GeoHealth

RESEARCH ARTICLE

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Jiawei Zhang and Zhihu Xu contributed equally to this work.

Key Points:

- Six pollutants have adverse effects, with O_3 exerting adverse effects only in the warm season
- Greenness has a modifying effect on the detrimental impact of NO_2, SO_2, O_3 (warm), and CO
- No moderating effect of Gross Domestic Product was found

Supporting Information:

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

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Exploring the Modifying Role of GDP and Greenness on the Short Effect of Air Pollutants on Respiratory Hospitalization in Beijing

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Abstract It is unclear whether Gross Domestic Product (GDP) and greenness have additional modifying effects on the association between air pollution and respiratory system disease. Utilizing a time-stratified case-crossover design with a distributed lag linear model, we analyzed the association between six pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3, and CO) and 555,498 respiratory hospital admissions in Beijing from 1st January 2016 to 31st December 2019. We employed conditional logistic regression, adjusting for meteorological conditions, holidays and influenza, to calculate percent change of hospitalization risk. Subsequently, we performed subgroup analysis to investigate potential effect modifications using a two-sample z test. Every 10 μg/m^3 increase in $PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3 led to increases of 0.26% (95%CI: 0.17%, 0.35%), 0.15% (95%CI: 0.09%, 0.22%), 0.61% (95%CI: 0.44%, 0.77%), 1.72% (95%CI: 1.24%, 2.21%), and 0.32% (95%CI: 0.20%, 0.43%) in admissions, respectively. Also, a 1 mg/m^3 increase in CO levels resulted in a 2.50% (95%CI: 1.96%, 3.04%) rise in admissions. The links with NO_2 ($p < 0.001$), SO_2 ($p < 0.001$), O_3 (during the warm season, $p < 0.001$), and CO ($p < 0.001$) were significantly weaker among patients residing in areas with higher levels of greenness. No significant modifying role of GDP was observed. Greenness can help mitigate the effects of air pollutants, while the role of GDP needs further investigation.

Plain Language Summary Numerous investigations have explored the connection between air pollution and respiratory disease hospital admissions. Nonetheless, the potential modifying roles of Gross Domestic Product (GDP) and the presence of green spaces remain inconclusive. To address this issue, our research utilized a time-stratified case-crossover design, analyzing electronic patient records from Beijing, China's capital city. Our analysis did not reveal any significant alteration in the relationship between air pollution and respiratory disease admissions due to sex or GDP. However, the data indicated that the correlation was amplified for individuals aged over 65, during different seasons, for those with differing marital statuses, and among those residing in areas with low greenness (Normalized Difference Vegetation Index levels). Drawing from an extensive data set, these results offer more detailed insight into strategies to mitigate the effects of air pollution on respiratory disease-related hospital admissions.

1. Introduction

According to the World Health Organization's report on the top 10 causes of death in 2019, two of the leading global causes of death were related to respiratory diseases, imposing a significant disease burden. Chronic obstructive pulmonary disease (COPD) ranked as the third leading cause of death worldwide, accounting for approximately 6% of total deaths. Additionally, lower respiratory infections continued to be the most lethal communicable disease in the world, occupying the fourth position on the list of leading causes of death (World Health Organization, 2022). Prevalence of respiratory diseases is an important contributor to the disease burden in low- and middle-income countries (Clark et al., 2022).

The leading risk factors for respiratory diseases include the unhealthy habit (tobacco smoking) and exposure to air pollution (including indoor air pollution, ambient air pollution, and occupational pollutants) (Adeloye et al., 2022; Eisner et al., 2010). Air pollution has a significant impact on health (Yee et al., 2021), resulting in up to 7 million premature deaths and causing a much greater number of hospital admissions annually (Orru

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et al., 2017). Recent studies have shown that air pollutants have a clear association with outpatient visits (Liu et al., 2017; Ma et al., 2020) hospitalizations (Moore et al., 2016; Renzi et al., 2022) and deaths (Nazar & Niedoszytko, 2022; Orellano et al., 2020) in respiratory diseases. One study revealed that the highest increases in total respiratory outpatient visits occurred at lag 05 for both NO_2 and SO_2. A 10 μg/m^3 increase in NO_2 corresponded to a 2.50% rise in total respiratory outpatient visits, whereas a similar increase in SO_2 was linked to a 3.50% increase (Ma et al., 2020). An elevation in pediatric respiratory outpatient visits was observed with every increase in the interquartile range (IQR) of $PM_{2.5}$, PM_{10}, NO_2, CO, and O_3 concentrations. Each IQR increase in $PM_{2.5}$ (lag 0) was associated with a 1.91% rise, while PM_{10} (lag 0) showed a 2.46% increase. Additionally, there was a 1.88% increase for NO_2 (lag 0), a 2.00% increase for CO (lag 0), and a 1.91% increase for O_3 (lag 4) concentrations (Liu et al., 2017). For the risk of air pollution on hospital admissions for respiratory diseases, Renzi et al. observed additional risks for total respiratory diseases amounting to 1.20% and 1.22% for every 10 μg/m^3 rise in PM_{10} and $PM_{2.5}$ at lag 0–5 days, respectively (Renzi et al., 2022). Many studies have found that greenness may interact with exposure to air pollutants (Ji et al., 2020). Greenness can reduce the negative effects of air pollution (Bloemsma et al., 2022; Jaafari et al., 2020; Zhang et al., 2022). Although there is prior research suggesting that greenness may reduce all-cause mortality (Ji et al., 2020), there has been little investigation exploring the connection between greenness and respiratory disease hospitalizations.

Social and environmental determinants play crucial roles in shaping individuals' health outcomes. Among these factors, socioeconomic status stands out as a key influence on health and well-being. The relationship between socioeconomic status and health is complex, but numerous studies have found that populations with lower socioeconomic backgrounds are more susceptible to Non-communicable Diseases. This vulnerability is attributed to factors such as material deprivation, psychosocial stress, unhealthy living conditions, and limited access to high-quality healthcare (World Health Organization, 2008; Xue et al., 2021). Many studies have analyzed the effects of Gross Domestic Product (GDP) on a variety of disease outcomes, including mental health (Xue et al., 2021), cardiovascular mortality (Sung et al., 2020), and others (Malicka et al., 2022), as well as studies examining the moderating effects of GDP (Gao et al., 2022). Nonetheless, no previous studies have investigated how GDP might influence the relationship between air pollution and respiratory disease hospitalizations. Considering the increasing significance of comprehending the effects of environmental factors on human health, it is essential to address these knowledge gaps through further research.

In the process of modern urbanization, greenness has become a crucial issue that cannot be ignored. Greenness not only plays a vital role in improving the ecological environment but also enhances the physical and mental health of the population. Therefore, there has been a growing scientific interest in the potential health benefits of exposure to greenness (Frumkin et al., 2017). A study in the United States found that greenness was positively associated with hospitalization for respiratory disease (Klompmaker et al., 2022). In a study utilizing data of the 2019 Global Burden of Disease, greenness was significantly negatively associated with the global burden of disease for lower respiratory infections (Liu et al., 2023). Few studies have examined whether greenness mediate the association between air pollution and respiratory hospitalization.

The combination of severe air pollution and rapid urbanization has contributed to an increased respiratory burden in China. Specifically, Beijing, located in the northern part of the North China Plain at 116°20′E and 39°56′N, is particularly affected. As the capital city, it has a high concentration of vehicles and a dense population, leading to a significant impact of air pollution on public health. In this context, Gao et al. conducted a study to examine the immediate effects of ambient air pollution on hospitalizations related to COPD in Beijing. The study found that the cumulative lag effect of a 10 μg/m^3 increase in air pollutant levels was most pronounced for nitrogen dioxide (NO_2) at lag 06, with a 3.03% increase. Similarly, short-term exposure to various air pollutants had adverse effects on COPD hospitalizations, with varying degrees of impact depending on the lag days (Gao et al., 2019). Another study conducted in Beijing demonstrated that the relative risks of various pollutants on hospitalization for acute exacerbations of COPD were greater than 1 (Liang et al., 2019). The above findings confirmed the negative effects of air pollutants on respiratory diseases. However, previous studies were based on group exposure with relatively small sample sizes, making it difficult to avoid common confounding factors in time-series studies. Currently, few large-sample studies based on individual exposure and advanced designs exist.

The objective of our study was to assess the effects of air pollutants on hospitalized patients with respiratory diseases using a time-stratified case crossover design, based on daily air pollutant concentrations. We also included age, sex, season, GDP, and greenness as moderating factors to compare the effect of air pollution on respiratory disease hospitalizations within each individual group.

2. Methods

2.1. Study Area and Data on Hospital Admissions

Our study was conducted in Beijing, the capital city of China. Beijing is divided into 16 districts, with a resident population of 21.536 million in 2019 and an area of 16,410.54 square kilometers.

We obtained admission records from 133 hospitals between 1st January 2016 and 31st December 2019 (a total of 1,461 days), including almost all inpatients in Beijing. These records contain basic information such as sex, age, address, date of admission, hospitalization diagnosis in Chinese and corresponding International Classification of Diseases, 10th Revision (ICD-10) code. We extracted daily inpatient visits with a main diagnosis of respiratory diseases (ICD-10 codes J00–J99) from the database. In this study, we considered a wide range of respiratory diseases, including but not limited to acute upper respiratory tract infections (J00–J06), influenza and pneumonia (J09–J18), other acute lower respiratory tract infections (J20–J22), other diseases of the upper respiratory tract (J30–J39), chronic lower respiratory diseases (J40–J47), lung diseases due to external agents (J60–J70), other respiratory diseases affecting mainly the interstitium (J80–J84), suppurative and necrotic conditions of the lower respiratory tract (J85–J86), other diseases of the pleura (J90–J94), and other diseases of the respiratory system (J95–J99). Among these respiratory diseases, influenza and pneumonia (J09–J18) accounted for 28.58% of the cases, making it the most prevalent category. Other respiratory system diseases (J80–J84) had a proportion of 24.09%, followed by chronic lower respiratory diseases (J40–J47) at 17.34%.

2.2. Environmental Exposure

2.2.1. Air Pollution and Meteorological Data

For our exposure data, we acquired satellite-derived air pollution data, encompassing daily concentrations of $PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3, and CO. In essence, it employed a machine learning technique known as "space–time extremely randomized trees" to predict daily air pollutant concentrations across China. Specifically, the spatial resolutions were 1 km for $PM_{2.5}$, PM_{10}, and O_3 and 10 km for NO_2, SO_2, and O_3. Results from the 10-fold cross-validations indicated a high prediction accuracy for each pollutant, with R-squared values of 0.90 for $PM_{2.5}$, 0.86 for PM_{10}, 0.84 for NO_2, 0.84 for SO_2, 0.87 for O_3, and 0.80 for CO. Further details about the air pollution data can be found in previous descriptions (Wei, Li, Lyapustin, et al., 2021; Wei, Li, Xue, et al., 2021; Wei et al., 2022, 2023). Figures S1–S6 in Supporting Information S1 show the distribution of six pollutants and the residential addresses of hospitalized patients on 1st January 2019 and 1st July 2019.

We also obtained daily meteorological data form 20 weather stations in Beijing, including relative humidity (%), mean temperature (°C) during the study period from the Institute of Geographic Sciences and Natural Resources Research. To capture the temperature around each individual's residential address, we utilized inverse distance weighted interpolation, incorporating all accessible site data for daily temperature and humidity. Meteorological data from January 2016 to December 2019 were obtained from Resource and Environment Science and Data Center.

2.3. GDP Data

The China Grid GDP data set comprehensively considers multiple factors closely related to human economic activity, such as land use types, night lights brightness, and residential density, based on county-level GDP statistical data in China. Using a multi-factor weighting allocation method, the GDP data of administrative regions is distributed to grid units, achieving the spatialization of GDP (Xu, 2017). The original data consisted of annual gridded data with a resolution of 1 km × 1 km. We matched GDP data to each patient based on their residential address. Figure S7 in Supporting Information S1 show the distribution of GDP and the residential addresses of hospitalized patients in 2019.

2.4. Greenness

The Normalized Difference Vegetation Index (NDVI) accurately reflects surface vegetation cover by measuring the differences between surface reflectance in red visible and near-infrared light, which results in values ranging from −1 to +1. Dense vegetation pixels are associated with high positive numbers. In this study, we obtained China's annual vegetation index spatial distribution data set from the Resource and Environmental Science and Data Center website (Xu, 2018). The data set was generated using continuous-time-series spot/vegetation NDVI satellite remote-sensing data and the maximum synthesis method. The NDVI data has a temporal resolution of 1 month and a spatial resolution of 1 km × 1 km. We matched corresponding NDVI values based on the addresses of our study subjects. Figure S8 in Supporting Information S1 show the distribution of NDVI and the residential addresses of hospitalized patients in January 2019 and July 2019.

2.5. Influenza

The influenza information from the influenza weekly of reports from January 2016 to December 2019 were obtained from the Chinese National Influenza Center.

2.6. Statistical Analysis

We conducted a time-stratified case-crossover design to examine the potential associations between air pollutants and hospital outpatient visits for respiratory diseases (ICD10: J00–J99) (Carracedo-Martínez et al., 2010). For each individual patient, the levels of air pollution exposures on the day of admission were compared with those of control periods. Three to four control days were matched to the date of admission by the same day of the week in the same month of the same year with the patient. For example, if the date of admission was on Friday, 3rd March 2017, we would define Friday, 3rd March 2017 as the case index day and all other Fridays in March 2017 (March 10th, 17th, 24th, and 31st) as the control index days. In this study, 1,331,023 control days were selected for the 555,498 hospitalized patients with respiratory diseases. We retrieved daily mean temperature and relative humidity at each patient's address on each of the corresponding case and control days. The study also designed each patient as its self-control to minimize the potential confounding of socio-economic (e.g., age, sex, etc.) and stratify time to exclude long-term impact of air pollutant (e.g., secular trend, seasonality, etc.).

We used conditional logistic regression models combined with distributed lag model (DLM) to quantify the associations between exposures to air pollutants and the admission of respiratory diseases through the odds ratio (OR) (Chen et al., 2022; Gasparrini et al., 2010; Guo et al., 2011). The lag effects of air pollutants were modeled by cross-basis, a bi-dimensional space of functions to reflect the exposure-responses and lag structure of the association. We plotted the lag structure over 5 days (lag 0–lag 4) to explore the lag structure of health effects of air pollutants.

$$\begin{aligned}&\mathrm{Logit}(P(\mathrm{case} = I \text{ in } \mathrm{stratum}_{ij} \mid \text{Air pollutant, Temp, Humidity, Holiday, Influenze}))\\&= \beta_{\mathrm{stratum}_{ij}} + \mathrm{cb}(\text{Air pollutant}) + \mathrm{ns}\big(\mathrm{Temp02}, df\\&= 3) + \mathrm{ns}(\mathrm{Humidity02}, df = 3) + \mathrm{Holiday} + \mathrm{influenza}\end{aligned}$$

where $\mathrm{stratum}_{ij}$ is the fixed time strata i in individual j (the same calendar month for case day and control days for the individual j), $\beta_{\mathrm{stratum}_{ij}}$ is the intercept of stratum i for individual j, cb(Air pollutant) is the cross basis function, a linear function was used for the air pollutant-response dimension and a natural cubic spline with two internal knots was selected at equally log values of lags to allow for more flexibility at shorter delays (Guo et al., 2011), Holiday is a binary variable indicating whether the date was a public holiday, Influenza is a binary variable indicating whether the date was influenza epidemic, ns(Temp02, $df = 3$) and ns(Humidity02, $df = 3$) are the natural cubic spline function to fit non-linear exposure-response relationship of temperature and relative humidity (Chen et al., 2022).

Because O_3 concentrations were much lower in the cold season (see Figure S9 in Supporting Information S1), the association of O_3 with the admission of respiratory diseases was evaluated in all year, the warm season (April–September) and the cold season (October–March) (Chen et al., 2022).

To explore the possibility of nonlinear concentration-response curves of air pollutants with the admission of respiratory diseases, the cross-basis functions for all air pollutants were rebuilt using the distributed lag nonlinear model (DLNM), where a natural cubic spline with two internal spline knots at equally spaced percentiles of concentrations was fitted to account for potential nonlinear relationships between pollutants and the admission of respiratory diseases, and a natural cubic spline with two internal knots placed at equally spaced log values of lags was used for the lag-structure. The relationship between ozone exposure and hospitalization in cold, warm and overall seasons can be seen in Supporting Information S1 (see Figure S10), in which we found the adverse effect of O_3 in the warm season under DLM assumption.

We also conducted stratified analyses by sex (male vs. female), age (≤65 vs. >65 years), marriage status (yes vs. no), season (warm [April–September] vs. cold [October–March]), GDP (high vs. low, based on median value) and NDVI (high vs. low, based on median value), to identify the possible effect modifications. Statistical differences between stratum were tested using 2-sample z tests with the following formula:

$$z = \frac{\beta_1 - \beta_2}{\sqrt{\mathrm{SE}_1^2 + \mathrm{SE}_2^2}}$$

where β_1 and β_2 were the group-specific regression coefficients (log OR) and SE_1 and SE_2 were the corresponding standard errors (Liu et al., 2021).

We conducted multiple sensitivity analyses to examine the robustness of the associations of air pollutants with the admission of respiratory diseases. First, we performed double-pollutants model to test the stability of the relationship due to high correlation among air pollutants. Second, we exchanged the lag structure with step function, where cut-off points were set day by day. Third, we changed the degree of freedom from 4 to 6 for natural cubic spline of temperature in the main model. Fourth, we trimmed the highest 1% of daily concentrations for all pollutants to test the potential influences of outliers on the analyses.

All analyses were performed in R (version 4.2.2) using 2-sided tests with an α of 0.05. Odds ratios and their 95% Cis were converted into percent change in risk of the admission of respiratory diseases with per 10 μg/m^3 (for CO, 1 mg/m^3), using the following equation:

$$\text{Percent change} = \left(e^{\beta \times 10} - 1\right) \times 100\%$$

$$\text{Percent change.lower95\%CI} = \left(e^{(\beta - 1.96 \times \mathrm{SE}) \times 10} - 1\right) \times 100\%$$

$$\text{Percent change.upper95\%CI} = \left(e^{(\beta + 1.96 \times \mathrm{SE}) \times 10} - 1\right) \times 100\%$$

where β is the regression coefficient (log OR) and SE is the standard error of the β.

3. Results

3.1. Baseline Characteristics

Among the total of 555,498 inpatient visits between 1st January 2016 and 31st December 2019, 60.1% were male, and the mean age at hospital admission was 54.93 years. 53.3% of the cases were hospitalized in cold season and 46.7% of the cases were hospitalized in warm season. Table 1 summarizes the basic descriptive information of patients.

Throughout the study period, the daily concentrations of pollutants were observed to fluctuate according to seasonal changes (see Figure S10 in Supporting Information S1), with a clear increase in pollutant concentrations during the cold season (except for O_3). Of the 1,461 days, 1,293 (88.5%) days of daily $PM_{2.5}$, 1,361 (93.2%) days of daily PM_{10}, 1,447 (99.0%) days of daily NO_2, 1,361 (93.2%) days of daily SO_2, 1,245 (85.2%) days of daily O_3 and 1,456 (99.7%) days of daily CO concentrations achieved the target of the Chinese Ambient Air Quality Standards Grade II standards ($PM_{2.5} \leq 75$ μg/m^3, $PM_{10} \leq 150$ μg/m^3, $NO_2 \leq 80$ μg/m^3, $SO_2 \leq 150$ μg/m^3, $O_3 \leq 160$ μg/m^3, CO ≤ 4 mg/m^3). Distribution of exposure to air pollutants and meteorological conditions on case days and control days is provided in Table 2.

Table 1
Demographic Characteristics of Respiratory Hospital Admissions in Beijing During 2016–2019

Baseline characteristic	Values
Respiratory disease hospitalizations (*n*)	555,498
Case days (*n*)	555,498
Control days (*n*)	1,331,023
Sex (*n* (%))	
Male	333,603 (60.1)
Female	221,895 (39.9)
Age at hospital admission (mean (SD))	54.93 (30.78)
Marriage (*n* (%))	
No	175,780 (31.6)
Yes	379,718 (68.4)
Season at hospital admission (*n* (%))	
Warm	259,182 (46.7)
Cold	296,316 (53.3)
GDP (mean (SD))	127,155.7 (193,672.6)
NDVI (mean (SD))	0.29 (0.15)

Note. SD standard deviation, GDP gross domestic product, NDVI normalized difference vegetation index.

The daily average concentrations for $PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3, and CO were 46.75, 85.25, 34.84, 85.25, 101.03, and 0.98 mg/m^3, respectively. $PM_{2.5}$, PM_{10}, NO_2, SO_2, and CO had strong positive correlation coefficients between each two pollutants. O_3 was negatively associated with other pollutants in significant correlations (Table S1 in Supporting Information S1).

3.2. Association of Daily Concentrations of Air Pollutants and Respiratory Disease Admissions

We found that there were significant correlations between the daily concentrations of air pollutants and the number of inpatients. Figure 1 displays the associations between pollutants and hospitalized patients with respiratory diseases at various lag days adopting single-pollutant models. For respiratory hospitalization, all pollutants displayed adverse effect. Most pollutants, including $PM_{2.5}$, PM_{10}, NO_2, O_3 (warm) and CO, exhibited immediate effects, often starting from the first day of exposure. The maximum single day effect for each pollutant was as follows: a 10-unit increase in $PM_{2.5}$ (lag0) corresponded to a 0.26% (95%CI: 0.17%, 0.35%) rise in hospitalization risk; for PM_{10} (lag 0), each 10-unit increase was linked to a 0.15% (95%CI: 0.09%, 0.22%) higher risk; NO_2 (lag 4) saw a 0.61% (95%CI: 0.44%, 0.77%) increase in risk for every 10-unit rise; SO_2 (lag 4) showed a substantial 1.72% (95%CI: 1.24%, 2.21%) increase in risk with a 10-unit rise; O_3 (warm, lag 0) indicated a 0.32% (95%CI: 0.20%, 0.43%) rise in risk for every 10-unit increase, and CO (lag 4) exhibited a significant 2.50% (95%CI: 1.96%, 3.04%) increase in risk for every 1-unit rise. Meanwhile, some pollutants had cumulative effects that persist from lag01 to lag04, such as $PM_{2.5}$, PM_{10}, NO_2, O_3 (warm) and CO. Concerning O_3, it's noteworthy that there was no significant association with health outcomes throughout the year. During the cold season, O_3 may even exhibit adverse effects. Conversely, we observed notable health benefits linked to O_3 during the warm season. It's worth noting that we observed a phenomenon known as harvesting effect for most pollutants, which means they exhibit contrasting effects in the first few days of exposure.

The concentration-response curves (both linear: DLM and nonlinear: DLNM) for six air pollutants can be seen in Figure 2. In general, both linear and non-linear curves showed similarity within the 99% concentration range (within the red dashed line) for all air pollutants. However, nonlinear analysis revealed that for $PM_{2.5}$, PM_{10}, and O_3 (warm), their exposure-response curves manifest negative effects at low concentrations, with a notable escalation in harmful effects at high concentrations. In the case of NO_2, a plateau period was observed at

Table 2
Distribution of Air Pollutants and Meteorological Conditions in Beijing During 2016–2019

Variable	Min	Q25	Median	Q75	Max	Mean	SD
Air pollutant							
$PM_{2.5}$ (μg/m^3)	10.63	29.21	39.77	55.45	209.46	46.75	26.83
PM_{10} (μg/m^3)	25.93	58.06	75.26	100.33	562.78	85.25	43.13
NO_2 (μg/m^3)	11.81	24.85	30.80	41.70	99.84	34.84	14.32
SO_2 (μg/m^3)	25.93	58.06	75.26	100.33	562.78	85.25	43.13
O_3 (μg/m^3)	15.18	63.60	93.62	133.53	239.35	101.03	49.09
CO (mg/m^3)	0.35	0.68	0.87	1.10	4.98	0.98	0.51
Meteorological condition							
Relative humidity (%)	10.24	37.54	52.41	69.73	95.68	53.32	19.43
Temperature (°C)	−16.88	0.53	13.23	22.63	30.38	11.88	11.56

Note. SD standardized deviation, Q25 the 25th percentile, Q75 the 75th percentile.

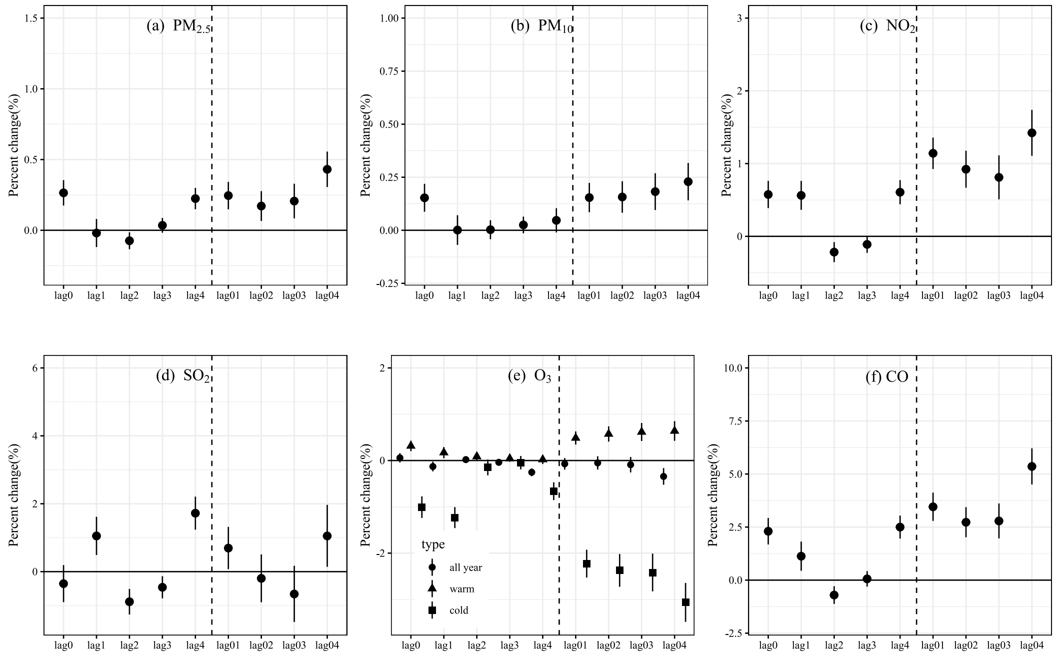

Figure 1. Percentage change (95%CI) of respiratory hospital admissions with a 10 μg/m^3 increase $PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3 and 1 mg/m^3 increase CO at different lags. Note: The effects of single-day lags (from current day to 4 days before: lag 0–lag 4) and cumulative lags (from lag 01 to lag 04) were plotted.

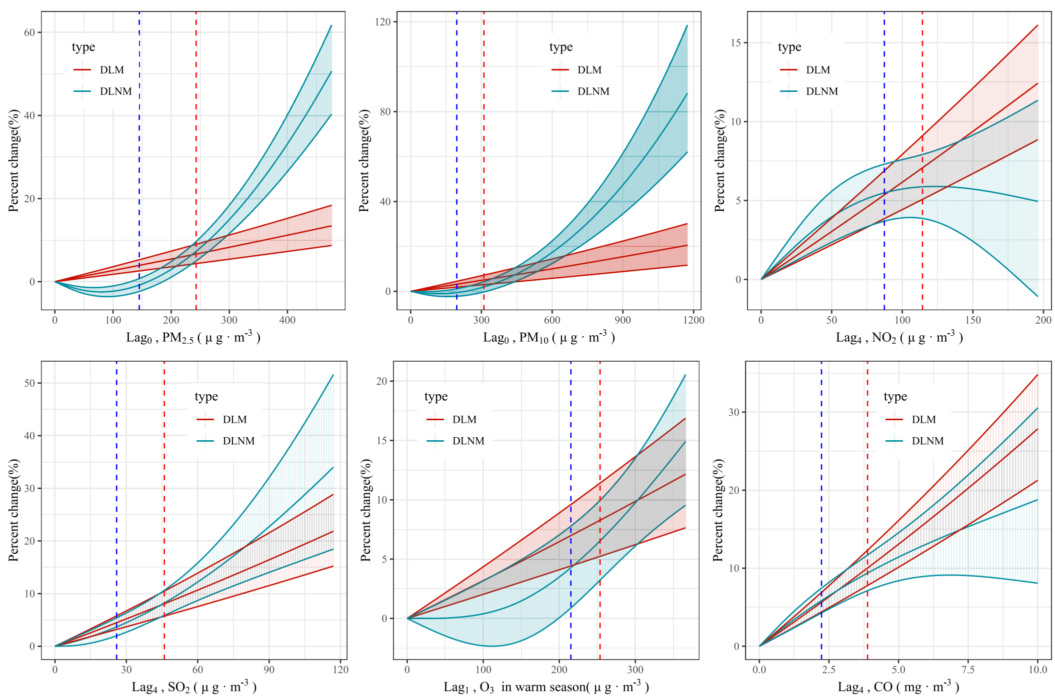

Figure 2. E-R curves of air pollutants and respiratory hospital admissions. Note: The blue (red) lines represent the percent change based on DLNM (DLM), with shadings in the corresponding colors indicative of 95% CI. The 95th (99th) percent of air pollutant is marked by the dashed blue (red) line.

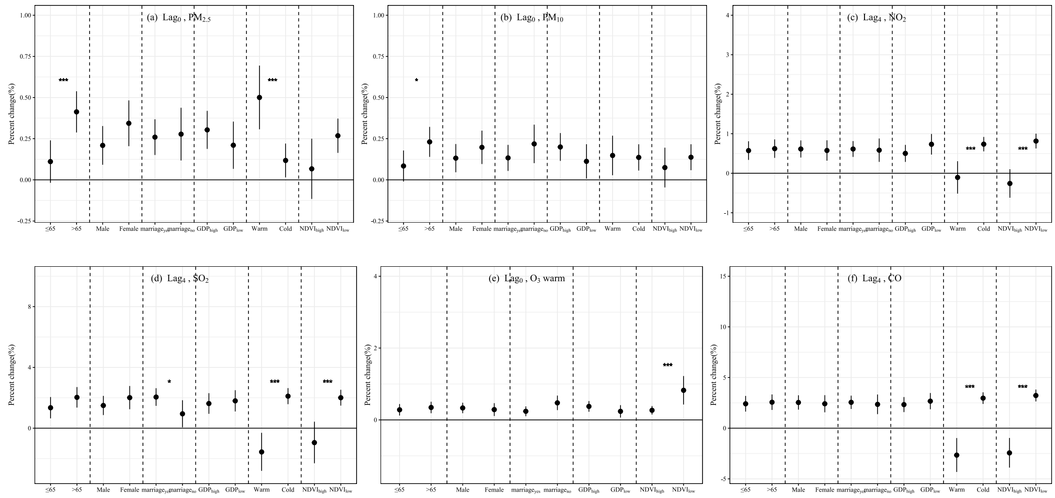

Figure 3. Percentage change (95%CI) of respiratory hospital admissions per 10 μg/m^3 increases in $PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3 and 1 mg/m^3 increase in CO at the maximum effect single day, stratified by age, sex, marriage, season, GDP and NDVI. Note:*p < 0.05; **p < 0.01; ***p < 0.001.

elevated concentrations. The nonlinear findings for SO_2 and CO aligned consistently with the linear results. The exposure-response relationships for ozone in different seasons can be seen in Figure S11 of the Supporting Information S1.

3.3. Stratified Analysis

Following the main effect, we reported the effect estimates of the stratified analysis based on the maximum effect single day. Figure 3 illustrates the impact of pollutants levels in different subgroups on hospitalization of respiratory diseases. In age-specific analysis, the elderly (>65 years) people were more vulnerable to $PM_{2.5}$ ($p < 0.001$), PM_{10} ($p < 0.05$). As for sex-specific and marriage analysis, all pollutants showed no significance in the subgroups. As for marriage-specific, we found married individuals were more susceptible to the effects of SO_2 ($p < 0.05$). We found that season may modify the association between $PM_{2.5}$ ($p < 0.001$), NO_2 ($p < 0.001$), SO_2 ($p < 0.001$), O_3 ($p < 0.001$), and CO ($p < 0.001$). $PM_{2.5}$ had a greater effect in warm season while other gaseous pollutants had a greater effect in cold season. O_3 could be found in Figure S12 of the Supporting Information S1. Similarly, all pollutants still showed no significant correlation with different level of GDP. According to an analysis of greenness, exposure risk to NO_2 ($p < 0.001$), SO_2 ($p < 0.001$), O_3 (warm, $p < 0.001$), and CO ($p < 0.001$) was inversely correlated with NDVI. The differences of $PM_{2.5}$ and PM_{10} exhibited similar trends but they were not statistically significant.

3.4. Sensitivity Analysis

The outcomes of the sensitivity analysis revealed the robustness of the results, indicating that variations in temperature degrees of freedom, adjustments to the lag structure of pollutants, or the imposition of concentration limits beyond the 99th percentile do not compromise the findings (Figure S13 in Supporting Information S1). In the double-pollutants model, we observed interdependence in the effects of certain pollutants. Specifically, the effects of $PM_{2.5}$ were not independent of NO_2 and CO, while the effects of PM_{10} were influenced by $PM_{2.5}$, NO_2, and CO. Additionally, the effects of NO_2 were not independent of CO. However, the effects of SO_2, O_3, and CO demonstrated independence from each pollutant.

4. Discussion

In this large time-stratified case-crossover study, short-term exposures to $PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3 (warm) and CO were significantly associated with hospital admission of respiratory disease. The associations were modified by age, marriage, season and greenness. No statistically significant differences were observed in terms of sex and GDP.

Our findings were consistent with numerous previous studies conducted at the individual level. Liu et al. explained that risk of hospital admission of respiratory disease was changed according to the pollution in the area, polluted and less polluted zones have 1.64 odds ratio (95%CI: 1.43,1.89) in India (Liu et al., 2013). In our study, the short-term effects of air pollutants varied depending on the type of pollutant, which likely reflects the differences in biological mechanisms and characteristics among each pollutant. Air pollution can accumulate and penetrate into lung tissue, and fine particulate matter can cause an increase in proinflammatory activity, leading to bronchial injury. In contrast, ozone caused invisible changes in lung structure that may result in chronic respiratory diseases (De Sario et al., 2013; Zhu et al., 2014).

Our study evaluated the impact of air pollutants on respiratory admission under different exposure windows. In this study, the majority of pollutants (except for SO_2) were found to increase the risk of hospitalization on the first day of exposure. Cai's study also revealed that PM_{10} and NO_2 exposure at lag 01 had the strongest adverse effects on asthma hospitalization in Shanghai (Cai et al., 2014). These findings suggested that both pollutants potentially exert immediate and acute effects on respiratory disease. Comparable outcomes have been reported in other studies as well (To et al., 2013). In addition, we found the strongest association between six air pollutants and respiratory admissions at lag 04 in terms of cumulative effect, highlighting the lag effect of air pollutants.

Nonlinear analysis unveiled contrasting patterns at low concentrations for $PM_{2.5}$, PM_{10}, and O_3, potentially influenced by residual confounding. For example, there was an inverted u-shaped relationship between income level and environmental degradation (Panayotou, 1993). China remains in a phase characterized by high emissions, and areas with elevated pollution levels often coincide with individuals of higher GDP (Wang et al., 2022). The atypical patterns noted at lower concentrations might be influenced by confounding stemming from economic conditions.

In certain lag days, we observed a negative association between air pollutants and respiratory admissions. This phenomenon could be attributed to the short-term acute exposure to air pollution that mainly affects vulnerable individuals. When the levels of air pollution rise and high-risk individuals fall sick or die, the total number of high-risk individuals reduces. Consequently, an incidence or mortality rate lower than the anticipated level is observed. This adverse correlation is commonly known as the harvesting effect (Rabl, 2005; Schwartz, 2001).

In our study, the analysis stratification revealed that the relationship between air pollution and hospitalization for respiratory diseases was moderated by age, marriage, season, and greenness. However, no significant associations were found between sex and GDP. Previous studies have found that older adults are more susceptible to the impacts of air pollution (Fan et al., 2022; Gaines et al., 2023; Gu et al., 2020; Kan et al., 2008), which may be a result of the vulnerability of respiratory function in the elderly. For stratified analysis by season, our study found that patients were more affected by pollutants except O_3, $PM_{2.5}$, and PM_{10} during cold seasons. Wang et al. found that under low temperature, PM_{10}, NO_2 and SO_2 had a more significant impact on the daily hospitalization caused by respiratory diseases based on the research in western China (Wang et al., 2013). Sun et al. reported significant increase in total incident respiratory diseases during winter in Hong Kong (Sun et al., 2018). This may be due to the easy occurrence of temperature inversion under low temperature conditions, which hinders the diffusion of pollutants and leads to a stronger effect (Trinh et al., 2019). O_3 mainly exhibits adverse effects during the warm season, because it is formed by the chemical reaction of volatile organic and nitrogen oxides compounds in sunlight and high temperature conditions (Crutzen, 1974; Sillman, 1999). Regarding marital status, it is speculated that the observed association could be attributable to unmeasured factors like social stress. For example, married individuals might experience increased social pressure due to financial obligations to support family. However, married individuals should have better health status, marriage can encourage healthy behaviors, such as visiting doctors (Umberson, 1992), and discourage risky behaviors, such as smoking (Lindström, 2009). It should be cautious when interpreting this result.

Regarding the impact of greenness, this study found that a high NDVI significantly reduced the exposure risk to $PM_{2.5}$, PM_{10}, and NO_2 on respiratory disease hospitalizations. Similar results were reported in study in urban U.S. counties, an IQR increase in NDVI corresponds to a 1.29% and 0.01% decrease in the association between PM_{10}, $PM_{2.5}$ and respiratory disease hospitalization (Heo & Bell, 2019). The commonly suggested mechanisms encompass trees' ability to absorb nitrogen oxides, ammonia, sulfur dioxide, and ozone, as well as their capability to filter particulate matter by capturing it on their leaves and bark (Jim & Chen, 2008; Shen & Lung, 2017). In addition, greenness promoted physical activity, which in turn enhanced antioxidant capacity and triggers an anti-inflammatory response (Beavers et al., 2010; Kimura et al., 2010).

Additionally, stratified analysis by sex and GDP in this study did not observe any differences. Due to the absence of precise measurement of individual economic levels, we resorted to matching gridded GDP with low accuracy to approximate individual economic levels. Consequently, we failed to observe the moderating effect of the GDP. Although GDP may represent other aspects, such as accessibility to healthcare services and social security, this study did not find any moderating effects of GDP.

In this study, a case-crossover design with a large sample size was used, which controlled individual covariates (some confounders which are fixed in the short term, e.g., sex, age, and GDP), meteorological conditions, holidays and influenza. Furthermore, the design used individual-level exposure assessment (high resolution machine learning product: 1–10 km) based on the patient's permanent address, making the results more reliable. Third, we found the modification of NDVI on air pollutants and admission due to respiratory diseases.

This study also has some limitations. First, given the observational nature of the studies, the possibility of residual confounding cannot be excluded. Second, we employed daily outdoor concentration data of various air pollutants to analyze their correlation with the daily hospitalizations of patients with respiratory diseases in Beijing. This method will have introduced bias to effects estimates because residents spend a long time indoors, but indoor air pollution was not considered. Moreover, this study only analyzed the strength of the association between inpatients and air pollution and hospital outpatients were excluded, further study should analyze the impact of air pollution on outpatients and inpatients to make the results more comprehensive.

5. Conclusions

Our study uncovered significant correlations between short-term exposure to $PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3 (warm), and CO, and respiratory disease hospitalizations. We observed that the relationships between short-term air pollutant exposure hospital admissions for respiratory diseases varied among different levels of greenness. The role of socioeconomic status need to be investigated in future studies.

Conflict of Interest

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

Data Availability Statement

Our code is available at Zenodo (Zhang et al., 2023). The patient data are not publicly available and the authors do not have permission to share data. Air pollution data can be found via CHAP data set (Wei, Li, Lyapustin, et al., 2021; Wei, Li, Xue, et al., 2021; Wei et al., 2022, 2023), Each data set of air pollutant has its link of Zenodo or National Tibetan Plateau Data Center, and everyone can download data freely after registering on the website. Meteorological data can obtain from the website (Resource and Environment Science and Data Center, 2023), The GDP data can be found from the website (Resource and Environment Science and Data Center, 2017). Both meteorological data and GDP data are not free to the public, the website provides contact information for the data manager, and it can be obtained through a paid method. The NDVI data can be found from Resource and Environment Science and Data Center (Resource and Environment Science and Data Center, 2018). It can be obtained freely after registering on the website. The influenza information from the influenza weekly of reports from January 2016 to December 2019 were obtained from the website (Chinese National Influenza Center, 2023). The original data is text-based, and we manually assessed the flu epidemic situation each week, compiling it into a data set indicating whether there was a flu epidemic each week.

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