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Effects of temperature variation between neighbouring days on daily hospital visits for childhood asthma: a time-series analysis

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ABSTRACT

Objectives: To identify the relationship between temperature variation between neighbouring days (TVN) and hospital visits for childhood asthma in age- and sex-specific groups.

Study design: An ecological design was used to explore the effect of TVN on hospital visits for childhood asthma.

Methods: A Poisson generalised linear regression model combined with a distributed lag non-linear model was used to analyse the association between TVN and hospital visits for childhood asthma. All hospital visits for childhood asthma from June 2010 to July 2013 were included ($n = 17,022$). Daily climate data were obtained from Hefei Meteorological Bureau. **Results:** A significant correlation was found between TVN and hospital visits for childhood asthma in age- and sex-specific groups. For different gender groups, the effect of TVN on childhood asthma was the greatest at 3 and 5 days lag for males and females. For different age groups, the effect of TVN on childhood asthma was the greatest at 1 and 5 days lag for 0–4 years and 5–14 years children, respectively. A 1 °C increase in TVN was associated with a 4.2% (95% confidence interval 0.9–7.6%) increase in hospital visits for childhood asthma.

Conclusions: TVN is associated with hospital visits for childhood asthma. Once the temperature change rapidly, guardians will be urged to pay more attention to their children's health, which may reduce the morbidity of childhood asthma.

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Introduction

Asthma poses serious risks to human health.^{1,2} Worldwide, approximately 180,000 patients die each year due to asthma, and approximately 1% of all disability-adjusted life years lost are attributable to asthma.^{3,4} The World Health Organisation estimated that approximately 300 million people suffer from asthma, and projected that the prevalence of asthma is increasing at 50% per annum (particularly among children). It has been estimated that the number of people with asthma will reach 400 million by 2025.^{4–6} In China, the prevalence of asthma among children was 1.5% in 2000,⁷ which was less than the world average (between 1% and 18%^{8,9}). However, given the large population in China, the increasing prevalence of childhood asthma is an important public health problem.¹⁰

Associations between asthma and environmental factors have been found in previous studies. Numerous environmental factors (e.g. temperature, humidity, rainfall, wind, intensity of solar irradiation and barometric pressure) have a significant effect on the prevalence and morbidity of asthma.^{11–13} In particular, the relationship between temperature and childhood asthma has attracted increasing attention in recent years, because children seem to be more vulnerable to respiratory diseases.⁵ Some studies have shown a significant negative correlation between asthma and temperature factors (daily mean temperature, lower minimum temperature^{14,15}), and implied that a low or cool temperature was the main environmental factor leading to asthma attacks. However, other studies have found a positive relationship between asthma and the diurnal temperature range and daily mean temperature.^{16,17} It has also been found that extremely hot temperatures could trigger asthma attacks.^{12,15} Previous studies have shown that asthma attacks are sensitive to regional climate.^{18,19} These factors indicate that asthma attacks may be attributed to rapid temperature variation rather than the simple temperature index.

Studies on asthma have not been undertaken evenly across the world, and most have been based in developed countries. However, developing countries have poorer resources for adapting to and preparing for weather variance than developed countries, so developing countries are at greater risk.²⁰ Although the relationship between climate factors and asthma has been studied extensively, the view is not uniform in different regions with different levels of development. Therefore, more studies are urgently required to discover the true relationship between hospital visits due to asthma and temperature variation in developing countries. This study was designed to explore the relationship between hospital visits for asthma and temperature variation between neighbouring days (TVN) among Chinese children in age- and sex-specific groups.

Methods

Data collection

Hefei is located in the east of China (31°52' N, 117°17' E), and is the capital city of Anhui province. It is one of the most

populous cities in China, with a total population of over 7.6 million in 2014 and land area of approximately 11,400 km². Hefei has a subtropical monsoon climate with four distinct seasons.²¹ The daily data on hospital visits for asthma from 1 June 2007 to 31 July 2013 were obtained from Anhui Provincial Children's Hospital, which is the largest children's hospital in Anhui province, responsible for the health and medical care of almost 20 million children. Asthma cases were diagnosed by clinicians. Data were divided into age groups (0–4 years and 5–14 years) and sex groups. Daily meteorological data were obtained from Hefei Meteorology Bureau, including maximum temperature (°C), mean temperature (°C), minimum temperature (°C) and relative humidity (%) in Hefei during the same period. The TVN was calculated as the mean temperature of one day minus the mean temperature of the following day. In this study, all patient information was de-identified prior to analysis, and there was no conflict of interest with patients or other organisations.

Statistical analyses

Daily hospital visits for childhood asthma followed a Poisson distribution.²² The relationship between TVN and hospital visits for childhood asthma was explored in the different age and sex groups using a Poisson generalised linear regression model combined with a distributed lag non-linear model (DLNM), which showed the effect of lagged and non-linear.^{23,24} The model was designed to describe response of two-dimensional TVN relationship with the dimensions of childhood asthma and lag day by using function of cross-basis. First, a significant relationship was found between the number of hospital visits for childhood asthma and temperature variation using time-series analysis. Second, as several previous studies had found potential confounding effects due to relative humidity, mean temperature, seasonal patterns and long-term trends, these factors were controlled in this study using natural cubic splines.^{22,25,26} Moreover, the day of the week (DOW) was adjusted in the model as a potential confounding factor. Finally, throughout the process, the optimal degree of freedom (df) was selected based on the minimum Akaike's Information Criterion (AIC), and the model fit was evaluated by analysis of residuals. The model is as follows:

$$Y_d \sim \text{Poisson}(U_d)$$

$$\text{Log}(U_d) = x + y\text{TVN}_{d,1} + y(\text{MT}_{d,5}) + z(\text{Humidity}_{d,4}) + z(\text{Time}_{d,7}) + g\text{DOW}_d$$

In the model, d is the day of observation; l is the number of lag days; x is the intercept of the model; z is natural cubic spline; y and g are the vectors of coefficients for $\text{TVN}_{d,1}$ and DOW_d , respectively; $\text{TVN}_{d,1}$ is a matrix obtained by using the DLNM to TVN; $\text{MT}_{d,5}$, $\text{humidity}_{d,4}$ and $\text{time}_{d,7}$ were used to control the mean temperature, relative humidity and seasonal patterns and long-term trends with 5 df, 4 df and 7 df, respectively; and DOW_d is the categorical day of the week with Sunday as a reference.

In this study, a lag of 10 days was used to compute the relative risk of TVN in DLNM models²⁷ as there was no effect between TVN and childhood asthma with lags of >10 days. In the model, all effect estimates were presented as relative risks. 0 °C, which was the mean TVN across the study period, was used as the reference value to calculate relative risk.

All statistical analyses were performed with R version 3.1.1, using the ‘splines’ package and ‘dlnm’ package to fit the regression model.²⁸

Results

This study used hospital visits for childhood asthma and daily climate data from 1 June 2010 to 31 July 2013. All these data are listed in Table 1, which includes the number of hospital visits for childhood asthma by sex and age groups, maximum temperature, mean temperature, minimum temperature and relative humidity. During the study period (total 1157 days), the mean values for daily maximum temperature, daily mean temperature, daily minimum temperature and relative humidity were 21.8 °C (range –1.0 to 39.0), 17.2 °C (range –2.8 to 34.0), 13.4 °C (range –7.6 to 30.5) and 72.8% (range 21.0–100.0), respectively. There were 17,022 hospital visits for childhood asthma, and the mean number of daily hospital visits for childhood asthma was 14.7 (range 0–49.0). The number of hospital visits for asthma was 2602 in children aged 0–4 years, and 14,420 in children aged 5–14 years. More males visited hospital with asthma than females (11,582 vs 5440, sex ratio 2.1:1).

Fig. 1 shows the cumulative effects of temperature variation on hospital visits for childhood asthma by age and sex. It indicates that the relationship between temperature variation and childhood asthma is significant. All groups shared a similar temperature variation–asthma pattern, and the relative risk increased rapidly when TVN exceeded 2 °C.

Fig. 2 shows the positive lagged effect of TVN (95th percentile [3.1 °C] relative to mean value [0 °C]). We found that female, male and children aged 5–14 years shared the similar general lagged effect pattern, which increases at first and then decreases with the number of lag days. The maximum lagged effect of TVN on females was greater than the effect on males, occurring five and three days after exposure, respectively. The TVN effect on males (seven days) lasted longer than that on

females (five days). On the one hand, the greatest effect of TVN on children aged 0–4 years was on the first day after exposure, but it decreased rapidly within six days. On the other hand, the effect of TVN on children aged 5–14 years was greatest on the fifth day after exposure, and lasted for six days. By checking the residuals, the adequacy of the model can be evaluated. A 1 °C increase in temperature variation was found to be associated with a 4.2% (95% CI 0.9–7.6%) increase in the number of hospital visits for childhood asthma (Table 2).

Fig. 3 shows the relationship between TVN and hospital visits for childhood asthma for different lags, with 0 °C as the reference. Overall, the estimated effect of TVN on morbidity was non-linear. Fig. 3 shows that large temperature increases have delayed adverse effects on asthma morbidity, and the risk of morbidity reduced with decreasing TVN. In Fig. 4, the residuals were checked to evaluate the model fit.

Discussion

The main purpose of this study was to analyze the relationship between TVN and childhood asthma, and to investigate the nonlinear nature and lagged effects of TVN on daily childhood asthma admissions in various age- and sex-specific groups. From 2010 to 2013, children in Hefei were exposed to the risk of relatively large TVN (2 °C) for over 360 days. The effect of TVN on childhood asthma was not acute, with a five-day lag for the greatest effect.

This study examined the impact of TVN on childhood asthma in China. Exposure to a large TVN was seen to increase the risk of childhood asthma. The greatest effect of TVN was seen in children aged 0–4 years; with a relative risk of 1.26 (95% CI 1.07–1.49) on the first day, this was larger and earlier than the relative risk of 1.08 (95% CI 1.03–1.13) seen on the fifth day in children aged 5–14 years. However, the exact mechanism remains unknown. Several previous papers have reported that short-term temperature variations can increase population mortality due to disturbed body function.^{26,29} Another study found that when sudden temperature variations exceeded the limit that people could bear, dysfunction of the automatic thermoregulation system might prevail³⁰ and affect either humoral or cellular immunity.³¹ In addition, younger children are particularly vulnerable to temperature

Table 1 – Summary statistics of daily asthma admissions, meteorological factors over 1157 days.

Variables	Mean	SD	Minimum	Percentiles			Maximum
				25	50	75	
Total	14.7	7.0	0	10.0	14.0	19.0	49.0
Male	10.0	5.2	0	6.0	9.0	13.0	29.0
Female	4.7	2.9	0	3.0	4.0	6.0	22.0
0–4 years	2.3	2.2	0	1.0	2.0	3.0	13.0
5–14 years	12.5	6.2	0	8.0	12.0	16.0	45.0
Meantem (°C)	17.2	9.8	–2.8	8.9	18.8	25.6	34.0
Maxtem (°C)	21.8	9.9	–1.0	13.5	23.5	30.0	39.0
Mintem (°C)	13.4	9.9	–7.6	4.5	14.6	22.5	30.5
Humidity (%)	72.8	15.4	21.0	64.0	75.0	85.0	100.0

Meantem = Daily mean temperature, Maxtem = Daily maximum temperature, Mintem = Daily minimum temperature, Humidity = Relative humidity.

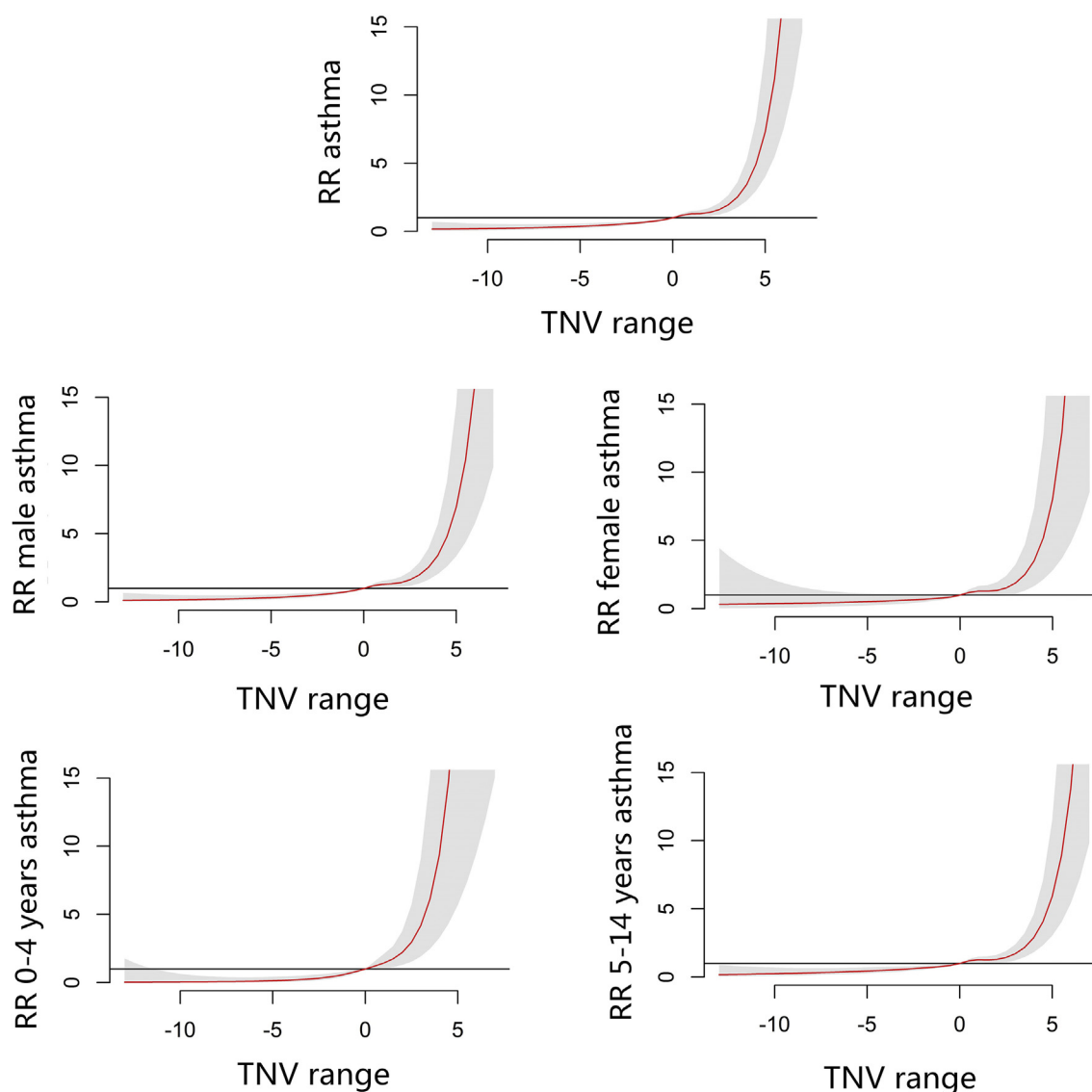


Fig. 1 – Cumulative effects of temperature variation between neighbouring days (TVN) on asthma among children under 15 years of age. RR, relative risk.

variation, possibly due to an immature immune system³² and poor self-care capacity.³³ The finding that young children are vulnerable to temperature variations suggests that children should be made aware of the possible threat posed by TVN. In order to protect susceptible individuals from the effect of sudden temperature variation, there is a need for research into biomarkers that are affected by TVN.

Another finding of this study was that the lagged effect of sex on asthma had an inverted U-shaped curvilinear relationship. The peak TVN lagged effect on females had a relative risk of 1.13 (95% CI 1.06–1.20) with a duration of five days, and this differed from males with a relative risk of 1.08 (95% CI: 1.03–1.13) and a duration of eight days. This implies that females will suffer more serious and abrupt asthma attacks after longer lagged days with innocent protection consciousness. In addition, females are more likely to be sensitive to asthma than males.^{34–36} It is not known why TVN has more serious and abrupt effects on females. The most likely reason

is variations in sex-specific body composition, living habits and personal situation (body mass, socio-economic status),^{36,37} which may contribute to females being more vulnerable to disease. This finding may enlighten future studies concerning sex-specific explanations, and provide scientific information to the children's caregivers for early protection.

This study found that an increase in TVN was a risk factor for childhood asthma. The overall effects of TVN on children increased rapidly, especially when TVN exceeded 2 °C, highlighting that both parents and healthcare workers should pay attention to the particularly high risk posed by large TVN and asthma-related morbidity in young children. What is more, the effects of TVN on children should be an important factor when developing health promotion strategies and policies to protect susceptible populations from harm due to short-term temperature changes. Warm weather leads to stimulated production and growth of pollen, mold spores and tiny

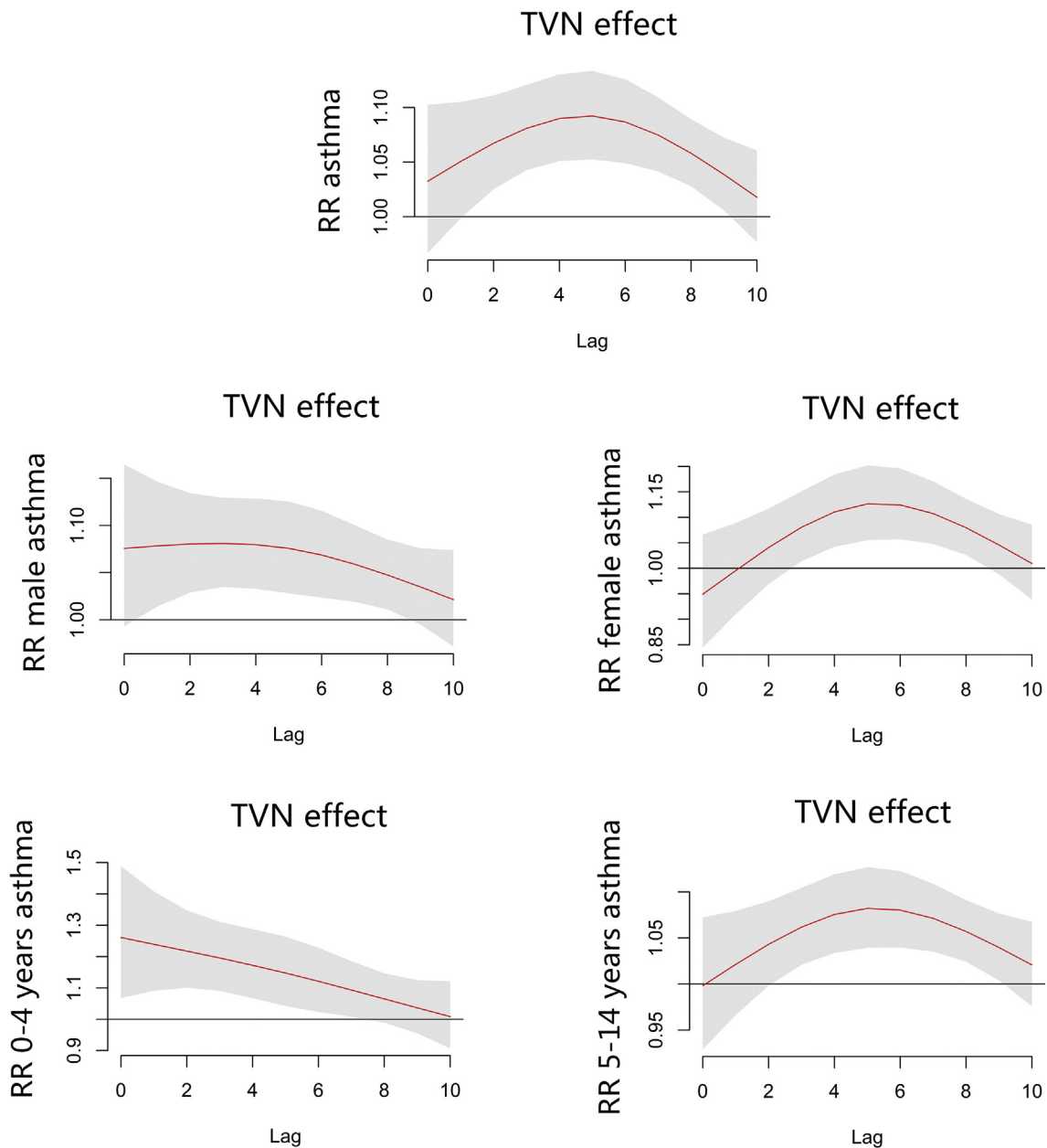


Fig. 2 – Lagged effects of temperature variation between neighbouring days (TVN) on asthma among children under 15 years of age. RR, relative risk; grey area, 95% confidence intervals of overall effects of mean temperature.

Table 2 – Relative risk of asthma in children under 15 years of age associated with one unit increase in temperature variation between neighbouring days.

	Relative risk (95% CI)			
	Lag 0	Lag 1	Lag 2	Lag 3–10
Total	1.042 (1.009–1.076) ^a	1.037 (1.012–1.062) ^a	1.032 (1.013–1.051) ^a	1.016 (0.987–1.032)
Male	1.041 (1.002–1.083) ^a	1.036 (1.007–1.067) ^a	1.031 (1.008–1.055) ^a	1.027 (0.983–1.049)
Female	1.043 (0.986–1.104)	1.038 (0.994–1.083)	1.032 (0.999–1.067)	1.028 (0.965–1.059)
0–4 years	1.087 (1.001–1.181) ^a	1.075 (1.010–1.144) ^a	1.063 (1.013–1.116) ^a	1.051 (0.923–1.100)
5–14 years	1.036 (1.001–1.073) ^a	1.031 (1.005–1.058) ^a	1.027 (1.006–1.048) ^a	1.023 (0.990–1.042)

CI, confidence interval.

^aP < 0.05.

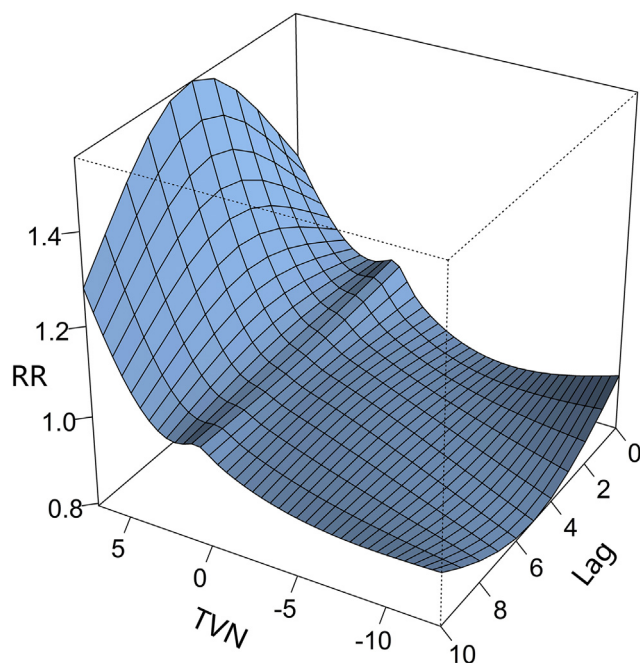


Fig. 3 – Three-dimensional plot of the effects of temperature variation between neighbouring days (TVN) on asthma, with 0°C as the reference, in China from June 2007 to July 2013. RR, relative risk.

animals,³⁸ and air concentrations of these allergens increase. In addition, people tend to spend more time outside in warm weather, leading to increased opportunities for outdoor physical activities and exposure to allergens, which may increase the risk of asthma attacks.³⁹ When it gets cold, severe convective weathers (including rain, wind etc.) will occur. Wind and rainfall can significantly reduce the concentration of allergens in the air, which could protect vulnerable populations effectively.¹³ However, this result is not consistent with the findings of previous studies in other regions.⁴⁰ As such, further research is needed to explore whether the effects of TVN vary with location and climate patterns. The results of this study may not be directly generalised to other regions with distinct weather patterns and target populations.

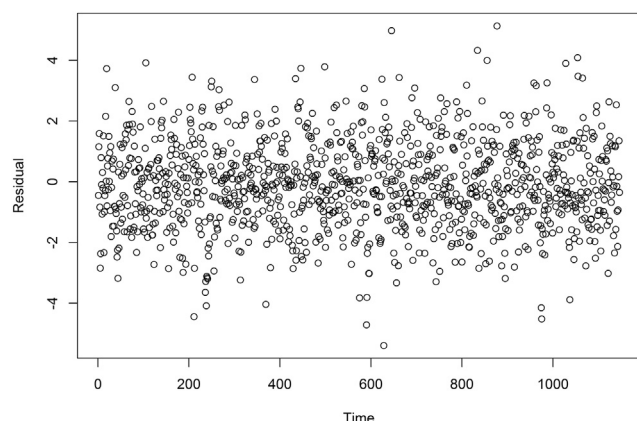


Fig. 4 – Scatterplot of residuals over time.

The strengths of this study are as follows. To the authors' knowledge, this is the first study to explore the effects of TVN on childhood asthma. Grouping the study population by sex and age made it possible to identify more detailed effects of TVN on childhood asthma; this could help in the provision of timely interventions for the target population. Lagged and non-linear effects of TVN on different age and sex groups were explored using advanced statistical methods. This study also has several limitations. First, the study may have some exposure bias because aggregated exposure on TVN data were used rather than personal exposure and identifiable individual information data, which may impact the effect of TVN on childhood asthma. Second, many factors, such as PM_{2.5}, PM₁₀ and social environmental factors, that may confound the effect of TVN on childhood asthma^{37,41} were not controlled in this study. Thirdly, the asthma data were obtained from a single hospital in a single city, so it may not be possible to extrapolate the results. However, the findings from this study may trigger further research in other regions.

Conclusion

This study demonstrated a significant relationship between hospital visits for childhood asthma and TVN. The relative risk increased rapidly, highlighting that guardians and healthcare workers should pay more attention to children's health when there is an increase in TVN. TVN has a lagged effect on childhood asthma, so it is important to consider this when caring for children. In future, with the environment getting worse, more studies and targeted health policies are needed to protect children from these risks.

Author statements

Ethical approval

Ethical approval was obtained from the Ethics Review Board of Anhui Medical University.

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Competing interests

None declared.

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