Sustainable Cities and Society 124 (2025) 106293

Contents lists available at ScienceDirect

Sustainable Cities and Society

journal homepage: www.elsevier.com/locate/scs

Individual and mixed associations between fine particulate matter components and hospital admissions for hypertension: Insights from a large-scale South Chinese cohort study

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ARTICLE INFO

Keywords:
Particle components
Hypertension hospitalization
Population susceptibility
Quantile-based g-computation (QGC)
Cohort study

ABSTRACT

Fine particulate matter ($PM_{2.5}$) pollution threatens urban sustainability. Few cohort studies have assessed hypertension risks linked to lagged and cumulative exposure to $PM_{2.5}$ components. Using data from a cohort study of 36,271 individuals in South China (2015–2020), we examined the individual associations between time-varying $PM_{2.5}$ and six components (NO_3^-, SO_4^{2-}, BC, CL^-, NH_4^+, and OM) with hypertension hospitalization through Cox proportional hazards regression. Mixed associations of simultaneous exposure to these components were analyzed at lag 0, lag 1, lag 2, lag 0–1, and lag 0–2 years using quantile-based g-computation models. Individual-effect analysis revealed strong associations, with each quantile increase in CL^-, NH_4^+, SO_4^{2-}, and NO_3^- linked to 17 %–32 % higher hypertension risks across different time windows. Co-exposure to $PM_{2.5}$ components at different lag times increased hospital admissions for overall hypertension, with hazard ratios (95 % confidence intervals) of 1.151 (1.136–1.166), 1.221 (1.205–1.238), 1.257 (1.241–1.273), 1.087 (1.073–1.101), and 1.197 (1.182–1.212). Secondary water-soluble ions (NO_3^-, SO_4^{2-}, NH_4^+, CL^-) were major contributors. Increased susceptibility was observed among those under 45, men, individuals with lower education, unhealthy weight, or limited green space exposure. These findings highlight the lagged and cumulative impacts of simultaneous exposure to $PM_{2.5}$ component on hypertension.

Abbreviations: HR, hazard ratio; CI, confidence interval; ICD-10, International classification of diseases–10th revision; $PM_{2.5}$, particulate matter with an aerodynamic diameter $\leq$ 2.5 μm; BMI, body mass index; NO_2, nitrogen dioxide; NDVI, normalized difference vegetation index; PRE, precipitation; TEMP, temperature; CL^-, chloride; NH_4^+, ammonium; BC, black carbon; SO_4^{2-}, sulfate; NO_3^-, nitrate; OM, organic matter.

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https://doi.org/10.1016/j.scs.2025.106293
Received 15 August 2024; Received in revised form 21 February 2025; Accepted 11 March 2025
Available online 12 March 2025
2210-6707/© 2025 Published by Elsevier Ltd.

1. Introduction

Hypertension is a common chronic disorder that is the primary cause of cardiovascular disease as well as premature mortality globally. By 2019, the worldwide number of hypertensive individuals has surpassed 1 billion (Nguyen & Chow, 2021). In the rapidly urbanizing regions, particularly in Asian countries, including China, the prevalence of hypertension has been rising alongside economic development (Kario et al., 2024). Mitigating the burden of hypertension is essential for attaining sustainable development and national health goals, as highlighted by programs such as "Healthy China 2030″ (Hou et al., 2020; Peng et al., 2024). Urbanization, a significant catalyst for economic advancement, also markedly elevates air pollution, especially fine particulate matter ($PM_{2.5}$). Recent evidence highlights urbanization as a major cause to increased $PM_{2.5}$ levels in China, emphasizing the necessity of comprehending its effects on hypertension (Huang et al., 2023; Liu et al., 2022). Such insights could inform targeted air pollution control strategies to alleviate disease burdens and promote sustainable urban development (Fu et al., 2024).

There is a growing body of evidence supporting a significant link between ambient $PM_{2.5}$ and hypertension, emphasizing the urgency of sustainable air quality policies (Hahad, Rajagopalan, Lelieveld, Sørensen, Frenis et al., 2023a, 2023b; Magnussen et al., 2023; Zhao et al., 2022). For instance, a recent meta-analysis containing 28 studies identified a positive correlation between prolonged $PM_{2.5}$ exposure and hypertension, although evident heterogeneity (Zhao et al., 2022). A study found that mice exposed to concentrated ambient $PM_{2.5}$ displayed elevated blood pressure, with sympathetic nervous system activation as a potential mediator, possibly linked to hypothalamic inflammation (Ying et al., 2014). Similarly, those exposed to greater $PM_{2.5}$ levels had higher blood pressure than people who used air purifiers, according to a double-blind, randomized controlled experiment carried out in China (Li et al., 2017). However, elevation in blood pressure has not been consistently demonstrated in humans and animal models following exposure to concentrated $PM_{2.5}$, partially due to variations in $PM_{2.5}$ composition, study population, and study design (Rajagopalan et al., 2024).

Importantly, $PM_{2.5}$ is a complex mixture that contains a variety of chemical elements, including nitrate (NO_3^-), sulfate (SO_4^{2-}), black carbon (BC), chloride (CL^-), ammonium (NH_4^+), organic matter (OM), and others (Zhang & Yao, 2024). Most existing studies primarily examine $PM_{2.5}$ as a whole, often overlooking the contributions of its individual chemical constituents. Since $PM_{2.5}$ composition and toxicity fluctuate across region, time periods, and concentration levels, such an oversight may introduce confounding bias (Barzeghar et al., 2020; Gangwar et al., 2020; Weichenthal et al., 2024; Zhao et al., 2022). Furthermore, based on a review of the existing literature, very few research has investigated the association between hypertension and the components of $PM_{2.5}$ (Li et al., 2022a; Li et al., 2022b; Li et al., 2023; Liu et al., 2021; Lv et al., 2023; Shen et al., 2022; Sun et al., 2024). Most available evidence stems from cross-sectional studies or research targeting specific population subgroups, such as pregnant women, middle-aged and older individuals, or children and adolescents. Considering that cohort studies yield more robust evidence than cross-sectional studies, there is an imperative for research utilizing a large-scale, general population cohort to examine the impact of $PM_{2.5}$ component exposure on hypertension risk (Liu et al., 2021; Zhao et al., 2022). Additionally, several investigations have demonstrated the lag and cumulative detrimental cardiovascular effects of PM (Bravo et al., 2017; Kazemiparkouhi et al., 2022; Zhang et al., 2024). For instance, a recent cohort-based investigation examining the long-term effects of $PM_{2.5}$ exposure on the initial hospitalization for major cardiac conditions has demonstrated the time-lagged and cumulative detrimental effects of $PM_{2.5}$ (Wei et al., 2024). Nonetheless, prior research has not examined the lag and cumulative impacts of prolonged simultaneous co-exposure to multiple $PM_{2.5}$ components over varied durations on hypertension, nor have they determined the individual contributions of each component. Such research could provide critical insights for shaping air pollution control strategies that not only improve public health but also contribute to achieving long-term sustainability goals by fostering cleaner, healthier urban environments.

To bridge the research gap, we designed a large cohort study to clarify the individual and combined relationships between $PM_{2.5}$ components (NO_3^-, SO_4^{2-}, BC, CL^-, NH_4^+, and OM) and the risk of first hospital admission from hypertension, while also examine the effects of lagged and cumulative mixture exposure. To assess the individual impacts of every component, we employed time-dependent Cox proportional hazards models. Additionally, the combined effects of $PM_{2.5}$ components on hospitalization for hypertension were investigated using quantile-based g-computation models, which could also be used to evaluate the individual contributions of each component to the overall mixture effect.

2. Methods

2.1. Study design and participants

As part of the Chinese 12th (2012–2017) Five-Year Plan Major Projects of Scientific Research, the Pearl River Cohort Study (PRCS), which conducted its baseline investigation from 2009 to 2015 in Guangzhou, Zhongshan, and Shenzhen, Guangdong province, provided the data for this research (Ruan et al., 2019). Our analysis focused on the sub-cohort of PRCS from Guangzhou, one of China's biggest cities, due to the availability of hospitalization data in this area. Between January and December 2015, a total of 49,985 residents were enrolled, as primary exposure data on $PM_{2.5}$ components became available starting in 2013, and the exposure of interest involves a three-year moving average, calculated over the current and previous two years. Participants who were under the age of 18 ($n = 9159$), had ambiguous residence addresses ($n = 3837$), or had hospitalization dates reported after their date of death ($n = 718$) were excluded from the analysis. A total of 36,271 adult residents were finally recruited in 2015, with follow-ups continuing until December 2020 (Fig. A.1). The comparison shows that the general characteristics of the included participants align well with those of the overall study population (Table A.1). Baseline information comprised of computer-based questionnaire data, encompassing various factors such as age, sex, ethnicity, health insurance categories, family history of cardiovascular diseases, marital status, education levels, exercise frequency, smoking status, and alcohol consumption. In addition, physical examination measurements were conducted, including parameters like height, weight, as well as body mass index (BMI). Face-to-face interviews were conducted by trained nurses, and physical examinations were completed following a standardized procedure. Before data collection, all participants signed a permission form and provided written informed consent. Ethical approval was granted by the Sun Yat-sen University Human Ethics Council (IRB No. L201703). Categories of each variable were described in depth in the *Cohort in this study* section of *the Supplementary Methods*.

Hospitalization data were gathered from the information systems of all 418 healthcare institutions throughout Guangzhou, encompassing the whole region. The causes of hospitalization were identified using the principal discharge diagnosis code (i.e., the first-listed diagnosis) for hypertension (I10-I16), with the primary outcome defined as the first hospital admission for hypertension. These diagnoses were determined through physician evaluations and categorized using the International Classification of Diseases, 10th edition (ICD-10) codes. Primary hypertension (also known as 'essential hypertension', I10) was specifically included due to its high prevalence as the most common type of hypertension (Carretero & Oparil, 2000; de Silva et al., 2020). The exact admission date was recorded for each hospitalization.

2.2. Environmental exposure

Between 2013 and 2020, yearly average concentration data of $PM_{2.5}$ and its components, with a geographical resolution of 1 km, were derived from a publicly available dataset of ChinaHighAirPollutants (CHAP). This dataset encompasses extensive, reliable ground-level air pollutant data for China, with its reliability having been validated in prior research (Han et al., 2024; Li et al., 2025; Liu et al., 2024). Both $PM_{2.5}$ mass data and component data were simulated using the four-dimensional spatiotemporal deep forest (4D-STDF) model, with both exposure datasets being derived from satellite-based remote sensing data. Calculations of PM components have been described in detail elsewhere and were briefly introduced as follows (Wei, Li, Chen et al., 2023). Daily ground-based measurements of $PM_{2.5}$ inorganic compositions were obtained via the Chinese Center for Disease Control and Prevention network, which is rather homogeneous with dense clusters situated in key megacities across mainland China. $PM_{2.5}$ samples were obtained using quartz filter membranes, and then after being ultrasonically extracted with clean water, ion chromatography was used to determine their chemical composition (Chen et al., 2020; Chen et al., 2019). To address the differences in the sources of ground-based measurements of $PM_{2.5}$ compositions and $PM_{2.5}$ mass used for model validation, we employed the 4DSTDF model to assess daily concentrations of $PM_{2.5}$ components at a resolution of 0.01°. Specifically, the 4D-STDF model integrated satellite-derived $PM_{2.5}$ mass data with additional auxiliary variables, including satellite remote sensing products, pollutant emission inventories, and meteorological reanalysis data. This model helps mitigate the impact of source variability and improves the separation and accuracy of the estimated components. The components estimated through the 4DSTDF model agreed well with ground measurements conducted in China and were widely utilized in epidemiological research examining the health effects of air pollution (Wang et al., 2023).The concentrations of $PM_{2.5}$ and its constituents were allocated to each participant according to the geocoded coordinates of their residential address. Based on the proximity to available air pollution data, the exposure value was assigned using a nearest-neighbor matching approach. Specifically, the concentrations were allocated for lag years 0, 1, and 2, which are referred to as lag 0, lag 1, and lag 2). Furthermore, moving averages for the current year and the years before, namely lag 0–1 and lag 0–2, were calculated to assess cumulative exposure levels (Wei et al., 2024).

2.3. Other covariates

To take into consideration the impact of environmental confounders, data on greenness exposure (specifically, the normalized difference vegetation index, or NDVI), nitrogen dioxide (NO_2) concentrations, temperature (TEMP), and precipitation (PRE) were also gathered. The Land Processing Distributed Active Archive Center and the CHAP dataset provided the greenness and NO_2 concentration data, respectively (Wei et al., 2023). Monthly data on TEMP and PRE were acquired from the National Science & Technology Infrastructure of China (http://loess.geodata.cn) (Peng et al., 2019). The annual average NDVI for each participant was determined within a 250-meter radius around each residence. Furthermore, NO_2 concentrations, TEMP, as well as PRE, were matched with their geocoded residential address (Cai et al., 2023; Wen et al., 2023).

2.4. Statistical analyses

2.4.1. Individual-effect analyses

We started our analysis by determining the individual impact of the annual average exposure to $PM_{2.5}$ and its constituent components (NO_3^-, SO_4^{2-}, BC, CL^-, NH_4^+, and OM) on hospital admissions using a time-dependent Cox proportional hazards model. In each model, the annual exposure levels of $PM_{2.5}$ or each component, along with NDVI, NO_2, TEMP, and PRE, were included as time-dependent terms. In model 1 (i.e., the base model), no adjustments were made for covariates. Model 2 included demographic factors including age at baseline, sex, ethnicity, health insurance categories, family history of cardiovascular diseases, marital status, education levels, and BMI. Model 3 further incorporated lifestyle and environmental factors, including smoking status, alcohol consumption, exercise frequency, TEMP, PRE, NDVI, and NO_2 concentrations. The probable confounders were chosen using a directed acyclic graph (DAG, Fig. A.2) and previous studies (Cai et al., 2023; Huang et al., 2023; Wen et al., 2023). The resulting hazard ratio (*HR*) and its corresponding 95 % confidence interval (*CI*) for a quantile increase in the exposure concentration were presented. Additionally, we reintroduced the exposure of interest as a smoothing factor in model 3 to investigate potential non-linear exposure-response correlations between the specific exposures at lag 0, lag 1, lag 0–1, or lag 0–2 years and the related outcome. The optimal degrees of freedom for the smoothing term were determined by minimizing the Bayesian Information Criterion (BIC) values (Malloy et al., 2009).

2.4.2. Mixture-effect analyses

We next used a quantile-based g-computation (QGC) model (designated as model 4) to explore the association between exposure to the combination of these six PM components and the risk of hospital admissions related to hypertension, controlling for the same confounders as in model 3. We further incorporated $PM_{2.5}$ concentrations into model 4 to investigate the mixture effects after controlling for $PM_{2.5}$ mass concentration. Briefly, the QGC approach initially transforms the six exposure components into quantized forms. It then fits an underlying model to assess the individual impacts of exposures on the outcome, generates predictions from this model at predefined exposure levels, and applies a marginal structural model to these predictions. Similar to the weighted quantile sum regression, the QGC approach estimates the mixture impact and the proportional contribution weight of each component. In this case, g-computation was used to estimate the parameters of a marginal structural model. The combined effect from the QGC is defined as the change in the outcome when all mixture components increase by one quantile concurrently. Overall, QGC is a robust methodology that enables the assessment of the mixture effect while allowing the direction of impact to vary across the exposures (Carrico et al., 2015; Keil et al., 2020). The QGC model differs from previous models by calculating marginal impact estimates using a joint marginal structural model, instead of providing conditional effect estimates. Although conditional estimates are frequently used in research to assess the adverse effects of exposure within certain groups, such as the exposed population, marginal estimates provide a population average exposure effect and are more easily interpretable than conditional hazard ratios. Within a fundamental model of Cox proportional hazards, the QGC model in this study incorporates 4 quantiles. The *quantile-based g-computation (QGC) model section* in the *Supplementary Methods* provides more information on the QGC technique.

2.4.3. Stratified analyses

The study also examined potential effect modifiers that could influence the mixed impacts of prolonged exposure to PM components on hypertension hospital admissions through stratified analyses. This involved assessing heterogeneity among different subgroups and testing intergroup disparities using a 2-sample z-test, with a significance threshold of 0.05 applied between each pair of subgroups (Altman & Bland, 2003; Liang et al., 2020). The potential modifiers included age categories at baseline (<45 years, 45–64 years, or ≥65 years), sex (Men or Women), BMI categories based on the criteria of the Working Group on Obesity in China (18.5 kg/m^2≤ BMI < 24.0 kg/m^2, or otherwise), education (≤Elementary school, Middle/High school, or ≥College), and greenness exposure (Low or High). *P*-values with a significance threshold of 0.05 were utilized in all statistical analyses. For all data cleansing, statistical modeling, and data visualization, R (version 4.2.2) was utilized.

2.4.4. Sensitivity analyses

To account for the mutual confounding effects among the components, we considered other components with correlation coefficients below 0.75 in the individual-effect analyses (model 3). To further assess the influence of gaseous pollutants, we acquired yearly concentrations of carbon monoxide, ozone, and sulfur dioxide from the CHAP datasets. Adjustments for carbon monoxide were made in this sensitivity analysis, while ozone and sulfur dioxide were excluded due to their high correlations (correlation coefficient $>$ 0.75) with $PM_{2.5}$. In the multi-pollutant models (model 4), carbon monoxide was also adjusted for. Next, to account for the impact of different NDVI buffers, we repeated model 4 using NDVI in 500-meter or 1000-meter buffers. Finally, to contend with missing covariates, we employed multiple imputations via chained equations (van Buuren & Groothuis-Oudshoorn, 2011) and conducted further studies using the complete datasets.

3. Results

3.1. Basic characteristics

The baseline characteristics of the participants are illustrated in Table 1 and Table A.2. Out of the initial 36,271 participants, 617 persons (1.7 %) were admitted to the hospital due to hypertension throughout an average follow-up duration of 5.8 years (standard deviation = 0.5), which amounts to a total of 209,835 person-years. The mean age of the participants was 50.9 years, with a standard deviation of 17.8 ages. 41 % of the participants were male. The Pearson correlation coefficients between the annual mean $PM_{2.5}$ and its components varied from 0.52 to 0.99 (Table 2). The annual average concentrations (*IQR*) of $PM_{2.5}$, NO_3^-, SO_4^{2-}, BC, CL^-, NH_4^+, and OM were 33.7 (5.8) μg/m^3, 6.0 (1.1) μg/m^3, 7.9 (0.9) μg/m^3, 3.3 (0.3) μg/m^3, 1.0 (0.3) μg/m^3, 3.8 (0.7) μg/m^3 and 11.7 (2.8) μg/m^3, respectively, exhibiting similar decreasing trends over person-years (Fig. A.3).

3.2. Associations of $PM_{2.5}$ and its constituents with hospitalization due to hypertension

HR estimates in the individual-effect analyses for model 1 and model 2 are presented in Table A.3. With full covariate adjustment (Model 3), we observed statistically positive associations between hypertension-related hospital admissions and a quantile increase in CL^-at lag 0, with corresponding *HR*s (and 95 % *CIs*) of 1.173 (1.046–1.314) for overall hypertension, and 1.208 (1.066–1.369) for primary hypertension. We found no evidence of an association between each quantile increase in $PM_{2.5}$, NH_4^+, BC, SO_4^{2-}, NO_3^-, or OM at lag 0 with hypertension-related hospital admissions (Table 3). For lagged and cumulative effects, we found that individual exposure to NH_4^+, NO_3^-, and SO_4^{2-} at lag 1 had harmful effects on overall hypertension hospital admissions, with *HRs* (and 95 % *CIs*) being 1.238 (1.063–1.442), 1.165 (1.019–1.333), and 1.189 (1.015–1.393), respectively. Similar *HR*s were found for primary hypertension hospitalizations. At lag 2, long-term exposure to NO_3^- and SO_4^{2-} were significantly linked to hypertension-related hospital admissions (Table A.4). Long-term NH_4^+ exposure at lag 0–1 and lag 0–2 was linked to an elevated risk of hypertension-related hospital admission (Table 3). After further adjustments for other components with correlation coefficients below 0.75 and for carbon monoxide concentrations, the estimated *HRs* obtained from the sensitivity analyses at each lag time were comparable to those from the main analysis (Fig. A.4). The exposure-response relationship of hypertension-related hospital admissions associated with six PM components generally showed a non-linear shape (Fig. 1, and Fig. A.5–Fig. A.8). As shown in Tables A.5–A.9, the optimal degrees of freedom were selected based on the minimization of BIC values.

Co-exposure to $PM_{2.5}$ components (NO_3^-, SO_4^{2-}, BC, CL^-, NH_4^+, and

Table 1
Characteristics of study participants.

	Total (*n* = 36,271)	Control group (*n* = 35,654)	Hospitalization from overall hypertension (*n* = 617)
Demographics			
Age (mean (SD), years)	50.9 (17.8)	50.7 (17.7)	66.7 (11.6)
Sex, (male %)	14,727 (40.6)	14,512 (40.7)	215 (34.8)
Ethnicity, (minority %)	280 (0.8)	278 (0.8)	2 (0.3)
Education levels (%)			
Illiterate or semiliterate	741 (2.0)	711 (2.0)	30 (4.9)
Primary school	5052 (13.9)	4897 (13.7)	155 (25.1)
Second school	7545 (20.8)	7406 (20.8)	139 (22.5)
High school	16,310 (45.0)	16,052 (45.0)	258 (41.8)
College or above	6623 (18.3)	6588 (18.5)	35 (5.7)
Marital status (%)			
Never married	5455 (15.0)	5425 (15.2)	30 (4.9)
Married	29,264 (80.7)	28,748 (80.6)	516 (83.6)
Widowed	1239 (3.4)	1177 (3.3)	62 (10.0)
Divorced	313 (0.9)	304 (0.9)	9 (1.5)
Health insurance (%)			
For urban workers	24,922 (68.7)	24,476 (68.6)	446 (72.3)
For urban residents	7308 (20.1)	7174 (20.1)	134 (21.7)
For rural residents	677 (1.9)	671 (1.9)	6 (1.0)
Others	3364 (9.3)	3333 (9.3)	31 (5.0)
Family history (%)			
No	21,241 (58.6)	20,921 (58.7)	320 (51.9)
Yes	15,030 (41.4)	14,733 (41.3)	297 (48.1)
BMI (mean (SD), kg/m^2)	22.6 (2.9)	22.6 (2.9)	23.8 (3.2)
Lifestyle behaviors			
Exercise frequency (%)			
Very low	13,954 (38.5)	13,728 (38.5)	226 (36.6)
Occasional	3403 (9.4)	3353 (9.4)	50 (8.1)
Often	2574 (7.1)	2536 (7.1)	38 (6.2)
High	16,340 (45.0)	16,037 (45.0)	303 (49.1)
Smoking status (%)			
Never	25,192 (69.5)	24,732 (69.4)	460 (74.6)
Former	529 (1.5)	513 (1.4)	16 (2.6)
Current	10,550 (29.1)	10,409 (29.2)	141 (22.9)
Alcohol consumption (%)			
Never	25,551 (70.4)	25,078 (70.3)	473 (76.7)
Ever	10,720 (29.6)	10,576 (29.7)	144 (23.3)
Environmental covariates			
NO_2 (mean (SD), (μg/m^3)	44.5 (3.8)	44.5 (3.8)	44.6 (2.9)
TEMP (mean (SD), °C)	22.6 (0.3)	22.6 (0.3)	22.5 (0.3)
PRE (mean (SD), mm)	150.0 (16.5)	150.0 (16.5)	151.0 (19.2)
NDVI (mean (SD))	0.23 (0.04)	0.23 (0.04)	0.23 (0.05)

Abbreviations: BMI, body mass index; NO_2: nitrogen dioxide; NDVI, normalized difference vegetation index; PRE, precipitation; TEMP, temperature.

Table 2
Exposure distribution of pollutants across person-years and Pearson correlation coefficients between the exposure levels.

Exposure	Mean ± SD	Median (Min, Max)	Interquartile Range	Pearson correlation coefficient						
				$PM_{2.5}$	CL^-	NH_4^+	BC	SO_4^{2-}	NO_3^-	OM
$PM_{2.5}$ (μg/m^3)	33.7 ± 5.2	33.7 (22.0, 42.3)	5.8	1.00	0.63	0.97	0.97	0.97	0.93	0.99
CL^- (μg/m^3)	1.0 ± 0.2	1.0 (0.5, 2.0)	0.3	0.63	1.00	0.74	0.59	0.59	0.67	0.52
NH_4^+ (μg/m^3)	3.8 ± 0.6	3.8 (2.4, 5.0)	0.7	0.97	0.74	1.00	0.94	0.93	0.96	0.92
BC (μg/m^3)	3.3 ± 0.4	3.3 (2.1, 4.0)	0.3	0.97	0.59	0.94	1.00	0.95	0.90	0.95
SO_4^{2-} (μg/m^3)	7.9 ± 1.0	7.9 (5.8, 9.8))	0.9	0.97	0.59	0.93	0.95	1.00	0.85	0.96
NO_3^- (μg/m^3)	6.0 ± 0.9	6.0 (3.7, 7.9)	1.1	0.93	0.67	0.96	0.90	0.85	1.00	0.87
OM (μg/m^3)	11.7 ± 2.4	11.7 (5.8, 15.5)	2.8	0.98	0.52	0.92	0.95	0.96	0.87	1.00

Table 3
Individual effects of hypertension-related hospitalizations associated with each quantile increase in $PM_{2.5}$ and its components at lag 0, lag 0–1, and lag 0–2 years.

Lagged exposure	Overall hypertension (n = 617)		Primary hypertension (n = 509)	
	HR (95 % *CI*)	*P* value	*HR* (95 % *CI*)	*P* value
Lag 0				
$PM_{2.5}$	0.998 (0.862–1.155)	0.979	0.959 (0.816–1.127)	0.609
CL^-	1.173 (1.046–1.314)	0.006	1.208 (1.066–1.369)	0.003
BC	0.886 (0.773–1.017)	0.086	0.877 (0.753–1.023)	0.095
NH_4^+	1.108 (0.966–1.272)	0.144	1.128 (0.970–1.311)	0.118
NO_3^-	1.011 (0.887–1.151)	0.874	1.033 (0.893–1.196)	0.658
SO_4^{2-}	1.134 (0.955–1.346)	0.152	1.105 (0.918–1.331)	0.293
OM	0.890 (0.786–1.006)	0.063	0.840 (0.734–0.960)	0.011
Lag 0–1				
$PM_{2.5}$	0.989 (0.960–1.019)	0.452	0.980 (0.948–1.013)	0.226
CL^-	1.098 (0.983–1.227)	0.099	1.111 (0.982–1.257)	0.096
BC	0.936 (0.805–1.088)	0.387	0.906 (0.769–1.068)	0.240
NH_4^+	1.278 (1.091–1.498)	0.002	1.315 (1.104–1.568)	0.002
NO_3^-	1.083 (0.952–1.232)	0.225	1.078 (0.933–1.246)	0.310
SO_4^{2-}	0.992 (0.834–1.180)	0.931	1.004 (0.832–1.211)	0.968
OM	0.905 (0.775–1.058)	0.211	0.870 (0.735–1.030)	0.107
Lag 0–2				
$PM_{2.5}$	0.996 (0.975–1.017)	0.684	0.991 (0.969–1.014)	0.422
CL^-	1.112 (0.989–1.250)	0.077	1.120 (0.983–1.275)	0.088
BC	0.975 (0.816–1.167)	0.785	0.978 (0.803–1.191)	0.825
NH_4^+	1.186 (1.001–1.405)	0.048	1.234 (1.018–1.494)	0.032
NO_3^-	1.164 (1.001–1.353)	0.049	1.166 (0.985–1.380)	0.075
SO_4^{2-}	1.193 (0.968–1.471)	0.097	1.146 (0.914–1.438)	0.237
OM	0.944 (0.788–1.131)	0.531	0.850 (0.699–1.034)	0.104

Note: Models were adjusted for age, sex, ethnicity, health insurance categories, family history of cardiovascular diseases, marital status, education levels, BMI, exercise frequency, smoking status, alcohol consumption, NDVI, TEMP, PRE, and NO_2 concentrations.

OM) at various lag times (0, 1, 2, 0–1, and 0–2 years) was positively associated with hospital admissions for overall hypertension in the mixture-effect analyses employing QGC models. The *HRs* (with 95 % *CIs*) were 1.151 (1.136–1.166), 1.221 (1.205–1.238), 1.257 (1.241–1.273), 1.087 (1.073–1.101), and 1.197 (1.182–1.212), respectively. Consistent findings were noted for hospital admissions due to primary hypertension (Table 4 and Table A.10). Furthermore, substantial associations remained significant after accounting for $PM_{2.5}$ mass concentrations (Table A.11).

Furthermore, we discovered that combined exposure to $PM_{2.5}$ constituents had distinct contributions (relative weights) to hypertension hospitalization. At lag 0, the component of SO_4^{2-} (43.0 %–43.3 %) exhibited the strongest contribution to the observed adverse relationships between co-exposures and hospitalizations for both overall hypertension and primary hypertension, followed by CL^- (36.7 %–41.6 %) and NH_4^+(15.4 %–20.0 %). For lagged and cumulative co-exposure, NH_4^+, SO_4^{2-}, and NO_3^- were the primary contributors to hypertension-related hospital admissions. Consistent findings were observed when additionally accounting for $PM_{2.5}$ mass concentrations (Fig. 2). The estimated HRs at different lag times remained consistent after further adjustments for carbon monoxide concentrations, incorporating NDVI in 500-meter and 1000-meter buffers, or using the complete dataset (Tables A.12–A.16).

3.3. Subgroup analyses

In the stratified analyses by demographics (Fig. 3 and Table A.17), we observed that men, younger participants, and those with lower educational levels were more vulnerable to hypertension hospitalization associated with mixed exposure to PM components. Men had significantly greater risks compared to women, with $P_{\text{interaction}} < 0.001$. The association between PM components and hypertension-related hospital admissions was greater among individuals under 45 years old than the older ones (all $P_{\text{interaction}} < 0.001$). Additionally, participants with elementary education or lower exhibited a 5 %–22 % increased risk of hospitalization for hypertension compared to those with higher educational attainment.

When stratified by controllable factors, participants with unhealthy weight (BMI < 18.5 kg/m^2 or BMI ≥24.0 kg/m^2) and those with limited exposure to greenness exhibited greater risks. Specifically, individuals with unhealthy weight experienced a higher risk of overall hypertension compared to their counterparts (*HR*: 1.22 vs. 1.11). Similarly, those with low greenness exposure had an 11 %–21 % higher risk of hypertension-related hospitalizations compared to those with greater greenness exposure.

4. Discussion

We conducted a large-scale prospective cohort study involving 36,271 adults in the Pearl River Delta region of China. Our findings revealed that prolonged concurrent exposure to various PM components (NO_3^-, SO_4^{2-}, BC, CL^-, NH_4^+, and OM) at different lag periods was associated with an increased risk of hospitalization for hypertension, ranging

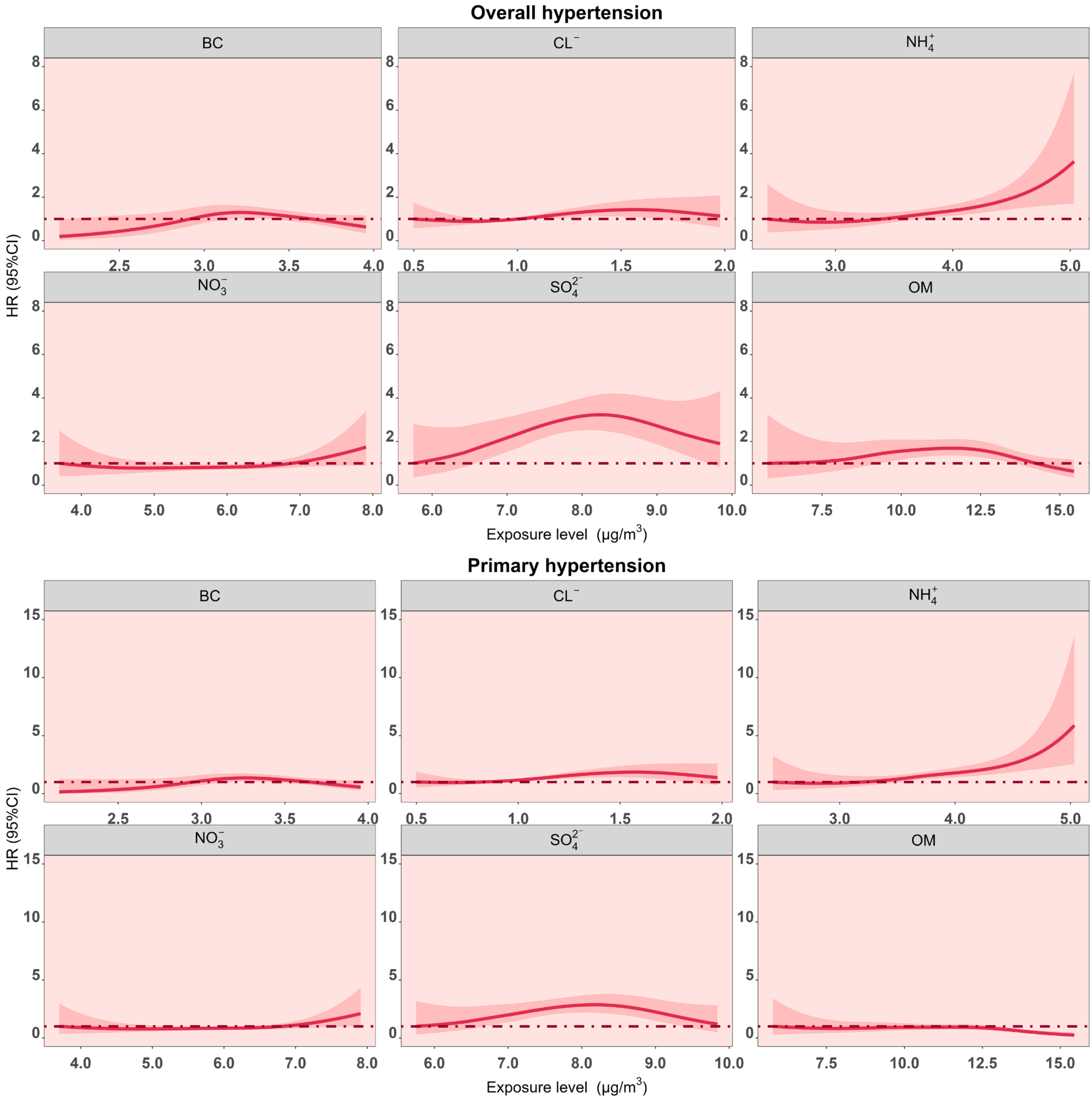

Fig. 1. The exposure-response curve for the association of annual $PM_{2.5}$ components with hospitalization from overall and primary hypertension. Models were adjusted for age, sex, ethnicity, health insurance categories, family history of cardiovascular diseases, marital status, education levels, BMI, exercise frequency, smoking status, alcohol consumption, NDVI, TEMP, PRE, and NO_2 concentrations.

from 8 % to 26 % within the general population. Among these mixed exposures, NH_4^+, SO_4^{2-}, NO_3^-, and CL^- played a predominant role, collectively contributing to over 90 % of the overall effect. Additionally, we observed that men, individuals under the age of 45, those with less education, those with unhealthy weight, and those with limited greenness exposure exhibited stronger associations between mixed exposure and elevated risks of hypertension-related hospital admissions. This study enhances existing evidence in China by being the first to examine both the lag and cumulative effects of combined exposure to PM components on hypertension hospitalization.

In our analysis of individual-effect models, we observed a significant increase in hospitalization risks for both overall and primary hypertension linked with prolonged exposure to various PM components. Specifically, for each quantile increase in CL^-, NH_4^+, SO_4^{2-}, and NO_3^- across different lag periods, the risk of hypertension hospitalization ranged from 17 % to 32 %. The associations observed in this study imply that extended exposure to PM components may have a substantial and enduring effect on the risk of hypertension-related hospitalization. Currently, the scarcity of extended PM composition monitoring data has hindered a comprehensive understanding of its relationship with hypertension (Zhao et al., 2022). Most existing knowledge is derived from cross-sectional studies, which may not fully capture the chronic impacts of PM exposure (Li et al., 2022a; Li et al., 2022b; Li et al., 2023; Liu et al., 2021; Lv et al., 2023; Shen et al., 2022; Sun et al., 2024). In a nationwide cross-sectional survey of 113,159 adults in China, NO_3^-, SO_4^{2-}, BC, NH_4^+, and OM were found to be positively correlated with hypertension prevalence (Lv et al., 2023). Similarly, another cross-sectional research in 7 Chinese provinces, involving 37,610 children and adolescents,

Table 4
Mixture impacts of each quantile increase in co-exposure to PM components on hospital admissions for overall and primary hypertension using QGC models across different lag years.

	Overall hypertension ($n = 617$)		Primary hypertension ($n = 509$)	
Lagged exposure	*HR* (95 % *CI*) [a]	*P* value	*HR* (95 % *CI*) [a]	*P* value
Lag 0	1.151 (1.136–1.166)	< 0.001	1.104 (1.089–1.120)	< 0.001
Lag 1	1.221 (1.205–1.238)	< 0.001	1.189 (1.172–1.205)	< 0.001
Lag 2	1.257 (1.241–1.273)	< 0.001	1.164 (1.148–1.179)	< 0.001
Lag 0–1	1.087 (1.073–1.101)	< 0.001	1.076 (1.061–1.090)	< 0.001
Lag 0–2	1.197 (1.182–1.212)	< 0.001	1.078 (1.064–1.092)	< 0.001

[a] Adjusted for age, sex, ethnicity, health insurance categories, family history of cardiovascular diseases, marital status, education levels, BMI, exercise frequency, smoking status, alcohol consumption, NDVI, TEMP, PRE, and NO_2 concentrations.

reported positive effect estimates for $PM_{2.5}$ components concerning hypertension prevalence (Li et al., 2022b). However, our results differ from these studies, particularly regarding the role of BC. While a strong relationship between BC and the risk of hypertension has been identified in previous studies, we did not find a similar effect. Interestingly, our results align more closely with a cross-sectional study performed in Australia, which also found no significant relationships between blood pressure and BC (Vander Hoorn et al., 2021). The observed discrepancies suggest that additional cohort studies are needed to clarify the intricate relationship between PM chemical components and health outcomes. These differences may stem from varying exposure assessment techniques, demographic variability, and regional differences in PM composition (Li, B. et al., 2021; Xue et al., 2021; Yang et al., 2020).

Additionally, although several previous investigations have examined the link between individual exposure to PM constituents and hypertension, there remains a significant dearth of general-population cohort investigations examining the collective effects of prolonged exposure to PM components. A notable instance is a pregnant women cohort study conducted in California, United States, spanning from 2008 to 2017, which investigated the relationships between five PM species and pregnancy-related hypertension problems (Sun et al., 2024). The study revealed that BC was the greatest contributor (71 %) of the mixture effects among all individual species. Another cohort research examined the cumulative impact of long-term exposure to PM components on blood pressure and hypertension, including 9031 middle-aged and elderly individuals in China. The results showed that NH_4^+ contributed more to the total mixture effects (Li et al., 2022a). The scarcity of general-population cohort studies investigating the collective effects of prolonged exposure to PM components is particularly noteworthy, as individuals in real-world environments are concurrently exposed to multiple PM components, which can lead to complex synergistic or antagonistic interactions (Qi et al., 2022; Wang et al., 2020). Such interactions can result in variable impacts on human cardiopulmonary function, complicating the assessment of their health effects (Jin et al., 2022). Our study addresses this gap by exploring both lagged and cumulative effects, offering new insights into how sustained exposure to PM components influences hypertension hospitalization. We observed stronger associations between mixed exposure to PM components and hypertension-related hospital admissions, particularly for NO_3^-, SO_4^{2-}, NH_4^+, and CL^- when considering lagged periods. This underscores the importance of developing targeted environmental policies that address specific PM components. While there are general air quality guidelines for the overall mass of PM_{10} and $PM_{2.5}$, many nations, including China, do not have precise criteria for individual PM components. This study offers valuable evidence for prioritizing specific PM components in air quality monitoring and regulation, with implications for developing

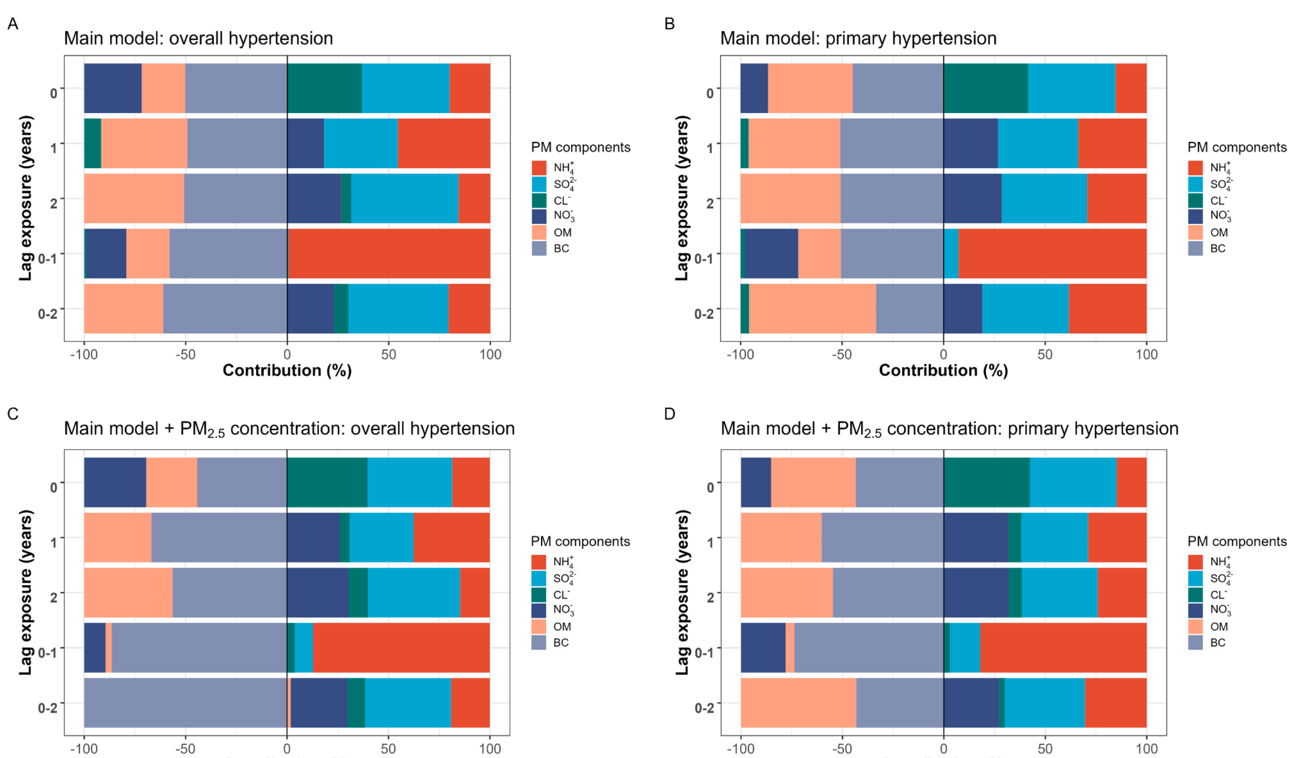

Fig. 2. The contributions assigned to each PM component from combined-effect analyses by using QGC models with a quantile number of 4. Main model: adjusting for age, sex, ethnicity, health insurance categories, family history of cardiovascular diseases, marital status, education levels, BMI, exercise frequency, smoking status, alcohol consumption, NDVI, TEMP, PRE, and NO_2 concentrations.

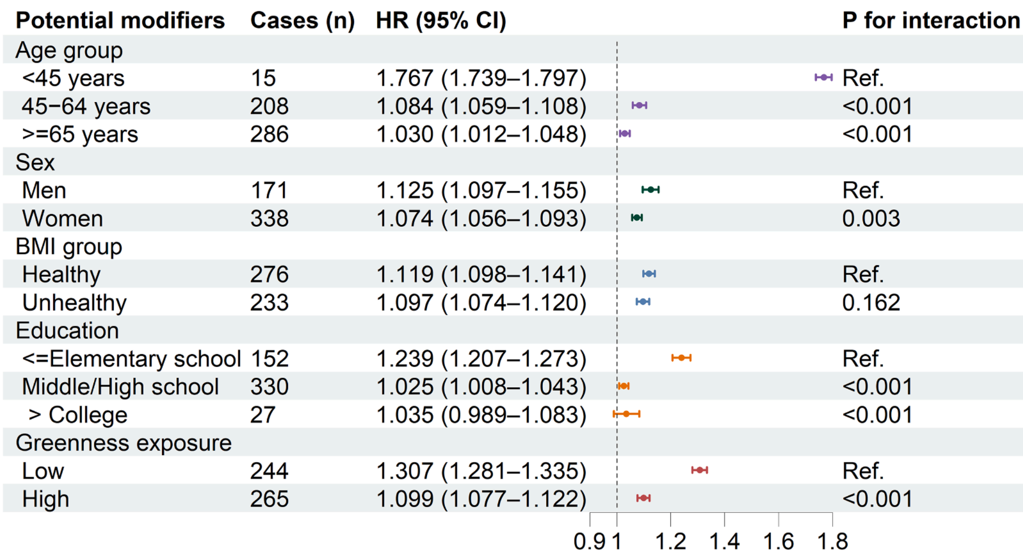

Fig. 3. Mixed impacts of co-exposure to PM components on hospitalization for primary hypertension, stratified by age group, sex, BMI category, education level, and greenness exposure.

Note: Normal or healthy weight was defined as 18.5 kg/m^2≤ BMI < 24.0 kg/m^2, and abnormal or unhealthy weight was defined as BMI < 18.5 kg/m^2 or BMI ≥24.0 kg/m^2, according to the criteria of the Working Group on Obesity in China. The *P* for interaction between subgroup-specific effects was assessed using a 2-sample z-test.

component-based standards that more effectively safeguard public health. Our results highlight the critical need to monitor those PM components most strongly linked to hypertension hospitalization, which can guide resource allocation and inform targeted emission control strategies. For instance, implementing stricter emission standards for traffic, industry, and biomass burning substantially mitigates the health burden associated with these components. Building on these findings, we recommend that policymakers integrate the health impacts of individual PM components into air quality regulations. This approach can more effectively mitigate the health risks associated with PM exposure. Specifically, monitoring and regulating key components such as NO_3^-, SO_4^{2-}, NH_4^+, and CL^- should be prioritized. Urban planners and public health officials could leverage our findings to allocate resources for targeted emission control measures, ensuring meaningful health benefits. Furthermore, advancing biological and toxicological research is crucial to fully understand the mechanisms underlying the interactions among combined exposures. These interdisciplinary efforts can provide a more comprehensive foundation for developing robust, evidence-based environmental policies.

While studies identifying susceptible subpopulations impacted by mixture effects are still limited, research focusing on PM mass or individual components has provided valuable insights. Our results support existing evidence that men and those with lower educational levels exhibit greater vulnerability to the adverse effects of prolonged exposure to multiple PM components (Li et al., 2022a; Li et al., 2021; Tibuakuu et al., 2018; Yang et al., 2020). Notably, we observed an unexpectedly high susceptibility in younger participants, contrasting with other studies on cardiovascular outcomes that reported greater effects of long-term $PM_{2.5}$ exposure in the elderly (Liu et al., 2021; Lv et al., 2023; Xi et al., 2022). Interestingly, Wang et al. found in a cohort study spanning ten US states that younger residents (<34 years) had a higher relative risk of MI hospitalizations from long-term $PM_{2.5}$ exposure compared to older individuals (Wang et al., 2023). Similarly, two meta-analyses showed that the harmful effects of $PM_{2.5}$ were more pronounced in younger populations than in the elderly (Chen & Hoek, 2020; Yang et al., 2018). Given that younger people can manage and control their hypertension more quickly and readily than older people, and that hospitalization rates for hypertension among young and middle-aged adults are rising globally (Harris et al., 2024; Meher et al., 2023), public health prevention efforts should place greater emphasis on this age group, especially in regions with severe $PM_{2.5}$ pollution. By enhancing air quality monitoring in these areas, it is possible to effectively reduce $PM_{2.5}$-related hypertension risks in young people, thereby lowering the long-term health hazards from air pollution in the broader population. Additionally, given the observed heightened susceptibility among younger populations, public health policies should incorporate younger adults as a high-risk group for hypertension monitoring and targeted interventions, especially in regions experiencing severe $PM_{2.5}$ pollution. These proactive measures could mitigate long-term health effects, promote health equity, and support sustainable urban development.

Modifiable factors like BMI and greenness exposure were shown to have a substantial impact on the modulation of health risks related to exposure to PM components and hypertension. Our findings align with existing evidence indicating that individuals who are underweight or overweight face greater health risks from $PM_{2.5}$ exposure compared to those with a normal weight (Li et al., 2020; Lin et al., 2017; Yang et al., 2018). Furthermore, our study emphasizes the protective effects of green spaces. Green spaces not only purify the air by capturing particulate matter and acting as noise barriers, but they also make substantial contributions to overall environmental cleanliness (Kim et al., 2023; Zhang et al., 2023). Additionally, regular exposure to green spaces provides numerous benefits, including enhancing environmental aesthetics, improving psychological well-being, and alleviating negative emotions (Yu et al., 2023). Therefore, beyond safeguarding vulnerable populations, promoting urban greenery could be a key strategy in mitigating hypertension risks associated with mixed pollutant exposure. Integrating green infrastructure into urban health policies not only reduces $PM_{2.5}$ exposure and its associated hypertension risks but also aligns with sustainable development goals by fostering cleaner air, reducing urban heat island effects, and creating healthier living environments. Such interventions contribute to addressing the long-term public health burden posed by air pollution, while building sustainable, resilient cities.

5. Strengths and limitations

This study utilized a substantially large cohort, providing ample statistical power to thoroughly investigate the correlations between $PM_{2.5}$ constituents and hypertension hospitalization across multiple subgroups. We utilized a QGC technique to evaluate the combined effects of mixed exposures over different spans of time, rather than focusing solely on the individual impacts of each constituent. This approach accounted for substantial collinearity and potential additive or synergistic interactions. Furthermore, we performed a series of sensitivity analyses to guarantee the reliability and consistency of our findings. Despite these novel contributions and advantages, it is essential to acknowledge certain limitations. First, while thorough sensitivity analyses were conducted to address potential confounding and correlations among gaseous pollutants, residual confounding and strong correlations between PM components may still limit the precision of estimating their individual effects, making it difficult to isolate their independent impacts. Second, residential addresses were not followed over the follow-up period; they were only gathered at baseline. Nevertheless, considering that participants were permanent residents with a consistent residence history, the likelihood of relocation is minimal. Third, by using only hospitalization data, our study likely underestimates the full impact of particulate matter exposure on hypertension, since this data predominantly includes the most severe cases. Research using outpatient data has been found to report larger effect sizes than studies using hospitalization data (Danesh Yazdi et al., 2021; Feng et al., 2024; Lee et al., 2022; Zaheer et al., 2025). However, the use of first hospitalization for hypertension as our primary outcome aligns with standard practice in hospitalization-based studies, enhancing comparability with existing research (Mork et al., 2023; Wei et al., 2024). To gain a deeper insight into the health consequences associated with hypertension, future research might include information from self-reported diagnoses, outpatient visits, or other medical interactions.

6. Conclusions

In conclusion, our study found a significant correlation between chronic exposure to PM components and an increased risk of hospitalization for hypertension. Participants under the age of 45, those with lower educational attainment, unhealthy body weight, or limited exposure to green spaces exhibited heightened vulnerability to the adverse hypertension-related effects resulting from combined exposure to these $PM_{2.5}$ components. Our research revealed that secondary water-soluble inorganic ions, including NO_3^-, SO_4^{2-}, NH_4^+, and CL^-, may be important sources of this danger. To promote sustainable urban development, upcoming urban strategic plans should prioritize monitoring and regulating these components, safeguarding vulnerable populations, and implementing green initiatives to alleviate the negative consequences linked to prolonged exposure to $PM_{2.5}$ components.

Funding

This work was supported by the National Key Research and Development Program of China (2022YFC3600804), National Natural Science Foundation of China (82204162), Young Elite Scientist Sponsorship Program by China Association for Science and Technology (2023QNRC001), Guangdong Provincial Pearl River Talents Program (0920220207), Basic and Applied Basic Research Foundation of Guangdong Province (2022A1515010823), Guangzhou Municipal Science and Technology Bureau (2023A04J2072), and Fundamental Research Funds for the Central Universities, Sun Yat-sen University (23qnpy108).

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Declaration of competing interest

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Acknowledgments

We would like to thank Wenmin Han and Xiuyuan Chen for their valuable contributions. We acknowledge the data support from "Loess Plateau SubCenter, National Earth System Science Data Center, National Science & Technology Infrastructure of China (http://www.geodata.cn). Professor Yuantao Hao gratefully acknowledges the support of KC Wong Education Foundation.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.scs.2025.106293.

Data availability

Data will be made available on request.

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