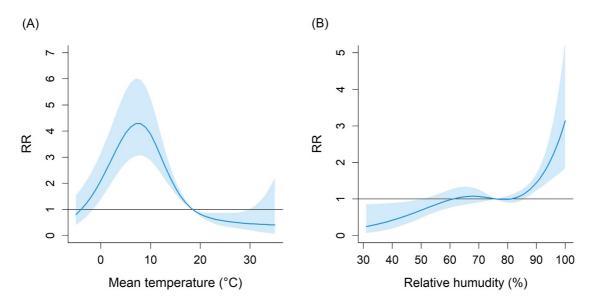
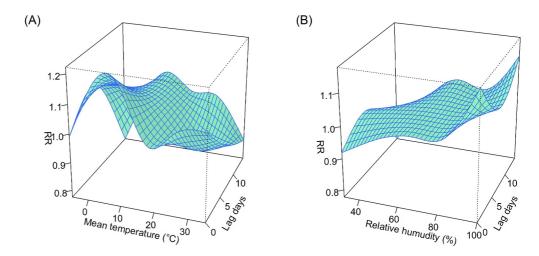


Figure 2. The cumulative relative risk effect of (a) mean temperature and (b) relative humidity on hospitalizations of RSV infections over a lag of 14 days. Median meteorological values (18.4°C for mean temperature, 76.0% for relative humidity) serve as references.

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**Figure 3.** Three-dimensional (3D) plot of the effect of (a) mean temperature and (b) relative humidity on hospitalizations of RSV infections over a lag of 14 days. *X*-axis, meteorological factors; *Y*-axis, lag days; *Z*-axis, relative risk (RR). Median meteorological values (18.4°C for mean temperature, 76.0% for relative humidity) serve as references.

relative humidity on RSV infections occurred on the day of exposure (lag 0 day), at a temperature of 6.8°C (RR = 1.22, 95% CI: 1.12–1.33) and a relative humidity of 100% (RR = 1.18, 95% CI: 1.07–1.29), respectively.

Based on the findings above, we further analyzed the lagged effects of mean temperature and relative humidity on RSV infections under extreme conditions, relative to median values (Figure 4). The risks of RSV infections associated with extremely low (RR = 1.14, 95% CI: 1.04–1.25) and low (RR = 1.22, 95% CI: 1.12–1.32) temperatures were highest on the concurrent day (lag 0 day), persisting until lag 11 days and lag 9 days, respectively. In contrast, high temperature demonstrated a protective effect on RSV infections, beginning on lag 9 days and persisting until lag 11 days, while the effect of extremely high temperature remained insignificant across all lag

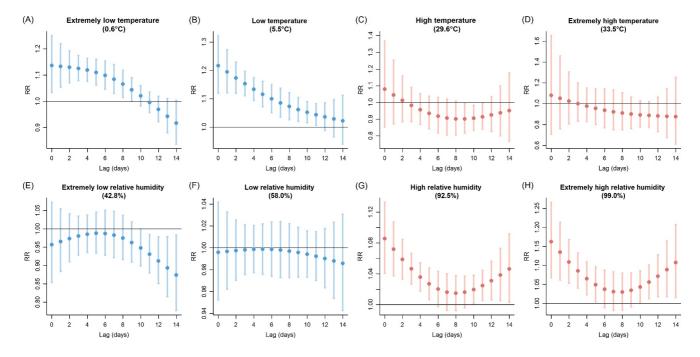


Figure 4. Lag-response associations at specific mean temperature and relative humidity levels of RSV infections. (a) Extremely low temperature (1st percentile,  $0.6^{\circ}$ C), (b) low temperature (10th percentile,  $5.5^{\circ}$ C), (c) high temperature (90th percentile,  $29.6^{\circ}$ C), (d) extremely high temperature (99th percentile,  $33.5^{\circ}$ C), (e) extremely low relative humidity (1st percentile, 42.8%), (f) low relative humidity (10th percentile, 58.0%), (g) high relative humidity (90th percentile, 92.5%), (h) extremely high relative humidity (99th percentile, 99.0%). Median meteorological values ( $18.4^{\circ}$ C for mean temperature, 76.0% for relative humidity) serve as references.

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**Table 2**Cumulative Relative Risks (95% CIs) for Extreme Meteorological Factors on RSV Infections Over 0–14 Lag Days, Stratified by Gender and Age Group

	Gender			Age group (years)		
Variables	Male	Female	P-value <sup>a</sup>	<1	1~5	P-value <sup>a</sup>
Mean temperature (°C)						
Extremely low <sup>b</sup> (0.6)	2.50 (1.59, 3.95)	2.06 (1.19, 3.56)	0.595	2.83 (1.84, 4.35)	1.38 (0.70, 2.74)	0.083
Low <sup>c</sup> (5.5)	4.27 (2.86, 6.38)	3.71 (2.28, 6.03)	0.659	4.71 (3.17, 6.99)	2.97 (1.73, 5.11)	0.178
High <sup>d</sup> (29.6)	0.46 (0.19, 1.11)	0.46 (0.16, 1.34)	0.988	0.38 (0.15, 0.98)	0.58 (0.20, 1.67)	0.579
Extremely high <sup>e</sup> (33.5)	0.35 (0.07, 1.75)	0.59 (0.08, 4.27)	0.688	0.22 (0.04, 1.29)	0.99 (0.15, 6.41)	0.251
Relative humidity (%)						
Extremely low <sup>b</sup> (42.8)	0.62 (0.30, 1.28)	0.32 (0.13, 0.79)	0.270	0.39 (0.20, 0.77)	0.61 (0.20, 1.87)	0.513
Low <sup>c</sup> (58.0)	0.95 (0.71, 1.28)	0.89 (0.62, 1.27)	0.781	0.90 (0.68, 1.20)	0.93 (0.61, 1.43)	0.900
High <sup>d</sup> (92.5)	1.72 (1.33, 2.21)	1.71 (1.26, 2.32)	0.982	1.50 (1.17, 1.92)	2.32 (1.63, 3.30)	0.048
Extremely high <sup>e</sup> (99.0)	2.76 (1.57, 4.87)	3.07 (1.56, 6.07)	0.814	2.36 (1.37, 4.07)	4.60 (2.08, 10.18)	0.176

*Note.* CIs, confidence intervals. Median meteorological values (18.4°C for mean temperature, 76.0% for relative humidity) serve as references. <sup>a</sup>*P*-value obtained from *Z*-test for the difference between the two risk estimates derived from subgroup analysis. <sup>b</sup>1st percentile of mean temperature or relative humidity. <sup>c</sup>10th percentile of mean temperature or relative humidity. <sup>d</sup>90th percentile of mean temperature or relative humidity.

days. The protective effect of extremely low relative humidity on RSV infections was observed on lag 10 days and reached its strongest at lag 14 days (RR = 0.87, 95% CI: 0.77–0.98). We found no significant association between RSV infections and low relative humidity. Conversely, the risk effects of high (RR = 1.09, 95% CI: 1.04–1.13) and extremely high (RR = 1.16, 95% CI: 1.07–1.27) relative humidity on RSV infections peaked on the day of exposure (lag 0 day), followed by a decline and a subsequent increase as lag days increased.

#### 3.3. Effect of Meteorological Factors in Subgroups

Table 2 and Figure S3 in Supporting Information S1 present the cumulative effects (lag 0–14 days) of meteorological factors on RSV infections, stratified by gender and age. The effects of extreme mean temperature were consistent across subgroups defined by gender and age (all P for difference >0.05). Similarly, the risk estimates for extreme relative humidity were comparable between males and females (all P for difference >0.05). In contrast, high relative humidity had a significantly stronger risk effect on children aged 1–5 years compared to those under 1 year of age (P for difference <0.05).

# 3.4. Attributable Burden of RSV Infections Due To Meteorological Factors

Table 3 shows the estimates of the attributable number and attributable fraction for RSV infections associated with cold or humid conditions over a lag of 0–14 days. Cold conditions were responsible for 55.23% (95% CI: 50.01%–64.03%) of RSV infections, corresponding to 2,765 cases (95% CI: 2502–3207). Among these, moderately cold conditions contributed the majority (AF = 54.62%, 95% CI: 40.84%–58.73%), while the fraction due to extremely cold conditions were limited (AF = 0.61%, 95% CI: 0.35%–1.38%). In comparison, 12.02% (95% CI: 9.36%–20.24%) of RSV infections were attributable to humid conditions, with a higher fraction of cases attributable to moderately humid conditions (AF = 11.68%, 95% CI: 9.47%–20.23%) than to extremely humid conditions (AF = 1.11%, 95% CI: 0.92%–2.42%).

### 3.5. Sensitivity Analyses

Sensitivity analyses were performed to check the robustness of the model. The results remained consistent with the main analysis when the degrees of freedom for the variables and the maximum lag days were adjusted (Figures S4–S7 in Supporting Information S1). Additionally, variations in the number and placement of knots for climatic variables did not result in any noticeable changes in the associations between climatic variables and RSV infections (Figure S8 and S9 in Supporting Information S1).

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Table 3
Attributable Numbers and Fractions (%) of RSV Infections Associated With Mean Temperature and Relative Humidity

Variables	AN (95% CI)	AF (95% CI)
Cold <sup>a</sup>	2765 (2502, 3207)	55.23 (50.01, 64.03)
Extremely coldb	31 (17, 69)	0.61 (0.35, 1.38)
Moderately cold <sup>c</sup>	2735 (2007, 2931)	54.62 (40.84, 58.73)
Humid <sup>a</sup>	601 (477, 1017)	12.02 (9.36, 20.24)
Extremely humid <sup>d</sup>	55 (46, 121)	1.11 (0.92, 2.42)
Moderately humid <sup>e</sup>	585 (468, 1015)	11.68 (9.47, 20.23)

*Note.* AN, attributable numbers; AF, attributable fractions; CI, confidence interval. <sup>a</sup>Components attributable to cold conditions were computed for mean temperatures lower than the median (18.4°C), while components attributable to humid conditions were computed for relative humidity higher than the median (76.0%). <sup>b</sup>Extremely cold conditions were defined as mean temperature lower than the first percentile. <sup>c</sup>Moderately cold conditions were defined as mean temperature ranging between the first percentile and the median. <sup>d</sup>Extremely humid conditions were defined as relative humidity higher than the 99th percentile. <sup>c</sup>Moderately humid conditions were defined as relative humidity ranging between the 99th percentile and the median.

### 4. Discussion

In this study, we explored the nonlinear and lagged associations between mean temperature and relative humidity and pediatric RSV infections in Suzhou, Eastern China. Additionally, to the best of our knowledge, this is the first study to evaluate the burden of RSV infections attributable to cold or humid conditions. Generally, we found that lower temperatures and higher relative humidity were associated with increased RSV activity, with lagged effects. Children aged 1–5 years were found to be more vulnerable to high relative humidity compared to children under 1 year old. Besides, the attributable burden of RSV infections associated with cold conditions (55.23%) was higher than that related to humid conditions (12.02%).

Our study identified an inverted U-shaped association between temperature and RSV, with the cumulative risk peaking at 7.5°C. This finding suggested that relatively low temperatures were most favorable for RSV transmission and aligned with previous studies (Darniot et al., 2018; Lee et al., 2023; Li, Wang, Broberg, et al., 2022; Nenna et al., 2017). RSV is known to have clear seasonal epidemics in temperate regions and certain subtropical areas, with peak activity typically occurring during the cold winter months (Li et al., 2019). Evidence has shown that climatic factors can affect the seasonality of RSV by influencing the virus's survival, infectivity, transmission,

and host immunity (B. Xu et al., 2021). Laboratory studies indicated that RSV tend to survive longer in lower temperatures (Pica & Bouvier, 2012). Besides, low temperatures can weaken the body's protective barrier by reducing respiratory mucosal secretion and impair immune function by lowering the erythrocyte sedimentation rate, thereby increasing host susceptibility to viral infections (Eccles & Wilkinson, 2015). Moreover, during colder periods, increased indoor crowding and poor ventilation further facilitate RSV transmission (Hajat & Haines, 2002). We observed a positive association between relative humidity and RSV, consistent with studies in temperate and subtropical regions (Darniot et al., 2018; Nenna et al., 2017). For instance, a study across 13 European countries reported a correlation between higher relative humidity and increased RSV activity (Li, Wang, Broberg, et al., 2022). This could be attributed to RSV's aerosol stability, as it inactivates rapidly in small aerosols under low humidity but remains stable in larger aerosols at high humidity (Meerhoff et al., 2009). An experimental study demonstrated that RSV exhibits maximum stability at 80%-90% humidity when temperature is constant at 20.5°C (Yusuf et al., 2007). Besides, a cross-sectional study in South Korea reported a negative association between higher relative humidity and lung function (Seok et al., 2024). Another potential explanation for our findings is that people tend to spend more time indoors during humid outdoor conditions (Ali et al., 2020). However, our findings differ from results observed in Guangzhou, a subtropical region in China, which reported a negative correlation between RSV prevalence and relative humidity (Liu et al., 2019). This discrepancy may be attributed to regional climatic differences, particularly Guangzhou's consistently high humidity, which could uniquely affect virus transmission dynamics.

This study also examined the lag-response relationship between mean temperature, relative humidity, and RSV infections. Our findings revealed that the maximum risk effects of temperature and relative humidity occurred on the day of exposure, consistent with a study on the delayed association between temperature and influenza in Jiangsu, China (Dai et al., 2018). Besides, the risk effects associated with extreme values of low temperature and high relative humidity both emerged on lag 0 day and persisted for a prolonged duration in our study. Comparatively, the protective effects of high temperatures and extremely low humidity exhibited a delayed onset and were short-lived, consistent with observations in other infectious diseases. For example, in Lanzhou, China, high temperatures reduced the risk of influenza in the second week of lag, while in Jiangsu, China, extremely low humidity showed a protective effect against hand-foot-mouth disease on the sixth day of lag (Wang et al., 2022; Yang et al., 2024). The lagged effects of climatic factors can be related to the incubation period of RSV infection, which is about 2–8 days (Wright & Piedimonte, 2011). Additionally, variability in healthcare-seeking behavior could play a role, as some individuals seek medical attention shortly after infection, while others delay until severe symptoms develop (Apostolidis et al., 2009). Furthermore, extreme weather can affect the human immune system, gradually altering susceptibility to viral infections, which in turn leads to a lag in infection risk (Yang et al., 2024). Notably, we found that the lag duration for low temperature (11 days) was longer than that for

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extreme low temperature (9 days). This difference may be attributed to the short-lived nature of extreme low temperatures, which prompt immediate protective measures and result in effects concentrated in the short term. In contrast, prolonged exposure to sustained low temperatures, coupled with reduced protective awareness, may contribute to extended lagged effects. The above findings suggest that prolonged preventive measures may be effective in mitigating the risks associated with cold-associated and humidity-associated RSV infections.

In the subgroup analyses, we found children aged 1–5 years to be more vulnerable to the effects of high relative humidity than those under 1 year of age, which aligns with previous findings. For instance, evidence from Hong Kong and Lanzhou, China, suggested that high relative humidity has a greater impact on lower respiratory infections in older children compared to younger ones (H. C. Y. Lam et al., 2019; W. Zhang et al., 2024). The larger risk estimates may largely be attributed to differences in the frequency of outdoor activities. Children under 1 year of age are typically cared for at home, whereas older children are more likely to engage in outdoor activities, thereby increasing their exposure to humidity. To better protect sensitive groups of children, the underlying pathology and mechanism behind this discrepancy should be further investigated in future research.

The findings of this study further substantiate the relationship between cold and humid conditions and RSV infections in children. Specifically, we quantified the burden of RSV infections attributable to cold or humid conditions and divided the attributable fractions into different components. Our results indicated that 55.23% of RSV infections were attributable to cold and 12.02% to humid conditions. As far as we know, no prior research has quantified the burden of pediatric RSV infections attributable to climatic conditions. However, a study on influenza, a respiratory virus with environmental sensitivities similar to RSV, found that 68% of influenza hospitalizations among children under five in China were attributed to sensitive temperatures (2.5–16.1°C), which aligns comparably with our findings (R. Zhang et al., 2022). Besides, we found that the majority of the attributable risk occurred under moderate weather conditions. This phenomenon may be attributed to the fact that moderate temperatures or humidity accounted for most of the days in the observed series. Additionally, during extreme weather events, work and school closures may encourage individuals to stay at home, reducing close interpersonal contact and lowering the risk of RSV infections. Furthermore, experimental studies indicated that RSV exhibits greater stability at relative humidity levels of 80%–90% compared to extremely humid conditions (99%) (Yusuf et al., 2007). Our estimates of the attributable burden provide strong evidence for incorporating meteorological factors into the prevention and control strategies for pediatric RSV infections.

This study has several limitations. First, the meteorological data were derived from fixed monitoring sites rather than individual exposure assessments, which may introduce some measurement error in the exposure. However, such exposure misclassification is unlikely to lead to substantial bias in time-series studies. Second, the data on RSV infections cases were based on hospital reports, which may be subject to selection bias or under-reporting bias. Third, this study was conducted in a single city in China, which may limit the generalizability of the findings to regions with different population demographics, climatic conditions, health behaviors, and healthcare systems. Therefore, caution should be exercised when extrapolating these results to other geographical and epidemiological contexts. Fourthly, data on other potential confounding factors, such as socio-economic status and air pollution, were not considered. These factors may influence the risk of RSV infections. Future research should consider expanding the study area, incorporating a wider range of relevant factors, and integrating additional data, such as individual-level data, to enhance the comprehensiveness and generalizability of the findings.

In conclusion, we identified nonlinear and lagged associations between mean temperature and relative humidity and pediatric RSV infections. Older children were at increased risk following exposure to high relative humidity. Moreover, we provide evidence that cold or humid conditions could account for a substantial proportion of RSV infections. This study will inform public health policies on preventing RSV infections, such as increasing intervention intensity and frequency during cold and humid periods. More importantly, with a few RSV prophylactic vaccine candidates on the horizon, our findings could help predict the RSV season, guide the timing of immunizations, and inform the planning of seasonal healthcare services.

#### **Abbreviations**

AF attributable fraction

AN attributable number

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CI confidence interval

Df degrees of freedom

DFA direct fluorescence antibody

DLNM distributed lag nonlinear model

LIS Laboratory Information System

PACF partial autocorrelation function

QAIC Quasi-Akaike Information Criterion

RR relative risk

RSV respiratory syncytial virus

SCH Soochow University Affiliated Children's Hospital

#### **Conflict of Interest**

The authors declare no conflicts of interest relevant to this study.

## **Data Availability Statement**

The meteorological data can be accessed at China National Meteorological Information Center (URL: https://data.cma.cn/dataService/cdcindex/datacode/A.0012.0001/show\_value/normal.html). Researchers need to register for free on this website in order to access the required data. The selection of "Suzhou" (observation site code: 58439) should be made to obtain data specific to the Suzhou area. The clinical data supporting this research were collected from Soochow University Affiliated Children's Hospital. The raw/processed patient data contain personal information and are not publicly accessible due to restrictions imposed by the Medical Ethics Committee of Soochow University Affiliated Children's Hospital. Other researchers must obtain permission from the relevant authorities in order to use this data. The R code used for the analysis presented in this manuscript is publicly available at https://github.com/FENG-ac/RSVmet. All analyses in this study are made with software R version 4.1.2 (R Core Team, 2021), licenses and other information can be found at https://www.R-project.org.

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