



RESEARCH ARTICLE



# Short-term exposure to PM<sub>2.5</sub> and its components and type 2 diabetes-related hospital admissions, length of stay, and hospital costs in Shanghai

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## ABSTRACT

The short-term influence of particles with an aerodynamic diameter  $\leq 2.5$   $\mu\text{m}$  (PM<sub>2.5</sub>) and its individual elements on hospital costs, the length of hospital stay (LOS), and hospital admissions caused by type 2 diabetes remains unclear. A generalized additive model (GAM) with quasi-Poisson distribution was utilized to assess the association of individual pollutants and mixtures. For every 10  $\mu\text{g}/\text{m}^3$  rise in PM<sub>2.5</sub> and a per-SD increase in NH<sub>4</sub><sup>+</sup> at lag0, hospital admissions increased by 0.93% (95% CI: 0.68, 1.19) and 2.81% (95% CI: 2.20, 3.42); hospital costs rose by 24.58 thousands of CNY (95% CI: 5.95, 43.22) and 77.06 thousands of CNY (95% CI: 33.07, 121.04); LOS increased by 9.53 days (95% CI: 0.44, 18.62) and 27.80 days (95% CI: 6.34, 49.27), respectively. Factor analysis showed that mixed-source particulate pollution was significantly associated with an increase in hospital admissions (0.27%, 95% CI: (0.20, 0.34)), LOS (2.87 days, 95% CI: (0.35, 5.40)), and hospital costs (71.68 thousands of CNY, 95% CI: (19.89, 123.46)). These findings suggested that short-term exposure to elevated levels of PM<sub>2.5</sub> as well as its components increased the risk of hospital costs, LOS, and hospital admissions due to type 2 diabetes.

## ARTICLE HISTORY

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## KEYWORDS

PM<sub>2.5</sub> components; type 2 diabetes; Hospital admissions; Hospital costs; Length of hospital stay

## Introduction

PM<sub>2.5</sub> (particles with an aerodynamic diameter  $\leq 2.5$   $\mu\text{m}$ ) can transport a multitude of toxic substances, posing a serious health threat (Yuan et al. 2020). Studies revealed that prolonged exposure to PM<sub>2.5</sub> has been linked with an elevated risk of diabetes mellitus (Sorensen et al. 2022). Within the Global Burden of Disease Study (GBD), PM<sub>2.5</sub> was identified as the third major contributory factor for type 2 diabetes (Murray et al. 2020). GBD 2019 findings suggested that approximately 20% of the global burden related to type 2 diabetes may be attributed to PM<sub>2.5</sub> exposure (Murray et al. 2020; Forray et al. 2023). While these studies primarily focus on long-term exposure, it is crucial to consider the implications of short-term exposure as well. Short-term exposure to PM<sub>2.5</sub> might influence hospital admissions for type 2 diabetes through several potential

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causal pathways, including the exacerbation of existing cardiovascular or respiratory conditions, which are common comorbidities in patients with type 2 diabetes (Bell et al. 2013).

PM<sub>2.5</sub> is made up of several components, such as black carbon (BC), chloride (Cl), nitrate (NO<sub>3</sub><sup>-</sup>), ammonium (NH<sub>4</sub><sup>+</sup>), sulfate radical (SO<sub>4</sub><sup>2-</sup>), and organic matter (OM) (Wei et al. 2023). The components of PM<sub>2.5</sub> and the prevalence of diabetes have been found to be significantly correlated in several studies (Sun et al. 2016, 2022; Yu et al. 2020). For instance, cohort study conducted in South Africa and China revealed a significant association between BC, NO<sub>3</sub><sup>-</sup> in the chemical fraction of PM<sub>2.5</sub> and an increased risk of gestational diabetes (Sun et al. 2016, 2022). However, these studies only focused on evaluating the risk of developing diabetes as an outcome indicator, and there are limited studies assessing the burden of disease indicators, such as hospital admissions, hospital costs and length of hospital stay (LOS).

Assessing the short-term impacts of PM<sub>2.5</sub> and its constituents on indicators of type 2 diabetes burden could lead to the discovery of novel approaches for reducing the disease burden of PM<sub>2.5</sub>-related diabetes. To achieve this goal, a time-series study was carried out in Shanghai to investigate the relationship between hospital costs, length of stay (LOS), and hospital admissions related to type 2 diabetes and PM<sub>2.5</sub> and its constituents.

## Materials and methods

### Data collection

#### Patient data

The Shanghai Municipal Health Insurance System (<http://ybj.sh.gov.cn/tjsj/>) provided comprehensive data on basic health insurance for residents of both rural and urban areas, as well as employees. It also provided comprehensive and complete data on hospital costs, LOS, and daily hospital admissions attributed to type 2 diabetes from 1 January 2016, to 31 December 2019. Additional information on the system can be found in the previously released publications (Peng et al. 2022; Zhou et al. 2023). A time-series of demographic information, hospital expenses, daily hospital admissions, and LOS for people with type 2 diabetes was rebuilt based on the system (Table S23).

Patient data were collected from all hospitals across all districts of Shanghai, including tertiary, secondary, and primary care facilities before implementing the COVID-19 lockdown measures. Based on the results of the secondary diagnosis, the diagnosis of type 2 diabetes was coded as E12 in accordance with the International Classification of Diseases, Tenth Revision (ICD – 10) coding system. Gender and age information was included in the demographic data, with age groups being 45 years and under, 45–64 years old, 65–74 years old, and 75 years and over. The Fudan University School of Public Health's Ethics Committee gave the study its approval.

#### Air pollutants and meteorological data

Data on the chemical composition of PM<sub>2.5</sub>, including NH<sub>4</sub><sup>+</sup>, SO<sub>4</sub><sup>2-</sup>, BC, NO<sub>3</sub><sup>-</sup>, Cl, and OM, gaseous pollutants, including carbon monoxide (CO), ozone (O<sub>3</sub>), nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>), and average temperature and relative humidity from the first day of 2016 to the last day of 2019 were completely obtained without missing values. The source of the daily concentrations of PM<sub>2.5</sub> and its constituents was the China High Air Pollutant (CHAP) dataset, which offers high-resolution data spanning a geographical resolution of 1 km<sup>2</sup> (<https://weijing-rs.github.io/product.html>). The PM<sub>2.5</sub> and its constituent dataset, sourced from the latest open-source version, was estimated using the Spatiotemporal Extra Trees (STET) model, with satellite remote sensing data (Wei et al. 2023). The daily concentrations of CO, O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub> were obtained from the Shanghai Municipal Bureau of Ecology and Environment (<https://sthj.sh.gov.cn/>), collected by 19 environmental monitoring stations across Shanghai.

Average temperature and daily relative humidity were obtained via the National Meteorological Information Center (<http://data.cma.cn/>), recorded by 11 surface meteorological stations in Shanghai.

To increase the precision of the recorded values, the total levels of PM<sub>2.5</sub> and its constituents in Shanghai were estimated through the first day of 2016 to the last day of 2019 (Feng et al. 2022). The computations in detail are available in our earlier articles (Peng et al. 2022). The arithmetic average of all monitoring stations was utilized to express the daily concentrations of NO<sub>2</sub>, O<sub>3</sub>, CO, and SO<sub>2</sub> (Li et al. 2022; Peng et al. 2022; Zhou et al. 2023)

### *The medical care CPI*

The Consumer Price Index (CPI) is a crucial measure that gives a detailed account of changes in the cost of consumer goods and services bought by locals (Burns et al. 2008). Previous research has demonstrated there was an association between CPI and hospital costs. Therefore, we obtained the Shanghai Statistics Bureau's monthly CPI statistics for medical care from 2016 to 2019 ([https://tjj.sh.gov.cn/ydsj61/index\\_2.html](https://tjj.sh.gov.cn/ydsj61/index_2.html)). We calculated the monthly fixed base CPI using the January 2016 CPI through a careful process. Then, we used this monthly fixed base CPI (Table S21) to adjust the monthly hospital expenses before including them in our analysis (Zhou et al. 2023).

## *Statistical analysis*

### *Characteristic statistics*

Means, standard deviations (SDs), and percentiles (P<sub>5</sub>, P<sub>25</sub>, P<sub>50</sub>, P<sub>75</sub>, and P<sub>95</sub>) were utilized to characterize the variance of data on patients, PM<sub>2.5</sub> and its constituents, gaseous pollutants, and meteorological conditions. The daily fluctuation in hospital admissions, hospital expenses, and LOS for people with type 2 diabetes was displayed using a calendar heat map. The relationship between PM<sub>2.5</sub> and its constituents (PM<sub>2.5</sub>, SO<sub>4</sub><sup>2-</sup>, BC, NO<sub>3</sub><sup>-</sup>, Cl, NH<sub>4</sub><sup>+</sup>, and OM), gaseous pollutants (NO<sub>2</sub>, O<sub>3</sub>, CO, and SO<sub>2</sub>), and meteorological factors (daily mean temperature, daily mean relative humidity) was assessed using Spearman correlation analysis.

### *Estimating associations*

The relationship between PM<sub>2.5</sub> and its constituents and daily hospital expenses, hospital admissions, and LOS related to type 2 diabetes was evaluated using a generalized additive model (GAM) with a quasi-Poisson distribution. Based on earlier research, a number of potential confounding variables were accounted for in the GAM model, including relative humidity (rh), the day of the week (dow), long-term trends, seasonality, public holidays (ph), and average temperature (temp). The degrees of freedom (df) for daily average temperature and relative humidity are six and three, respectively, and that the df for seasonality and long-term trends is seven for every year (Peng et al. 2022). In this model, we added dow and ph as categorical variables. Here is how the primary model appears:

$$\log(E(Yt)) = \alpha + \beta * Zt + \text{ns}(\text{temp}, 6) + \text{factor}(\text{ph}) + \text{factor}(\text{dow}) + \text{ns}(\text{rh}, 3) + \text{ns}(\text{time}, 7)$$

$$Y't = \alpha + \beta * Zt + \text{ns}(\text{temp}, 6) + \text{factor}(\text{ph}) + \text{factor}(\text{dow}) + \text{ns}(\text{rh}, 3) + \text{ns}(\text{time}, 7)$$

where  $Y't$  represents the projected daily hospital expenses or LOS owing to type 2 diabetes,  $E(Yt)$  represents daily hospital admissions.  $Zt$  represents the PM<sub>2.5</sub> and its components concentration on lag(t),  $\alpha$  denotes the intercept,  $\beta$  is the coefficient of regression for  $Zt$ , and ns() stands for natural spline.

A variety of time lags(t) were investigated, including multi-day moving averages (from lag01 to lag07) and single-day lags (from a given day to a week prior: lag0-lag7).

The daily admissions change as a percentage and the daily LOS and hospital costs rise as an absolute were computed using the following formulas (Li et al. 2022; Peng et al. 2022; Zhou et al. 2023):

$$\text{Absolute increase} = \beta * \Delta c$$

$$\text{Percentage Change} = [\exp(\beta * \Delta c) - 1] * 100$$

where  $\beta$  is the GAM model's regression coefficient for  $\text{PM}_{2.5}$  and its constituents.  $\Delta c$  is set to  $10 \text{ ug/m}^3$  for  $\text{PM}_{2.5}$ , and per SD for  $\text{PM}_{2.5}$  components.

### Subgroup analysis

A stratified subgroup analysis by age (less than 45, 45–64, 65–74, and more than 74 years) and sex (women and men) was conducted to compare effect values. The statistical significance of the differences between subgroups was tested using the Z-test (Altman and Bland 2003). Below is a list of the equation:

$$Z = \frac{(\beta_1 - \beta_2)}{\sqrt{SE_1^2 + SE_2^2}}$$

where the subgroups' effect values are denoted by  $\beta_1$  and  $\beta_2$ , respectively. The standard errors are denoted by  $SE_1$  and  $SE_2$ , respectively.

### Exposure–response relationship

We investigated dose–response relationships between absolute increases in hospital expenses, LOS, variations in the percentage of daily admissions, and  $\text{PM}_{2.5}$  and its components concentration (Peng et al. 2022).

### Principal component analysis

To identify the main pollution sources, a principal component analysis (PCA) with varimax rotation was employed on the daily concentrations of  $\text{PM}_{2.5}$  components and gaseous pollutants ( $\text{O}_3$ ,  $\text{SO}_2$ ,  $\text{NO}_2$ ,  $\text{CO}$ ). The number of factors retained was determined based on the Kaiser criterion (eigenvalues  $>1$ ) and the scree plot. Varimax rotation was applied to maximize the variance of the squared loadings, enhancing the interpretability of the components. The extracted factors were interpreted based on their component loadings, with loadings greater than 0.5 considered significant. Generalized additive models (GAMs) with a quasi-Poisson distribution were then applied to evaluate the association between these extracted components and hospital admissions, LOS, and hospital costs due to type 2 diabetes.

### Sensitivity analysis

In order to verify the robustness of the data and look for interactions or potential multi-collinearity, five sensitivity analyses were carried out. Initially, the data were fitted to a two-pollutant model ( $\text{PM}_{2.5}$  and its components and  $\text{O}_3$ ,  $\text{SO}_2$ ,  $\text{NO}_2$ ,  $\text{CO}$ ). Second, there was an increase in calendar time degrees of freedom from 5 to 9 every year. Third, there was an increase in the temperature degrees of freedom from 4 to 8. Fourth, the relative humidity degrees of freedom were adjusted from 1 to 5. Lastly, the lag effect of temperature from lag1 to lag7 was evaluated.

R version 4.2.1 was used for all statistical analyses, and the splines, sf, ggplot2, rgdal, MGCV, and raster packages were utilized. Two-sided tests were used, and statistical significance was defined as P-values less than 0.05.

## Results

### *The characteristics of the population*

This analysis included 172,291 people with type 2 diabetes spanning from 2016 to 2019, which equates to 1,935,512 days of hospital stays and 4,382,333 Chinese yuan (CNY) in hospital expenses. The data included 94,598 (54.9%) men and 77,693 (45.1%) women. There were 58,410 (33.9%) patients aged 65–74 (Table 1). In order to display daily fluctuations in LOS, hospital admissions, and hospital expenses for type 2 diabetes, we also produced a calendar heat map (Figure S1).

### *PM<sub>2.5</sub> and its components characteristics*

The average daily value of PM<sub>2.5</sub> was 37.73 µg/m<sup>3</sup>. Of the entire PM<sub>2.5</sub> mass, OM had the highest average concentration at 32.7% (12.32 µg/m<sup>3</sup>), while Cl had the lowest at 3.6% (1.37 µg/m<sup>3</sup>) (Table 2). The PM<sub>2.5</sub> components and PM<sub>2.5</sub> had Spearman correlation values ranging from 0.71 to 0.94. NH<sub>4</sub><sup>+</sup> had the strongest correlation with PM<sub>2.5</sub> (0.94). The Spearman correlation coefficients between the components varied from 0.55 to 0.91. The two variables with the highest degree of correlation were BC and OM (0.91). Temperature and relative humidity had a negative correlation with PM<sub>2.5</sub> and its constituents. Cl had the highest correlation coefficient with temperature (−0.71). OM had the highest correlation coefficient with relative humidity (−0.28) (Table S1).

**Table 1.** The study population's distributional characteristics and those of the three indicators.

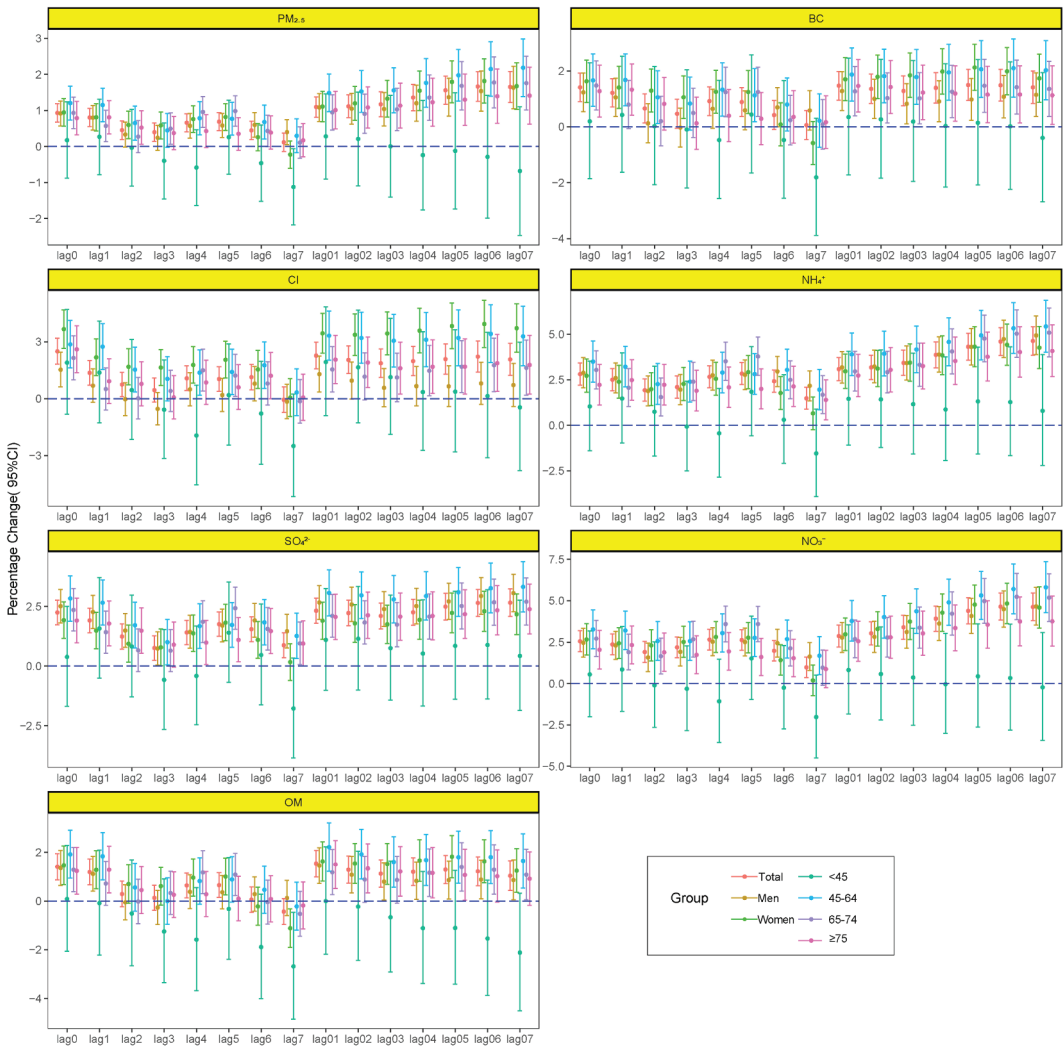
Variable	Total	Mean	SD	P <sub>5</sub>	P <sub>25</sub>	P <sub>50</sub>	P <sub>75</sub>	P <sub>95</sub>
Hospital admissions	172,291	117.93	57.03	24	71	124	160	332
LOS (days)	1,935,512	1324.79	639.26	278.5	772	1397	1797.5	3421.5
Hospital costs (1000 CNY)	4,382,333	3000	1470	623	1739	3145	4066	8498
Gender								
Men	94,598(54.9%)	64.75	32.58	12	38	67	89	184
Women	77,693(45.1%)	53.18	25.56	11	33	56	72	153
Age group (years)								
<45	10,689(6.2%)	7.32	5.13	1	3	6	11	33
45–64	52,337(30.4%)	35.82	19.70	6	20	35	50	120
65–74	58,410(33.9%)	39.98	20.30	7	23	42	54	122
≥75	50,855(29.5%)	34.81	15.87	8	22	38	46	90

LOS for duration of hospital stay. SD stands for standard deviation. Hospital costs were determined in the Chinese Yuan within January 2016. CNY: Chinese Yuan.

**Table 2.** Distributional characteristics of PM<sub>2.5</sub> components and meteorological factors.

Variable	Mean	SD	P <sub>5</sub>	P <sub>25</sub>	P <sub>50</sub>	P <sub>75</sub>	P <sub>95</sub>
PM <sub>2.5</sub> , µg/m <sup>3</sup>	37.73	21.39	13.82	22.24	32.35	47.34	78.61
BC, µg/m <sup>3</sup>	2.38(6.3%)	1.02	1.23	1.64	2.15	2.83	4.31
Cl, µg/m <sup>3</sup>	1.37(3.6%)	0.74	0.57	0.83	1.15	1.77	2.81
NH <sub>4</sub> <sup>+</sup> , µg/m <sup>3</sup>	5.10(13.5%)	2.46	1.80	3.22	4.75	6.49	9.42
SO <sub>4</sub> <sup>2-</sup> , µg/m <sup>3</sup>	8.12(21.5%)	2.98	4.04	5.83	7.79	9.87	13.50
NO <sub>3</sub> <sup>-</sup> , µg/m <sup>3</sup>	8.44(22.4%)	5.49	1.95	4.33	7.13	11.33	19.05
OM, µg/m <sup>3</sup>	12.32(32.7%)	10.19	2.04	5.45	9.59	15.79	32.93
O <sub>3</sub> , µg/m <sup>3</sup>	97.47	41.6	43	68	90	120	182
NO <sub>2</sub> , µg/m <sup>3</sup>	40.09	18.12	16	27	37	50	75
SO <sub>2</sub> , µg/m <sup>3</sup>	10.01	4.75	5	7	9	12	19
CO, µg/m <sup>3</sup>	0.67	0.22	0.4	0.5	0.6	0.8	1.1
Temperature, °C	17.66	8.72	3.80	10.10	18.50	24.70	30.70
Relative humidity, %	73.33	12.37	51.00	65.00	74.00	83.00	92.00

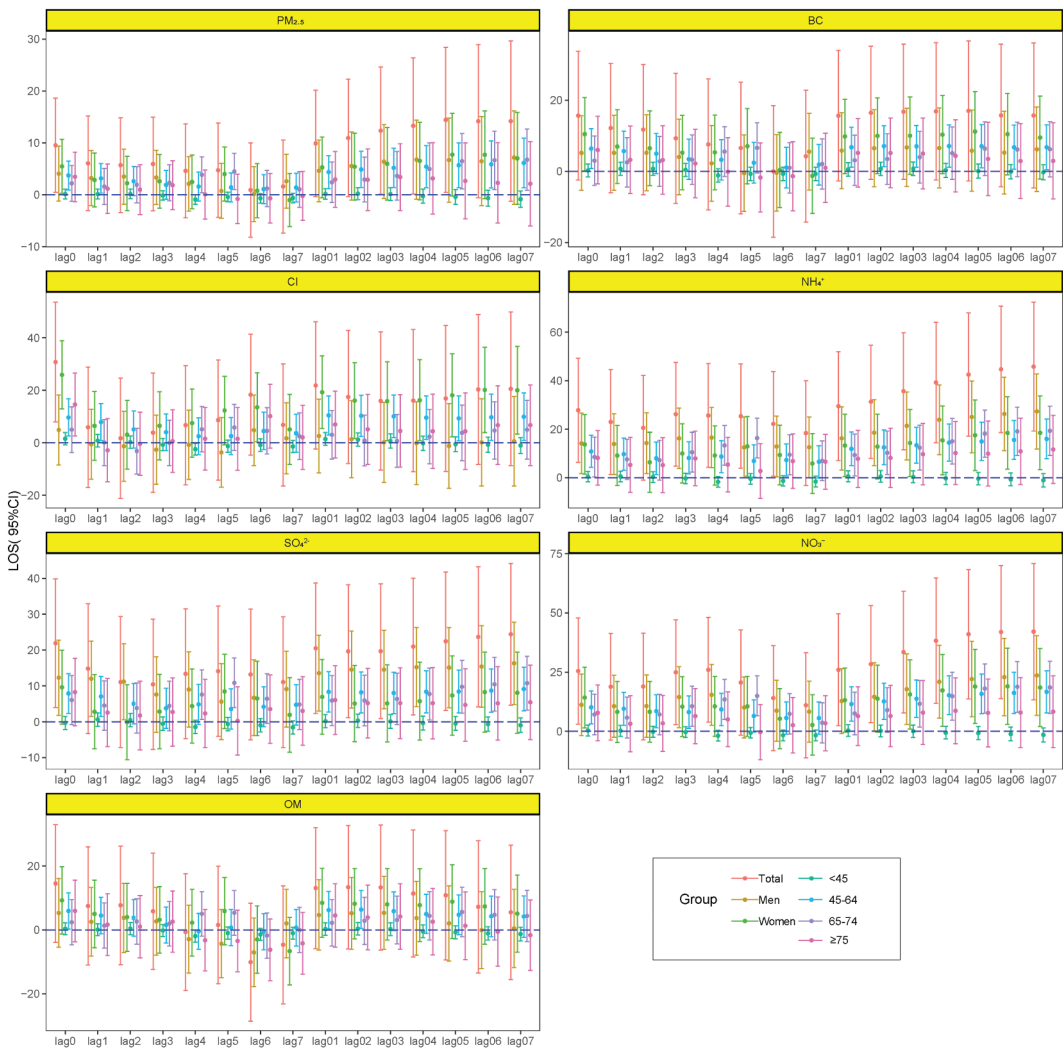
SD: Standard deviation.



**Figure 1.** Percentage change in daily hospital admissions. point estimates and 95% CIs are used to show how the percentage change in daily hospitalizations will vary in response to a  $10 \mu\text{g}/\text{m}^3$  rise in  $\text{PM}_{2.5}$  and a per-SD increase in its constituent parts. <45: age less than 45 years old. 45–64: the age range between 45 and 64 years old. 65–74: the age range between 65 and 74 years old.  $\geq 75$ : age over or equal to 75 years old.

### Effects of $\text{PM}_{2.5}$ and its components on type 2 diabetes

Figure 1 and Table S2 show there was a positive association between daily hospital admissions and  $\text{PM}_{2.5}$  and its constituents. The maximum effect value's lag day differed for  $\text{PM}_{2.5}$  and its constituent parts, where  $\text{PM}_{2.5}$  was 1.66% (95% CI: 1.25, 2.08) at lag 06, BC was 1.50% (95% CI: 0.95, 2.06) at lag 05, Cl was 2.50% (95% CI: 1.83, 3.18) at lag 0,  $\text{NH}_4^+$  was 4.63% (95% CI: 3.85, 5.41) at lag 07,  $\text{SO}_4^{2-}$  was 2.66% (95% CI: 2.09, 3.24) at lag 07,  $\text{SO}_4^{2-}$  was 4.63% (95% CI: 3.80, 5.47) at lag 07 and OM was 1.41% (95% CI: 0.88, 1.94) at lag 0. Women were found to have a greater influence of Cl on daily hospital admissions than men, according to gender stratification (Tables S3–S9). Hospital admissions in the age group of  $\leq 45$  were found to be less impacted by  $\text{PM}_{2.5}$  and its constituents, according to age stratification (Tables S10–S16).

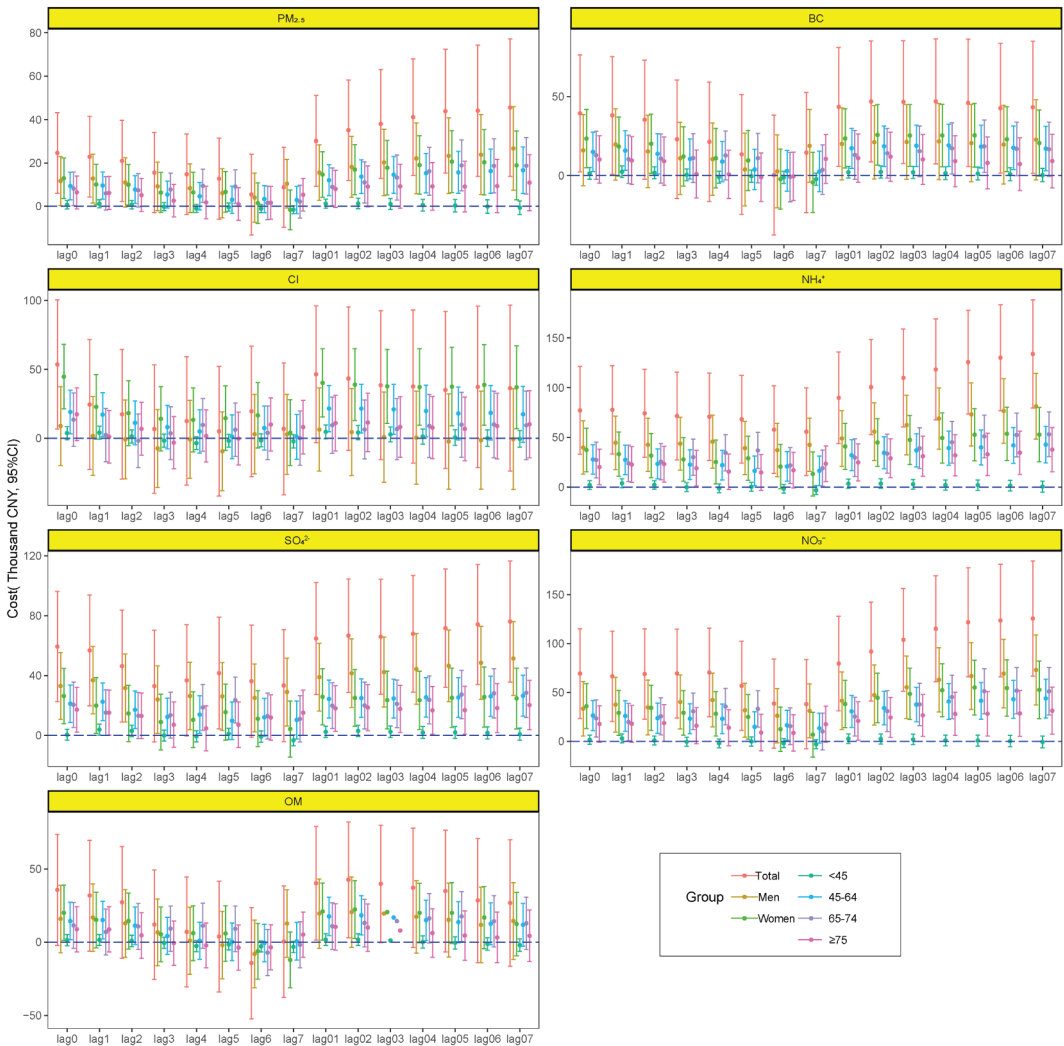


**Figure 2.** Absolute increase in LOS. Note: point estimates and 95% CIs are used to show how the absolute increase in LOS will vary in response to a 10- $\mu\text{g}/\text{m}^3$  rise in PM<sub>2.5</sub> and a per-SD increase in its constituent parts. <45: age less than 45 years old. 45–64: the age range between 45 and 64 years old. 65–74: the age range between 65 and 74 years old. ≥75: age over or equal to 75 years old.

The absolute increase in LOS for PM<sub>2.5</sub> and its constituents that vary in lag days is displayed in Figure 2 and Table S2. The rise for PM<sub>2.5</sub> was 14.42 days (95% CI: 0.46, 28.38) for lag 05, Cl was 30.75 days (95% CI: 7.89, 53.62) at lag 0, NH<sub>4</sub><sup>+</sup> was 45.80 days (95% CI: 19.16, 72.44) at lag 07, SO<sub>4</sub><sup>2-</sup> was 24.41 days (95% CI: 4.62, 44.20) at lag 07 and NO<sub>3</sub><sup>-</sup> was 42.12 days (95% CI: 13.30, 70.94) at lag 07. According to the subgroup analysis, women had a greater significant effect of Cl on LOS than men (Tables S3–S9). For the LOS in the ≤45 age group, PM<sub>2.5</sub> and its constituents had less of an impact (Tables S10–S16).

Figure 3 and Table S2 show an absolute increase in hospital cost for PM<sub>2.5</sub> and its constituents that vary in lag days. For hospital costs in thousands of CNY, the rise for PM<sub>2.5</sub> was 45.51 (95% CI: 13.83, 77.19) at lag 07, BC was 47.00 (95% CI: 7.38, 86.62) at lag 04, Cl was 53.5 (95% CI: 6.53, 100.47) at lag 0, NH<sub>4</sub><sup>+</sup> was 133.83 (95% CI: 79.37, 188.28) at lag 07, SO<sub>4</sub><sup>2-</sup> was 76.08 (95% CI: 35.56, 116.60) at lag 07 and OM was 42.62 (95% CI: 2.96, 82.28) at lag 02. The effect of Cl on hospital costs was more significant in women than in men (Tables S3–S9). Hospital costs in the ≤45 age group were less impacted by PM<sub>2.5</sub> and its constituents (Tables S10–S16).





**Figure 3.** Absolute increase in hospital costs. point estimates and 95% CIs are used to show how the absolute increase in hospital costs will vary in response to a  $10\text{-}\mu\text{g}/\text{m}^3$  rise in  $\text{PM}_{2.5}$  and a per-SD increase in its constituent parts. <45: age less than 45 years old. 45–64: the age range between 45 and 64 years old. 65–74: the age range between 65 and 74 years old.  $\geq 75$ : age over or equal to 75 years old.

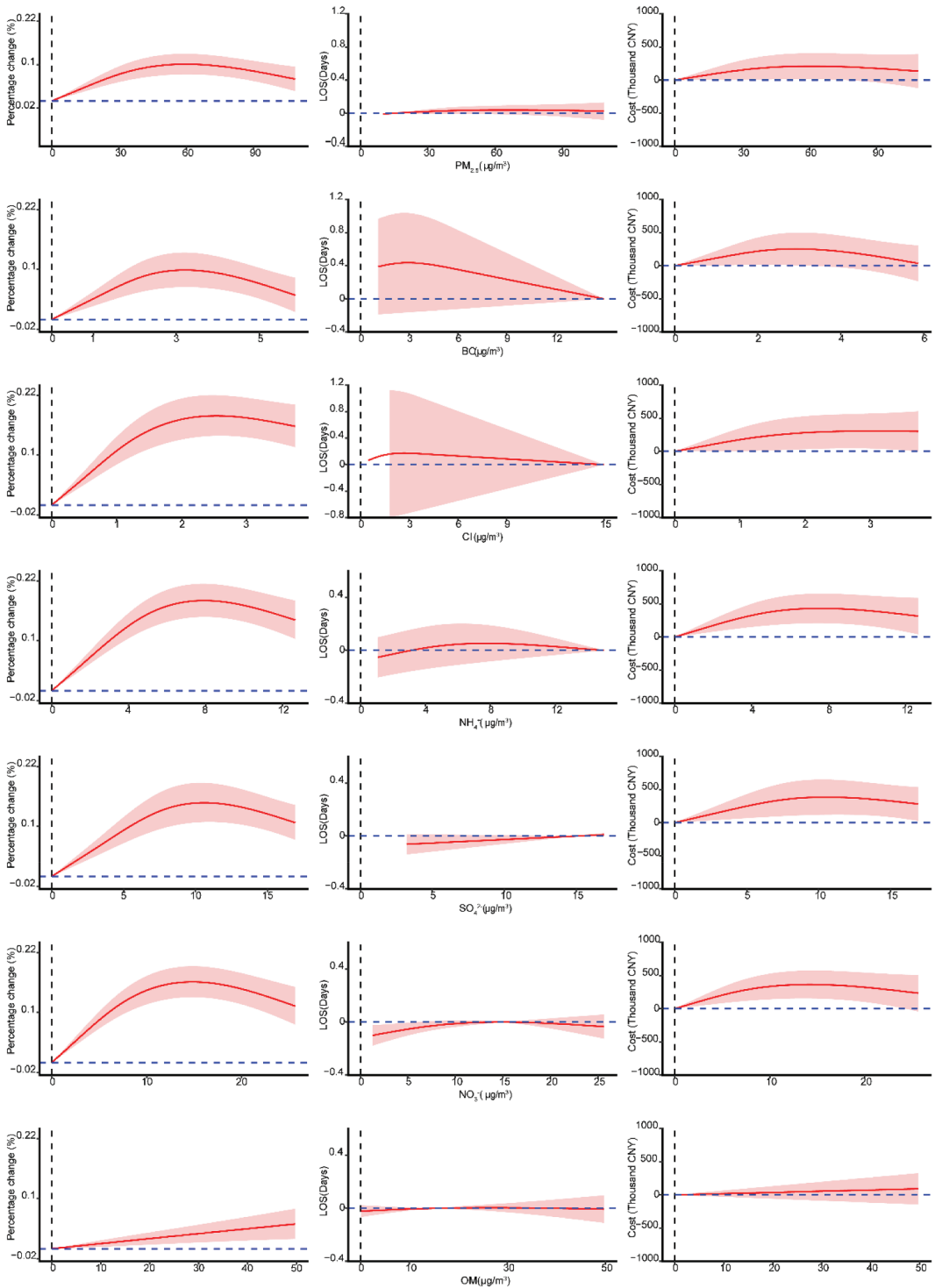
### Effect of varying concentrations of $\text{PM}_{2.5}$ and its constituent parts

At low concentrations, the associations between hospital costs, hospital admissions, and  $\text{PM}_{2.5}$  and its constituent levels were roughly linear ( $\text{PM}_{2.5}$ :  $0\text{--}60\text{ }\mu\text{g}/\text{m}^3$ , BC:  $0\text{--}3.2\text{ }\mu\text{g}/\text{m}^3$ , Cl:  $0\text{--}2.5\text{ }\mu\text{g}/\text{m}^3$ ,  $\text{NH}_4^+$ :  $0\text{--}7.9\text{ }\mu\text{g}/\text{m}^3$ ,  $\text{SO}_4^{2-}$ :  $0\text{--}10.5\text{ }\mu\text{g}/\text{m}^3$ ,  $\text{NO}_3^-$ :  $0\text{--}14.8\text{ }\mu\text{g}/\text{m}^3$ ). However, at higher concentrations, there was a saturation or decline. A linear relationship existed between OM and hospital costs, LOS, and hospital admissions (Figure 4).

### Association between components and type 2 diabetes outcomes

PCA with variance-maximizing rotation identified two main pollution components (Figure S2–S3). Component 1 (Mixed-source particulate pollution) was primarily composed of high loadings of  $\text{PM}_{2.5}$  (0.99), OM (0.92), BC (0.96), Cl (0.82),  $\text{NH}_4^+$  (0.95),  $\text{SO}_4^{2-}$  (0.87),  $\text{NO}_3^-$  (0.95),  $\text{NO}_2$  (0.79),





**Figure 4.** The relationship of different levels of  $PM_{2.5}$  and its components with hospital costs, LOS, and daily hospital admissions. Note: CNY is Chinese Yuan.

CO (0.87), SO<sub>2</sub> (0.75). These pollutants were typically associated with industrial emissions and traffic pollution. Component 2 (photochemistry pollution) was dominated by O<sub>3</sub> (0.97), indicating its close association with photochemical oxidation processes. The association between the two components and hospital admissions, LOS, and hospital costs related to type 2 diabetes suggested that component 1 was significantly correlated with an increase in hospital admissions (0.27%, 95% CI: (0.20, 0.34)), LOS (2.87 days, 95% CI: (0.35, 5.40)), and hospital costs (71.68 thousands of CNY, 95% CI: (19.89, 123.46)). Component 2 was significantly correlated with an increase in hospital admissions (0.59%, 95% CI: (0.06, 1.13)) (Table S23).

### **Sensitivity analysis**

The two-pollutant models gave similar results for the impacts of PM<sub>2.5</sub> and its constituent parts on hospital costs, LOS, and hospital admissions after adjustment for other pollutants (Table S17). The effect estimates were not significantly altered by varying the df for calendar time, relative humidity, and temperature. In addition, considering longer lags of temperature did not meaningfully change the estimated risks for PM<sub>2.5</sub> and its components (Tables S18–S21).

### **Discussion**

Based on data from 18 million diabetic patients in Shanghai, PM<sub>2.5</sub> and its components were positively associated with hospital costs, LOS, and hospital admissions owing to type 2 diabetes. NH<sub>4</sub><sup>+</sup>, SO<sub>4</sub><sup>2-</sup> and NO<sub>3</sub><sup>-</sup> had maximum effects at lag 07. Hospital costs, LOS, and hospital admissions increased approximately linear with OM concentrations at all levels tested and specific concentration ranges of PM<sub>2.5</sub> and other constituents.

While a large number of studies have delved into the connection between PM<sub>2.5</sub> and type 2 diabetes, there is still a scarcity of literature on PM<sub>2.5</sub> constituents and the indicators of the disease burden of type 2 diabetes. The effects of PM components on type 2 diabetes – related hospital admissions have been studied in studies (Sun et al. 2016). One research demonstrated PM<sub>2.5</sub> with elevated levels of SO<sub>4</sub><sup>2-</sup> had a positive association with diabetes hospitalization rates (Zanobetti et al. 2009). Increased NO<sub>3</sub><sup>-</sup> concentrations in PM<sub>10</sub> were also linked to a higher likelihood of emergency hospitalizations for type 2 diabetes, according to another study (Sun et al. 2016). This study found that NH<sub>4</sub><sup>+</sup>, SO<sub>4</sub><sup>2-</sup> and NO<sub>3</sub><sup>-</sup> were associated with hospital costs, LOS, and hospital admissions, which was consistent with the abovementioned studies. In addition, our study found significant cumulative and delayed effects on the onset of type 2 diabetes within the short-term exposure window. While this study focused on short-term exposure, future research could further explore the impact of long-term exposure to better understand the chronic consequences of PM<sub>2.5</sub> exposure.

According to earlier research, younger people were somewhat less affected by PM<sub>2.5</sub> than those over 65 years old (Li et al. 2023). This research also revealed PM<sub>2.5</sub> and its components had a lower impact on hospital costs, LOS, and hospital admissions for people with type 2 diabetes under 45 years old. This is possibly because the elderly people are more susceptible to the adverse consequences of PM<sub>2.5</sub> and its components. Consistent with earlier research (Zanobetti et al. 2009; Tian et al. 2022; Zhou et al. 2022), this research also found that gender was not a statistically significant moderator. There were gender differences in hospital admissions, LOS, and hospital costs due to CI exposure in the PM<sub>2.5</sub> components only.

This research revealed a linear relationship between hospital expenses, LOS, and hospital admissions for PM<sub>2.5</sub> and other constituents (OM excluded). The associations remained stable or decreased at high concentrations. This is consistent with earlier findings (Peng et al. 2022). This could be because at high PM<sub>2.5</sub> concentrations, people tend to stay indoors more or wear protective masks when they do outdoor activities (Christoffersson et al. 1988; Zhou et al. 2023).

The findings from PCA highlighted the significant role of mixed-source particulate pollution in exacerbating type 2 diabetes-related health outcomes, including increased hospital admissions,

longer hospital stays, and higher healthcare costs. This aligns with our previous analysis of individual pollutants, which also emphasized the adverse health impacts of particulate matter. The mixed-source nature of component 1, combining industrial and traffic-related emissions, is consistent with prior studies that have linked similar pollution mixtures to increased emergency department visits (Billionnet et al. 2012). These results underscore the importance of considering pollution as a mixture rather than individual components. The synergistic effects of pollutants from different sources may exacerbate their health impacts, particularly for chronic conditions such as type 2 diabetes. Future research should further explore these associations and the underlying mechanisms.

There are still no clear mechanisms explaining the connection of hospital expenses, LOS, and hospital admissions and PM<sub>2.5</sub> and its constituents. The following are possible underlying mechanisms:

PM<sub>2.5</sub> and its components can lead to the deterioration of hospitalization status of patients with type 2 diabetes, including an increase in the number of hospital admissions and the length of hospital stay, through multiple mechanisms. Specifically, during the *in vivo* metabolic process, they can generate reactive oxygen species (ROS) such as superoxide anion radicals and hydroxyl radicals. These ROS can damage pancreatic islet cells (Eguchi et al. 2021). For example, they can destroy the mitochondrial structure within pancreatic islet cells and affect the electron transport chain, thereby interfering with the energy supply required for insulin synthesis. Meanwhile, they can also act on the relevant regulatory factors in the transcription and translation processes of the insulin gene, ultimately disrupting the function of pancreatic islet cells and exacerbating the condition of patients with type 2 diabetes (Bhatti et al. 2022).

In terms of vascular endothelial cells, PM<sub>2.5</sub> and its components can damage their function. Specifically, it is manifested as a change in the structural integrity of vascular endothelial cells, an increase in the permeability of the vascular wall, and further promotion of thrombus formation. This not only affects the microcirculation, leading to insufficient perfusion of tissues and organs, but also increases the risk of cardiovascular complications in diabetic patients, such as accelerated formation of atherosclerotic plaques, thereby affecting the overall metabolic state of patients, further deteriorating the condition and increasing the demand for hospitalization (Liang et al. 2020).

Exposure to PM<sub>2.5</sub> and its components can also activate inflammatory signaling pathways, prompting the activation of inflammatory cells such as macrophages and neutrophils and the release of inflammatory factors. These inflammatory factors can interfere with key molecules in the insulin signal transduction pathway, exacerbate insulin resistance, and simultaneously promote the occurrence of complications such as atherosclerosis, resulting in increased difficulty in blood glucose control and elevated risk of complications in diabetic patients, thereby increasing the number of hospital admissions and prolonging the length of hospital stay to maintain stable disease conditions (Bhatti et al. 2022).

PM<sub>2.5</sub> exposure can disrupt the balance of the cardiac autonomic nerve, which is specifically manifested as affecting the normal activities of the sympathetic and parasympathetic nerves, resulting in dysregulation of vascular contraction function, increased peripheral vascular resistance, abnormal characteristics of blood pressure fluctuations, and changes in heart rate variability (Basith et al. 2022). Such physiological changes can affect the secretion of hormones related to glucose metabolism, increase the pressure of metabolic control, and increase the risk of hospitalization due to cardiovascular events such as myocardial ischemia and arrhythmia (Wang et al. 2020).

The association of PM<sub>2.5</sub> and its constituents with type 2 diabetes hospital admissions seems to be more about exacerbating existing diabetes conditions rather than inducing new cases of type 2 diabetes. Considering the chronic nature of type 2 diabetes and the relatively short exposure periods examined in this study, it is improbable that PM<sub>2.5</sub> exposure would directly induce diabetes within such a brief timeframe. Instead, PM<sub>2.5</sub> and its constituents are likely to worsen pre-existing conditions, resulting in increased hospital admissions.

To our knowledge, this study was the initial attempt to quantify the association between  $PM_{2.5}$  and its components and hospital admissions, LOS and hospital costs, as well as the burden of type 2 diabetes caused by  $PM_{2.5}$  and its component exposure in Shanghai, China. Nonetheless, this study has certain shortcomings. Initially, the study's data regarding diabetes patients were collected from three different levels of hospitals in Shanghai, which may have introduced some degree of categorization bias. Second, the average concentrations determined from fixed monitoring stations and PM raster data comprised the  $PM_{2.5}$  and its constituents data, rather than the exact data from the patients' residences, which may have measurement errors. Third, the study was an ecological study that was unable to demonstrate a causal link of  $PM_{2.5}$  and its constituents and the incidence of diabetes, and it may be susceptible to ecological fallacy.

Conclusion

According to this research, high levels of  $PM_{2.5}$  and its components were linked to increased hospital admissions, LOS, and hospital costs due to type 2 diabetes. The government should proactively put initiatives in place to lower the concentration of  $PM_{2.5}$  and place greater emphasis on the protection of high-risk groups, especially those who already have diabetes to alleviate the deterioration of the disease and ease the economic burden of  $PM_{2.5}$ -associated diabetes. Considering the limitations of this study, we recommend that a more rigorously designed study would involve considering comorbidities, such as cardiovascular and respiratory-related diagnoses, to better understand the extent to which  $PM_{2.5}$  exacerbates versus induces type 2 diabetes.

Abbreviations

Abbreviations	Full names
CHAP	China High Air Pollutant
BC	Black carbon
CI	Confidence interval
Cl	Chloride
CNY	Chinese yuan
CO	Carbon monoxide
CPI	Consumer Price Index
Df	Degree of freedom
Dow	Day of the week
GAM	A generalized additive model
GBD	Global Burden of Disease Study
ICD-10	International Classification of Diseases, Tenth Revision
$NH_4^+$	Ammonium
$NO_2$	Nitrogen dioxide
$NO_3^-$	Nitrate
$O_3$	Ozone
OM	Organic matter
PC	Percentage change
Ph	Public holidays
Rh	Relative humidity
SD	Standard deviations
SDs	Standard deviations
$SO_2$	Sulfur dioxide
$SO_4^{2-}$	Sulfate radical
Temp	Average temperature

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## Authors' contributions

**Hongyu Liang:** Conceptualization, Data Curation, Software, Formal analysis, Writing – Original Draft. **Wenyong Zhou:** Conceptualization, Data Curation, Software, Formal analysis, Writing – Original Draft. **Zexuan Wen:** Conceptualization, Data Curation, Software, Formal analysis, Writing – Original Draft. **Jing Wei:** Resources. **Weibing Wang:** Conceptualization, Resources, Methodology, Writing – Review & Editing, Project administration, Funding acquisition. **Jun Li:** Conceptualization, Resources, Methodology, Writing – Review & Editing, Project administration. All authors read and approved the final manuscript.

## Availability of data and materials

The source data and R code of this study can be available on request.

## Consent for publication

All authors have approved the manuscript for submission.

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