Long-term associations of PM_1 *versus* $PM_{2.5}$ and PM_{10} with asthma and asthma-related respiratory symptoms in the middle-aged and elderly population

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Abstract

Background Few studies have compared the associations between long-term exposures to particulate matters (aerodynamic diameter ⩽1, ⩽2.5 and ⩽10 µm: PM_1, $PM_{2.5}$ and PM_{10}, respectively) and asthma and asthma-related respiratory symptoms. The objective of the present study was to compare the strength of the aforementioned associations in middle-aged and elderly adults.

Methods We calculated the mean 722-day personal exposure estimates of PM_1, $PM_{2.5}$ and PM_{10} at 1 km×1 km spatial resolution between 2013 and 2019 at individual levels from China High Air Pollutants (CHAP) datasets. Using logistic regression models, we presented the associations as odds ratios and 95% confidence intervals, for each interquartile range (IQR) increase in PM_1/$PM_{2.5}$/PM_{10} concentration. Asthma denoted a self-reported history of physician-diagnosed asthma or wheezing in the preceding 12 months.

Results We included 7371 participants in COPD surveillance from Guangdong, China. Each IQR increase in PM_1, $PM_{2.5}$ and PM_{10} was associated with a greater odds (OR (95% CI)) of asthma (PM_1: 1.22 (1.02–1.45); $PM_{2.5}$: 1.24 (1.04–1.48); PM_{10}: 1.30 (1.07–1.57)), wheeze (PM_1: 1.27 (1.11–1.44); $PM_{2.5}$: 1.30 (1.14–1.48); PM_{10}: 1.34 (1.17–1.55)), persistent cough (PM_1: 1.33 (1.06–1.66); $PM_{2.5}$: 1.36 (1.09–1.71); PM_{10}: 1.31 (1.02–1.68)) and dyspnoea (PM_1: 2.10 (1.84–2.41); $PM_{2.5}$: 2.17 (1.90–2.48); PM_{10}: 2.29 (1.96–2.66)). Sensitivity analysis results were robust after excluding individuals with a family history of allergy. Associations of PM_1, $PM_{2.5}$ and PM_{10} with asthma and asthma-related respiratory symptoms were slightly stronger in males.

Conclusion Long-term exposure to PM is associated with increased risks of asthma and asthma-related respiratory symptoms.

Introduction

Air pollution, an important environmental component, has been associated with blunted therapeutic responses to inhaled corticosteroids, more frequent use of healthcare resources and a poorer control of chronic respiratory diseases, including asthma and asthma-respiratory symptoms [1–8].

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Accumulating evidence has demonstrated that exposure to ambient particulate matters (PMs) with an aerodynamic diameter ⩽2.5 and ⩽10 µm ($PM_{2.5}$ and PM_{10}, respectively) was adversely associated with respiratory health, including asthma and asthma-related symptoms [8–12], despite inconsistent conclusions. This might be, at least partially, interpreted by the regional differences in the compositions and concentrations of PMs [10–12]. Furthermore, previous studies were mainly conducted in Europe and America where there were comparatively low exposure levels. Studies regarding the associations between air pollution and asthma and asthma-related respiratory symptoms in higher exposure settings (such as mainland China) have been scarce [13], where there was rapid population growth and industrial development and urbanisation. Guangdong, one of the most developed provinces of China, is characterised by lower concentrations of PMs with more toxic components [14, 15]. Therefore, it would be worthwhile to explore the associations between air pollutants and asthma and asthma-related respiratory symptoms in Guangdong province.

Ambient PMs, including PM with an aerodynamic diameter ⩽1 µm (PM_1) [16], $PM_{2.5}$ [17] and PM_{10}, are major drivers of urban air pollution. PM_1 is smaller than $PM_{2.5}$ and PM_{10}, and is characterised by a higher surface area to volume ratio, which might elicit greater adverse impact on the respiratory tract and other health outcomes [18, 19]. PM_1 conferred greater cellular toxicity and elicited more notable inflammation compared with $PM_{2.5}$ and PM_{10} [20]. The association between asthma and asthma-related respiratory symptoms and PM_1 (the smaller and potentially more toxic PM) in China has not been well characterised, except for a single study focusing on children and adolescents in Northeast China [13].

We conducted a population-based study of 7371 middle-aged and elderly residents in Guangdong province. We compared the strength of associations of long-term ambient exposure to PM_1 *versus* $PM_{2.5}$ and PM_{10} on asthma and asthma-related respiratory symptoms, and identified the more vulnerable subpopulations (*e.g.* males).

Methods

Study design and participants

We employed a multistage, probability-based sampling strategy in six surveillance points: Panyu district (Guangzhou city), Doumen district (Zhuhai city), Yingde (Qingyuan city), Taishan (Jiangmen city), Luoding (Yunfu city) and Wengyuan county (Shaoguan city). We included adults who were aged ⩾40 years, and who had participated in the 2014–2015 and 2019–2020 COPD surveillance in Guangdong [21, 22]. We combined the data from the two surveys as a larger cross-sectional study. Briefly, we included residents who had been living in their current residence for >6 months within the year of the survey. We excluded residents with paraplegia, malignancy, cognitive defects, linguistic or mental disorders and pregnant or breastfeeding women. Data were collected during an interview in a healthcare facility by trained staff from the local health stations or community clinics.

The study protocol was approved by the Ethics Review Committee of the National Center for Chronic and Noncommunicable Disease Control and Prevention, China Center for Disease Control and Prevention (201410 and 201901). All participants provided written informed consent.

Ambient and personal air pollution assessment

Daily concentrations of ambient PM_1, $PM_{2.5}$ and PM_{10} at 1 km×1 km (km^2) spatial resolution between 2013 and 2019 were obtained from the China High Air Pollutants (CHAP) datasets. Home addresses of all participants were geocoded using the Baidu Maps API (https://lbsyun.baidu.com) for matching the geocodes of each pollutant from the CHAP datasets. The first participant was recruited on 23 December 2014, while the concentration of air pollutants could be obtained on the earliest date (1 January 2013) by matching the geocode in the CHAP datasets.

In light of the fact that long-term exposure has been conventionally defined among participants who have been exposed to air pollutants for >1 year [23–25], the total exposure window was extended to 722 days (the longest duration within the CHAP database), which allowed us to investigate the associations between the 722-day averaged exposure levels of PMs and asthma and asthma-related respiratory symptoms. Details of PM_1, $PM_{2.5}$ and PM_{10} estimates have been described previously [26–28]. Briefly, a space-time extremely randomised tree model was developed to generate the daily time-series dataset of PM_1, $PM_{2.5}$ and PM_{10} concentrations at 1 km^2 grids from 2013 to 2019 in China. The data (model input) mainly included satellite remote sensing (MAIAC AOD), Multiresolution Emission Inventory for China (MEIC) pollution emissions, meteorological characteristics, land use and urban form (land use, road, population), and spatiotemporal terms. Hence, a time-series and full-coverage dataset of PM_1, $PM_{2.5}$ and PM_{10} at 1 km^2 cell grids from 2013 to 2019 was generated. The spatiotemporal terms were included to capture the

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spatiotemporal autocorrelation of PM_1, $PM_{2.5}$ and PM_{10} concentrations. Based on 10-fold cross-validation [26–28], greater consistency was observed between the estimated PM_1 (coefficient of determination (R^2) =0.83, root-mean-square error (RMSE)=6.2 μg·m^{-3}), $PM_{2.5}$ (R^2=0.92, RMSE=10.8 μg·m^{-3}) and PM_{10} (R^2=0.90, RMSE=21.13 μg·m^{-3}) and ground-level measurements at a daily scale. Geocoding was performed at each residential location of study participants to estimate the exposure concentration of PMs, which allowed for the calculation of the 722-day averaged concentration prior to the survey for each participant.

For other criteria pollutants, the daily concentrations of ambient sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO) and ozone (O_3) at 10 km^2 grids between 2013 and 2019 were also obtained from the CHAP datasets. As reported previously [26–31], the consistency between the estimated SO_2, NO_2, CO and O_3 data and ground-based measurements was high.

Clinical assessments

Respiratory symptoms (wheeze, persistent cough, dyspnoea and persistent phlegm) were captured from the Epidemiologic Standardization Project Questionnaire of the American Thoracic Society (ATS-DLD-78-A) [32], which has been extensively validated.

Participants were considered as having wheezing if they had a positive response to "Does your chest ever sound wheezy or whistling, including the time when you had a cold?" [13].

Persistent cough denoted coughing on most days (⩾4 days per week) for ⩾3 months annually in the absence or presence of cold (positive responses to several items on cough) [13].

Persistent phlegm denoted phlegm, sputum or mucus brought up from the chest in the morning on most days (⩾4 days per week) for ⩾3 months of the previous year in the absence or presence of cold (positive responses to several items on phlegm) [13].

The questionnaire inquired about shortness of breath during daily activity and its severity based on the modified Medical Research Council (mMRC) dyspnoea scale. Only 8.2% of participants had a documented mMRC dyspnoea scale because it was only applied to the participants with COPD. To account for the heterogeneity of participants and study-specific assessment items, the harmonised dyspnoea symptom variables were defined as "shortness of breath during daily life activity" [33].

Asthma was defined on the basis of a self-reported history of asthma diagnosis by physicians or by the presence of wheezing in the preceding 12 months, which has also been adopted in the China Pulmonary Health (CPH) Study [34]. The European Community Respiratory Health Survey (ECRHS) asthma questionnaire served as the source of reference for this definition [35].

A family history of allergic rhinitis or asthma was defined as any biological parent who had ever been diagnosed as having allergic rhinitis or asthma. If participants answered "Yes" to a family history of allergic rhinitis or asthma, then she/he would be defined as having a family history of allergy (supplementary table E1) [36].

Covariates

A standardised questionnaire was employed to examine the potential confounding and mediating effects. We captured the following variables from the questionnaire: sex (male, female), age, region (urban, rural), educational level (primary school or lower, middle school, university or higher), marital status (unmarried, married, widowed/divorced), biomass fuel exposure (yes, no), household ventilation (yes, no), smoking status (yes, no), passive smoking (yes, no), occupational exposure (yes, no), family history of allergy (yes, no) and body mass index (BMI) category (underweight, normal weight, overweight, obesity). The definition of the covariates is summarised in supplementary table E2 [22, 37].

Statistical analysis

The odds ratios and 95% confidence intervals were calculated to determine the association between each interquartile range (IQR) change in ambient PM_1/$PM_{2.5}$/PM_{10} concentration and asthma and asthma-related respiratory symptoms by using logistic regression models [6]. We compared the Akaike Information Criterion value of three models to avoid over-fitting. The magnitude of collinearity was assessed based on the variance inflation factor (VIF). VIF ⩾5 indicated collinearity among the variables. Variables with a significant collinearity were excluded. Finally, we included age, sex, education, marital status, region, occupational exposure, household ventilation, passive smoking, biomass fuel exposure, smoking status,

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family history of allergy and BMI categories to adjust for confounding. The statistical significance for the difference between the groups was examined by using a two-sample z-test, whose 95% confidence interval was calculated as: $(\beta_1-\beta_2)\pm1.96\sqrt{(SE_1^2+SE_2^2)}$, where β_1 and β_2 are the coefficient estimates from the model for each stratum and SE_1 and SE_2 are the standard errors.

Spearman's rank correlation test was used to determine the association of air pollutants. Strong, moderate and weak correlations were defined as coefficients (r_s) >0.60, 0.30–0.60 and <0.30, respectively. In light of the moderate-to-high correlation between PM_1/$PM_{2.5}$/PM_{10} and other pollutant models (except for O_3), we applied a two-pollutant model of PM_1/$PM_{2.5}$/PM_{10} and O_3 to exclude the inclusion of parameters with a significant collinearity.

For subgroup analysis, we further explored the effect modification according to sex. To evaluate the robustness of our estimates, we conducted the sensitivity analyses by excluding participants with a family history of allergy.

Statistical analyses were performed with R version 4.2.2 (https://cran.r-project.org). The threshold of statistical significance for main effects and interactions was set at $p<0.05$.

Results

Participant characteristics

Of 7510 participants screened, 139 had ineligible data (three did not answer the symptom-related questions and 136 did not report height). Therefore, 7371 participants were finally included, whose characteristics are presented in table 1. The mean age was 57.26 years and 3764 participants (51.06%) were males. The overall prevalence of wheeze (9.96% *versus* 7.37%), persistent cough (4.33% *versus* 1.19%) and persistent phlegm (7.62% *versus* 2.27%) was significantly higher in males than in females (all $p<0.05$). The overall prevalence of asthma (4.57% *versus* 3.91%) and dyspnoea (8.55% *versus* 7.98%) did not differ significantly between males and females (both $p>0.05$).

Air pollutant concentrations

The mean daily ambient concentration of PM_1, $PM_{2.5}$, PM_{10} from each surveillance point is presented in table 2. The mean daily ambient concentration of PM_1, $PM_{2.5}$ and PM_{10} was 20.85, 34.92 and 54.35 $\mu g \cdot m^{-3}$, respectively. The IQR of ambient PM_1, $PM_{2.5}$ and PM_{10} concentrations was 6.72, 10.81 and 16.39 $\mu g \cdot m^{-3}$, respectively. Overall, the concentration of PM_1, $PM_{2.5}$ and PM_{10} yielded a medium-to-high correlation with that of the other pollutants, with r_s ranging from 0.40 to 0.99, except for the weak correlation between O_3 and PM_1, $PM_{2.5}$ and PM_{10} (figure 1). The PM_1:$PM_{2.5}$ and PM_1:PM_{10} ratios at the residential address were 59.69% and 38.36%, respectively. There was a strong positive correlation between PM_1 and $PM_{2.5}$ (Spearman's γ correlation coefficient (γ_s)=0.99) and PM_{10} (γ_s=0.96).

Associations between PMs and asthma and asthma-related respiratory symptoms

Based on the single-pollutant model, each IQR increase in the 722-day mean exposure of PM_1, $PM_{2.5}$ and PM_{10} was associated with a significantly higher odds (OR (95% CI)) of having asthma (PM_1: 1.22 (1.02–1.45); $PM_{2.5}$: 1.24 (1.04–1.48); PM_{10}: 1.30 (1.07–1.57)), wheeze (PM_1: 1.27 (1.11–1.44); $PM_{2.5}$: 1.30 (1.14–1.48); PM_{10}: 1.34 (1.17–1.55)), persistent cough (PM_1: 1.33 (1.06–1.66); $PM_{2.5}$: 1.36 (1.09–1.71); PM_{10}: 1.31 (1.02–1.68)) and dyspnoea (PM_1: 2.10 (1.84–2.41); $PM_{2.5}$: 2.17 (1.90–2.48); PM_{10}: 2.29 (1.96–2.66)) in the overall population. We did not identify significant positive associations between PM_1/$PM_{2.5}$/PM_{10} exposures and persistent phlegm (table 3). The strengths of associations between the 722-day means of PMs concentration and asthma and asthma-related respiratory symptoms in single-pollutant models and two-pollutant models were similar with minor differences. Therefore, we present the results of single-pollutant models only hereafter. Overall, the associations of PM_1, $PM_{2.5}$ and PM_{10} with asthma and asthma-related respiratory symptoms were comparable. When stratified by sex, the associations were slightly stronger in males (table 4). The plots of the exposure–response relationships of PM_1, $PM_{2.5}$ and PM_{10} exposure with asthma and asthma-related respiratory symptoms are shown in supplementary figure E1.

Sensitivity analyses

Overall, we found similar results when excluding participants with a family history of allergy in sensitivity analyses (supplementary tables E3 and E4, and figure 2). There were significant associations between PM_1/$PM_{2.5}$/PM_{10} exposures and asthma, wheeze and dyspnoea in the participants without a family history of allergy. Stratified analyses among individuals with no family history of allergy showed that the associations of asthma and dyspnoea were slightly stronger in males.

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TABLE 1 Baseline characteristics of the study participants

	All participants (n=7371)	Males (n=3764)	Females (n=3607)
Age (years)#	57.26±9.26	57.90±9.35	56.58±9.12
Educational level#			
Primary school or lower	4231 (57.40)	1756 (46.65)	2475 (68.62)
Middle school	2989 (40.55)	1901 (50.50)	1088 (30.16)
University or higher	151 (2.05)	107 (2.84)	44 (1.22)
Marriage status#			
Unmarried	94 (1.28)	68 (1.81)	26 (0.72)
Married	6720 (91.17)	3536 (93.94)	3184 (88.27)
Widowed/divorced	557 (7.56)	160 (4.25)	397 (11.01)
Region of residence#			
Urban	2745 (37.24)	1291 (34.30)	1454 (40.31)
Rural	4626 (62.76)	2473 (65.70)	2153 (59.69)
Occupational exposure#			
Yes	3676 (49.87)	2009 (53.37)	1667 (46.22)
No	3695 (50.13)	1755 (46.63)	1940 (53.78)
Household ventilation#			
Yes	5835 (79.16)	2893 (76.86)	2942 (81.56)
No	1536 (20.84)	871 (23.14)	665 (18.44)
Passive smoking#			
Yes	4200 (56.98)	2256 (59.94)	1944 (53.90)
No	3171 (43.02)	1508 (40.06)	1663 (46.10)
Biomass fuel exposure#			
Yes	2738 (37.15)	1331 (35.36)	1407 (39.01)
No	4633 (62.85)	2433 (64.64)	2200 (60.99)
Smoking status#			
Yes	3183 (43.18)	3107 (82.55)	76 (2.11)
No	4188 (56.82)	657 (17.45)	3531 (97.89)
BMI category#			
Underweight	295 (4.00)	165 (4.38)	130 (3.60)
Normal	3684 (49.98)	2035 (54.06)	1649 (45.72)
Overweight	2547 (34.55)	1212 (32.20)	1335 (37.01)
Obesity	845 (11.46)	352 (9.35)	493 (13.67)
Family history of allergy#			
Yes	502 (6.81)	300 (7.97)	202 (5.60)
No	6869 (93.19)	3464 (92.03)	3405 (94.40)
Asthma			
Yes	313 (4.25)	172 (4.57)	141 (3.91)
No	7058 (95.75)	3592 (95.43)	3466 (96.09)
Wheeze#			
Yes	641 (8.70)	375 (9.96)	266 (7.37)
No	6730 (91.30)	3389 (90.04)	3341 (92.63)
Persistent cough#			
Yes	206 (2.79)	163 (4.33)	43 (1.19)
No	7165 (97.21)	3601 (95.67)	3564 (98.81)
Persistent phlegm#			
Yes	369 (5.01)	287 (7.62)	82 (2.27)
No	7002 (94.99)	3477 (92.38)	3525 (97.73)
Dyspnoea			
Yes	610 (8.28)	322 (8.55)	288 (7.98)
No	6761 (91.72)	3442 (91.45)	3319 (92.02)

Data are presented as mean±SD or n (%). BMI: body mass index. #: significant difference between males and females ($p<0.05$), tested with the Chi-squared test for categorical variables and the t-test for continuous variables.

Discussion

This is the first study which has compared the associations of long-term exposure of PM_1 *versus* $PM_{2.5}$ and PM_{10} with asthma and asthma-related respiratory symptoms in the middle-aged and elderly population in China. Our study has added to the existing evidence by demonstrating robust associations between

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TABLE 2 Descriptive statistics of particulate matter concentrations stratified by surveillance points

	Mean±SD	Median	Minimum	Maximum	IQR
Panyu, Guangzhou (n=1230)					
PM_1 ($\mu g \cdot m^{-3}$)	23.49±5.43	18.97	17.44	31.54	10.88
$PM_{2.5}$ ($\mu g \cdot m^{-3}$)	40.09±7.94	32.74	31.87	48.74	15.95
PM_{10} ($\mu g \cdot m^{-3}$)	61.59±9.42	52.92	51.03	73.05	18.41
Doumen, Zhuhai (n=1184)					
PM_1 ($\mu g \cdot m^{-3}$)	18.86±2.92	17.50	15.36	22.99	5.34
$PM_{2.5}$ ($\mu g \cdot m^{-3}$)	32.09±4.51	28.07	27.19	37.07	9.00
PM_{10} ($\mu g \cdot m^{-3}$)	52.58±10.72	44.18	39.50	66.42	22.85
Yingde, Qingyuan (n=1231)					
PM_1 ($\mu g \cdot m^{-3}$)	22.37±4.72	18.15	17.36	28.24	9.38
$PM_{2.5}$ ($\mu g \cdot m^{-3}$)	37.74±7.89	30.58	29.62	47.34	15.72
PM_{10} ($\mu g \cdot m^{-3}$)	56.88±11.07	47.13	45.18	70.88	21.98
Taishan, Jiangmen (n=1353)					
PM_1 ($\mu g \cdot m^{-3}$)	19.84±3.23	17.98	14.96	24.81	6.42
$PM_{2.5}$ ($\mu g \cdot m^{-3}$)	32.58±5.03	29.22	24.13	41.04	9.90
PM_{10} ($\mu g \cdot m^{-3}$)	51.61±7.28	47.67	39.83	63.70	13.83
Luoding, Yunfu (n=1210)					
PM_1 ($\mu g \cdot m^{-3}$)	20.11±3.01	22.59	15.89	23.74	5.78
$PM_{2.5}$ ($\mu g \cdot m^{-3}$)	33.34±4.91	37.31	26.67	39.23	9.21
PM_{10} ($\mu g \cdot m^{-3}$)	51.91±6.80	57.21	41.97	59.78	13.70
Wengyuan, Shaoguan (n=1163)					
PM_1 ($\mu g \cdot m^{-3}$)	20.39±4.34	17.05	15.31	25.50	8.59
$PM_{2.5}$ ($\mu g \cdot m^{-3}$)	33.75±6.71	28.47	26.13	42.09	13.12
PM_{10} ($\mu g \cdot m^{-3}$)	51.56±9.04	44.30	41.08	63.04	16.69

PM_1, $PM_{2.5}$ and PM_{10}: particulate matter with an aerodynamic diameter ⩽1, ⩽2.5 and ⩽10 µm, respectively; IQR: interquartile range.

long-term exposure to ambient PM_1, $PM_{2.5}$ and PM_{10} and asthma and asthma-related respiratory symptoms in Guangdong province. The associations were slightly stronger in males than females.

Our findings have further complemented the studies which demonstrated the detrimental associations of $PM_{2.5}$ exposure with respiratory health [8–12]. Per-IQR-increase analyses have been essential pertaining to

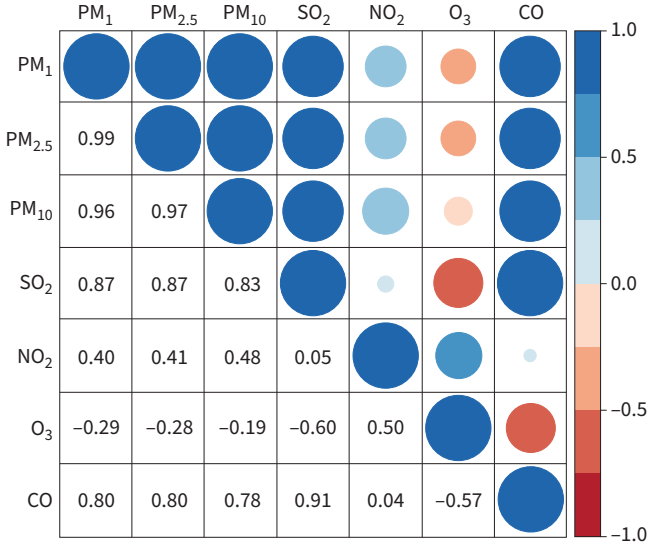

FIGURE 1 Pairwise correlation (r_s) of different ambient air pollutants. PM_1, $PM_{2.5}$ and PM_{10}: particulate matter with an aerodynamic diameter ⩽1, ⩽2.5 and ⩽10 µm, respectively; SO_2: sulfur dioxide; NO_2: nitrogen dioxide; O_3: ozone; CO: carbon monoxide.

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TABLE 3 Associations between per interquartile range increase in particulate matter with an aerodynamic diameter ⩽1, ⩽2.5 and ⩽10 µm (PM_1, $PM_{2.5}$ and PM_{10}, respectively) and asthma and asthma-related respiratory symptoms for the whole study population (n=7371 for all analyses)

	Single-pollutant model			Two-pollutant model ($PM+O_3$)		
	OR (95% CI)	AIC	Adjusted p-value	OR (95% CI)	AIC	Adjusted p-value
Asthma						
PM_1	1.22 (1.02–1.45)	2523.99	0.03*	1.20 (1.00–1.44)	2525.70	0.05*
$PM_{2.5}$	1.24 (1.04–1.48)	2523.00	0.01*	1.23 (1.03–1.47)	2524.68	0.02*
PM_{10}	1.30 (1.07–1.57)	2521.71	0.008**	1.28 (1.06–1.56)	2523.33	0.01*
Wheeze						
PM_1	1.27 (1.11–1.44)	4156.12	<0.001***	1.25 (1.10–1.43)	4157.73	<0.001***
$PM_{2.5}$	1.30 (1.14–1.48)	4153.10	<0.001***	1.29 (1.13–1.47)	4154.68	<0.001***
PM_{10}	1.34 (1.17–1.55)	4151.66	<0.001***	1.33 (1.15–1.53)	4153.05	<0.001***
Persistent cough						
PM_1	1.33 (1.06–1.66)	1770.09	0.01*	1.29 (1.02–1.63)	1771.36	0.03*
$PM_{2.5}$	1.36 (1.09–1.71)	1768.79	0.007**	1.33 (1.06–1.68)	1770.03	0.01*
PM_{10}	1.31 (1.02–1.68)	1771.40	0.03*	1.28 (0.99–1.64)	1772.27	0.06
Persistent phlegm						
PM_1	1.07 (0.91–1.27)	2780.95	0.42	1.06 (0.89–1.26)	2782.53	0.55
$PM_{2.5}$	1.09 (0.93–1.29)	2780.51	0.29	1.08 (0.91–1.28)	2782.12	0.38
PM_{10}	1.10 (0.92–1.31)	2780.60	0.32	1.08 (0.90–1.30)	2782.15	0.39
Dyspnoea						
PM_1	2.10 (1.84–2.41)	3933.66	<0.001***	1.98 (1.73–2.27)	3921.06	<0.001***
$PM_{2.5}$	2.17 (1.90–2.48)	3923.48	<0.001***	2.05 (1.79–2.35)	3909.25	<0.001***
PM_{10}	2.29 (1.96–2.66)	3935.27	<0.001***	2.15 (1.84–2.51)	3917.53	<0.001***

AIC: Akaike Information Criterion; O_3: ozone. The model was adjusted by age, educational level, marital status, body mass index category, region, passive smoking, occupational exposure, household ventilation, biomass fuel exposure, smoking status, sex and family history of allergy. *: p<0.05; **: p<0.01; ***: p<0.001.

TABLE 4 Associations between per interquartile range increase in particulate matter with an aerodynamic diameter ⩽1, ⩽2.5 and ⩽10 µm (PM_1, $PM_{2.5}$ and PM_{10}, respectively) and asthma and asthma-related respiratory symptoms among males and females

	Males (n=3764)			Females (n=3607)		
	OR (95% CI)	AIC	Adjusted p-value	OR (95% CI)	AIC	Adjusted p-value
Asthma						
PM_1	1.32 (1.04–1.68)	1358.67	0.02*	1.12 (0.86–1.45)	1184.86	0.41
$PM_{2.5}$	1.31 (1.03–1.66)	1359.11	0.03*	1.18 (0.91–1.53)	1184.03	0.22
PM_{10}	1.40 (1.07–1.81)	1357.60	0.01*	1.20 (0.91–1.60)	1183.92	0.20
Wheeze						
PM_1	1.28 (1.08–1.52)	2343.80	0.004**	1.25 (1.03–1.52)	1827.40	0.02*
$PM_{2.5}$	1.30 (1.10–1.54)	2342.97	0.003**	1.31 (1.08–1.59)	1825.21	0.007**
PM_{10}	1.37 (1.14–1.65)	2340.57	<0.001***	1.31 (1.06–1.62)	1826.21	0.01*
Persistent cough						
PM_1	1.35 (1.05–1.75)	1313.56	0.02*	1.22 (0.75–1.98)	466.35	0.43
$PM_{2.5}$	1.38 (1.07–1.78)	1312.78	0.01*	1.30 (0.80–2.10)	465.87	0.29
PM_{10}	1.34 (1.01–1.77)	1314.70	0.04*	1.21 (0.72–2.06)	466.45	0.47
Persistent phlegm						
PM_1	1.03 (0.84–1.25)	1993.21	0.78	1.26 (0.91–1.75)	794.51	0.17
$PM_{2.5}$	1.04 (0.86–1.26)	1993.12	0.68	1.32 (0.95–1.84)	793.71	0.10
PM_{10}	1.04 (0.84–1.28)	1993.17	0.73	1.37 (0.95–1.97)	793.58	0.10
Dyspnoea						
PM_1	2.23 (1.85–2.70)	2054.39	<0.001***	2.01 (1.66–2.43)	1890.82	<0.001***
$PM_{2.5}$	2.23 (1.85–2.69)	2053.06	<0.001***	2.13 (1.76–2.58)	1882.12	<0.001***
PM_{10}	2.44 (1.97–3.03)	2054.38	<0.001***	2.16 (1.74–2.69)	1892.03	<0.001***

AIC: Akaike Information Criterion. The model was adjusted by age, educational level, marital status, body mass index category, region, passive smoking, occupational exposure, household ventilation, biomass fuel exposure, smoking status and family history of allergy. *: p<0.05; **: p<0.01; ***: p<0.001.

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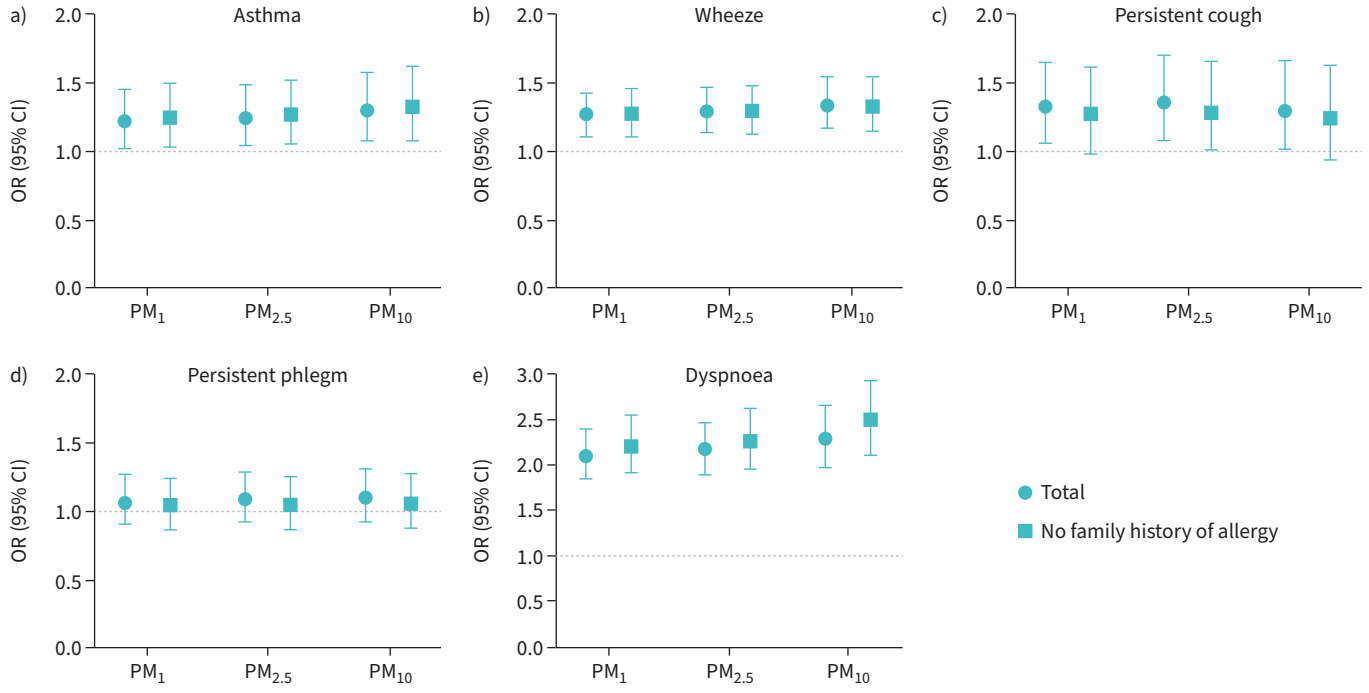

FIGURE 2 Sensitivity analysis on the associations between particulate matter with an aerodynamic diameter ⩽1, ⩽2.5 and ⩽10 µm (PM_1, $PM_{2.5}$ and PM_{10}, respectively) and asthma and asthma-related respiratory symptoms among participants without a family history of allergy: a) asthma, b) wheeze, c) persistent cough, d) persistent phlegm and e) dyspnoea. The associations were adjusted for age, sex, educational level, marriage status, body mass index, region, passive smoking, occupational exposure, ventilation, biomass fuel exposure and smoking status. Adjusted odds ratios and 95% confidence intervals were estimated per interquartile range increase in PM_1, $PM_{2.5}$ and PM_{10} for asthma and asthma-related respiratory symptoms.

air pollutants such as PMs in the published epidemiological studies. The rationale is that PM_1 is the essential component of both $PM_{2.5}$ and PM_{10}, and that it would be impossible under any real-life conditions for an individual to be exposed to an equal concentration of all three PMs. We have analysed the association per IQR increase in concentration of the respective pollutant, showing that the associations of PM_1, $PM_{2.5}$ and PM_{10} were comparable. The association of the respective pollutant per 10 $\mu g \cdot m^{-3}$ increase also supported a similar conclusion (supplementary tables E5–E7). This finding was consistent with the results among children and adolescents residing in 33 communities in cities of Northeast China, in which the adjusted OR (95% CI) of asthma and asthma-related respiratory symptoms per 10 $\mu g \cdot m^{-3}$ increase in PM_1 (asthma: 1.56 (1.46–1.66)) was similar to $PM_{2.5}$ (asthma: 1.50 (1.41–1.59)) [13]. However, the drivers of the associations for PM_1, $PM_{2.5}$ and PM_{10} were notably different between the two studies. Consistent with most previous studies in China [38–40], PM_1 accounted for >85% and >50% for the ambient $PM_{2.5}$ and PM_{10} in seven cities in Northeast China [13] and Beijing [39]. Therefore, PM_1 was an essential driver of the PM pollution, accounting for the main components and concentrations of $PM_{2.5}$ and PM_{10} in most areas (more than 26 cities) across mainland China [38–40]. However, the PM_1:$PM_{2.5}$ (59.69%) and PM_1:PM_{10} (38.36%) ratios in our study were similar to those reported in other European countries (PM_1:$PM_{2.5}$ ratio: 48–69%; PM_1:$PM_{2.5}$ ratio: 40%) [41, 42], but remained much lower compared with other areas in China. We posited that the adverse health effects of $PM_{2.5}$ and PM_{10} in Guangdong province could be partially attributed to PM_1 [38]. Additional studies comparing the associations of PM_1, $PM_{2.5}$ and PM_{10} (particularly their specific components) are needed to shed light on how the different PM sizes and compositions could have affected asthma and asthma-related respiratory symptoms in humans.

We have identified slightly stronger associations between PM concentrations and asthma and asthma-related respiratory symptoms in males than in females. Consistent with the study focusing on children in Northeast China, stronger associations between PM concentration and asthma and asthma-related respiratory symptoms were observed among boys compared with girls [13]. A study of 12 Southern California communities has evaluated the associations between different ambient air pollutant concentrations and asthma [43]. The study showed that asthma-related symptoms among 3676 children correlated positively with PM levels in boys, but not in girls. In three studies reporting a greater impact of

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air pollution among males, the higher levels of work-related exposures and the more time spent outdoors might help collectively explain the higher likelihood of developing asthma and asthma-related respiratory symptoms [13, 44, 45]. Other sex-related traits, such as hormonal status and body size, could have influenced the biological transportation of environmental chemicals, potentially leading to different associations between males and females [9, 46].

Notably, PM exposures did not significantly increase the risk of asthma among participants with a family history of allergy. The discordant findings between participants with *versus* without a family history of allergy could be partly interpreted by the non-equivalence between the history of documented diseases and the currently symptomatic diseases. Participants with a family history of allergy might be more likely to avoid contact with risk factors of allergic diseases and more proactively seek prescription refills to maintain asthma or allergic symptom control. Identification of the underlying causes, however, would benefit from more in-depth analysis *via* longitudinal assessments within our study setting.

Although our study did not aim to identify the underlying mechanisms of the noxious effects of PMs on asthma and asthma-related respiratory symptoms, the systemic inflammation, oxidative stress responses, immune injury, disease-associated gene polymorphisms and DNA methylation, regulation of the gene expression, and altered signalling pathways associated with oxidative stress responses might collectively help explain our findings [47–52]. First, compared with $PM_{2.5}$ and PM_{10}, the smaller diameter of PM_1 could elicit inflammatory responses *via* inducing oxidative stress after internalisation by airway epithelial cells [53, 54]. PM_1 could penetrate deeper to the more distal airways and be better adsorbed to the cellular surface, resulting in similar levels of toxicity despite the lower concentration. Second, the effects of airborne PMs on lung function might depend primarily on the pro-inflammatory responses [55, 56]. Third, PMs may also absorb aeroallergens released by pollen grains, partially contributing to the enhanced IgE antibody-mediated immune response with the prolonged retention of the allergens [57]. Moreover, both B-cells and T-cells could sense intercellular signals and utilise cellular and humoral immunity to induce potent inflammatory responses. Studies have shown that PMs can cause an imbalance in Th1/Th2 T-helper cell ratios and functional dysregulation by skewing towards the Th2 inflammatory responses and inhibiting Th1 inflammatory responses [18, 58].

Some limitations should be considered. First, the causality between long-term exposure to ambient PMs and asthma and asthma-related respiratory symptoms cannot be inferred because of the cross-sectional study design. Second, the definitions of self-reported asthma and asthma-related respiratory symptoms could only be regarded as a proxy for the typical clinical diagnosis; however, these definitions were consistent with those adopted in major large-scale epidemiological studies [8, 13, 32, 34, 35, 59, 60]. Third, information on multiple food intake, physical activity and vaccination was lacking. Fourth, PMs might interact with multiple indoor air pollutants (*e.g.* mould, household fuels, allergens, furniture, paints and cleaning agents) [61], which cannot be readily disentangled. Fifth, our study has addressed the association between PMs and asthma and asthma-related respiratory symptoms in Guangdong only, and hence a wider distribution of geographic locations should be taken into account in future studies. We will also conduct long-term analysis and follow-up studies to further verify the current findings. In addition, our study has highlighted the need for ongoing research on PM_1, especially its constituents and toxicity, which might help broaden the scope of the study. Finally, exposure measurement errors have not been thoroughly considered. We have enrolled participants who had been living at the current location for >6 months within the year of the survey. The 722-day averaged exposure levels of the air pollutants might have been biased for those living at the location for <722 days. However, high-quality PM estimates at finer spatiotemporal scales were lacking at the global and regional levels, which has hampered more comparative analyses using various exposure datasets.

Despite these limitations, our study has included a relatively large sample of the middle-aged and elderly population, allowing for a robust analysis to detect the associations for PMs with asthma and asthma-related respiratory symptoms based on a comprehensive panel of covariates for adjustment. Second, we have estimated the residential concentrations of PMs at a spatial resolution of 1 km^2, a reasonably fine precision of exposure modelling which has been validated in previous studies [26–28] to safeguard the accuracy of the exposure assessment. Additionally, despite excluding the participants with a known family history of allergy, the overall results were not altered materially. Results of the single- and two-pollutant models remained robust.

Our study has ascertained the associations between the respiratory health status of middle-aged and elderly residents in Guangdong province and the multiple airborne PMs, thus providing a more solid basis for policymakers to formulate updated policies for continuous air quality improvement. Our findings call

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for continued monitoring of the dynamics between atmospheric PMs pollution and the burden of chronic respiratory diseases at the population level.

Conclusions

Long-term ambient PM_1 air pollution is associated with asthma, wheeze, persistent cough and dyspnoea in the middle-aged and elderly population. The strength of associations of PM_1, $PM_{2.5}$ and PM_{10} is comparable. Males appear more susceptible to the adverse associations of PMs than females. Future longitudinal studies incorporating individual-level monitoring for outdoor and indoor air pollutants as well as comprehensive measures of pollen are needed to confirm the findings.

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