Received: 9 July 2024 | Accepted: 19 November 2024

DOI: 10.1111/resp.14864

ORIGINAL ARTICLE

Official Journal of the Asian Pacific Society of Respirology Respirology APSR WILEY

Association of short-term exposure to PM_1 with hospital admission from total and cause-specific respiratory diseases

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Funding information
Guangzhou Municipal Health Commission, Grant/Award Number: 20191A010054

Associate Editor: Alexander N. Larcombe; **Senior Editor:** Paul King

Abstract

Background and Objective: Evidence of short-term exposure to particulate matter with an aerodynamic diameter ≤1 μm (PM_1) on hospital admission for respiratory diseases (RDs) is limited. We aimed to estimate the associated risk of PM_1 on hospital admissions for RDs.

Methods: In this time-stratified case-crossover study, we assigned cases who had been admitted to hospital for RDs in Guangdong, China between 2016 and 2019. Exposure to PM_1 was assigned on the basis of the patient's residence for each case day and its control days. Conditional logistic regression models and distributed lag nonlinear models were used to quantify the association of PM_1 exposure with hospital admission for RDs at lag 0–1 days.

Results: A total of 408, 658 hospital admissions for total RDs were recorded in the study period. Each 10 μg/m^3 increase in PM_1 was significantly associated with a 1.39% (95% confidence interval [CI]: 0.87%–1.91%), 1.97% (95% CI: 1.06%–2.87%) and 1.69% (95% CI: 0.67%–2.71%) increase in odds of hospital admissions for total RDs, chronic obstructive pulmonary disease (COPD) and pneumonia. The excess fraction of hospital admission for total RDs attributable to PM_1 exposure was 6.03%, while 6.59% for COPD and 7.48% for pneumonia. Besides, higher excess fractions were more pronounced for hospital admission of total RDs in older patients (>75 years).

Conclusion: Our results support that PM_1 is associated with increased risks of hospital admissions for RDs. It emphasizes the needs to pay attention to the effects of PM_1 on respiratory health, especially among elderly patients.

KEYWORDS
air pollution, case-crossover study, distributed lag nonlinear models, hospital admission, PM_1, respiratory disease

INTRODUCTION

Numerous epidemiological studies have shown that fine particles ($PM_{2.5}$) exposure is closely related to a variety of RDs such as COPD,[1–3] pneumonia,[4,5] and asthma.[6,7] Smaller sized particulate matters like PM_1 is considered to be more toxic than $PM_{2.5}$ due to its capability to carry more toxic carcinogens and deposit deeper in the lung.[8–12] Although accumulating experimental studies have demonstrated the respiratory toxicity of PM_1 by activating inflammatory responses and oxidative stress,[13–15] the epidemiological evidence is limited.

To date, only a limited number of studies in Shenzhen, China and Vietnam, specifically reported the positive links between PM_1 exposure and increased hospitalizations for total RDs, while the effect estimates were inconsistent.[16–18] These inconsistent findings might be due to differences in age and the categories of diseases among study participants. Additionally, the aforementioned studies used data from single monitoring stations or station-based measurements rather than individual exposures, potentially resulting in imprecise and incomparable estimates. Furthermore, it is still unknown whether PM_1 exposure is associated with an

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elevated risk of hospital admission for specific types of RDs such as acute exacerbation of chronic obstructive pulmonary disease (AECOPD), bacterial pneumonia, emphysema and chronic bronchitis, which is very important for early prevention, and standardized treatment of related sensitive population of specific RDs. In addition, all the above studies obtained data on PM_1 exposures from monitoring stations, which are crude for exposure assessment. In 2019, we developed an open-access dataset called ChinaHighAirPollutants (CHAP) using combination of artificial intelligence models with ground-based measurements, satellite remote sensing, model simulations and atmospheric reanalysis.[19] This high spatial resolution dataset provides more accurate estimates of daily levels PM_1 in China.

Inhalation is the main route of ambient particulate matter entering the human body. Compared to external exposure, respiratory tract deposition dose represents the actual exposure level and therefore recommended to be considered when estimating the adverse effect of particles on respiratory health.[20] Current studies have supported the internal dose of exposures depends on the size distributions and population characteristics, including gender and age.[21,22] However, few studies have estimated the deposition of PM_1 in human airways and further assessed the associated risk of hospital admission for respiratory diseases.[21,22]

To fill the gap, we applied high-resolution grid air pollution dataset (CHAP), combined with multiple-path particle dosimetry (MPPD) model to assess the deposited PM_1. Besides, we conducted a large case-crossover study in Guangdong province to evaluate the risk of total and cause-specific respiratory hospitalizations attributable to PM_1, and to estimate the corresponding excess hospital admissions. Stratified analysis was further performed to explore the impact in hospitalization between age, gender and seasons.

SUMMARY AT A GLANCE

This study assessed the impact of PM_1 exposure on hospital admissions for respiratory diseases (RDs) in Guangdong, China. An increase in PM_1 was significantly associated with higher hospital admissions for RDs, especially among older patients, highlighting the need to focus on the effects of PM_1 on respiratory health.

METHODS

Study population

Based on the data from the Guangzhou Health Technology Identification and Human Resources Assessment Center, we included 408,658 patients who lived in Guangdong province, China and were admitted for RDs between 1 January 2016, and 31 December 2019. Besides, we extracted information including the date of admission, date of birth, gender, race and residential address of each patient from the database. The study was approved by the Ethics Committee of Sun Yat-sen University and informed consent was waived (ID: 2020–61).

Outcomes

The study outcome was hospital admissions for total RDs (International Statistical Classification of Diseases and Related Health Problems 10th Revision [ICD-10] codes: J00-J99) and 7 main types of RDs including asthma (ICD-10 codes: J45-J46), COPD (ICD-10 codes: J41-J44), acute exacerbation of chronic obstructive pulmonary disease (AECOPD) (ICD-10 codes: J44.0-J44.1), chronic bronchitis (ICD-10 codes: J41-J42), emphysema (ICD-10 codes: J43), pneumonia (ICD-10 codes: J12-J18) and bacterial pneumonia (ICD-10 codes: J15).

Study design

We adopted a time-stratified case-crossover study, which is widely applied to evaluate the acute effect of ambient pollution on health.[23,24] For each patient admitted to hospital, the admission date was defined as the case day, and the corresponding control days were the days on the same day, month and year as the case day. According to the approach, each case day could match for 3 or 4 control days.[24] For instance, if a case was admitted to the hospital on September 8, 2023 (Friday), the September 1, 2023 was the case day and other Fridays in September 2023 (i.e., September 15, 22 and 29) were the corresponding control days. As individual-level covariates were less likely to alter during case and corresponding control days, we did not consider them as confounders in our analysis.[25]

Exposure assessment

Daily ambient PM_1 data used in the study was obtained from the CHAP dataset (spatial resolution: 10 km × 10 km).[19,26,27] This dataset was produced by artificial intelligence model combination with ground-based measurements, satellite remote sensing, model simulations and atmospheric reanalysis of the big data, which had a full spatiotemporal coverage in China during 2015–2020 and good agreement with measured air pollutant concentrations in China. The cross-validated coefficient of determination (R^2) was 0.82 for PM_1. Based on the address for each patient, the daily 24-h average concentrations of PM_1 on the case and control days were extracted from the CHAP dataset.

The deposited fraction of PM_1 was further calculated by MPPD model based on Wang et al.[22] Briefly, PM deposits in different regions of the respiratory system, including the head (mouth cavity and nasopharyngeal

passages), tracheobronchial and pulmonary regions. The deposited fractions in each lung region, along with physiological parameters such as age and sex, significantly impact the calculation of deposition amounts and can be effectively used to predict PM deposition in the human respiratory system.[8,22,28,29] In this study, we defined deposited PM_1 as the sum of PM_1 concentrations in the tracheobronchial and pulmonary regions, excluding the head region. This is because PM_1 particles are less likely to deposit in the head region due to their small size and are typically cleared by breathing and coughing.[30] Therefore, to better capture the particles that are likely to remain and potentially cause health effects, we focused on the TB and pulmonary regions where PM_1 are more likely to deposit and persist. Because the study population was mostly elderly, we only considered notable differences in PM_1 deposition by gender. Therefore, we calculated the corresponding doses of PM_1 deposited in the different groups using the following equation:

$$\text{Male: Deposited } PM_1\left(\mu g/m^3\right) = PM_1 \times 11.57\% \quad (1)$$

$$\text{Female: Deposited } PM_1\left(\mu g/m^3\right) = PM_1 \times 12.83\% \quad (2)$$

Equations (1) and (2) represent the estimated amount of PM_1 deposited in the respiratory tract for males and females, respectively. The coefficients of 11.57% and 12.83% represent the deposition factors for males and females, which were derived based on physiological differences in lung structure and respiratory patterns between the gender.

Covariates

Daily concentrations of multiple gaseous pollutants, including sulfur dioxide (SO_2) (CV-$R^2 = 0.84$), nitrogen dioxide (NO_2) (CV-$R^2 = 0.84$), carbon monoxide (CO) (CV-$R^2 = 0.80$) and ozone (O_3) (CV-$R^2 = 0.87$), were collected from the CHAP dataset. Meteorological variables, included 24-h average temperature (°C) and relative humidity (%) were gained from China Meteorological Administration Land Data Assimilation System (CLDAS), with spatial resolution of 0.0625° × 0.0625° and temporal resolution of 1 day. The above covariates were extracted separately for case and control days according to the residential addresses of each case.

Statistical analysis

Exposure-response analysis

Spearman's correlation coefficient was used to evaluate the correlation between air pollutants. We applied conditional logistic regression model and distributed lag models (DLMs) to investigate short-term effect of PM_1 including ambient PM_1 and deposited PM_1 on total and cause-specific RDs hospitalizations. Percent change in odds ($[\text{odds ratio} - 1] \times 100\%$) of hospital admissions and their 95% confidence interval associated with per 10 $\mu g/m^3$ increase in ambient/deposited PM_1 on the day of hospitalization and within 1 day before hospitalization.[31] We separately included ambient PM_1 and deposited PM_1 as continuous variables, and adjusted for temperature and humidity terms to assess exposure-response curves using natural spline functions with 6 degrees of freedom (*df*) and 3*df*, respectively.[32] The cross-basis function for PM_1 exposure, established using DLM, consists of a linear function of the space of PM_1 exposure and the space of 2 d lag.[33] Besides that, distributed lag nonlinear models (DLNMs) were further applied. A likelihood ratio test was used to analyse the nonlinearity of their association. The lowest level of PM_1 concentration was used as a reference when assessing the association between PM_1 and hospitalizations for RDs.

TABLE 1 Baseline characteristics of the study population, 2016–2019.

Characteristics	Value
Case days, no.	408,658
Control days, no.	1387,734
Cause-specific, no. (%)	
Pneumonia (J12-J18)	121,979 (29.8)
Bacterial pneumonia (J15)	40,729 (10.0)
COPD (J41-J44)	130,266 (31.9)
Chronic bronchitis (J41-J42)	12,614 (3.1)
Emphysema (J43)	1063 (0.3)
AECOPD (J44.0-J44.1)	102,497 (25.1)
Asthma (J45-J46)	8628 (2.1)
Other respiratory diseases	147,785 (36.2)
Gender, no. (%)	
Male	247,517 (60.6)
Female	161,141 (39.4)
Age, year	
Mean (SD)	76.4 (9.33)
≤75 years (no. [%])	184,084 (45.0)
>75 years (no. [%])	224,574 (55.0)
Race, no. (%)	
Han	406,718 (99.5)
Other	994 (0.2)
Unknown	946 (0.2)
Season, no. (%)	
Warm	191,471 (46.8)
Cool	217,187 (53.2)

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary diseases.

Excess hospital admission

We further assessed excess hospital admission by estimating excess fraction and number of excess hospital admission. Based on a previously proposed method,[34,35] excess fraction was calculated using the following equation:

$$\text{Excess fraction}_{x,t} = 1 - e^{\left(-\sum_{l=l_0}^{L}\beta_{x_{t-l},l}\right)}$$

$$\text{Number of excess hospital admission}_{x,t} = N_t \times \text{excess fraction}_{x,t}$$

In above equation, $\sum\beta_{x_t,l}$ corresponds to the logarithm of the cumulative odds ratio of pollutant exposure in DLMs or DLNMs at time t; N_t is the number of hospital admission for RDs at time t. The excess $\text{fraction}_{x,t}$ and number of excess hospital $\text{admission}_{x,t}$ on behalf of the amount of time during time t-l_0, ⋯, t-L that can be attributed to exposure to pollutant, compared to the reference level of exposure to pollutant, that is, the minimum pollutant exposure level. The empirical confidence intervals (eCIs) were calculated for estimated excess fraction and number of excess hospital admission by Monte Carlo simulation.

Stratified analysis

Gender (male, female), age (≤75 years old, 75 years old), season (Cool season, October to March of next year; Warm season, April–September) were conducted for subgroup analyses, to investigate possible susceptible modification.

Sensitivity analysis

To evaluate the robustness of this finding, we fitted single- and multi-pollutant model to control for co-exposure to air pollutants (NO_2, SO_2, CO and O_3). Principal component analysis (PCA) was used for dimensionality reduction, and several correlated pollutants were transformed into a set of linearly uncorrelated mixed variables, called principal components. Principal components (PC) choosed by Kaiser's eigenvalue greater than 1.0 rule and Cattell's Scree test[36] were selected as covariate for the multi-pollutant models, and likelihood ratio test was used to examine the heterogeneity between the single- and multi-pollutant. In this study, all analyses were performed using R version 4.1.1. All p-values were two-sided, and a p-value <0.05 was considered as statistically significant.

TABLE 2 Distribution of exposure to ambient air pollutants and meteorological conditions on case days and control days.

			Percentile				
	Mean	SD	5th	25th	50th	75th	95th
On case days (n = 408,658)							
Air pollutant							
PM_1, μg/m^3	22.2	11.9	7.9	13.6	19.3	28.1	45.3
Deposited PM_1, μg/m^3	2.7	1.5	0.9	1.6	2.3	3.4	5.5
CO, mg/m^3	0.89	0.22	0.61	0.74	0.85	0.99	1.33
SO_2, μg/m^3	10.7	4.0	6.0	7.8	9.9	12.7	18.5
NO_2, μg/m^3	46.9	21.5	20.6	32.4	42.9	56.1	87.1
O_3, μg/m^3	93.1	50.6	20.0	55.0	88.0	124.1	185.1
Meteorological condition							
Temperature, °C	23.2	6.0	12.5	18.9	24.0	28.3	31.1
Relative humidity, %	76.0	13.9	48.4	68.5	79.1	86.7	92.7
On control days (n = 1,387,734)							
Air pollutant							
PM_1, μg/m^3	22.0	11.8	7.8	13.5	19.1	27.9	44.9
Deposited PM_1, μg/m^3	2.7	1.4	0.9	1.6	2.3	3.4	5.4
CO, mg/m^3	0.89	0.22	0.61	0.74	0.85	0.99	1.32
SO_2, μg/m^3	10.7	4.0	5.9	7.7	9.9	12.6	18.4
NO_2, μg/m^3	46.3	21.1	20.4	32.1	42.5	55.3	85.7
O_3, μg/m^3	93.1	50.4	19.7	55.1	87.9	123.8	184.4
Meteorological condition							
Temperature, °C	23.2	6.1	12.3	18.8	24.1	28.3	31.2
Relative humidity, %	76.1	13.7	49.0	68.5	79.0	86.7	92.7

Abbreviations: CO, carbon monoxide; NO_2, nitrogen dioxide; O_3, ozone; PM_1, particulate matter with aerodynamic diameter ≤1 μm; SO_2, sulfur dioxide.

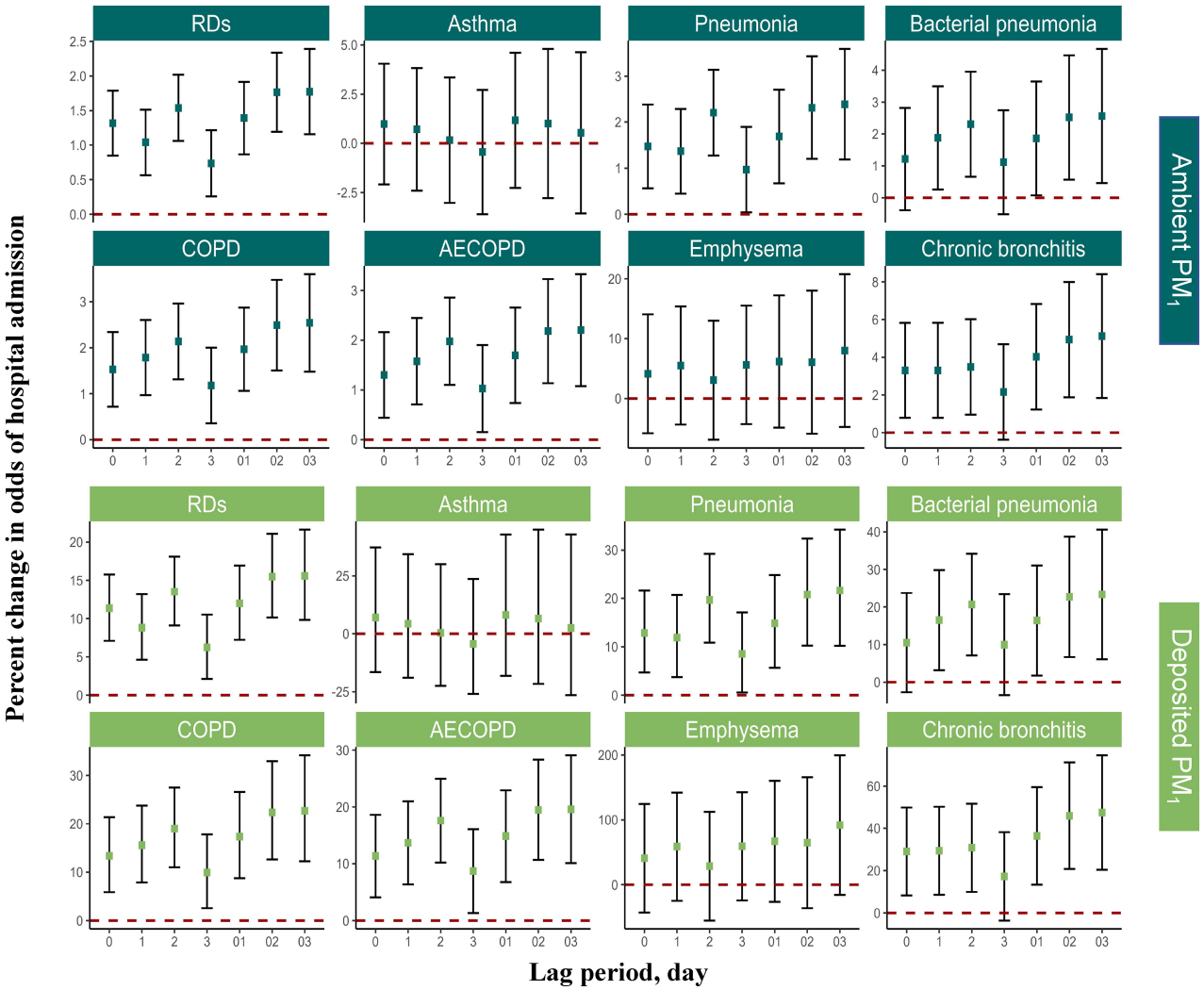

FIGURE 1 Percent change in odds of hospital admission associated with each 10 μg/m^3 increase of exposure to ambient/deposited PM_1 in different lag days. AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary diseases; PM_1, particulate matter with aerodynamic diameter ≤1 μm.

RESULTS

Descriptive outcomes

We collected a total of 408,658 hospitalized records for total RDs from 1 January 2016, to 31 December 2019, including 130,266 COPD (31.8%), 121,979 pneumonia (29.8%), 8628 asthma cases (2.1%) and other respiratory disease cases (36.3%). Over half of the patients were male (60.6%), 45.2% were aged ≤75 years and 46.8% of admissions were in warm season (Table 1). The distribution of air pollutants and meteorological conditions in case and control days are shown in Table 2. The mean concentrations of PM_1, deposited PM_1, CO, SO_2, NO_2 and O_3 on the case day were 22.2 μg/m^3, 2.7 μg/m^3, 0.89 mg/m^3, 10.7 μg/m^3, 46.9 μg/m^3 and 93.1 μg/m,^{3} respectively, which was similar to those in control days. PM_1 was strongly correlated with deposited PM_1 ($r = 0.99$), while moderately correlated with SO_2, NO_2 and CO ($r = 0.58$, 0.53 and 0.51, respectively; all p-values <0.001; shown in Figure S1 in the Supporting Information).

Exposure-response analysis

Each 10 μg/m^3 increase of ambient PM_1 was significantly associated with 1.39% (95% CI: 0.87%–1.91%), 1.69% (0.67%–2.71%), 1.97% (1.06%–2.87%), 1.90% (0.88%–2.92%), 1.86% (0.08%–3.64%) and 4.02% (1.22%–6.82%) in total RDs, pneumonia, COPD, AECOPD, bacterial pneumonia and chronic bronchitis at lag 01 days, respectively. No significant associations were observed between PM_1 and hospital admission on asthma and emphysema with any different lag days. We also observed that deposited PM_1 had similar short-term effects as did ambient PM_1 (Figure 1). J-shaped associations were observed between ambient PM_1

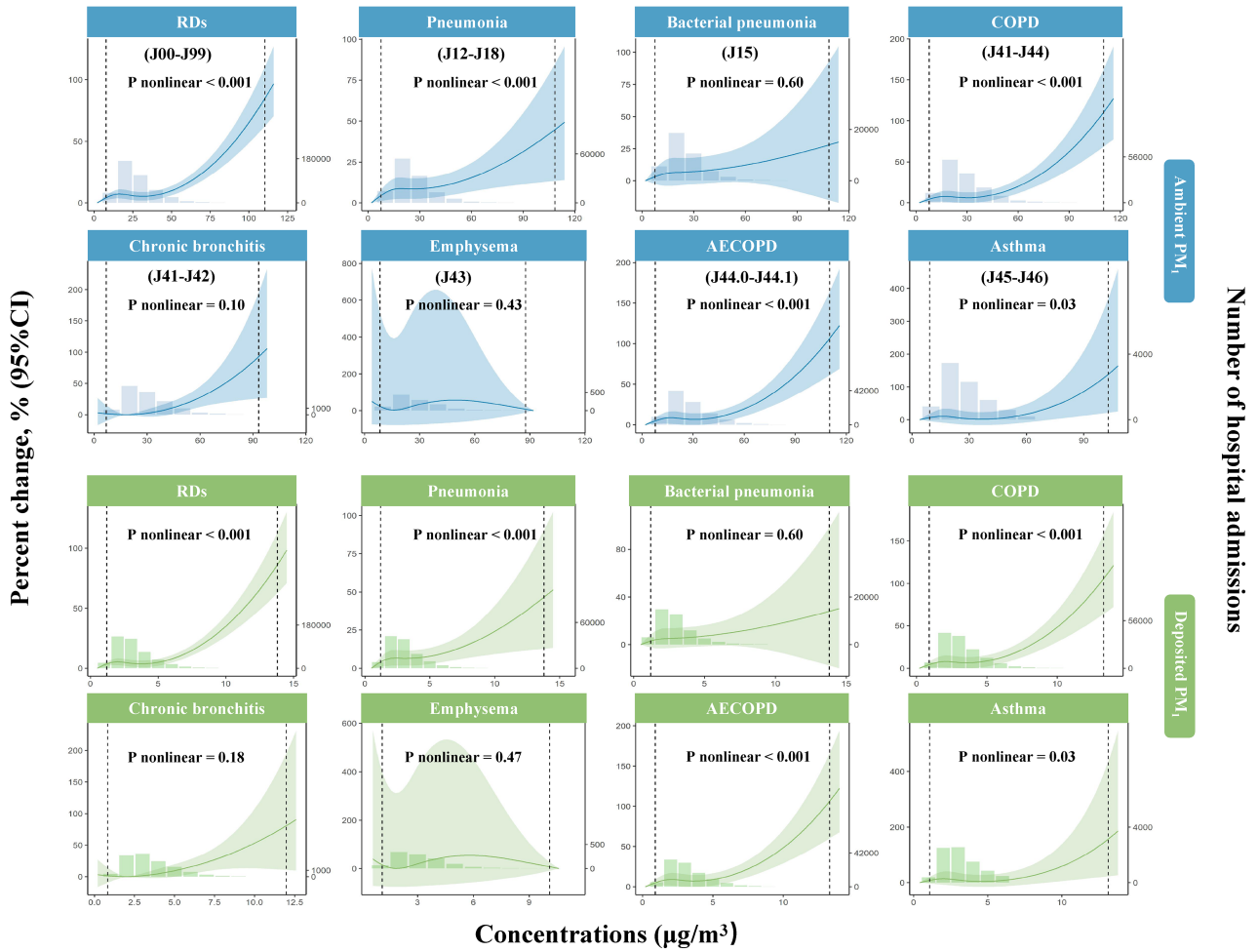

FIGURE 2 Cumulative exposure–response curves for associations of lag 0–1 day exposure to ambient/deposited PM$_1$ with hospital admission from total and cause-specific respiratory diseases. The solid lines with shaded regions indicate percent changes in odds of hospital admission and their corresponding 95% confidence intervals, while the two dotted lines represent 5% and 95% of the ambient PM$_1$ exposure, respectively. AECOPD, acute exacerbation of chronic obstructive pulmonary disease; CI, confidence interval; COPD, chronic obstructive pulmonary diseases; PM$_1$, particulate matter with aerodynamic diameter ≤1 μm.

and deposited PM$_1$ with hospital admissions for total RDs, COPD, AECOPD, pneumonia and asthma (p for nonlinear <0.05); while the associations of PM$_1$ with hospital admissions for emphysema, bacterial pneumonia and chronic bronchitis were linear (Figure 2). In multi-pollutant models, we observed the lower estimates of ambient PM$_1$ and deposited PM$_1$ on hospital admissions on total RDs, COPD, AECOPD and pneumonia when exposure to gaseous pollutants (NO_2, SO_2, CO and O_3) were adjusted, though the exposure-response curves still represented as J-shapes (Figure S2 in the Supporting Information).

Excess hospital admission

The excess fraction of hospital admission for total RDs attributed to ambient PM$_1$ was 6.03% (95% eCI: 2.95%–8.7%), which corresponds to 24,631 (95% eCI: 12,044, 35,573) (Table 3). The excess fraction computed using estimates from the DLNMs was 7.48%, 6.59% and 7.2%, of hospital admission for pneumonia, COPD and AECOPD, respectively, and the estimates from the DLMs was 9.08% of hospital admission for chronic bronchitis. Nevertheless, no significant excess fraction was observed of hospital admission of asthma, bacterial pneumonia and emphysema. The excess fraction remained or slightly changed with adjustment for deposited PM$_1$.

Stratified analysis

Figure 3 show excess fraction of hospital admission for RDs stratified by age, season and sex. We observed higher excess fractions of hospital admission for total RDs in patients aged >75, female and in warm season. In addition, the association of PM$_1$ with hospital admissions for total RDs were J-shaped in subtype except warm season (Figures S3 and S4 in the Supporting Information).

TABLE 3 Excess fraction and number of excess hospital admissions from respiratory disease associated with lag 0–1 day exposure to ambient/deposited PM_1, using DLM or DLNM.

		Ambient PM_1			Deposited PM_1		
Disease	*N*	Excess fraction, % (95% eCI)[a]	Number of excess hospital admissions, *N* (95% eCI)[a]	*p* for nonlinear[b]	Excess fraction, % (95% eCI)[a]	Number of excess hospital admissions, *N* (95% eCI)[a]	*p* for nonlinear[b]
Total respiratory disease (J00-J99)	408,658	6.03 (2.95, 8.7)	24,631 (12,044, 35,573)	<0.001	4.45 (2.07, 6.62)	18,197 (8450, 27,049)	<0.001
Pneumonia (J12-J18)	121,979	7.48 (2.17, 12.03)	9130 (2650, 14,676)	<0.001	5.75 (1.70, 9.28)	7015 (2072, 11,315)	<0.001
Bacterial pneumonia (J15)	40,728	2.49 (−0.70, 5.58)	1014 (−284, 2274)	0.60	2.2 (−0.61, 4.93)	896 (−248, 2009)	0.60
COPD (J41-J44)	130,266	6.59 (0.94, 11.48)	8589 (1226, 14,952)	<0.001	6.83 (1.00, 11.81)	8899 (1304, 15,389)	<0.001
AECOPD (J44.0-J44.1)	102,496	7.2 (0.87, 12.59)	7332 (892, 12,909)	<0.001	8.12 (2.17, 14.12)	8321 (2229, 14,468)	<0.001
Emphysema (J43)	1062	13.78 (−5.44, 28.63)	146 (−58, 304)	0.43	13.00 (−4.92, 26.97)	138 (−52, 286)	0.47
Chronic bronchitis (J41-J42)	12,613	9.08 (3.21, 14.61)	1146 (405, 1843)	0.10	8.83 (2.86, 14.44)	1114 (361, 1822)	0.18
Asthma (J45-J46)	8628	6.23 (−11.28, 20.28)	537 (−974, 1749)	0.03	8.96 (−9.9, 23.36)	773 (−854, 2015)	0.03

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; CI, confidence interval; COPD, chronic obstructive pulmonary diseases; eCI: empirical confidence interval.

[a]Estimated using the DLNM if the *p* value for nonlinear was <0.05 or using the DLM if the *p* value for nonlinear was >0.05.

[b]Estimated using the likelihood ratio test.

DISCUSSION

In this large case-crossover study, short-term effect of PM_1 was significantly associated with an increased risk of RDs hospital admissions. Furthermore, our findings suggest J-shaped associations between PM_1 exposure and hospitalization for total RDs, as well as COPD and pneumonia. The excess fraction of hospital admission for total RDs was 6.03%, which equivalents to 24,631. And the excess fraction was 7.48% and 6.59% of hospital admission for pneumonia and COPD, respectively. The higher excess fraction of admissions for total RDs was observed in patients older than 75 years, females, and in the warmer seasons.

Similarly, three previous case-crossover studies (one conducted in Shenzhen, China and two in Hanoi, Vietnam) also estimated acute impacts of PM_1 on hospital admissions of RDs and reported positive associations,[16–18] but the estimates are inconsistent. Each 10 $\mu g/m^3$ increase in PM_1 was associated with a 2.5% elevated risk of total RDs hospitalization among 8934 Vietnamese children,[17] while a 9% increase in 6078 Chinese adults.[16] Another study in Vietnam among 302,345 children, reported a 1.4% increase in risk.[18] All of the results are higher than that in our study, with a 1.39% increase risk of total RDs. Although the average concentration of PM_1 in our study (22.2 $\mu g/m^3$) was close to that in Shenzhen city (19 $\mu g/m^3$), the sample size in our study was larger than that study conducted in Shenzhen, which may have enhanced the robustness of our results. Furthermore, the study in Shenzhen incorporated a substantial proportion of patients with respiratory infections. Nevertheless, it neglected to target chronic non-communicable respiratory diseases such as chronic obstructive pulmonary disease (COPD), which constitute a considerable proportion of respiratory diseases in China. In addition, the possible reasons for the inconsistent estimates between Vietnam and our study could be related to heterogeneity in the characteristics of subjects and PM_1 concentration.

Apart from the significant associations between PM_1 and hospital admission for total RDs, we have new findings that short-term exposure to PM_1 is significantly associated with increased risk of hospital admission for specific RDs (including COPD, pneumonia, AECOPD, chronic bronchitis and bacterial pneumonia), which may be attributed to shared underlying pathological mechanisms associated with PM_1-related RDs. Inhaled PM can be deposited in the trachea, bronchus and distal lungs through oral and nasopharyngeal passages, causing lung injury.[37] Fine particles mainly deposit in the surrounding small airways and alveoli. When the particle size is less than 1 μm, the particles can remain in the alveolar region for several years.[38] Hence, when assessing the health effects of PM_1, it is crucial to consider the internal exposure dose alongside the potential

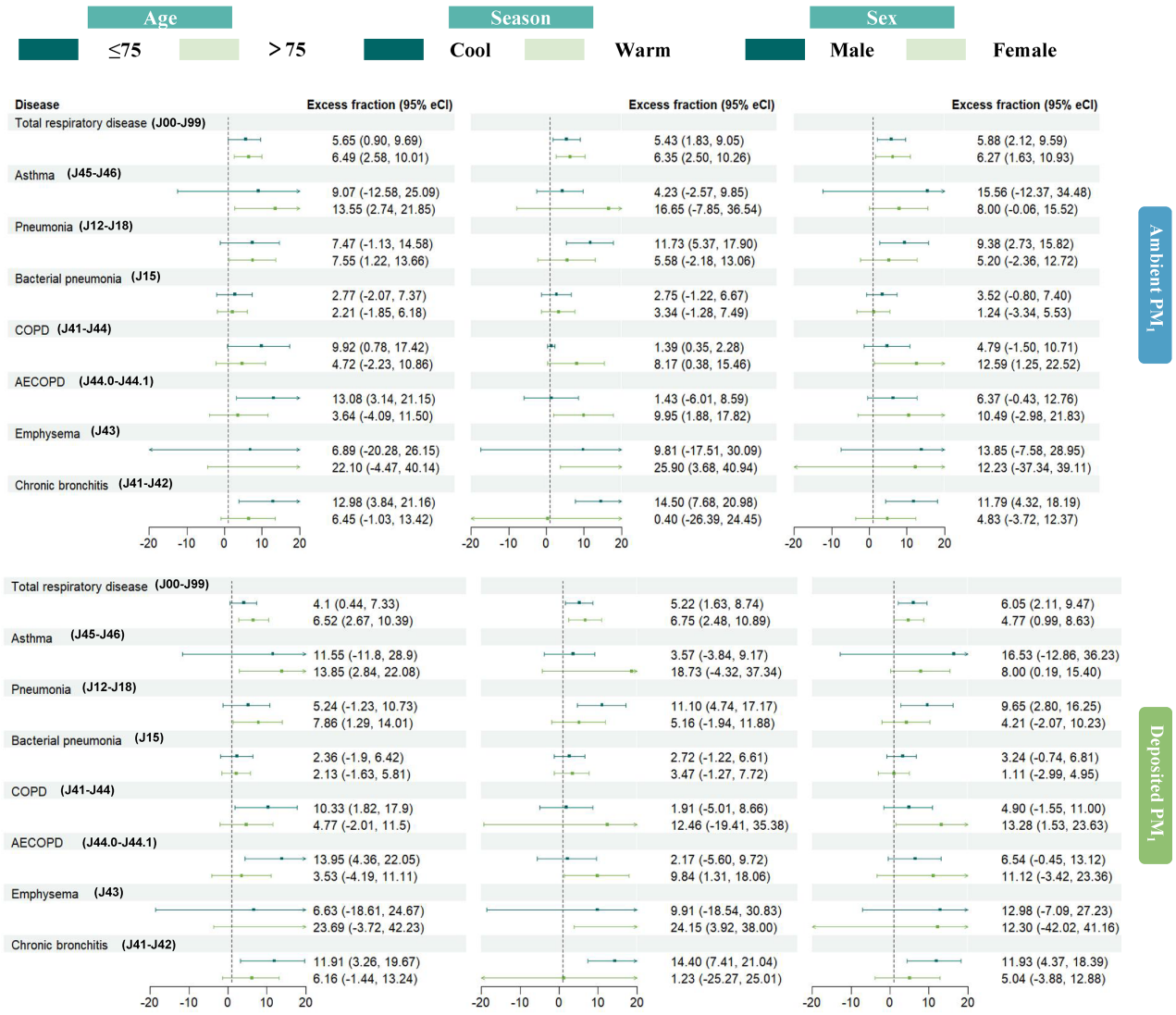

FIGURE 3 Excess fraction of hospital admission from respiratory diseases associated with lag 0–1 day exposure to ambient/deposited PM_1, stratified by age, season and sex. The dotted black lines indicate the estimates of 0. PM_1, particulate matter with aerodynamic diameter ≤1 μm; AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary diseases; eCI: empirical confidence interval; PM_1, particulate matter with aerodynamic diameter ≤ 1 μm.

toxicity of the chemicals contained in PM_1 itself. Thus, we applied MPPD model to calculate deposited PM_1, combined with individual-level on PM_1 concentrations, to obtain more accurate effect estimate. In addition, few studies have specifically focused on the chemical characteristics of PM_1 (e.g., heavy metals, polycyclic aromatic hydrocarbons, organic compounds and black carbon) and their impact on respiratory disease hospitalizations. We acknowledged that future studies should aim to identify and quantify these toxic components to better understand which chemicals within PM_1 contribute most to the adverse respiratory health effects observed.

Besides that, our study suggested that ambient PM_1 exposure may have a greater adverse impact on hospital admission of RDs in older adults. The elderly may generally have an elevated risk of particulate air pollutions related effects due to the degradation of biological functions and immune systems, as well as underlying chronic diseases.[39] Simultaneously, exposure to PM may exacerbate lower respiratory tract inflammation, especially in susceptible populations such as the elderly.[40] Monitoring ambient PM_1 could be a valuable tool in protecting the elderly, as short-term exposure to elevated PM_1 levels has been shown to have significant adverse effects on their health. It is therefore crucial to minimize outdoor activities for older adults during periods of high PM_1 exposure. Practical interventions, such as improving indoor air quality through the use of air purifiers, issuing health advisories on days with elevated PM_1 levels, and encouraging healthcare providers to adjust treatment plans for high-risk individuals, could help mitigate these effects.

Most existing studies focus on $PM_{2.5}$, whose relationship with the occurrence and mortality of respiratory diseases is

well-established.[3,23,41] However, research on PM_1 is severely lacking. Although PM_1 is an important component of $PM_{2.5}$, the correlation between PM_1 and $PM_{2.5}$ varies depending on environmental factors, such as emission sources and seasonality. In areas dominated by combustion processes (e.g., vehicle emissions or industrial activities), PM_1 can form a larger proportion of $PM_{2.5}$, resulting in stronger correlations. Resuspended road dust contributes primarily to $PM_{2.5}$ but is largely absent in PM_1.[42] A European study found that PM_1's contribution to $PM_{2.5}$ varied significantly between summer (58%) and winter (29%).[43] Additionally, the smaller size of PM_1 allows it to penetrate deeper into the lungs, reaching the alveolar region, where it may cause more severe damage than larger particles like $PM_{2.5}$.[16,44]

This study has several strengths. First, we investigated associations between PM_1 and hospital admissions for RDs with considerably large sample size, ensuring the adequate statistical power of our results. Second, the PM_1 exposure data we evaluated were extracted from a high spatial grid dataset based on individual addresses, rather than directly using pollution data from monitoring stations, which facilitates the assessment of more accurate individual level exposures. Third, we applied the MPPD model to simulate the deposition of PM_1, and the quantification of PM_1 deposition helps refine the risk assessment. At the same time, the effect of deposited PM_1 on respiratory hospitalization was taken into account in this study, which has not been considered in any study to date. In addition, by applying a time-stratified case-crossover design, we could effectively control potential confounders in all analyses, including individual-level covariates (e.g., age and sex) and behaviour like smoking.

This study has several limitations that should be acknowledged. First, the lack of information on actual inhalation may have led to an underestimation of the true measure of effect. Second, we focused on the elderly population (aged >60) in our study limits the generalizability of the findings. Furthermore, this restricted age range prevented us from accounting for the effects of age when calculating PM_1 deposition using the MPPD model. Third, as this study was conducted in a single province (Guangdong) in China, the generalizability of the results to other regions should be considered with caution.

In conclusion, short-term exposure to PM_1 was significantly associated with an increased risk of hospitalization for RDs, with older adults potentially being a particularly sensitive population. Our finding highlights the importance of reducing ambient PM_1 exposure as a possible strategy to mitigate RDs-related hospitalizations. Furthermore, the exposure-response relationship between PM_1 and hospitalizations for RDs could provide valuable data for the refinement of air quality standards for PM_1.

AUTHOR CONTRIBUTIONS

Chenghui Zhong: Formal analysis (lead); writing – original draft (lead). **Qi Tian:** Formal analysis (equal); writing – original draft (equal). **Jing Wei:** Data curation (lead); formal analysis (equal); writing – review and editing (equal). **Wenfeng Lu:** Formal analysis (equal); writing – review and editing (equal). **Ruijun Xu:** Formal analysis (equal); writing – review and editing (equal). **Meiqi Lan:** Formal analysis (equal); writing – review and editing (equal). **Nan Hu:** Formal analysis (equal); writing – review and editing (equal). **Lan Qiu:** Formal analysis (equal); writing – review and editing (equal). **Han Zhang:** Formal analysis (equal); writing – review and editing (equal). **SaiFeng Li:** Formal analysis (equal); writing – review and editing (equal). **Chunxiang Shi:** Formal analysis (equal); writing – review and editing (equal). **Yuewei Liu:** Conceptualization (equal); writing – review and editing (equal). **Yun Zhou:** Conceptualization (equal); writing – review and editing (equal).

ACKNOWLEDGEMENTS

We thank the Dr. Jing Wei from the Department of Atmospheric and Oceanic Science, Earth System Science Interdisciplinary Center, University of Maryland for kindly providing us with the air pollution data.

FUNDING INFORMATION

This work was supported by the Guangzhou Municipal Health Commission (Grant number 20191A010054).

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

Data are available in a public, open access repository. The air pollution data are available at (weijing-rs.github.io/product.html). The clinical and meteorological data are not publicly available.

HUMAN ETHICS APPROVAL DECLARATION

The study was approved by the Ethical Committee of School of Public Health, Sun Yat-sen University with a waiver of informed consent.

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How to cite this article: Zhong C, Tian Q, Wei J, Lu W, Xu R, Lan M, et al. Association of short-term exposure to PM_1 with hospital admission from total and cause-specific respiratory diseases. Respirology. 2025;30(3):242–52. https://doi.org/10.1111/resp.14864