Letter

Short-term Effects of Fine Particulate Matter and its Constituents on Acute Exacerbations of Chronic Bronchitis: A Time-stratified Case-crossover Study

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Chronic bronchitis (CB), characterized by persistent coughing with mucus production for at least three consecutive months in two successive years and caused by multiple factors[1], is a progressive condition. Acute exacerbation of chronic bronchitis (AECB), marked by recurrent episodes of bronchial inflammation, have been linked to various adverse health outcomes[2]. Environmental $PM_{2.5}$ results from complex interactions among multiple emissions and chemical compositions. It comprises a complex mixture of chemical components, including black carbon (BC), nitrate (NO_3^-), sulfate (SO_4^{2-}), ammonium (NH_4^+), and organic matter (OM)[3]. While several epidemiological studies have explored the link between long-term exposure to ambient air pollutants and CB[4,5], no studies have focused on the relationship between $PM_{2.5}$, its constituents, and acute exacerbation of CB. In addition, the specific populations and seasons most susceptible to the effects of $PM_{2.5}$ and its constituents remain unclear. Therefore, this study aimed to (1) evaluate the association of short-term exposure to $PM_{2.5}$ and its constituents and the risk of AECB, and (2) identify seasons and populations that are more susceptible to the adverse effects of $PM_{2.5}$ and its constituents.

Shanghai, a densely populated first-tier city in the Yangtze River Delta region, belongs to the north subtropical monsoon climate zone. Considering its demographics, location, and urban development, it is an ideal setting to study the interactions between $PM_{2.5}$, its constituents, and AECB. A total of 269,101 case records were obtained from the Jinshan District Community Health Service Center and Shanghai Hospital System. Patients diagnosed with the International Classification of Diseases, 10th edition [ICD-10]: J44.1, from October 2018 to December 2022, with a total of 2,202 AECB cases, were included in the study. Among these, 1,815 cases were hospitalized before the COVID-19 pandemic, while 387 patients were hospitalized during the pandemic. Basic demographic details of these patients, including sex, age, date of hospitalization, and specified disease codes were extracted. The geographic distribution of AECB cases is shown in Supplementary Figure S1.

$PM_{2.5}$ and its constituents were obtained as follows: case records provided detailed residential addresses, which were aggregated at the natural village and community level. These addresses were geocoded using Baidu Maps API to generate precise latitudinal and longitudinal coordinates. During the study period, $PM_{2.5}$ and its constituent data with a spatial resolution of 10 km were obtained from the Tracking Air Pollution in China (TAP) dataset (https://tapdata.org.cn/)[6]. TAP uses multiscale air quality (CMAQ) simulations of operating communities. To correct the simulation deviation of the CMAQ model, the dust emission simulation module was first improved, and then a model was built based on the observed $PM_{2.5}$, and the extreme gradient boost (XGBoost) algorithm was used to adjust the relative contribution of the simulated $PM_{2.5}$, to obtain a more accurate conversion factor for $PM_{2.5}$ constituents. This allowed the acquisition of concentration data of $PM_{2.5}$ constituents[7]. The $PM_{2.5}$ constituent data released by TAP included BC, NO_3^-, SO_4^{2-}, NH_4^+ and OM. The resulting exposure data can be viewed as individual horizontal exposure data, based on precise geographic matching.

In this study, we employed a time-stratified case-crossover design to investigate the acute effects of exposure to $PM_{2.5}$ and its constituents, on AECB. This

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methodology incorporated temporal strata, such as years and months, into its framework. Each AECB case served as its own control by comparing exposures during the reference periods preceding and following the event day (case day). Specifically, for each individual AECB episode, the environmental exposure to $PM_{2.5}$ and its constituents on the actual event date was contrasted with that of three or four corresponding matched days (control days) within the same geographic location, identical year, month, and day of the week (DOW). This design effectively mitigated for seasonal fluctuations, long-term trends, DOW effects, spatial variations, and personal-level confounding factors that remain constant over time, including age, sex, behavior, and metabolic factors[8].

The Spearman correlation coefficient (r_s) was used to determine the correlation between $PM_{2.5}$ and its constituents. Conditional logistic regression (CLR) model was utilized to estimate this association between short-term exposure to $PM_{2.5}$, its constituents, and AECB. Various lag structures were assessed, including single-day lags (0-day to 7-day) and moving-average lags (1-day to 7-day). Lag-0 represented pollutant concentrations on the same day, while lag-1 represented the moving average concentration from the present day to the previous day, with subsequent lag periods following suite. The lag period producing the maximum impact estimate was selected for further analysis. The resulting effect estimates provided the odds ratios (*ORs*) and their corresponding 95% confidence intervals (*CIs*) for each increase of 10 μg/m³ in $PM_{2.5}$ and its constituents. A restricted cubic spline (RCS) model was used to fit the relationship of $PM_{2.5}$ and its constituents, with the AECB concentration-response[9]. Subgroup analyses stratified the data by sex (men and women) and age (< 80 years *vs.* ≥80 years) to identify potentially susceptible populations. To examine seasonal variations, the study period was divided into two seasonal categories: warm (April–September) and cold (October–March). To ensure the robustness of the findings, multiple sensitivity analyses were conducted by altering specific parameter configurations within the modeling framework. Based on the original model, gaseous pollutants such as O_3 were added to test the two-pollutant model. In addition, we used other high-resolution $PM_{2.5}$-datasets to fit the high-resolution component data to test the robustness of our results. At the same time, the exposure concentration of $PM_{2.5}$, was obtained using a previous formula[10]. Given that the study period included the COVID-19 pandemic, the population after December 2019 was excluded from the analysis to test the stability and reliability of the results.

All statistical analyses were conducted using R software (version 4.3.2, R Foundation for Statistical Computing, Vienna, Austria). The “ggcorrplot” package was employed to conduct Spearman’s correlation analysis, while the “survival” package was used to implement conditional logistic regression modeling. Additionally, the “splines” package was utilized for NCS smoothing. In this study, a bilateral test *P*-value < 0.05 was considered statistically significant.

As shown in Table 1, the study included 2,202 cases of AECB from the Jinshan District in Shanghai, China, between October 2018 and December 2022. Included cases were aged from 42 to 102 years [mean ± SD (standard deviation): 78.47 ± 8.53 years]. Among these cases, 1,348 were men (constituting 61.22% of the total), and more than half (62.85%) of AECB cases occurred in colder months.

Supplementary Table S1 summarizes the distribution of ambient $PM_{2.5}$ and its constituents on case and control days. The mean daily concentrations of $PM_{2.5}$ were recorded as 34.52 μg/m³ on case days, and 34.53 μg/m³ on control days. Among the five constituents analyzed, their collective contribution to the total $PM_{2.5}$, was 87.02%, with individual constituent contributions ranging from 4.08% to 23.70%. The average daily concentrations of $PM_{2.5}$ constituents, including BC, NO_3^-, SO_4^{2-}, NH_4^+, and OM, were found to be 1.41, 8.18, 6.66, 5.33, and 7.46 μg/m³, respectively (Supplementary Table S2). Supplementary Figure S2 presents a heat map of Spearman’s correlation showing the relationship between $PM_{2.5}$ and its constituents. The figure shows a moderate-to-high correlation between $PM_{2.5}$ and its five constituents (r_s > 0.6).

The *OR* values for AECB incidence at different lag days are estimated in Figure 1, and they correspond to each increment of 10 μg/m^3; in $PM_{2.5}$ and its constituents’ exposure. $PM_{2.5}$ constituents were found to exert detrimental effects on AECB. The relative risks associated with $PM_{2.5}$ and its constituents, showed a roughly similar lagged structure, with risks peaking on the 5th day of lagged exposure. This study selected the lag 5th day as the main lag for further analyses The CLR model estimates revealed that a single-day lagged exposure on the 5th day to $PM_{2.5}$ and its constituents (BC, NO_3^-, SO_4^{2-}, NH_4^+, OM) were linked with an increased incidence of AECB, as indicated by elevated odds ratios (*ORs*) values of 1.033 (95% *CI*: 1.010–1.055), 1.862 (1.038–3.342), 1.129 (1.049–1.216), 1.145 (1.021–1.284), 1.190 (1.051–1.346) and 1.105 (1.009–1.209), respectively, for every 10 μg/m^3; increase in exposure. The detailed risk estimates for different lag periods can be found in the supplementary material, specifical Supplementary Table S3. Supplementary Table S4 shows that after excluding the COVID-19 population, the *OR* value of $PM_{2.5}$ and its components on the risk of AECB reached a maximum on the 7th day lag, and the *OR* and 95% *CI* were 1.035 (1.009, 1.061), 2.227 (1.116, 4.444), 1.150 (1.054, 1.255), 1.120 (0.981, 1.279), 1.236 (1.071, 1.427), and 1.183 (1.066, 1.312).

The C-R curves indicating the connection between the fifth day of exposure to $PM_{2.5}$, its constituents, and the incidence of AECB are shown in Figure 2. There was an increasing trend in the exposure risks linked to $PM_{2.5}$, NO_3^-, and NH_4^+. However, no significant exposure risks were observed for BC, SO_4^{2-}, or OM. All *P*-values > 0.05,

Table 1. Summary statistics and characteristics of AECB cases

Characteristic	Number	Percentage (%)
AECB (ICD-10 code: J44.1)	2,202	100
Case days	2,202	–
Control days	7,381	–
Sex		
Men	1,348	61.22
Women	854	38.78
Age of onset (years, mean ± SD)	78.47 ± 8.53	–
< 80 years	1,057	48.00
≥ 80 years	1,145	52.00
Season at happen		
Cold (January to March, October to December)	1,384	62.85
Warm (April to September)	818	37.15

Note. Number is frequency, or mean ± SD, or n (%). ICD-10, International Classification of Diseases–Tenth Revision; AECB, acute exacerbation of chronic bronchitis.

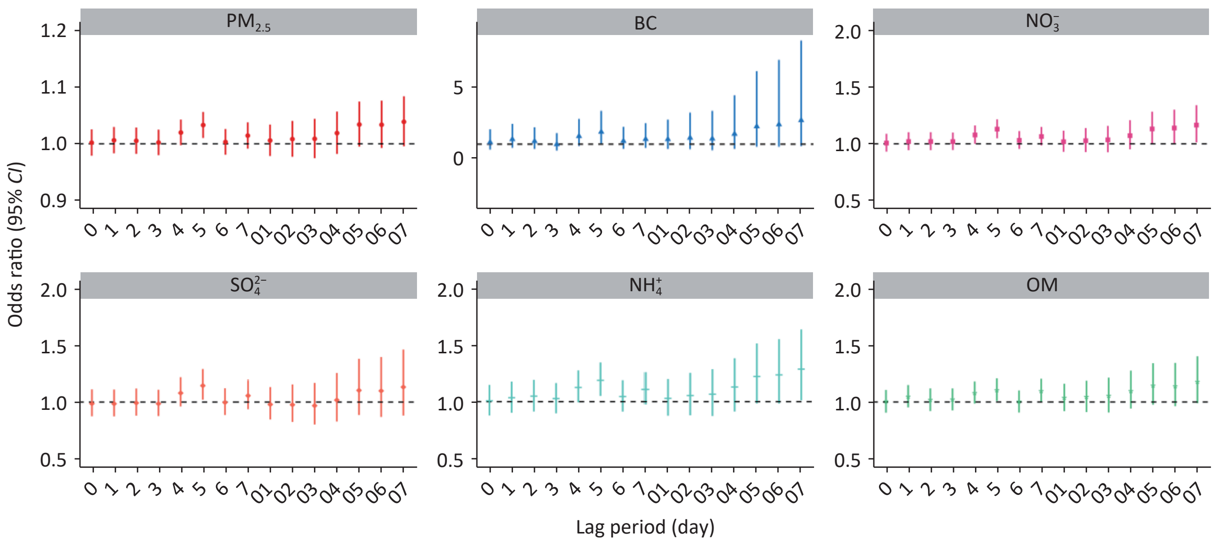

Figure 1. Odds ratios (with 95% *CIs*) for the increased incidence of acute exacerbation of chronic bronchitis associated with a 10 μg/m³ increment increase in $PM_{2.5}$ and its constituents at various lag days.

which corroborated this conclusion, showed that there was no significant deviation from linearity in the correlations between these constituents and the prevalence of AECB when examined using nonlinear likelihood ratio tests.

Based on single-day lagged exposure on the fifth day, Supplementary Table S5 shows the stratified analysis estimates of the connection between $PM_{2.5}$, its constituents, and AECB. Men were found to have slightly higher illness occurrence risks in the sex-stratified analysis, but there were no statistically significant differences in susceptibility to sex modification (with interaction effects of *P*.int > 0.05). With respect to age, individuals aged ≥ 80 years demonstrated a higher risk of BC exposure, whereas those < 80 years of age showed a heightened risk of NH_4^+ exposure. Further contrast across different seasons revealed that $PM_{2.5}$ and its constituents exerted a greater influence on AECB during colder periods. No significant differences were observed between subgroups.

A sensitivity analysis verified the robustness of the main findings. Results using the dual-pollutant model showed little change in *OR* estimates compared to the main model refer to Supplementary Table S6. Similar results were obtained with the high-resolution exposure assessment datasets, as detailed in Supplementary Figures S3 and S4.

This study has some limitations. First, the data were sourced from the Jinshan District Health Service Medical Center in Shanghai, China, which implies that the findings may not be universally applicable to other regions with distinct meteorological and geographical attributes. Second, as smoking status and indoor air pollutant data were not accessible, we could not adjust for these potential confounders. Instead, we relied on a time-stratified case crossover design, assuming that these conditions remained relatively constant throughout the study period. Third, the high inter-correlation among individual fine particulate matter constituents (r_s: 0.62–0.98) constrained our capacity to construct multi-pollutant models that accurately determined the individual contribution of each constituent to the incidence of acute episodes of chronic bronchitis. In addition, because $PM_{2.5}$ and its constituents with a spatial resolution of 10 km, may lack the accuracy required for research at the level of natural villages and communities, higher-resolution data of $PM_{2.5}$ and its components are needed for further research. Finally, owing to the limited sample size, there is a possibility of error, and the sampled data may not fully represent the overall population characteristics.

In summary, short-term exposure to $PM_{2.5}$ and its constituents was associated with an increased AECB incidence. Men exhibited greater susceptibility to $PM_{2.5}$ and its constituents. Research has demonstrated that during colder seasons, patients are more susceptible to the detrimental effects of fine particulate matter constituents. This study presents novel evidence on the immediate adverse health impacts resulting from exposure to $PM_{2.5}$ and its constituents in relation to AECB occurrences.

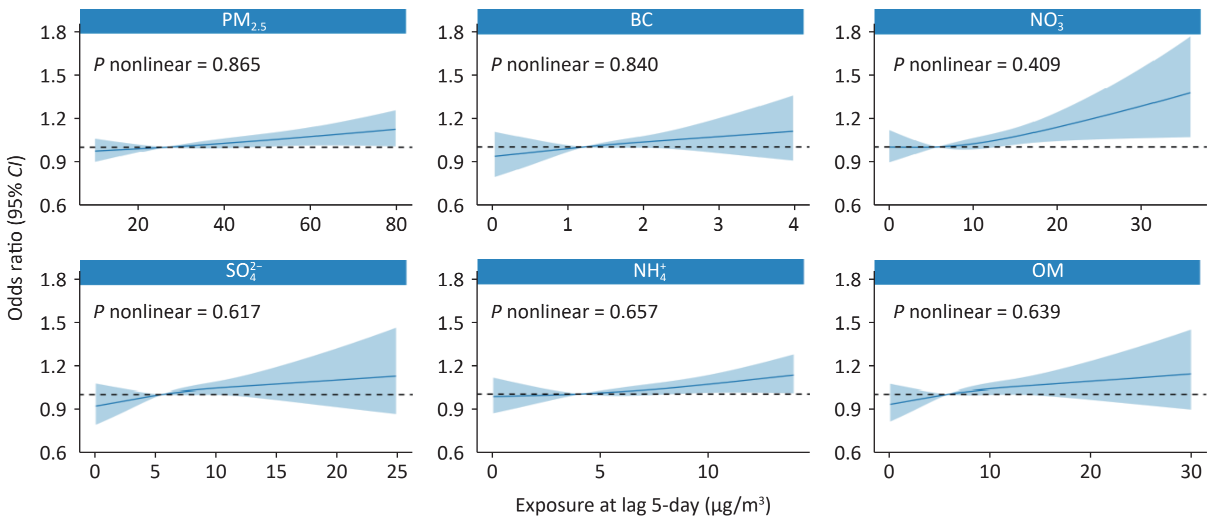

Figure 2. Concentration-response curves $PM_{2.5}$ and its constituents associated with acute exacerbation of chronic bronchitis. *P* nonlinear: Likelihood ratio tests for non-linearity with the null hypothesis that there was no difference between the linear assumption and NSC smoothing function. NSC: natural spline cubic.

These findings underscore the importance of implementing rigorous emission reduction strategies and sustainable environmental management practices in regions with elevated air pollution levels, particularly $PM_{2.5}$.

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