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RESEARCH ARTICLE

Observed causative impact of fine particulate matter on acute upper respiratory disease: a comparative study in two typical cities in China

Xiaolin Xia [1,3] · Ling Yao [2,3,5] · Jiaying Lu [2,3,4] · Yangxiaoyue Liu [1,3] · Wenlong Jing [1,3] · Yong Li [1,3]

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Abstract

Association between fine particulate matter ($PM_{2.5}$) and respiratory health has attracted great concern in China. Substantial epidemiological evidences confirm the correlational relationship between $PM_{2.5}$ and respiratory disease in many Chinese cities. However, the causative impact of $PM_{2.5}$ on respiratory disease remains uncertain and comparative analysis is limited. This study aims to explore and compare the correlational relationship as well as the causal connection between $PM_{2.5}$ and upper respiratory tract infection (URTI) in two typical cities (Beijing, Shenzhen) with rather different ambient air environment conditions. The distributed lag nonlinear model (DLNM) was used to detect the correlational relationship between $PM_{2.5}$ and URTI by revealing the lag effect pattern of $PM_{2.5}$ on URTI. The convergent cross mapping (CCM) method was applied to explore the causal connection between $PM_{2.5}$ and URTI. The results from DLNM indicate that an increase of 10 μg/m^3 in $PM_{2.5}$ concentration is associated with an increase of 1.86% (95% confidence interval: 0.74%-2.99%) in URTI at a lag of 13 days in Beijing, compared with 2.68% (95% confidence interval: 0.99–4.39%) at a lag of 1 day in Shenzhen. The causality detection with CCM quantitatively demonstrates the significant causative influence of $PM_{2.5}$ on URTI in both two cities. Findings from the two methods consistently show that people living in low-concentration areas (Shenzhen) are less tolerant to $PM_{2.5}$ exposure than those in high-concentration areas (Beijing). In general, our study highlights the adverse health effects of $PM_{2.5}$ pollution on the general public in cities with various $PM_{2.5}$ levels and emphasizes the needs for the government to provide appropriate solutions to control $PM_{2.5}$ pollution, even in cities with low $PM_{2.5}$ concentration.

Keywords Fine particulate matter · Health effect · Causative impact · Acute upper respiratory disease · Convergent cross mapping · Distributed lag nonlinear model

Introduction

The health effects associated with fine particulate matter ($PM_{2.5}$) have attracted great public attention in recent decades. Substantial epidemiological evidences have confirmed the correlation between respiratory disease and a certain time exposure in contaminated air environment (especially $PM_{2.5}$) for general population (Huang 2014; Cohen et al. 2017; Shaddick et al. 2018; Wang et al. 2018; Burnett et al. 2014). A variety of time series and case-crossover studies are carried out to

Responsible Editor: Lotfi Aleya

✉ Ling Yao
yaoling@lreis.ac.cn

1 Guangdong Open Laboratory of Geospatial Information Technology and Application, Key Laboratory of Guangdong for Utilization of Remote Sensing and Geographical Information System, Engineering Technology Center of Remote Sensing Big Data Application of Guangdong Province, Guangzhou Institute of Geography, Guangdong Academy of Sciences, 510070 Guangzhou, People's Republic of China

2 State Key Laboratory of Resources and Environmental Information System, Institute of Geographic Sciences and Natural Resources Research, Chinese Academy of Sciences, Beijing 100101, People's Republic of China

3 Southern Marine Science and Engineering Guangdong Laboratory, Guangzhou 511458, People's Republic of China

4 College of Resources and Environment, University of Chinese Academy of Sciences, Beijing 100101, People's Republic of China

5 Jiangsu Center for Collaborative Innovation in Geographical Information Resource Development and Application, Nanjing Normal University, Nanjing 210023, People's Republic of China

investigate the short-term health effects of exposures to $PM_{2.5}$ on the respiratory system by analyzing the variation trend of mortality or healthcare visits in a certain area. Significant associations between $PM_{2.5}$ pollution episodes and the morbidity as well as the mortality of respiratory diseases are commonly found in cities around the world (Lin et al. 2016; Atkinson et al. 2015; Shang et al. 2013).

In recent decades, $PM_{2.5}$ pollution has always been a challenging environmental concern in a great number of cities in China (Liu et al. 2016; Song et al. 2017), especially the first-tier cities. Acute upper respiratory disease is one of the most common health issues, whose infection rates could be exacerbated by air pollution (Cheng et al. 2021). The nose and upper respiratory tract act as sentinels in the respiratory system. Inhalation particles of different sizes tend to impact and interact with the upper airway mucosa, thereby resulting in viral infection. Many studies have investigated short-term effects of air pollution on the respiratory infections, and significant associations between $PM_{2.5}$ levels and respiratory disease have been observed in heavily polluted regions, including Beijing (Li et al. 2018), Shanghai (Chen et al. 2008), Wuhan (Qian et al. 2007), and Lanzhou (Tao et al. 2013). However, evidences in other countries have shown that exposure to $PM_{2.5}$, even at levels which are not much greater than normal background concentration (e.g., 3–5 μg/m^3 in Western Europe), may lead to increased risk of mortality due to respiratory diseases (Kioumourtzoglou et al. 2016; WHO Regional Office for Europe 2013). A similar conclusion has been confirmed in China. Li et al. (2020) found out that short-term PM exposures were associated with increased respiratory diseases among children, even for $PM_{2.5}$ levels below current Chinese National Ambient Air Quality Standards II in certain cities in China. Yu and Chien (2016) also pointed out that $PM_{2.5}$ increase at relatively lower levels can increase the same-day respiratory health risks of children under 14 years old in China.

As the rising demands of harmless air environment from the Chinese public, a great number of researches concerning the relationship between air pollution and respiratory health have been conducted nationwide and demonstrated this correlation in cities with various levels of $PM_{2.5}$ pollution. However, there are still some insufficiency in current researches. On one hand, the most of the researches are conducted in a single city and lack the comparative analysis on effect pattern of $PM_{2.5}$ among cities with different pollution levels. On the other hand, time series analysis based on the regression model which mainly focuses on the correlational relationship is widely used in current researches; the causal connection between the two is still uncertain. In this research, we intended to investigate the health effect of $PM_{2.5}$ on the upper respiratory tract in two typical cities with rather different ambient air environment conditions and compare the effect pattern of $PM_{2.5}$ in distinct levels. Except for exploring the correlational relationship between $PM_{2.5}$ concentration and upper respiratory diseases using a time series analysis based on the regression model, the causal connection between the two was also detected by applying a model-free method, which helps to distinguish causality from standard correlations.

Methods and materials

Study areas

This study aims to explore the relationship between $PM_{2.5}$ pollution and acute upper respiratory disease in two typical cities with rather different ambient air environment conditions. For highly polluted city, Beijing where has suffered severe haze weather in recent years is chosen, while for a slightly polluted city, Shenzhen is picked since its air quality is always among the best in China.

Beijing, as the capital city, is the political and economic center of China. Located in the Jing-Jin-Ji metropolitan area which is dominated by heavy industry, Beijing has been deeply affected by the surrounding anthropogenic pollution emissions as a result of the rapid development in this area (Dominici and Mittleman 2012). In addition, the geographical location of Beijing generally tends to prevent the air pollutants from spreading out, which also aggravates the air pollution in Beijing. In view of this, Beijing urban area, including Dongcheng, Xicheng, Chaoyang, Haidian, Fengtai, and Shijingshan), is chosen as the typical area the suffered from heavy air pollution in this study.

Shenzhen, a young city in China, was once praised as an Environmental Protection Model City in 1997 for its favorable air environment. In recent years, as a member of the Pearl River Delta (PRD) region which is one of the most developed regions with the highest aggregation of industry in China, Shenzhen has experienced deterioration in its air environment quality. Influenced by local pollution as well as pollution from surrounding areas, air quality in Shenzhen has deteriorated gradually and affected the living quality of local people to some extent (Xia et al. 2017a, Xia and Yao 2019). However, the air environment condition in Shenzhen is still considered pleasant compared with Beijing (Xia et al. 2017b). In this study, Shenzhen city is chosen as the typical area with mild air pollution for comparison.

Data collection

Daily counts of respiratory illness cases from Jan 1 to Dec 31, 2013, were collected from ten comprehensive hospitals located in urban areas in Beijing (obtained from Xu et al. (2016)) and 66 major hospitals in Shenzhen City. According to the International Classification of Diseases 10th Revision Code (ICD-10), cases of upper respiratory tract infection (URTI)

(ICD-10: J00, J02-J06) were picked out from all the respiratory illness cases. In this study, we only focus on the association between short-term exposure to $PM_{2.5}$ and URTI, since URTI is generally considered to be associated with the external environment.

Hourly concentrations of $PM_{2.5}$ are released by the Ministry of Ecology and Environment of the People's Republic of China (http://air.cnemc.cn:18007), following the Chinese National Ambient Air Quality Standards (GB3095-2012) (MEP 2012). Daily-averaged concentration $PM_{2.5}$ (μg/m^3) data during the study period were collected to represent the degree of the exposure to $PM_{2.5}$, including data from 17 ambient air quality monitoring stations located in urban areas in Beijing city and 19 stations in Shenzhen City. The spatial distributions of the hospitals and monitoring sites are shown in Figure 1. The rate of the missing values from the 17 monitoring stations in Beijing is relatively high. To solve this problem, we use the linear interpolation method to fill the missing date range when it is less than or equal to 3 days. No missing date is observed in the time series of daily concentration of $PM_{2.5}$ in Shenzhen during the study period.

Meanwhile, to control for the effects of weather conditions during the same period, daily meteorological data were collected from the official website of the Chinese Meteorological Bureau, including daily mean temperature (°C) and relative humidity daily (%).

Distributed lag nonlinear model

Distributed lag nonlinear model (DLNM) has been widely used to estimate the exposure-response relationship between environmental pollution and diseases in a lot of epidemiological studies (Lall et al. 2010; Shrestha 2007). The exposure-response relationship generally represents the correlational relationship between the level of exposure and the occurrence of certain diseases of the human body.

Based on the generalized additive model, DLNM is developed to evaluate the lag effect by involving a detailed time-course representation of the exposure-response relationship (Gasparrini et al. 2010). The main advantage of the DLNM is that it is able to provide an estimate of the cumulative lag effect as the sum of the single-day lag effect upon the whole period. Considering the confounding factors, penalized smoothing splines of calendar time and metrological conditions (temperature, relative humidity) were added to improve the performance of the model. Degrees of freedom (*df*) for the smoothers are determined using the generalized the cross validation until the sum of absolute difference reached the

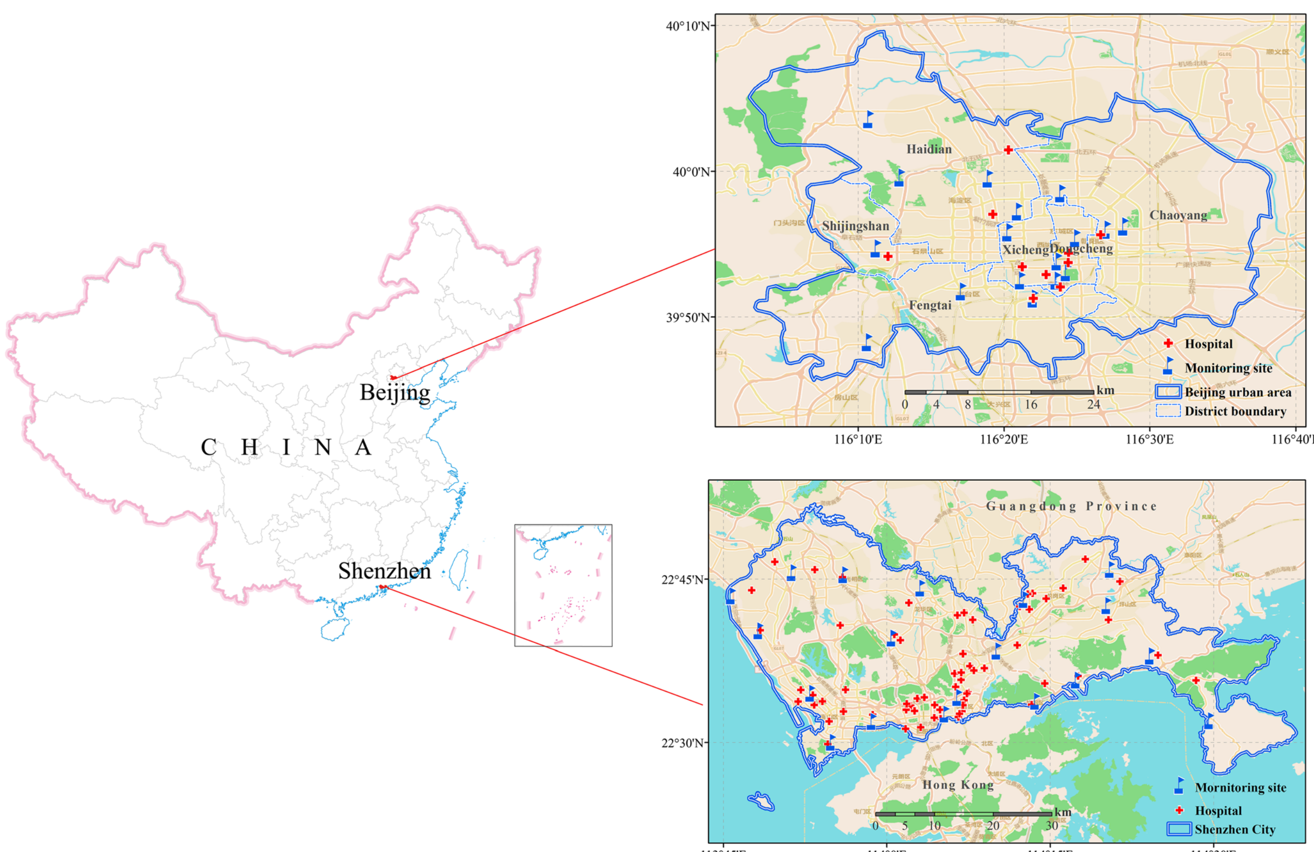


Figure 1 Distributions of involved hospitals and monitoring sites in Beijing urban areas and Shenzhen City

minimum. In this study, *df* for calendar time is set to 7, and *df* for temperature and relative humidity is set to 3 in both two study areas to account for the potential nonlinear effects. We also include two dummy variables for the day of the week and holiday, respectively. The model is of the form:

$$Log[E(Y_t)] = \alpha + \sum_{i=1}^{L} \beta_i X_{t-L,i} + S(time, df) + \beta_w DOW_t + \beta_h Holiday_t + S(Z_t, df) \quad (1)$$

where t is the day of observation; X_{t-L} represents the concentration of $PM_{2.5}$ on L days ahead day t; $E(Y_t)$ is the expected number of cases on day t; α is the intercept term; β represents the log-relative risk (RR) of cases associated with a unit increase of $PM_{2.5}$.; $S(time, df)$ and $S(Z_t, df)$ are the penalized smoothing splines of calendar time and metrological conditions (temperature, relative humidity); and *DOW* and *Holiday* stand for the day of week and holiday with β_w and β_h as the corresponding coefficients.

To perform the model, DLNM and Mixed GAM Computation Vehicle (MGCV) packages in R (Wood 2017) were used. All results are presented as relative risk (RR) or percent change in daily case amount and its 95% confidence interval (CI) in association with a 10-μg/m^3 increase of $PM_{2.5}$ concentration.

Convergent cross mapping method

The convergent cross mapping (CCM) method is the first proposed by Sugihara and May (1990) to deal with the illusory correlation in the complex system. It helps in distinguishing the causality from standard correlations between pairs of time series (at least 25 observations) (Maher and Hernandez 2015).

Based on Takens' theorem, the CCM algorithm is model-free and robust to unmeasured confounding which may induce false associations (Deyle and Sugihara 2011). It allows reconstructing high dimensional system dynamics with a time series of a single variable under mild assumptions. In CCM, the complex and nonlinear systems are analyzed through state-space reconstruction, which has advantages in solving problems in various fields, e.g., wildlife management and cerebral autoregulation (Vanderweele and Arah 2011). Unlike the most frequently used Granger causality analysis (Granger 1980) which behaves poorly in a weak-to-moderate coupling, CCM is more suitable for detecting illusory correlation and revealing potential causality in complex ecosystems (Sugihara et al. 2012).

Giving two time series of variables X $\{x_1,x_2,\ldots,x_L\}$ and $Y\{y_1,y_2,\ldots y_L\}$ (L is the length of time period), dimension E in which the reconstructed attractor is embedded and time lag τ, CCM algorithm is implemented in the following steps:

Step 1. Rebuild the shadow manifold M_x and M_y from the lagged-coordinate vectors X and Y, which is:

$$x(t) = \left\langle x_t, x_{t-\tau}, x_{t-2\tau}, \ldots, x_{t-(E-1)\tau} \right\rangle \quad (2)$$

$$y(t) = \left\langle y_t, y_{t-\tau}, y_{t-2\tau}, \ldots, y_{t-(E-1)\tau} \right\rangle \quad (3)$$

where $t = 1+(E-1)\tau$ to $t = L$. A small region around y_t will map to a small region around x_t to estimate x_t since M_y is diffeomorphic to M_x. Note that at least E+1 points are needed to form a bounding simplex around y_t (Sugihara and May 1990).

Step 2. Create a cross mapped estimation of y_t, denoted by $\widehat{y}_t|M_x$. Firstly, find the simultaneous lagged-coordinate vector on M_x, $x(t)$ and its $E+1$ nearest neighbors. For each $x(t)$, the nearest neighbor search gets a set of distances sorted from the closest to the outermost by an associated set of time $\{t_1,t_2,\ldots,t_{E+1}\}$. The distance $d[x(t), x(s)]$ is measured by the Euclidean distance between the two vectors.

Step 3. Calculate with a weighted mean the nearest neighbors in M_y. The weight w_i is defined as:

$$w_i = \frac{u_i}{\sum_{j=1}^{E+1} u_j} \quad (4)$$

where

$$u_i = exp\left(-\frac{d[x(t), x(t_i)]}{d[x(t), x(t_1)]}\right)$$

Step 4. Explore neighbors in y with $\{t_1, t_2, \ldots, t_{E+1}\}$. The estimate of y_t is a locally weighted mean of the E+1, and y_{t_i} is calculated as:

$$\widehat{y}_t|M_x = \sum_{i=1}^{E+1} w_i y_{t_i} \quad (5)$$

Step 5. . Calculate the CCM correlation. The Pearson correlation coefficient between original and estimated time series is expressed as:

$$\rho_{Y\widehat{Y}} = \rho\left(y_t, \widehat{y}_t|M_x\right) \quad (6)$$

Meanwhile, a t-statistic for correlation coefficient at a level of significance is calculated as:

$$t = {}^{\rho_{Y\widehat{Y}}}/_{S_\rho} where\ S_\rho = \sqrt{\frac{1-\rho_{Y\widehat{Y}}^{\ 2}}{N-2}} \quad (7)$$

where N is the length of the time series process. The Pearson correlation coefficient ρ_{YX} between the L true values from Y, and the L cross mapped estimates are an indicator of how much the dynamics of Y impacts the dynamics of X (Dan et al. 2017).

For CCM method, E and τ are two important parameters which need to be optimized. Based on previous findings, CCM is suggested to be insensitive to the manual setting of parameters and can extract reliable causality between diverse variables (Chen et al. 2017). Assuming that $E_{\max}$ is the optimal dimension, Whitney's theorem indicates that the dimensionality is generically between ($E_{\max}$ −1)/2 and $E_{\max}$ (Deyle and Sugihara 2011). In this study, dimension (E) from the two times series equals 2 using the false nearest neighbor method, and the value of τ is set to 2 based on the average mutual information criterion for both study areas.

Results and discussion

Descriptive statistics

A total of 51134 and 18354 URTI cases were recorded, respectively, from the hospitals in Beijing and Shenzhen in 2013. Table 1 summarizes the statistical characteristics of URTI, $PM_{2.5}$ concentration, and meteorological factors in Beijing and Shenzhen in 2013. The daily mean count of URTI was 140 in Beijing (ranged from 65 to 347) and 50 in Shenzhen (ranged from 1 to 87). The time series graph in Figure 2 shows the daily variations of URTIs and $PM_{2.5}$ concentrations in 2013.

During the study period, the overall daily mean $PM_{2.5}$ concentration was 102 μg/m^3 (ranged from 6.7 μg/m^3 to 508.5 μg/m^3) in Beijing and 37 μg/m^3 (ranged from 7.9 μg/m^3 to 129.8 μg/m^3) in Shenzhen. Referring to the Chinese Ambient Air Quality Standards (Grade II, 75 μg/m^3 for 24-hour average $PM_{2.5}$ concentration), 45.7% (155 days) of the daily $PM_{2.5}$ concentrations in Beijing and 88% (321 days) in Shenzhen were below the standard. While referring to the WHO Air Quality Standards (25 μg/m^3 for 24-h average $PM_{2.5}$ concentration), only 30 days in Beijing and 120 days in Shenzhen met the standard. Judging by the number of days which meet the two kinds of standard, $PM_{2.5}$ pollution in Beijing was much more severe than that in Shenzhen in 2013. In addition, meteorological conditions in the two cities are also different. Located in relatively lower latitudes, Shenzhen has a warmer and wetter climate than Beijing.

Table 1 Summary of the URTI, $PM_{2.5}$ concentration, temperature, and relative humidity in Beijing and Shenzhen during the study period. SD means standard deviation, and P(25), P(50), and P(75) represent the lower quartile, the mean value, and the upper quartile, respectively

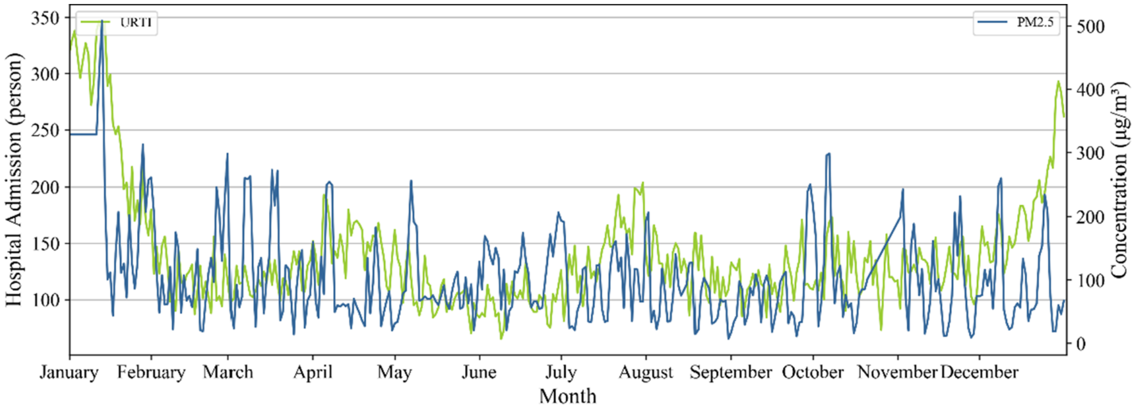
Variable	Mean ±SD	Min	P(25)	P(50)	P(75)	Max
URTI						
Beijing	140±52	65	108	126	155	347
Shenzhen	50±14	1	42	50	59	87
$PM_{2.5}$(μg/m^3)						
Beijing	102±73.6	6.7	53.1	82.4	129.5	508.5
Shenzhen	37±23.7	7.9	20.8	34.7	61.2	129.8
Temperature (°C)						
Beijing	11.3±11.6	-12.6	1.2	11.0	22.2	29.0
Shenzhen	23.2±5.2	4.4	18.8	25.6	27.3	35
Relative humidity (%)						
Beijing	58.7±17.3	18.9	46.7	59.0	73.3	93.3
Shenzhen	73±12.8	22	59	77	93	100

The lag effect of $PM_{2.5}$ on URTI

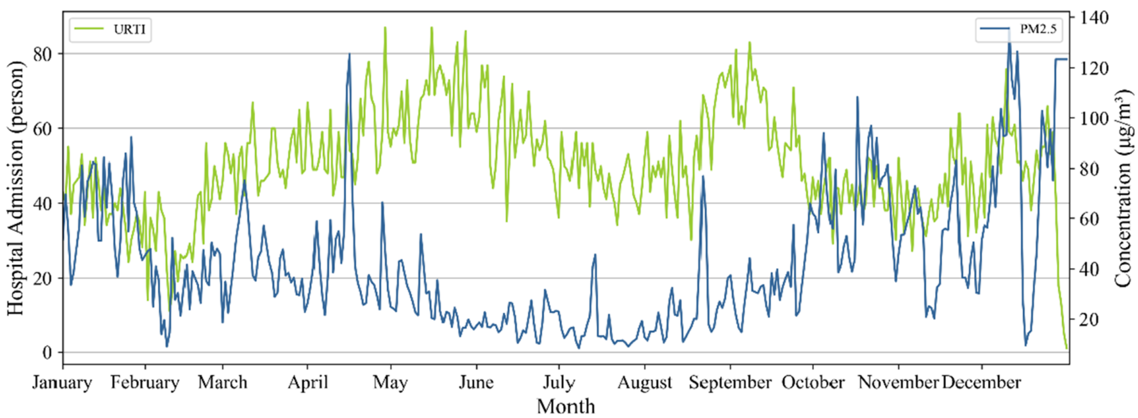
To explore the lagged health effect of $PM_{2.5}$ on the upper respiratory tract of the human body, a time series analysis based on DLNM was carried out. We investigated the lag effect of $PM_{2.5}$ up to a lag of 7 days in Shenzhen and 14 days in Beijing. There were clear exposure-response relationships between $PM_{2.5}$ concentration and URTI cases. As shown in Figure 3, the exposure-response patterns for Beijing and Shenzhen are both approximately linear, with slight fluctuations when the $PM_{2.5}$ concentrations are below a certain value (300 μg/m^3 for Beijing and 70 μg/m^3 for Shenzhen) and a sharper rise at higher $PM_{2.5}$ concentrations. Different patterns of response at the same $PM_{2.5}$ levels are observed in the two study areas, which implies that citizens in Shenzhen are more sensitive to $PM_{2.5}$ exposure while citizens in Beijing are more tolerant to $PM_{2.5}$ exposure.

In this study, the DLNM was applied to evaluate the effects of $PM_{2.5}$ on the upper respiratory track as a linear exposure-response relationship between them. The relative risk for URTI was denoted as a change in the number of daily URTI cases associated with a 10-μg/m^3 increase of $PM_{2.5}$ concentration. The resulting exposure-response patterns for both single-day lag effect and cumulative lag effect are shown in Figure 4, with black bars and gray areas representing the 95% CI. The cumulative lag effect was obtained by applying a polynomial curve fitting on single-day lag effect at a degree of 3.

Table 2 and Table 3 show the relative risk for URTI associated with a 10-μg/m^3 increase in $PM_{2.5,}$ together with the 95% CI in Beijing urban area and Shenzhen City. For Beijing urban area, significant single-day lag effects were observed at a lag ranging from 6 days to 12 days, with the maximum appeared at a lag of 10 days; significant cumulative lag effects appeared at a lag of 6 days and remained significant until a lag of 14 days. For Shenzhen City, a significant single-day lag effect was only observed at a lag of 1 day, and significant cumulative lag effects were observed at a lag ranging from 1 day to 5 days. Considering the cumulative lag effect, each 10-μg/m^3 increase in $PM_{2.5}$ concentration was maximally associated with 1.86% (95%CI: 0.74–2.99%) and 2.68%



(a) Time series graph in Beijing



(b) Time series graph in Shenzhen

Figure 2. Time series graph of URTI (number of daily cases) and daily PM2.5 concentrations in (**a**) Beijing and (**b**) Shenzhen in 2013

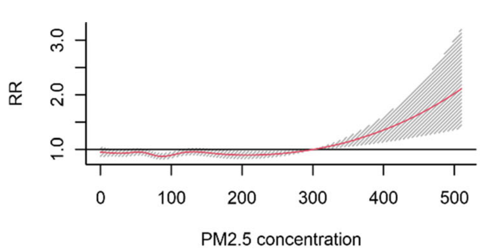
(95%CI: 0.99–4.39%) increase in URITs in Beijing (at a lag of 13 days) and Shenzhen (at a lag of 1 day), respectively.

Although significant lag effects were detected in both two study areas, the lag patterns were quite different. The lag effect of $PM_{2.5}$ on URTI in Beijing was more delayed and lasts longer than that in Shenzhen. Judging by the RR values, the same amounts of increases in $PM_{2.5}$ concentration in Shenzhen had a greater effect on URTI than in Beijing.

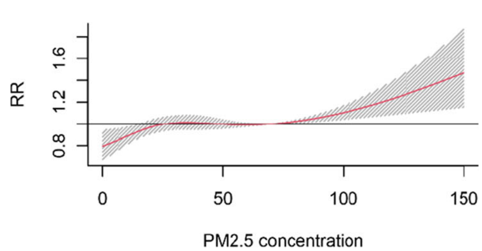
This section focused on the comparison of the exposure-response relationship between $PM_{2.5}$ and URTI in a highly polluted area and a slightly polluted area. It was found out that, after a short-term exposure in $PM_{2.5}$, response on URTI in the slightly polluted area (Shenzhen) was more significant than in the highly polluted area (Beijing), in terms of response time and degree of effect.

The causative influence of $PM_{2.5}$ on URTI

The lag effect analysis using DLNM in section 3.2 is a regression analysis which can only detect whether the two variables have a correlational relationship. However, correlation does not mean causality [33]. To explore the causative influence of



(a) Beijing



(b) Shenzhen

Figure 3 Smoothed exposure-response graph of daily mean PM2.5 concentrations at a lag of 0–1 day against the risk of URTI. The X-axis shows the moving averages of PM2.5 concentrations. The Y-axis is the predicted relative risk (RR). The red line represents central estimates, and the grey-shaded area represents the 95% CI

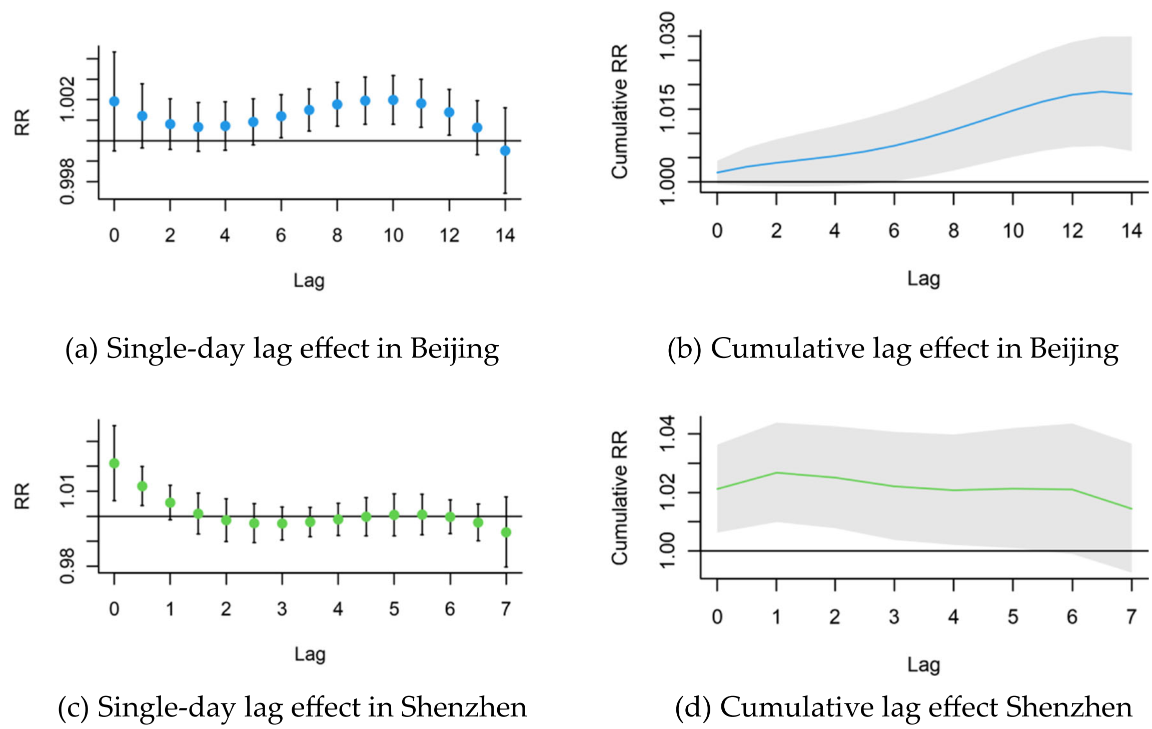


Figure 4. Lag-response relationship between PM2.5 and relative risk (RR) of URTI for (**a**) single-day lag effect in Beijing, (**b**) cumulative lag effect in Beijing, (**c**) single-day lag effect in Shenzhen, and (**d**) cumulative lag effect in Shenzhen

$PM_{2.5}$ on URTI, a time series analysis based on the CCM method was applied.

The convergent cross maps of Beijing urban area and Shenzhen City are shown in Figure 5, where the red lines represent the causative influence of the number of URTI cases on $PM_{2.5}$ concentrations while the blue lines represent the opposite.

Table 2 Relative risk for URTI on different lag days in associations with 10-μg/m^3 increase in $PM_{2.5}$ concentrations in Beijing urban area in 2013. (Value with * is significant at the 0.05 level)

Lag (days)	RR (95% CI) (Single-day lag effect)	Cumulative RR (95% CI) (Cumulative lag effect)
0	1.0019 (0.9995, 1.0043)	1.0019 (0.9995, 1.0043)
1	1.0012 (0.9996, 1.0028)	1.0031 (0.9992, 1.0070)
2	1.0008 (0.9996, 1.0020)	1.0039 (0.9991, 1.0088)
3	1.0007 (0.9995, 1.0019)	1.0046 (0.9991, 1.0101)
4	1.0007 (0.9995, 1.0019)	1.0053 (0.9992, 1.0115)
5	1.0009 (0.9998, 1.0020)	1.0062 (0.9995, 1.0130)
6	1.0012 (1.0001, 1.0022)*	1.0074 (1.0001, 1.0148)*
7	1.0015 (1.0005, 1.0025)*	1.0089 (1.0011, 1.0168)*
8	1.0018 (1.0007, 1.0028)*	1.0107 (1.0023, 1.0192)*
9	1.0019 (1.0008, 1.0031)*	1.0127 (1.0037, 1.0217)*
10	1.0020 (1.0008, 1.0032)*	1.0147 (1.0052, 1.0243)*
11	1.0018 (1.0006, 1.0030)*	1.0165 (1.0064, 1.0268)*
12	1.0014 (1.0003, 1.0025)*	1.0179 (1.0072, 1.0288)*
13	1.0006 (0.9993, 1.0020)	1.0186 (1.0074, 1.0299)*
14	0.9995 (0.9974, 1.0016)	1.0181 (1.0063, 1.0299)*

The ρ value itself cannot indicate the positive or negative impact, and only the positive ρ value with a stable convergent trend implies the causative impact may exist between the two variables. Significant convergent patterns of blue lines are observed for two study areas, indicating that $PM_{2.5}$ concentration causatively impacts the number of URTI in Beijing and Shenzhen. While regard to the red lines, no significant patterns were detected, which implies that the number of URTI has no impact on $PM_{2.5}$ concentration. This logical result also verifies the feasibility and effectiveness of CCM method. Quantitative results (ρ value) in Table 4 represent the strength of the causative impact, and it shows that the strength of the impact in Shenzhen is larger than that in Beijing.

Table 3 Relative risk for URTI on different lag days in associations with 10-μg/m^3 increase in $PM_{2.5}$ concentrations in Shenzhen City in 2013. (Value with * is significant at the 0.05 level)

Lag (days)	RR (95% CI) (Single-day lag effect)	Cumulative RR (95% CI) (Cumulative lag effect)
0	1.0212 (1.0063, 1.0364)*	1.0212 (1.0063, 1.0364)*
1	1.0054 (0.9985, 1.0124)	1.0268 (1.0099, 1.0439)*
2	0.9984 (0.9899, 1.0070)	1.0251 (1.0078, 1.0427)*
3	0.9971 (0.9905, 1.0037)	1.0221 (1.0038, 1.0407)*
4	0.9987 (0.9923, 1.0052)	1.0208 (1.0020, 1.0398)*
5	1.0005 (0.9921, 1.0090)	1.0213 (1.0010, 1.0420)*
6	0.9997 (0.9930, 1.0065)	1.0210 (0.9990, 1.0436)
7	0.9935 (0.9796, 1.0077)	1.0144 (0.9926, 1.0367)

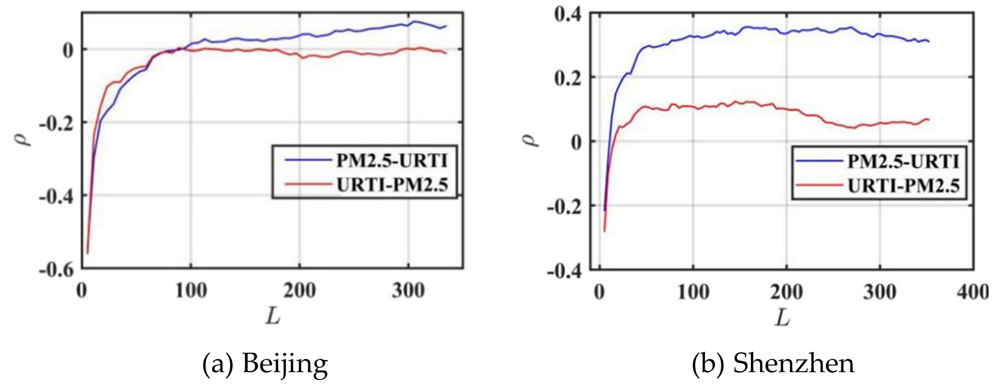


Figure 5 Convergent cross maps demonstrating the causality between PM2.5 concentration and URTI in (**a**) Beijing and (**b**) Shenzhen in 2013. PM2.5-URTI indicates the influence of PM2.5 on URTI, and URTI-PM2.5 is the opposite

Comparative discussions on the finding

Significant associations between $PM_{2.5}$ concentration and URTI cases in terms of correlation relationship as well as causal connection were both observed in Beijing urban area and Shenzhen City. That is, short-term exposure to $PM_{2.5}$ does have a significant adverse effect on the upper respiratory track of the general population regardless of the pollution level of $PM_{2.5}$. However, when concerning the effect patterns, such as the lag period and strength of effect, it shows quite different outcomes. The results from DLNM and CCM both show that the strength of the impact of $PM_{2.5}$ in Shenzhen City is larger than that in Beijing urban areas. This finding is consistent with other studies carried out in China and other countries. Table 5 summarizes the findings in relevant studies concerning the associations between $PM_{2.5}$ and respiratory disease in recent years.

Table 5 contains the study area, $PM_{2.5}$ level, increased percent of the respiratory disease (including the number of all diseases, number of upper respiratory infection, mortality of all disease) from the recent studies, and they are arranged in the order of $PM_{2.5}$ level from low to high. We can see that increased risks in the study areas with lower $PM_{2.5}$ levels are generally higher than those with higher $PM_{2.5}$ levels. For mortality of all respiratory disease, for each 10-μg/m^3 increase in $PM_{2.5}$ concentration, it showed 2.0–4.01% (95% CI: 0.15–7.52%) increases in Tokyo, Shenzhen, and Zhuhai (mean $PM_{2.5}$: 16.0–34.23 μg/m^3), 0.90–0.97% (95% CI: 0.01–1.94%) increases in Hefei and Shenyang (mean $PM_{2.5}$: 66.18–75 μg/m^3), while only 0.63% (95% CI: 0.07–1.19%) increase in Shijiazhuang (mean $PM_{2.5}$: 118.8 μg/m^3). Besides, for numbers of all respiratory disease, each 10-μg/m^3 increase in $PM_{2.5}$ concentration showed 1.06–1.19% (95% CI: 0.20–2.19%) increases in Shenzhen and Guangzhou (mean $PM_{2.5}$: 23.7–35.8 μg/m^3), 0.53–0.73% (95% CI: 0.22–0.87%) increases in Shanghai and Lanzhou (mean $PM_{2.5}$: 55.5–61.11 μg/m^3), while only 0.23–0.57% (95% CI: 0.02–0.66%) increases in Chengdu and Jinan (mean $PM_{2.5}$: 96.9–100 μg/m^3). As for upper respiratory infection, for each 10-μg/m^3 increase in $PM_{2.5}$ concentration, it showed 4.8% (95% CI: 2.8–6.9%) in Korea (mean $PM_{2.5}$: 21.1 μg/m^3), 2.68% (95% CI: 0.99–4.39%) in Shenzhen (mean $PM_{2.5}$: 50 μg/m^3), while 1.86% (95% CI: 0.74–2.99%) in Beijing (mean $PM_{2.5}$: 140 μg/m^3). A systematic review study conducted by Sun et al. (2020) similarly found out that a low increased risk of respiratory disease (0.62%, 95% CI: 0.57–0.66%) was identified at a high level of annual mean $PM_{2.5}$ concentrations (41.36–110.80 μg/m^3) with 1.82% (95% CI: 1.72–1.92%) at a low level of annual mean $PM_{2.5}$ concentrations (29.86–40.20 μg/m^3), which can also support the finding in this study.

Table 4. Quantitative causative influence (ρ value) between $PM_{2.5}$ and URTI in Beijing urban areas and Shenzhen City; value with * is significant at the 0.05 level

Pairs	Causative impact (ρ value)
$PM_{2.5}$ – URTI in Beijing	0.089*
URTI – $PM_{2.5}$ in Beijing	0.001
$PM_{2.5}$ – URTI in Shenzhen	0.347*
URTI – $PM_{2.5}$ in Shenzhen	0.102

Conclusions

In this study, a comparative analysis on the health effect of $PM_{2.5}$ is conducted in two typical cities with different pollution levels, by applying time series analysis based on the DLNM and CCM method. Both correlational relationship and causal connection between $PM_{2.5}$ concentration and URTI cases are detected in two study areas. In addition, the results from DLNM and CCM method consistently show that the strength of the impact of $PM_{2.5}$ in Shenzhen is larger than that in Beijing, which implies that people living in low-concentration areas (Shenzhen) are less tolerant to $PM_{2.5}$ exposure than those in high-concentration areas (Beijing). In conclusion, our study highlights the adverse health effects of $PM_{2.5}$ pollution on the general public in cities with various $PM_{2.5}$ levels in China and emphasizes the need for the government to provide appropriate solutions to control $PM_{2.5}$ pollution, even in cities with low $PM_{2.5}$ levels.

Table 5 Findings concerning the associations between $PM_{2.5}$ and respiratory disease in relevant studies in recent years

Study area	$PM_{2.5}$ level (μg/m^3)	Increase percent (95%CI)/ 10μg/m^3	Respiratory disease
Tokyo (Michikawa et al. 2020)	16.0±8.9[a]	2.00% (95% CI: 0.20–3.90%)	Mortality of all disease
Korea (Kim et al. 2020)	21.1 (0.3, 137.3)[b]	4.80% (95% CI: 2.80–6.90%)	Upper respiratory infection
Shenzhen (Zhang et al. 2019)	23.7 (3.4, 91.2)[b]	1.06% (95% CI: 1.02–1.10%)	All disease
Shenzhen (Zhu et al. 2021)	32.7[c]	4.01% (95% CI: 0.84–7.52%)	Mortality of all disease
Guangzhou (Yang et al. 2021)	35.8 (27.5)[d]	1.19% (95% CI: 0.20–2.19%)	All disease
Zhuhai (Wu et al. 2017)	34.23[c]	3.23% (95% CI: 0.15–6.40%)	Mortality of all disease
Shenzhen (Cai et al. 2019)	35 (7, 137)[b]	3.04% (95% CI: 0.60–5.55%)	Mortality of all disease
Hongkong (Lin et al. 2016a)	37.5 (5.8, 172)[b]	1.40% (95% CI: 0.35–2.46%)	Mortality of all disease
Guangzhou (Lin et al. 2016b)	47.7 (6.9, 153.7)[b]	1.06% (95% CI: 0.19–1.94%)	Mortality of all disease
Wuhan (Ren et al. 2020)	48.2 (2.5, 238)[b]	1.95% (95% CI: 1.63–2.27%)	All disease
Shenzhen (this study)	50±14[a]	2.68% (95% CI: 0.99–4.39%)	Upper respiratory infection
Changzhou (Yu et al. 2018)	50.98[c]	1.65% (95% CI: 0.18–3.15%)	Mortality of all disease
Shanghai (Yang et al. 2017)	55.50[c]	0.73% (95% CI: 0.59–0.87%)	All disease
Lanzhou (Chai et al. 2019)	61.11±30.89[a]	0.53% (95% CI: 0.22–0.84%)	All disease
Hefei (Sui et al. 2021)	66.18 (4.6, 373)[b]	0.90% (95% CI: 0.23–1.57%)	Mortality of all disease
Shenyang (Ma et al. 2011)	75 (10, 339)[b]	0.97% (95% CI: 0.01–1.94%)	Mortality of all disease
Beijing (Li et al. 2015)	82.02 (20.02, 249.3)[b]	1.70% (95% CI: 0.92–3.33%)	mortality of all disease
Beijing (Lu et al. 2017)	87.4[c]	0.66% (95% CI: 0.58–0.75%)	All disease
Chengdu (Duan et al. 2015)	96.9[c]	0.57% (95% CI: 0.48–0.66 %)	All disease
Jinan (Liu et al. 2019)	100 (16, 443)[b]	0.23% (95% CI: 0.02–0.45%)	All disease
Shijiangzhuang (Feng et al. 2018)	118.80[c]	0.63% (95% CI: 0.07–1.19%)	Mortality of all disease
Beijing (this study)	140±52[a]	1.86% (95% CI: 0.74–2.99%)	Upper respiratory infection

[a] mean ± standard deviation; [b] mean (minimum, maximum); [c] mean; [d] median (IQR)

Author contribution XX and LY developed the concept of research work. XX, LY, and JL conceived and designed the study, collected the data, and carried out research works. XX and JL analyzed the data. LY provided oversight for the research. XX prepared the initial draft of the manuscript. YXL, WJ, and YL revised the subsequent versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

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