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Association of temperature variability with the risk of initial outpatient visits for allergic rhinitis: a time-series study in Changchun

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Abstract: Epidemiological studies have revealed associations between several temperature parameters and allergic rhinitis (AR). However, few studies has reported the association of AR with daily temperature variability, which indicates both short-term intra- and inter-day temperature change. This study aimed to analyze associations between temperature variability and initial outpatient visits for AR. The analysis was conducted with an overdispersed Poisson model using daily time-series data on temperature and the number of initial AR outpatients from 2013 to 2015 in Changchun, China. The composite index of temperature variability was derived by calculating the standard deviation of daily minimum temperature and maximum temperature over exposure days. Stratified analysis by season was also conducted. There were 23,344 AR outpatients during the study period. In the total period, per 1˚C increase in temperature variability at 0–2 days (TV_{0-2}), 0–3 days (TV_{0-3}), and 0–4 days (TV_{0-4}) was associated with a 4.03% (95%CI: 0.91%–7.25%), 4.40 % (95%CI: 0.95%–7.97%), and 4.12% (95%CI: 0.38%–8.01%) increase in the number of AR outpatients, respectively. When stratified by season, the strongest effect was shown in spring. Our results suggested that temperature variability was associated with increased initial outpatient visits for AR, which may provide helpful implications for formulating public health policies to reduce adverse health impacts of unstable temperature.

Keywords: Temperature variability; Initial outpatient visits; Allergic rhinitis; Risk; Time-series study; Changchun

Introduction

Allergic rhinitis (AR) is a symptomatic disorder of the nose, induced by an IgE-mediated inflammation following allergen exposure (Pawankar et al. 2013), which is charactered by sneezing, nasal congestion, pruritus, and rhinorrhea (Cingi et al. 2017). It often influences patients' quality of life and work or school performance and increases direct and indirect medical expenses costs due to health care resource consumption (Del Cuvillo et al. 2017; Vandenplas et al. 2018). Risk factors for AR mainly include genetic factors (Kim et al. 2012) and environmental factors, such as meteorological factors (Gao et al. 2021; Hu et al. 2020; Kim et al. 2018), air pollution (Hu et al. 2020; Lin et al. 2021), and indoor allergens (Kim et al. 2012). Recently more attention has been paid to the impacts of temperature in the process of AR (Carreras et al. 2015; Gao et al. 2021; Kim et al. 2018; Wang et al. 2020).

Several temperature parameters have been examined as risk factors for respiratory diseases, including temperature range (Carreras et al. 2015) and daily mean temperature (Gao et al. 2021; Kim et al. 2018). For example, Carreras et al. have identified temperature range as a strong risk factor for hospital admissions by upper and lower respiratory infections (Carreras et al. 2015). In a study of Xinxiang, China, Gao et al. have observed greater risks of AR outpatients when mean temperature rose to 1.6-9.3 ˚C at a lag of 0-7 days and 23.5-28.5 ˚C at a lag of 0-3 days (Gao et al. 2021). In addition to temperature range and mean temperature, two another temperature indices, interday variability (e.g., temperature variation between neighboring days) and intraday variability (e.g., diurnal temperature range (DTR)) have been assessed to examine the associations of short-term unstable weather with respiratory outcomes (Lim et al. 2012;Wang et al. 2020). For instance, Lim et al. have reported a positive association between DTR and respiratory hospital admissions in Korea (Lim et al. 2012). Wang et al. have observed significant association of temperature variation between two neighboring days with increased risk of AR in Hefei, China (Wang et al. 2020). Some plausible explanations have been postulated to support the effect of temperature change on respiratory health. Temperature variation may affect the ability of the human immune system to resist infectious pathogen, and sudden cold temperature can cause the cooling of nasal and bronchial mucosa and seriously impair ciliar motility, which may finally trigger respiratory diseases (Bull 1980, Clary-Meinesz et al. 1992)

However, these studies abovementioned focused on the relationships between either intraday or interday changes of temperature and respiratory outcomes. Since unstable weather is an ongoing process, considering both interday and intraday temperature variation together may be better to apprehend its effect on respiratory health (Guo et al. 2016). Therefore, using a composite index of temperature variability, indicating both interday and intraday temperature variation, our study aimed to explore the short-term association of temperature variability with the number of initial AR outpatient visits from 2013-2015 in Changchun, China.

Material and methods

Study Area

Changchun (center : 124°18'～127°05' E, 43°05'～45°15' N), the capital of Jilin Province, is a city situated in the northeast of China. It has humid temperate continental climate, and has great annual and diurnal temperature variation with hot summer and cold winter. It has a registered population of 753.8 million by 2015, covering a total area of 20593.5 km^2 (Changchun Bureau of Statistics, 2015).

Study population

Daily counts of AR cases between 2013 and 2015 were gained from the Departments of Otolaryngology-Head and Neck Surgery from the First and Second Affiliated Hospitals of Jilin University. The study population comprised of all outpatients for AR symptoms examined by general practitioners and specialties during the period. Seated in the central districts in Changchun, the two hospitals are Grade-III Level-A comprehensive university hospitals, which integrate medical treatment, teaching, scientific research and disease prevention. They cover the largest number of patients in the city as well as nearby areas. The diagnosis of AR was based on medical history, clinical symptoms and signs, and relevant laboratory indicators such as skin prick test and serum-specific IgE test. Clinical symptoms included nasal congestion, nasal itching, sneezing, clear water nose, etc, which may be accompanied by eye itching, conjunctival congestion, and others. And signs included nasal watery secretions, nasal mucosal edema, and others (Editorial Committee of Chinese Journal of Otolaryngology Head and Neck Surgery, 2010). Moreover, for avoiding repeated counting, only one visit per patient per day was used as daily visit count, and subsequent follow-ups within 30 days of the initial visit were not included (Teng et al. 2017).

Meteorological data and air pollution parameters

Daily mean temperature and relative humidity in Changchun from 2013 to 2015 were derived from China Meteorological Data Sharing Service System (http://cdc.cma.gov.cn). 24-hour concentrations of PM_{10}, $PM_{2.5}$, and NO_2 in Changchun for the same study period were derived from China's National Urban Air Quality Real-time Publishing Platform (http://106.37.208.233:20035). The city-wide daily concentration of each air pollutant were estimated by averaging the 10 air-quality-monitoring stations within the core area of Changchun. Locations of meteorological stations and air-quality-monitoring stations in Changchun were displayed on a map (**Fig. S1**).

Definition of temperature variability

Temperature variability index was a composite index of both interday and intraday temperature variation, as well as an indicator accounting for the lag effects of temperature variation, which was previously described (Guo et al. 2016). This indicator was calculated as the standard deviation (SD) of the minimum temperature and the maximum temperature during the exposure days. For instance, if we defined $MinTemp_{lagi}$ and $MaxTemp_{lagi}$ as the minimum temperature and the maximum temperature for the preceding day i, then we derived the temperature variability for the preceding 2 days' exposure from the following formula: $TV_{0-1} = SD\ (MinTemp_{lag0}, MaxTemp_{lag0}, MinTemp_{lag1}, MaxTemp_{lag1})$. Similarly, we calculated the temperature variability for the preceding 3 days' exposure using the formula: $TV_{0-2} = SD\ (MinTemp_{lag0}, MaxTemp_{lag0}, MinTemp_{lag1}, MaxTemp_{lag1}, MinTemp_{lag2}, MaxTemp_{lag2})$.

Statistical analysis

Correlations between daily air pollutant concentrations and meteorological parameters were analyzed by Spearman's correlation analysis. Allowing for over-dispersed AR counts, a quasi-Poisson regression model was employed to obtain the risk estimates of initial outpatient visits for AR associated with temperature variability exposure, which adopted a standard method for time-series analysis (Bhaskaran et al. 2013). Since there was a linear relationship between DTR and health outcome, and increased risks of health outcomes are observed for large changes in temperature between neighboring days (Guo et al. 2016), the following formula was fitted to estimate the effects of temperature variability on the number of daily AR outpatient visits:

$\text{Log}(\mu_t) = \alpha + TV_j + \beta temp_{t,l} + \gamma dow + \delta holiday + ns(time,3*7) + ns(rhu\_avg,3)$

Where α is the intercept. $Temp_{t,l}$ is a cross-basis matrix obtained by applying a distributed lag non-linear model to control for nonlinear and delayed effects of daily mean temperature (Gasparrini et al. 2010), in which natural cubic splines with 5 and 2 degrees of freedom (df) were used, respectively, to fit the nonlinear effects of daily mean temperature and to capture the lags over time up to 10 days, with internal knots placed at equally spaced temperature percentiles or log-value of the lag (Guo et al. 2016). All the knots were determined based on the model fit using akaike's information criterion (Gasparrini et al. 2010, Guo et al. 2014). Given that the lag effect of daily mean temperature on the hospital admission of AR lasted no more than 10 days in a Korean study (Kim et al. 2018), the maximum lag of mean temperature was determined to be 10 days. Instead of an adjustment of daily minimum temperature or maximum temperature in the model, daily mean temperature was controlled, as it can better represent the exposure during all the day and night for daily AR outpatients. A natural cubic spline with 7 df per year was controlled in the model to remove the long-term and seasonal trends. Categorical variables "day of week (DOW)" and public holidays were used to exclude possible variance of initial AR outpatient visits within a week and during the public holidays. β is the coefficient for $temp_{t,l}$, and λ and δ stand for coefficients of the categorical variable for DOW and public holidays. The non-linear effects of relative humidity was also controlled for by fitting a natural cubic spline with a priori 3 df (Chen et al. 2017). Several lengths of exposure to temperature variability, from TV_{0-1} toTV_{0-7}, were estimated separately to make clear which length of temperature variability exposure was associated with the number of AR outpatients (Guo et al. 2016). The effect estimates of AR outpatients associated with per 1°C increase in temperature variability during the exposure days were presented as percentage changes and 95% confidence intervals (CIs).The percentage changes were calculated using the following formula: percentage changes = (relative risks -1)/100.

To assess whether the impacts of temperature variability on AR outpatients varied by different seasonal characteristics, a season-stratified analysis also conducted. In the season-stratified model, a natural cubic spline of day of year with 3 df and an indicator variable for year took place of the natural cubic spline of time variable to take into account the long-term trend in each season (Kim et al. 2018). The season-stratified model for calculating the temperature variability effect is as follows:

$\text{Log}(\mu_t) = \alpha + TV_j + \beta temp_{t,l} + ns(DOY,3) + factor(year) + \gamma dow + \delta holiday + ns(rhu\_avg,3)$

In addition, the confounding effects of air pollutants were also explored. As PM_{10}, $PM_{2.5}$, and NO_2

were known risk factors for AR (Teng et al. 2017), daily PM_{10}, $PM_{2.5}$, and NO_2 concentration was further adjusted in the model as a linear term one by one.

Sensitivity analysis

To assess the robustness of our model, we chose a maximum lag of 21 days used for the confounding adjustment for daily mean temperature and changed the df for daily relative humidity from 3 to 4–6 for the total period, respectively. We also obtained estimations for an interquartile range increase of temperature variability. All the statistical analyses were employed in R software version 3.5.0.

Results

Summary statistical analysis

The trends of daily number of initial AR outpatient visits, mean temperature, relative humidity, and air pollutant concentrations during 2013 to 2015 in Changchun were presented in **Fig. 1**, which showed a clear seasonality.

Summary statistics of the number of AR outpatients, meteorological variables, air pollutants, and temperature variability for the total and season-specific periods are displayed in **Table 1**. There were 23,344 AR outpatients over the study period, with a daily mean 21.7 AR outpatients. The mean counts of season-specific daily AR outpatients were 14.4 (2.0–42.0) for spring, 17.7(2.0–99.0) for autumn, and 12.6 (0–34.0) for winter, respectively. During the total study period, the annual-average daily mean temperature was 6.2˚C, ranging from −26.7˚C to 28.6˚C. The season-specific daily mean temperature was 7.5℃ (-13.8˚C–27.3˚C) for spring, 6.9℃ (-15.5˚C–22.0˚C) for autumn, and -14.0℃ (-26.7˚C–5.6˚C) for winter, respectively. The annual-average TV_{0-1} was 7˚C, with a range from 1.2˚C to 13.5˚C. The distributions of temperature variability presented similar from TV_{0-1} to TV_{0-7}. The relative humidity in spring was relatively lower than that in other seasons. The annual-average mean concentrations of PM_{10}, $PM_{2.5}$, and NO_2 were 97.2, 74.7, and 39.0 μg/m^3, which were higher in winter and lower in spring.

Daily hospital visit count by AR was negatively correlated with PM_{10}, $PM_{2.5}$, and NO_2, and was positively correlated with daily mean temperature, maximum temperature, minimum temperature, and relative humidity (*P*<0.001). Daily mean temperature, maximum temperature, and minimum temperature were negatively correlated with all air pollutant concentrations (*P*<0.001) (**Table S1**).

Effects of temperature variability on AR outpatients

Fig. 2 presents the overall exposure-response curve between $TV_{0\text{-}2}$, $TV_{0\text{-}3}$, $TV_{0\text{-}4}$ and AR outpatients. Broadly linear associations between temperature variability and the number of AR outpatients were noted. The curve of $TV_{0\text{-}2}$ rose rapidly at levels > 2˚C. The $TV_{0\text{-}3}$ and $TV_{0\text{-}4}$ curves increased at levels > 3˚C and then became relatively flat at levels > 6 ˚C.

Fig. 3 summarizes the percentage changes in AR outpatients associated with per 1°C increase in temperature variability at different exposure days for the total period and season-specific period. The effects of temperature variability increased at exposure 0–2 days for the total period, showing a decreasing pattern at exposure 0–5 days. In general, positive associations between temperature variability and AR outpatients were observed at exposure 0–2 days, at 0–3 days, and at 0–4 days. The largest estimates appeared at exposure 0–3 days among the total population. For per 1°C increase in $TV_{0\text{-}3}$, a 4.40% (95% CI: 0.95%–7.97%) increase in the number of AR outpatients was observed. Our main results were robust when changing the lag structure of 21 days for mean temperature (**Table S2**) and modifying the dfs for relative humidity (4–6df) for the total period (**Table S3**).The estimated effects for an interquartile range increase of temperature variability (from $TV_{0\text{-}1}$ to $TV_{0\text{-}7}$) are presented in **Table S4**.

In the season-stratified analysis, the impacts of temperature variability on AR in spring were the greatest, which were higher than those during the total period (**Fig. 3**). For per 1˚C increase in $TV_{0–2}$, $TV_{0\text{-}3}$, and $TV_{0–4}$, significant increases of 9.83% (95%CI: 5.32%–14.54%), 9.84% (95%CI: 4.81%–15.11%), and 5.59% (95%CI: 0.39%–11.06%) in AR outpatients were observed, respectively. In autumn season, suggestively significant effects of temperature variability on AR outpatients appeared at exposure 0–3 days (percentage change: 3.06% (95%CI: -0.07%–6.30%)). However, for winter season, no significant effect of temperature variability on AR outpatients was observed (**Table 2**).

To examine any possible confounding effects by air pollutants, including NO_2, $PM_{10,}$ and $PM_{2.5}$, each air pollutant was additionally adjusted in the model one by one. After adjusting for NO_2 and PM_{10}, the risk estimates for the effects of temperature variability slightly decreased but remained (suggestively) significant at exposure 2-days, 3-days, and 4-days (**Table 2**). After adjusting for $PM_{2.5}$, the estimates were attenuated at exposure 2-days and 3-days, but became non-significant at exposure 4-days (**Table 2**).

Discussion

Association between temperature variability and initial outpatient visits for AR

Our study found positive associations of temperature variability with the number of initial outpatient visits for AR in Changchun, Northeastern China. The associations between temperature variability and AR outpatients in the whole year appeared at exposure 0–2 days, 0–3 days, and 0–4 days. In general, individuals were more sensitive to the exposure to temperature variability in spring and autumn.

Few studies at present have considered both intra- and interday temperature changes to comprehensively assess the acute effect of temperature variation on AR. To take into account both intraday and interday variations of temperature, this study used a composite index of temperature variability to evaluate the burden of AR attributable to temperature variability. To our knowledge, our study was the first study to link temperature variability with AR outpatients, which may enrich the understanding of health impacts of temperature variability on respiratory disease. Moreover, temperature variations within a day or a few neighbouring days in the literature have offered some evidence to support our findings. For example, a recent study in Hefei, China, has demonstrated that a large temperature drop of 3.8°C between two adjacent days has a short-lasting lag effect on childhood AR, with a 2% increase in the childhood AR at lag 12 day (Wang et al. 2020). Lim et al. have reported positive associations of DTR with total respiratory, asthma, and pneumonia hospital admissions in Seoul (Lim et al. 2012).

There are some potential biological explanations for the effects of temperature variability on AR outpatients. AR patients may feel uncomfortable with sudden changes in interday and intraday temperatures as they are not well prepared for temperature variability physiologically and behaviorally (Garrett et al. 2011; Havenith 2005; Martinez-Nicolas et al. 2015). Living in the weather conditions featured with greater intra- and interday temperature variation, the body's thermoregulator centers may work via vasodilation or vasoconstriction against the sharp increase or decrease in the unstable temperature (Sanchez-Gonzalez &Figueroa 2013), and the imbalance of the autonomic nerve system involved in regulation of vasomotor tone is expected to induce rhinitis symptoms via increasing the vascular permeability (Hoshino et al. 2015). Moreover, sudden temperature changes may result in a more pronounced inflammatory nasal response in patients with persistent AR, by recruiting and activating eosinophils (Graudenz et al. 2006)

Some studies have identified the potential health effects of seasonal temperature variability on respiratory diseases (Kim et al. 2018; Sun et al. 2018). In our study, (suggestively) positive associations between temperature variability and the number of initial outpatient visits for AR were observed in spring and autumn, showing somewhat different compared to that in the whole study period. Spring and autumn are the transition periods with seasonal temperature changes, which would cause large variance in temperature. In the study of Seoul, Korea, which has a similar latitude and a similar climatic characteristics in terms of temperature and precipitation to Changchun, significant cold temperature effects on hospital visits for AR were observed among the adults and the elderly for the spring and among the total population for the autumn (Kim et al. 2018). Moreover, a study in Finland showed that young adults with AR experienced more cold-related respiratory symptoms than healthy young adults (Hyrkäs et al. 2014), partially explaining the cold temperature effects on triggering patients with AR for initial outpatient visits. Therefore, cold temperature effects may play an important role in the impacts of temperature variability on AR outpatients, as cold temperature can cause airway hyper-reactivity, contraction of the tracheal smooth muscle, as well as reduction of the pulmonary circulation (Cruz &Togias 2008). Additionally, the strongest effects were observed in spring, which may be affected by the interactive roles of increased length and severity of the pollen season, the higher relative humidity, and other environmental factors.

In addition, air pollution is another environmental factor for AR (Hu et al. 2020; Teng et al. 2017). The association of temperature variability with AR outpatients was attenuated after adjusting NO_2 and PM_{10}, and became non-significant after adjustment of $PM_{2.5}$ at some exposure days. Even there was only one related study showing a robust association of wintertime temperature variability with hospitalisations for respiratory diseases after further adjustment of time-varying $PM_{2.5}$ exposure (Sun et al. 2018), the finding in our study suggested that some air pollutants played as a confounder of the association.

Strengths and Limitation

Studies about the association of temperature parameters with AR mainly have revealed the impacts of mean temperature, and intraday or interday temperature variance on AR. However, to our knowledge, this study was the first to indicate the association of both intra and inter-daily temperature variance with

AR outpatients, as well as showing seasonal differences. Our findings were helpful for better understanding the impacts of climate change for AR patients, providing more evidence for reducing the adverse health effects of unstable temperatures on AR. Nevertheless, several limitations of our study should be acknowledged. First, similar to other time-series studies, this study used temperature data from surface weather observation stations as a surrogate of individual exposure to explore the effect of temperature variability, which may lead to some inevitable exposure-measurement errors to some degree. However, it is likely that this error is random, which may cause the underestimation of risk estimations (Guo et al. 2013). Second, our study did not consider residents' socioeconomic and demographic information and behavioral characteristics such as the usage of heater or air conditioner, which may make an influence on the assessment of individual exposure to temperature variability. Finally, our study was limited to a single city. As the health effects of temperature variability could be modified by climate conditions and locations (Guo et al. 2016), a multi-center study to comprehensively examine the impacts of temperature variability on AR in China is needed.

Conclusion

In conclusion, our study provided evidence on the association of temperature variability with increased outpatient visits for AR, particularly in spring, as well as implications for taking timely preventive and protective measures to reduce the adverse health impacts of unstable temperature on AR.

Declarations

Ethics approval and consent to participate

The numbers of outpatients for AR symptom in this study were derived from the archived data in previous clinical diagnosis and treatment from the Departments of Otolaryngology-Head and Neck Surgery from the First and Second Affiliated Hospitals of Jilin University. The data were at the group level and did not involve individual-level information, which could be exempted from informed consent and ethical review.

Consent for publication

Not applicable.

Available of data and materials

The data supporting the findings of our study are available on request from the corresponding author Li Ke.

Competing interests

The authors declare that they have no competing interests.

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Author Contributions

LK determined the ideas about the association between temperature variability and AR outpatients; MX and PK wrote the original draft; MX and JH developed the model for the association of temperature variability with AR outpatients, and conducted the formal analysis; MX and JH implemented the computer code; BL, LK, and PH reviewed and revised the manuscript.

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Table 1 Summary statistics of daily AR outpatients, meteorological variables, air pollutants, and temperature variability in Changchun, 2013–2015.

Variable	Whole year	Spring	Autumn	Winter
	Mean (range)	Mean (range)	Mean (range)	Mean (range)
Total AR (person/day)	21.7 (0.0–177.0)	14.4 (2.0–42.0)	17.7 (2.0–99.0)	12.6 (0.0–34.0)
Mean Temperature (˚C)	6.2 (-26.7–28.6)	7.5 (-13.8–27.3)	6.9 (-15.5–22.0)	-14.0 (-26.7–5.6)
Relative humidity (%)	64.4 (14.0–93.0)	54.0 (14.0–90.0)	63.1 (31.0–92.0)	68.4 (40.0–93.0)
PM$_{10}$, μg/m^3	97.2 (8.8–617.0)	91.2 (8.8–429.0)	109.3 (9.7–617.0)	128.1 (24.7–480.0)
PM$_{2.5}$, μg/m^3	74.7 (10.7–445)	61.9 (12.7–296.1)	84.3 (13.5–445.0)	110.3(15.8–381.0)
NO$_2$, μg/m^3	39.0 (4.2–137.6)	35.3 (4.5–77.3)	37.9 (5.0–111.3)	59.3 (14.7–137.6)
TV				
TV$_{0\text{-}1}$ (˚C)	7.0 (1.2–13.5)	7.4 (2.6–20.5)	7.7 (1.2–17.7)	7.3 (3.5–11.3)
TV$_{0\text{-}2}$ (˚C)	6.9 (1.5–12.5)	7.3 (3.3–18.6)	7.6 (1.5–17.2)	7.2 (3.5–11.4)
TV$_{0\text{-}3}$ (˚C)	6.8 (1.9–11.7)	7.3 (3.6–18.2)	7.6 (1.9–17.6)	7.2 (3.4–10.5)
TV$_{0\text{-}4}$ (˚C)	6.8 (2.9–11.3)	7.4 (3.5–17.5)	7.7 (2.9–17.4)	7.2 (3.5–10.0)
TV$_{0\text{-}5}$ (˚C)	6.8 (3.3–10.9)	7.5 (3.8–17.1)	7.8 (3.7–16.8)	7.3 (3.6– 9.6)
TV$_{0\text{-}6}$ (˚C)	6.9 (3.2–11.0)	7.5 (3.8–16.8)	7.9 (4.0–16.7)	7.3 (4.1–10.0)
TV$_{0\text{-}7}$ (˚C)	6.9 (1.5–12.5)	7.6 (3.3–18.6)	7.9 (1.5–17.2)	7.3 (3.5–11.4)

Abbreviations: AR, allergic rhinitis; PM$_{10}$, particulate matter < 10 μm in aerodynamic diameter; PM$_{2.5}$, particulate matter <2.5 μm in aerodynamic diameter; NO$_2$, nitrogen dioxide; TV$_{0\text{-}1}$, temperature variability at 0–1 days.

Table 2 Associations between temperature variability and AR outpatients after controlling for air pollutants

Variable	Adjust for NO_2		Adjust for PM_{10}		Adjust for $PM_{2.5}$	
	PC	95%CI	PC	95%CI	PC	95%CI
TV_{0-1} (˚C)	2.32	-0.38–5.10	1.78	-0.84–4.46	1.80	-0.82–4.49
TV_{0-2} (˚C)	4.01	0.83–7.30	3.59	0.48–6.81	3.54	0.41–6.76
TV_{0-3} (˚C)	4.36	0.86–7.98	4.03	0.59–7.59	3.89	0.43–7.46
TV_{0-4} (˚C)	4.06	0.28–7.97	3.71	-0.03–7.58	3.56	-0.19–7.45
TV_{0-5} (˚C)	3.07	-0.89–7.20	2.67	-1.27–6.77	2.57	-1.38–6.68
TV_{0-6} (˚C)	3.03	-1.11–7.35	2.63	-1.50–6.92	2.55	-1.58–6.86
TV_{0-7} (˚C)	3.70	-0.60–8.20	3.41	-0.88–7.88	3.31	-0.99–7.79

Abbreviations: AR, allergic rhinitis; CI, confidence interval; PC, percentage change; TV_{0-1}, TV at 0–1 days.

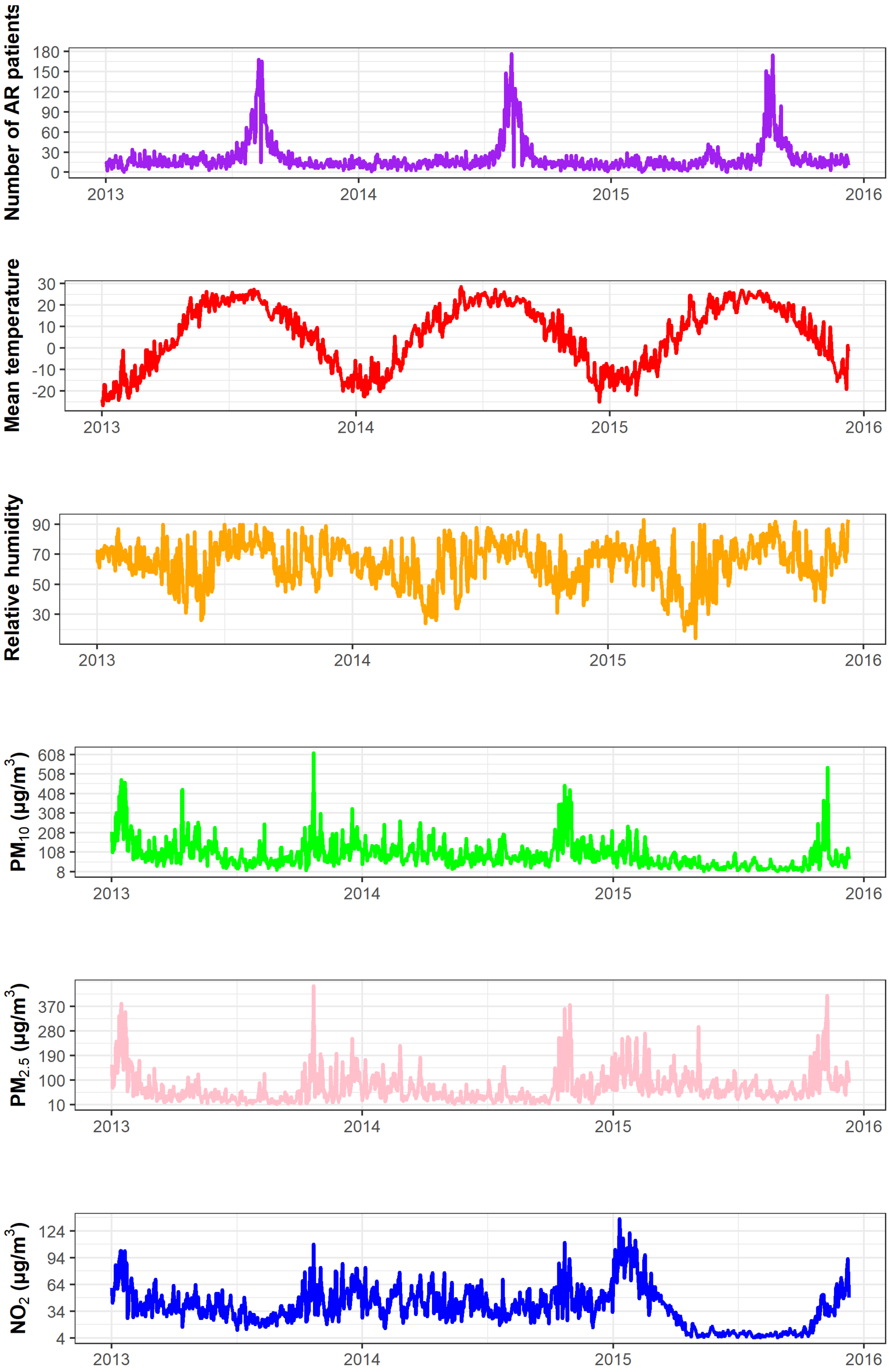
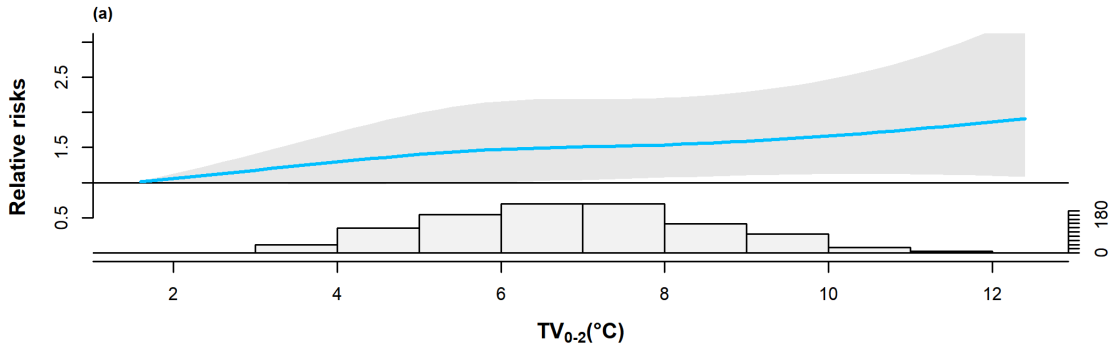


Fig.1 The trend of daily counts of hospital visit by AR in Changchun during 2013 to 2015.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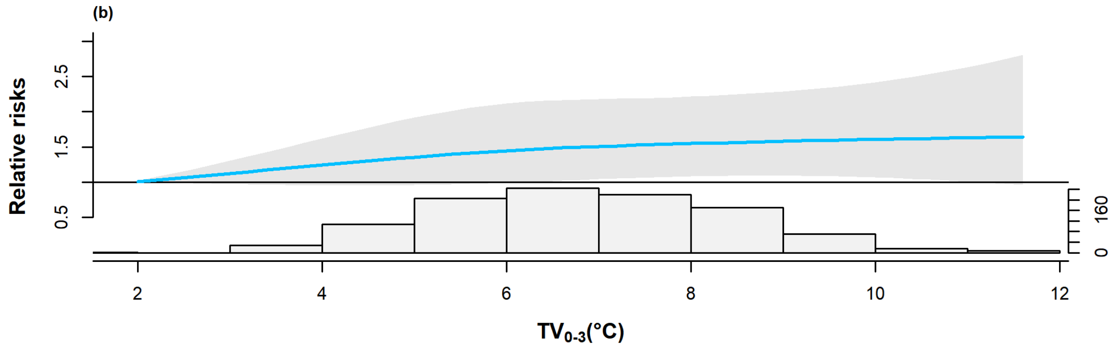
1.5
2.5
180
0
2
4
6
8
10
12
TV0-2(°C)


(b)
Relative risks
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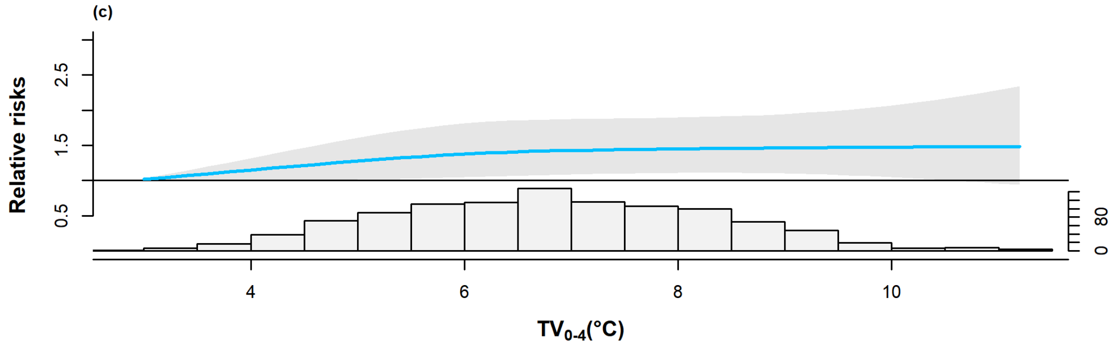
1.5
2.5
160
0
2
4
6
8
10
12
TV0-3(°C)


(c)
Relative risks
0.5
1.5
2.5
80
0
4
6
8
10
TV0-4(°C)

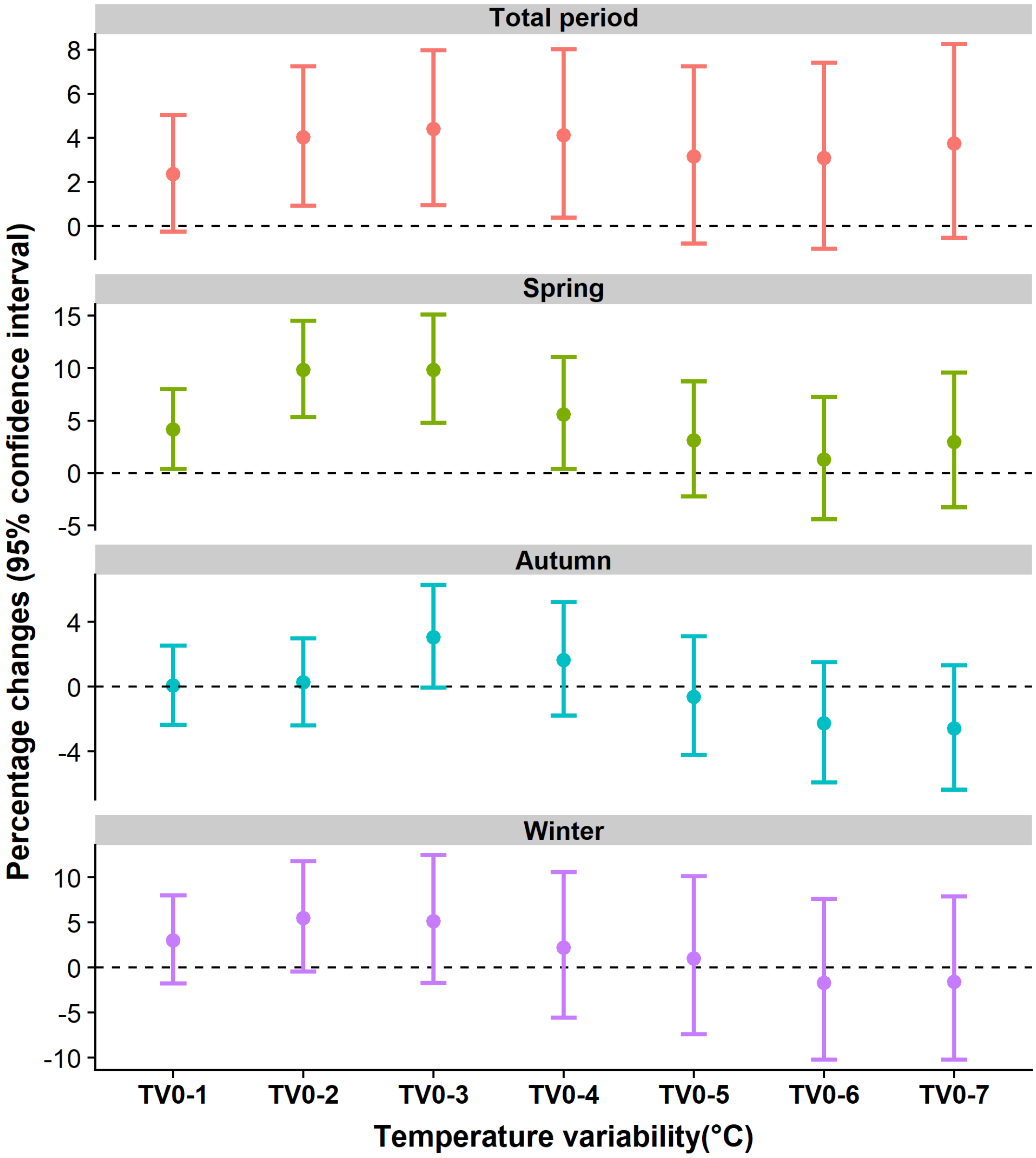


Fig.3 Total period and season-specific percentage changes with 95% confidence interval in daily number of AR outpatients for per 1˚C increase in the temperature variability.

Environmental Science and Pollution Research

Association of temperature variability with the risk of initial outpatient visits for allergic rhinitis: a time-series study in Changchun

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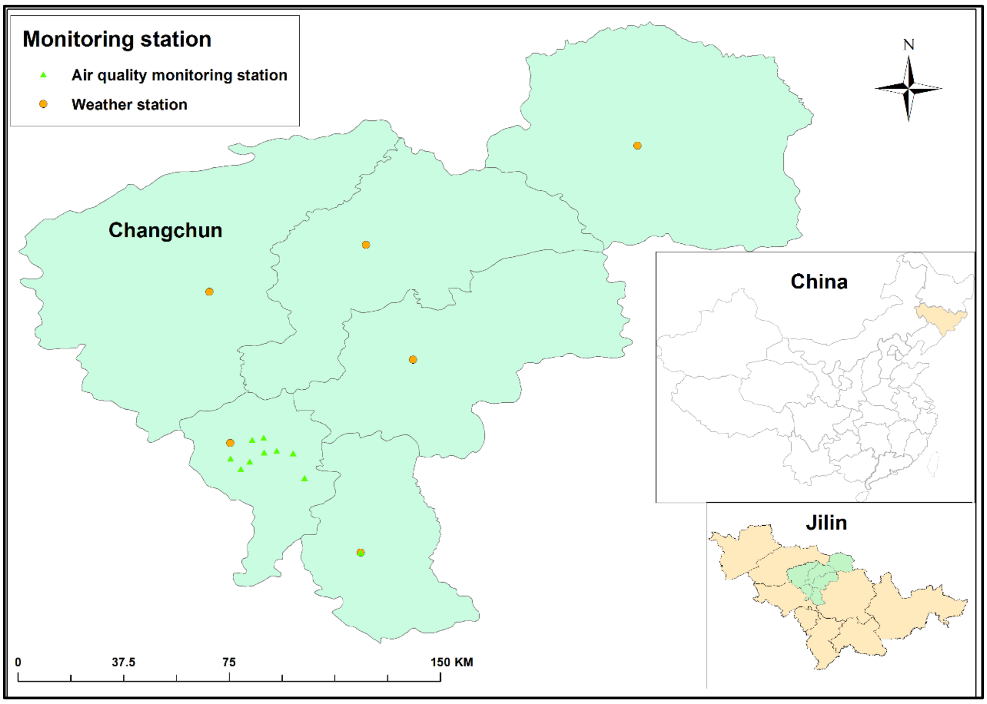

Fig S1 Locations of meteorological monitoring stations and air quality monitoring stations in Changchun

Table S1 Spearman's correlation coefficients for daily number of AR, air pollutants, and meteorological parameter

	Count	PM_{10}	PM25	NO_2	Mean temperature	Maximum temperature	Minimum temperature	Relative humidity
Count	1	-0.21**	-0.26**	-0.28**	0.40**	0.39**	0.41**	0.25**
PM_{10}		1	0.56**	0.69**	-0.33**	-0.30**	-0.36**	-0.15**
$PM_{2.5}$			1	0.45**	-0.40**	-0.37**	-0.43**	-0.10**
NO_2				1	-0.53**	-0.50**	-0.56**	-0.06
Mean temperature					1	0.99**	0.98**	0.08*
Maximum temperature						1	0.95**	0.02
Minimum temperature							1	0.17**
Relative humidity								1

[*] Correlation is significant at the 0.05 level (2-tailed);

[**] Correlation is significant at the 0.001 level (2-tailed).

Table S2 Total period percentage changes with 95% CI in daily number of AR Outpatients for per 1˚C increase in the temperature variability after changing the maximum lag of mean temperature

Modified model parameters	Variable	PC	95% CI
Maximum lag of mean temperature (10 days)			
	$TV_{0\text{-}1}$ (˚C)	2.35	-0.25–5.02
	$TV_{0\text{-}2}$ (˚C)	4.03	0.91–7.25
	$TV_{0\text{-}3}$ (˚C)	4.40	0.95–7.97
	$TV_{0\text{-}4}$ (˚C)	4.12	0.38–8.01
	$TV_{0\text{-}5}$ (˚C)	3.15	-0.80–7.25
	$TV_{0\text{-}6}$ (˚C)	3.09	-1.04–7.40
	$TV_{0\text{-}7}$ (˚C)	3.75	-0.54–8.24
Maximum lag of mean temperature (21 days)			
	$TV_{0\text{-}1}$ (˚C)	2.19	-0.23-4.67
	$TV_{0\text{-}2}$ (˚C)	4.14	1.24-7.11
	$TV_{0\text{-}3}$ (˚C)	4.40	1.17-7.73
	$TV_{0\text{-}4}$ (˚C)	3.73	0.18-7.41
	$TV_{0\text{-}5}$ (˚C)	2.22	-1.55-6.14
	$TV_{0\text{-}6}$ (˚C)	1.53	-2.43-5.64
	$TV_{0\text{-}7}$ (˚C)	1.49	-2.63-5.78

Abbreviations: AR: allergic rhinitis; CI, confidence interval; PC, percentage change; $TV_{0\text{-}1}$, TV at 0–1 days.

Table S3 Total period percentage changes with 95% CI in daily number of AR outpatients for per 1˚C increase in the temperature variability after changing the degree of freedom of relative humidity

Modified model parameters	Variable	PC	95% CI
Relative humidity (df=3)			
	TV_{0-1} (˚C)	2.35	-0.25–5.02
	TV_{0-2} (˚C)	4.03	0.91–7.25
	TV_{0-3} (˚C)	4.40	0.95–7.97
	TV_{0-4} (˚C)	4.12	0.38–8.01
	TV_{0-5} (˚C)	3.15	-0.80–7.25
	TV_{0-6} (˚C)	3.09	-1.04–7.40
	TV_{0-7} (˚C)	3.75	-0.54–8.24
Relative humidity (df=4)			
	TV_{0-1} (˚C)	2.34	-0.26-5.00
	TV_{0-2} (˚C)	4.14	1.02-7.36
	TV_{0-3} (˚C)	4.80	1.33-8.38
	TV_{0-4} (˚C)	4.64	0.88-8.53
	TV_{0-5} (˚C)	3.77	-0.20-7.90
	TV_{0-6} (˚C)	3.74	-0.41-8.08
	TV_{0-7} (˚C)	4.39	0.07-8.91
Relative humidity (df=5)			
	TV_{0-1} (˚C)	2.38	-0.22-5.04
	TV_{0-2} (˚C)	4.20	1.07-7.42
	TV_{0-3} (˚C)	4.89	1.42-8.47
	TV_{0-4} (˚C)	4.70	0.94-8.60
	TV_{0-5} (˚C)	3.77	-0.20-7.89
	TV_{0-6} (˚C)	3.73	-0.42-8.06
	TV_{0-7} (˚C)	4.35	0.03-8.86
Relative humidity (df=6)			
	TV_{0-1} (˚C)	2.32	-0.28-4.99
	TV_{0-2} (˚C)	4.12	0.99-7.34
	TV_{0-3} (˚C)	4.81	1.34-8.39
	TV_{0-4} (˚C)	4.58	0.83-8.48
	TV_{0-5} (˚C)	3.63	-0.34-7.75
	TV_{0-6} (˚C)	3.59	-0.56-7.91
	TV_{0-7} (˚C)	4.20	-0.12-8.71

Abbreviations: AR: allergic rhinitis; CI, confidence interval; PC, percentage change; df, degree of freedom; TV0-1, TV at 0–1 days.

Table S4 Total period percentage changes with 95% CI in daily number of AR outpatients for per interquartile range increase in the temperature variability

Variable	PC	95% CI
TV_{0-1} (˚C)	6.61	-0.59-14.33
TV_{0-2} (˚C)	9.99	2.50-18.03
TV_{0-3} (˚C)	11.46	3.26-20.30
TV_{0-4} (˚C)	10.72	2.10-20.07
TV_{0-5} (˚C)	8.37	-0.43-17.94
TV_{0-6} (˚C)	8.08	-0.89-17.86
TV_{0-7} (˚C)	9.33	0.07-19.44

Abbreviations: AR: allergic rhinitis; CI, confidence interval; PC, percentage change; TV_{0-1}, TV at 0–1 days.