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Particulate matter of different sizes associated with acute lower respiratory infection outpatient visits in children: a counterfactual analysis in Guangzhou, China

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Abstract

Background

The burden of lower respiratory infection is primarily borne by developing countries. However, the association between particulate matter of different sizes and acute lower respiratory infection (ALRI) outpatient visits in developing countries is less studied.

Methods

We obtained data on ALRI outpatient visits (N = 105,639) from a tertiary hospital in Guangzhou, China between 2013 and 2019. Over-dispersed generalized additive Poisson models were employed to evaluate the excess risk (ER) associated with particulate matter [inhalable particulate matter (PM_{10}), coarse particulate matter (PM_c), and fine particulate matter ($PM_{2.5}$)]. Counterfactual analyses were used to examine the potential percent reduction of ALRI outpatient visits if the levels of air pollution were as low as those recommended by the World Health Organization (WHO).

Results

There were 35,310 pneumonia, 68,218 bronchiolitis, and 2,111 asthma outpatient visits included. Each 10 $\mu g/m^3$ increase of three-day moving averages of particulate matter was associated with significant ER [95% confidence interval (CI)] of outpatient visits of pneumonia [$PM_{2.5}$: 3.71% (2.91%, 4.52%); PM_c: 9.19% (6.94%, 11.49%); PM_{10}: 4.36% (3.21%, 5.52%)], bronchiolitis [$PM_{2.5}$: 3.21% (2.49%, 3.93%); PM_c: 9.13% (7.09%, 11.21%); PM_{10}: 3.12% (2.10%, 4.15%)], and asthma [$PM_{2.5}$: 3.45% (1.18%, 5.78%); PM_c: 11.69% (4.45%, 19.43%); PM_{10}: 3.33% (0.26%, 6.49%)]. The association between particulate matter and pneumonia outpatient visits was stronger among male patients and in cold seasons. Counterfactual analyses suggested that $PM_{2.5}$ was associated with the largest potential decline of ALRI outpatient visits [pneumonia: 3.89%, 95% CI: (3.24%, 5.52%); bronchiolitis: 4.35% (3.06%, 4.82%); asthma: 5.98% (1.92%, 10.37%)] if the air pollutants were reduced to the level of the reference guidelines.

Conclusion

Short-term exposure to $PM_{2.5}$, PM_c, and PM_{10} is associated with significant risk of ALRI outpatient visits, among which $PM_{2.5}$ is associated with the highest potential decline in outpatient visits if it could be reduced to the WHO recommended level.

Introduction

Lower respiratory infections, also known as pneumonia or bronchiolitis, are the sixth leading cause of death for all ages, resulting in around 2.4 million deaths worldwide in 2016(1). The burden of lower respiratory infections is unevenly distributed across the globe and primarily born in developing countries and socioeconomically disadvantaged communities, where adequate nutrition, clean fuel, sanitation, and clean air are unavailable(2, 3).

Exposure to ambient particulate matter (PM) has been widely reported to be associated with lower respiratory infection(4–6). However, evidence on the association between different sizes of PM and lower respiratory infections, especially that from developing countries in which the level of air pollution is high, is relatively little(7–9). Meanwhile, it is widely acknowledged that short-term exposure to particulate matter is associated with ALRI hospitalizations(10–14), but we have not found any study that investigated the association between exposure to particulate matter and ALRI outpatient visits.

In this time-series analyses of outpatient visits in a tertiary hospital in Guangzhou, China from 2013 to 2019, we investigate the association between PM of different sizes (PM_{10}, PM_c, and $PM_{2.5}$) and the outpatient visits of ALRI, potential mediators, and the potential percent reduction of ALRI outpatient visits if the levels of particulate matter were as low as those recommended by the WHO.

Methods

Acute lower respiratory infection data

Data on hospital outpatient visits for ALRI were retrieved from the Guangdong Second Provincial General Hospital located in the southwest of the city (Figure 1), which is one of the highest-level (tertiary) hospitals in Guangzhou(15). According to the International Classification of Diseases, Tenth Revision (ICD-10), hospital outpatient visits with the primary diagnoses of pneumonia (J12-J18), bronchiolitis (J20-J21), and asthma (J45-J46)(16) were obtained between February 2013 and December 2019. We aggregated the three subtypes of ALRI to a series of daily time-series data(17-20).

Air pollution and meteorological data

Daily concentrations of air pollution during the study period were obtained from 11 air monitoring stations in Guangzhou (Figure 1), including inhalable particulate matter (PM_{10}), coarse particulate (PM_c), fine particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2), sulfur dioxide (SO_2) and ozone (O_3). Following previous study(19), the PM_c concentrations were calculated by subtracting $PM_{2.5}$ from PM_{10}, because PM_{10} was consisted of $PM_{2.5}$ and PM_c. Air pollution measurement details have been previously described(21). Approximately 1% of observation days had missing data for the air pollution, the missing data were imputed using a linear interpolation approach (the “na.approx” function in “zoo” package in R).

Daily meteorological data (mean temperature and relative humidity) were obtained from the National Weather Data Sharing System (http://data.cma.cn/). Because there is potentially high correlation among different air pollutants and meteorological factors, we examined the pairwise Pearson correlation coefficients among these variables.(22, 23)

Statistical models

The ALRI data, daily air pollution concentrations and meteorological data were linked by date. Following prior similar epidemiology studies(24), the association between PM pollution and hospital outpatient visits for acute lower respiratory infections diseases was examined by an over-dispersed generalized additive Poisson model (GAM). In the model, public holidays (PH) and day of the week (DOW) were adjusted for as categorical variables. Seasonal patterns, long-term trends, temperature, and relative humidity were controlled for as smoothing splines. In accordance with the approaches used in previous studies(25, 26), we selected six degrees of freedom (df) per year for temporal trends, a df of 6 for moving average temperature of the current day and previous three days (Temp03) and relative humidity (RH).

Considering the delayed health effects of air pollutants, we examined the lag effects for different lag structures. We begin with the same day (lag0) up to five days lag (lag5) in the single-lag day models. We also considered the accumulated effects of multi-day lags (moving averages for the current day and the previous 1, 2 and 3 days [lag01, lag02, and lag03]).

Stratified analyses

In order to evaluate the potential effect modifiers of the PM pollution-ALRI associations, we conducted stratified analyses by gender (male vs. female), age group (age <5 vs. age 5-14), and season (warm vs. cold). The warm season was defined as from April to September, and the cold season was from October to March. The 95% confidence interval (CI) of the difference between group was calculated by the formula below:

$$Q_1 - Q_2 \ \pm \ 1.96\sqrt{(\mathrm{SE}_1)^2 + (\mathrm{SE}_2)^2}$$

where Q represents the estimated coefficient in each stratum, and SE is the corresponding standard error(27). The difference was considered as statistically significant if the 95% CI did not include unity.

Sensitivity analyses

To examine the robustness of the main models, we applied a series of sensitivity studies. The main findings were assessed by changing the df in the smooth functions for temporal trends and meteorological factors. Additionally, we adjusted for gaseous air pollutants (SO_2, NO_2, and O_3) in two-pollutant models. The models were regarded as robust if there were no significant changes after df-changed or further adjustment for gaseous air pollutants.

Counterfactual analyses on the burden of ALRI attributable to air pollution

We estimated the burden of ALRI attributable to $PM_{2.5}$, PM_c, and PM_{10} by calculating the difference between the observed ALRI outpatient visits and the counterfactual visits predicted using well-recognized reference values of air pollution recommended by the World Health Organization (WHO) and our previously built over-dispersed generalized additive Poisson models. This difference between the observed and counterfactual ALRI outpatient visits represents the estimated burden of ALRI outpatient visits associated with particulate matter of different sizes. The counterfactual scenarios were set to be hypothetical values of $PM_{2.5}$, PM_c, and PM_{10} set by the WHO Air Quality Guidelines (24 hours mean: 25 $\mu g/m^3$ for $PM_{2.5}$, 25 $\mu g/m^3$ for PM_c, and 50 $\mu g/m^3$ for PM_{10}). The observed air pollution levels lower than the reference values were kept the same in the counterfactual scenario. The 95% CIs were constructed using 1,000 bootstrap replicates with replacement for each model.(28, 29)

In all statistical analyses, a P value 0.05 was considered statistically significant. All data cleaning, aggregation, and visualization, and statistical analyses were done using statistical computing environment R (version 4.0.5)(30).

Results

Figure 1 presents the geographical location of Guangzhou city and the sample hospital, as well as the geographical distribution of the air monitoring stations in Guangzhou. A total of 35,310 pneumonia, 68,218 bronchiolitis, and 2,111 asthma cases were included in our analyses. Table 1 shows the summary statistics of ALRI subtypes, particulate matter of different sizes (PM_{10}, PM_c, and $PM_{2.5}$), and gaseous pollutants (SO_2, NO_2, and O_3). The daily averages [standard deviations (SD)] of pneumonia, bronchiolitis, and asthma cases were 12.5 (9.1), 24.3 (11.5), and 0.8 (1.4). The mean concentrations of PM_{10}, PM_c, and $PM_{2.5}$ in our study were 58.3, 21.0, and 37.8 $\mu g/m^3$. The mean (SD) of temperature and relative humidity was 22.8 (5.9) °C and 81.8% (10.2%).

Table 1
Summary statistics of acute lower respiratory infections outpatient visits, air pollutants, and meteorological variables.

	Mean	SD	Percentile				
			Min	25th	50th	75th	Max
Acute lower respiratory infections							
Pneumonia	12.5	9.1	0.0	6.0	11.0	16.0	73.0
Bronchiolitis	24.3	11.5	0.0	16.0	23.0	31.0	81.0
Asthma	0.8	1.4	0.0	0.0	0.0	1.0	12.0
Air pollution, μg/m^3							
PM_{10}	58.3	28.1	10.0	38.2	51.1	73.4	217.8
PM_c	21.0	9.9	0.8	14.7	18.8	25.3	77.7
$PM_{2.5}$	37.8	21.2	4.6	22.7	32.3	48.3	156.4
SO_2	13.6	8.5	2.8	8.6	11.9	16.5	166.4
NO_2	45.2	18.6	4.4	33.6	41.2	53.7	177.7
O_3	51.6	30.2	3.5	30.0	47.2	67.1	294.6
Meteorological variables							
Temperature, °C	22.8	5.9	1.7	19.0	25.0	27.5	32.8
Relative humidity, %	81.8	10.2	30.5	77.0	83.1	89.3	100.0
SD: standard deviation							

Figure 2 shows the correlation plot of the air pollutants and meteorological variables in our sample. All the Pearson correlation coefficients were statistically significant except for the correlation between NO_2 and O_3. PM_{10} was significantly and strongly correlated with PM_c and $PM_{2.5}$ (Pearson correlation coefficients: 0.81 and 0.93); NO_2 was moderately correlated with particulate matters (Pearson correlation coefficients for PM_{10}, PM_c, and $PM_{2.5}$: 0.78, 0.66, and 0.70). Meteorological variables were negatively correlated with air pollutants except for the positive correlation between temperature and O_3.

Table 2 exhibits the ER of pneumonia, bronchiolitis, and asthma outpatient visits associated with per 10 μg/m^3 increase of $PM_{2.5}$, PM_c, and PM_{10} in lag03. The results revealed that particulate matters of different sizes were significantly associated with pneumonia, bronchiolitis, and asthma, respectively in single-pollutant models, where the ER of PM_c is the largest, followed by those of $PM_{2.5}$ and PM_{10}. The results were consistent and robust in two-pollutant models with further adjustment for SO_2, NO_2, and O_3, except for those asthma models controlling for NO_2. The corresponding exposure-response nonlinear curves for daily particulate matter and log relative risk are provided in Supplemental Fig. 1.

Table 2
Excess risk and 95% confidence intervals of pneumonia, bronchiolitis, and asthma for each 10 μg/m^3 increase in $PM_{2.5}$, PM_c, PM_{10} using single- and two-pollutants models.

Pollutants	Models	Pneumonia	Bronchiolitis	Asthma
PM_{10}				
	Single-pollutant model	3.71 (2.91, 4.52)	3.21 (2.49, 3.93)	3.45 (1.18, 5.78)
	Two-pollutant models			
	Control for SO_2	3.81 (2.97, 4.66)	3.44 (2.69, 4.21)	3.46 (1.13, 5.85)
	Control for NO_2	2.47 (1.47, 3.47)	1.48 (0.58, 2.37)	0.26 (-2.58, 3.19)
	Control for O_3	4.06 (3.22, 4.91)	3.48 (2.72, 4.25)	3.72 (1.30, 6.20)
PM_c				
	Single-pollutant model	9.19 (6.94, 11.49)	9.13 (7.09, 11.21)	11.69 (4.45, 19.43)
	Two-pollutant models			
	Control for SO_2	9.32 (6.98, 11.72)	9.72 (7.58, 11.91)	11.70 (4.29, 19.63)
	Control for NO_2	5.58 (3.03, 8.19)	4.80 (2.45, 7.20)	3.26 (-4.88, 12.09)
	Control for O_3	9.52 (7.21, 11.87)	9.47 (7.37, 11.61)	12.09 (4.56, 20.17)
$PM_{2.5}$				
	Single-pollutant model	4.36 (3.21, 5.52)	3.12 (2.10, 4.15)	3.33 (0.26, 6.49)
	Two-pollutant models			
	Control for SO_2	4.61 (3.37, 5.87)	3.50 (2.39, 4.63)	3.45 (0.14, 6.87)
	Control for NO_2	2.30 (0.96, 3.65)	0.39 (-0.78, 1.58)	-0.40 (-3.86, 3.18)
	Control for O_3	4.85 (3.63, 6.09)	3.38 (2.29, 4.48)	3.54 (0.26, 6.91)

Similar patterns of ER of ALRI outpatient visits associated with per 10 μg/m^3 increase in different size fractions could be observed in Fig. 3. Each 10 μg/m^3 increase in $PM_{2.5}$, PM_c, PM_{10} was associated with outpatient visits of pneumonia, bronchiolitis, and asthma in different lag days. In contrast, the effects of matter of different sizes on asthma are less robust: the moving average lags of PM_c, and $PM_{2.5}$ were still significantly associated with ALRI outpatient visits, but the effects of lag0 to lag5 of PM_c and $PM_{2.5}$ and different lags of PM_{10} were nonsignificant or at borderline significant.

Table 3 presents the estimated ER with 95% CI of pneumonia, bronchiolitis, and asthma stratified by gender, age group, and season, where the bold numbers indicate significant differences across strata. We can observe that each 10 $\mu g/m^3$ increases in PM_{10}, PM_c, and $PM_{2.5}$ were consistently associated with significantly different effects on pneumonia outpatient visits by gender and season groups. Similar differential effects can be observed for bronchiolitis associated with increases in PM_{10} and PM_c by different season strata, but not for $PM_{2.5}$. However, the differential effects across strata were much less significant for asthma outpatient visits: it was only significantly different between warm and cold seasons.

Table 3
Excess risk and 95% confidence intervals of pneumonia, bronchiolitis, and asthma for each 10 μg/m^3 increase in $PM_{2.5}$, PM_c, and PM_{10} stratified by gender, age group, and season.

Pollutants	Stratum	Pneumonia	Bronchiolitis	Asthma
PM_{10}				
	Gender			
	Male	**4.49 (3.54, 5.45)**	3.44 (2.68, 4.21)	4.46 (1.62, 7.39)
	Female	**2.68 (1.61, 3.75)**	2.76 (1.84, 3.69)	1.78 (-1.51, 5.18)
	Age			
	< 5	3.50 (2.66, 4.34)	3.09 (2.36, 3.82)	1.78 (-0.97, 4.60)
	5–14	4.50 (2.71, 6.33)	3.70 (2.49, 4.92)	6.01 (2.39, 9.75)
	Season			
	Warm	**-0.06 (-1.24, 1.13)**	**2.13 (1.03, 3.23)**	6.53 (2.52, 10.69)
	Cold	**5.12 (4.00, 6.25)**	**3.76 (2.74, 4.79)**	1.76 (-1.00, 4.61)
PM_c				
	Gender			
	Male	**11.07 (8.36, 13.83)**	10.02 (7.82, 12.25)	15.65 (6.36, 25.74)
	Female	**6.70 (3.78, 9.71)**	7.57 (4.99, 10.21)	5.94 (-3.96, 16.87)
	Age			
	< 5	8.69 (6.37, 11.06)	8.76 (6.69, 10.88)	6.96 (-1.69, 16.38)
	5–14	10.76 (5.65, 16.13)	10.75 (7.34, 14.27)	17.98 (6.46, 30.74)
	Season			
	Warm	**-0.93 (-4.33, 2.60)**	**3.77 (0.40, 7.26)**	22.14 (6.92, 39.53)
	Cold	**13.57 (10.46, 16.77)**	**11.92 (9.07, 14.84)**	9.39 (0.93, 18.56)
$PM_{2.5}$				
	Gender			
	Male	**5.31 (3.95, 6.69)**	3.48 (2.39, 4.58)	4.13 (0.30, 8.09)

The bold type represents the statistically significant differences ($p < 0.05$).
Warm season: April to September; cold season: October to March.

Pollutants	Stratum	Pneumonia	Bronchiolitis	Asthma
	Female	**3.11 (1.58, 4.65)**	2.45 (1.14, 3.78)	1.92 (-2.54, 6.58)
	Age			
	< 5	4.07 (2.87, 5.28)	2.88 (1.84, 3.93)	1.53 (-2.16, 5.35)
	5–14	5.59 (3.07, 8.17)	4.10 (2.39, 5.85)	6.13 (1.22, 11.28)
	Season			
	Warm	**0.08 (-1.49, 1.67)**	3.00 (1.56, 4.46)	**7.73 (2.62, 13.08)**
	Cold	**6.08 (4.42, 7.77)**	3.01 (1.51, 4.53)	**-0.30 (-4.05, 3.60)**
The bold type represents the statistically significant differences ($p < 0.05$).				
Warm season: April to September; cold season: October to March.				

Table 4 shows the proportion reduction of ALRI (pneumonia, bronchiolitis, and asthma) outpatient visits attributable to $PM_{2.5}$, PM_c, and PM_{10} in Guangzhou from 2013 to 2019 using counterfactual analysis that compares to the WHO recommended levels (25 μg/m^3 for $PM_{2.5}$, 25 μg/m^3 for PM_c, and 50 μg/m^3 for PM_{10}). We found that $PM_{2.5}$ was associated with the largest decline of ALRI outpatient visits [pneumonia: 3.89%, 95% CI: (3.24%, 5.52%); bronchiolitis: 4.35%, 95% CI: (3.06%, 4.82%); asthma: 5.98%, 95% CI: (1.92%, 10.37%)] if the levels of air pollution were reduced to the level of the reference guidelines specified by the WHO.

Table 4
Counterfactual analysis on the percent of decline (95% confidence intervals) in acute lower respiratory infection outpatient visits if the level of $PM_{2.5}$, PM_c, and PM_{10} were reduced to the reference levels in Guangzhou from 2013 to 2019.

	Pneumonia	Bronchiolitis	Asthma
PM_{10}	3.89% (3.24%, 5.52%)	4.35% (3.06%, 4.82%)	5.98% (1.92%, 10.37%)
PM_c	1.42% (1.10%, 1.82%)	1.91% (1.48%, 2.36%)	1.79% (0.60%, 3.09%)
$PM_{2.5}$	4.63% (3.47%, 5.98%)	4.38% (2.68%, 5.97%)	6.07% (0.08%, 12.37%)
The references of PM_{10}, $PM_{2.5}$, and PM_c concentration were based on the World Health Organization's Ambient Air Quality guidelines (24h mean: 50 μg/m^3 for PM_{10}, 25 μg/m^3 for PM_c, and 25 μg/m^3 for $PM_{2.5}$, respectively).			

Discussion

In this seven-year time-series analyses of daily ALRI outpatient visits data (N = 105,639) in Guangzhou, China from 2013 to 2019, we observed statistically significant ERs and potential declination of ALRI (including pneumonia, bronchiolitis, and asthma) outpatient visits associated with particulate matter of different sizes. The results were consistent in exposure assessment using different lags (lag 0 to 5 and moving averages of 1 to 3 days), two-pollutant models adjusting for SO_2, NO_2, and O_3, and various degrees of freedom. In counterfactual analyses that are of more public health significance, $PM_{2.5}$ was associated with the largest decline of ALRI outpatient visits if the exposure were as low as the WHO guideline reference.

Different effect estimates were observed among different sized PM with the largest ER being observed in PM_c, followed by $PM_{2.5}$ and PM_{10}. However, these results should be interpreted with caution that $PM_{2.5}$, PM_c, and PM_{10} have different means and standard deviations: the mean of PM_c in our sample (21.0 μg/m^3) was lower than the WHO recommended level (25 μg/m^3); the SD of PM_c (9.9 μg/m^3) was much smaller compared to those of $PM_{2.5}$ (21.2 μg/m^3) and PM_{10} (28.1 μg/m^3). Therefore, the ER of ALRI associated with PM_c appeared to be the largest, which likely results from its small standard deviation.

In view of the limitation that the calculation of ER largely depends on the statistical distribution of the exposures, we further examined the potential proportion declination that would occur if exposure to particulate matter of different sizes were reduced to the WHO recommended levels (25 μg/m^3 for $PM_{2.5}$, 25 μg/m^3 for PM_c, and 50 μg/m^3 for PM_{10}). In contrast to the result that PM_c was associated with the highest ER, our counterfactual analysis suggested that reducing $PM_{2.5}$ to the WHO reference was associated with the largest potential decline in ALRI outpatient visits, followed closely by the reduction of PM_{10}; while reducing PM_c to the WHO reference is associated with the lowest potential decline in ALRI outpatient visits, which is likely explained by the fact that the mean level of PM_c (21.0 μg/m^3) in our sample is lower than that of WHO reference level (25 μg/m^3).

Our counterfactual analysis results have much more practical public health meaning than those of ER. The implication that reducing the level of $PM_{2.5}$ may be associated with the largest decline in ALRI outpatient visits is consistent with previous reports about the toxicity of smaller-sized particulate matter on lower respiratory infection hospitalizations(10–14). For example, Wang et al. specifically focused on the association between particulate matter of different sizes and childhood pneumonia, and they reported a graded impact of particulate matter of different sizes on childhood pneumonia ($PM_1 > PM_{2.5} > PM_{10}$). Smaller-sized particulate matter is more likely to enter lower and deeper lobes of lung and cause more severe consequences of health.

Although the air quality has been substantially improved attributable to the effort of air quality management in China over the past decade(31, 32), the average level of particulate matter (especially $PM_{2.5}$ and PM_{10}), are still above the WHO recommended level. Northern China cities with high population density can experience anomalously high levels of air pollution during the winter(33). Our results highlight the importance of focusing on smaller-sized particulate matter due to its harmful effect on ALRI outpatient visits.

This study should be interpreted in view of several limitations. First, similar to previous time-series studies on air pollution associated health outcomes, we used daily aggregated data to evaluate the short-term effect of particulate matter on health outcomes, but this aggregated nature of data could be subject to ecological bias. Second, we used fixed-site measurement of particulate matter instead of personal exposure, which could lead to inaccurate exposure measurement. Third, we included relatively small number of asthma outpatient visits, which led to unstable point estimates and CIs. Fourth, since we used secondary data collected from the hospital administrative database, environmental and behavior variables that could serve as confounders were not available to us. Lastly, COVID-19 has greatly reshaped the behavior of patient inpatient and outpatient visits, but we were not able to investigate the potential effect of the COVID-19 pandemic on ALRI outpatient visits since the data in this period is not available (34, 35).

Nonetheless, this study has several strengths. First, this is the first study that investigates the association between particulate matter of different sizes and subtypes of ALRI outpatient visits, while previous studies either reported the exposure of $PM_{2.5}$ or hospitalization as the health outcome. Second, we used counterfactual analyses to estimate the potential percent reduction in ALRI outpatient visits compared to the WHO recommended levels. The results of counterfactual analyses have more substantial public health significance compared to ER,OR, and any other estimates associated with fixed amount of increase in particulate matter (such as 10 μg/m^3 increase in $PM_{2.5}$).

Conclusions

In summary, this study suggests a larger potential percent of reduction in ALRI outpatient visits if $PM_{2.5}$ could be as low as the level recommended by the WHO. The association between particulate matter and pneumonia outpatient visits was stronger among male patients and in cold seasons. The results highlight the need for a consolidated effort to reduce the particulate matter pollution of smaller sizes and consequently improve the health outcomes of residents in China.

Abbreviations

ALRI: Acute lower respiratory infection; CI: Confidential intervals; RR: Relative risk; ER: Excess risk; WHO: World Health Organization; PM: Particulate matter; PM_{10}: Particulate matter with an aerodynamic diameter ≤ 10mm; PM_c: Particulate matter between 2.5 and 10μm in aerodynamic diameter; $PM_{2.5}$: Particulate matter with an aerodynamic diameter ≤ 2.5mm SO_2: Sulfur dioxide; NO_2: Nitrogen dioxide; O_3: Ozone; GAM: Generalized additive models; DOW: Day of the week; PH: Public holidays; df: Degrees of freedom; ICD-10: International Classification of Diseases, Tenth Revision

Declarations

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Availability of data and materials

Please contact author for data requests.

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Authors’ contributions

Study concept and design were contributed by ZL; statistical analysis was contributed by QM and QY; drafting of the manuscript was contributed by ZL, NC, and CY; All authors contributed to the interpretation of results and manuscript editing; All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing of interests

The authors declare that they have no competing interests.

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Tables

Table 1. Summary statistics of acute lower respiratory infections outpatient visits, air pollutants, and meteorological variables.

	Mean	SD	Percentile				
			Min	25th	50th	75th	Max
Acute lower respiratory infections							
Pneumonia	12.5	9.1	0.0	6.0	11.0	16.0	73.0
Bronchiolitis	24.3	11.5	0.0	16.0	23.0	31.0	81.0
Asthma	0.8	1.4	0.0	0.0	0.0	1.0	12.0
Air pollution, μg/m^3							
PM_{10}	58.3	28.1	10.0	38.2	51.1	73.4	217.8
PM_c	21.0	9.9	0.8	14.7	18.8	25.3	77.7
$PM_{2.5}$	37.8	21.2	4.6	22.7	32.3	48.3	156.4
SO_2	13.6	8.5	2.8	8.6	11.9	16.5	166.4
NO_2	45.2	18.6	4.4	33.6	41.2	53.7	177.7
O_3	51.6	30.2	3.5	30.0	47.2	67.1	294.6
Meteorological variables							
Temperature, °C	22.8	5.9	1.7	19.0	25.0	27.5	32.8
Relative humidity, %	81.8	10.2	30.5	77.0	83.1	89.3	100.0

SD: standard deviation

Table 2. Excess risk and 95% confidence intervals of pneumonia, bronchiolitis, and asthma for each 10 μg/m^3 increase in $PM_{2.5}$, PM_c, PM_{10} using single- and two-pollutants models.

Pollutants	Models	Pneumonia	Bronchiolitis	Asthma
PM_{10}				
	Single-pollutant model	3.71 (2.91, 4.52)	3.21 (2.49, 3.93)	3.45 (1.18, 5.78)
	Two-pollutant models			
	Control for SO_2	3.81 (2.97, 4.66)	3.44 (2.69, 4.21)	3.46 (1.13, 5.85)
	Control for NO_2	2.47 (1.47, 3.47)	1.48 (0.58, 2.37)	0.26 (-2.58, 3.19)
	Control for O_3	4.06 (3.22, 4.91)	3.48 (2.72, 4.25)	3.72 (1.30, 6.20)
PM_c				
	Single-pollutant model	9.19 (6.94, 11.49)	9.13 (7.09, 11.21)	11.69 (4.45, 19.43)
	Two-pollutant models			
	Control for SO_2	9.32 (6.98, 11.72)	9.72 (7.58, 11.91)	11.70 (4.29, 19.63)
	Control for NO_2	5.58 (3.03, 8.19)	4.80 (2.45, 7.20)	3.26 (-4.88, 12.09)
	Control for O_3	9.52 (7.21, 11.87)	9.47 (7.37, 11.61)	12.09 (4.56, 20.17)
$PM_{2.5}$				
	Single-pollutant model	4.36 (3.21, 5.52)	3.12 (2.10, 4.15)	3.33 (0.26, 6.49)
	Two-pollutant models			
	Control for SO_2	4.61 (3.37, 5.87)	3.50 (2.39, 4.63)	3.45 (0.14, 6.87)
	Control for NO_2	2.30 (0.96, 3.65)	0.39 (-0.78, 1.58)	-0.40 (-3.86, 3.18)
	Control for O_3	4.85 (3.63, 6.09)	3.38 (2.29, 4.48)	3.54 (0.26, 6.91)

Table 3. Excess risk and 95% confidence intervals of pneumonia, bronchiolitis, and asthma for each 10 $\mu g/m^3$ increase in $PM_{2.5}$, PM_c, and PM_{10} stratified by gender, age group, and season.

Pollutants	Stratum	Pneumonia	Bronchiolitis	Asthma
PM_{10}				
	Gender			
	Male	**4.49 (3.54, 5.45)**	3.44 (2.68, 4.21)	4.46 (1.62, 7.39)
	Female	**2.68 (1.61, 3.75)**	2.76 (1.84, 3.69)	1.78 (-1.51, 5.18)
	Age			
	<5	3.50 (2.66, 4.34)	3.09 (2.36, 3.82)	1.78 (-0.97, 4.60)
	5-14	4.50 (2.71, 6.33)	3.70 (2.49, 4.92)	6.01 (2.39, 9.75)
	Season			
	Warm	**-0.06 (-1.24, 1.13)**	**2.13 (1.03, 3.23)**	6.53 (2.52, 10.69)
	Cold	**5.12 (4.00, 6.25)**	**3.76 (2.74, 4.79)**	1.76 (-1.00, 4.61)
PM_c				
	Gender			
	Male	**11.07 (8.36, 13.83)**	10.02 (7.82, 12.25)	15.65 (6.36, 25.74)
	Female	**6.70 (3.78, 9.71)**	7.57 (4.99, 10.21)	5.94 (-3.96, 16.87)
	Age			
	<5	8.69 (6.37, 11.06)	8.76 (6.69, 10.88)	6.96 (-1.69, 16.38)
	5-14	10.76 (5.65, 16.13)	10.75 (7.34, 14.27)	17.98 (6.46, 30.74)
	Season			
	Warm	**-0.93 (-4.33, 2.60)**	**3.77 (0.40, 7.26)**	22.14 (6.92, 39.53)
	Cold	**13.57 (10.46, 16.77)**	**11.92 (9.07, 14.84)**	9.39 (0.93, 18.56)
$PM_{2.5}$				
	Gender			
	Male	**5.31 (3.95, 6.69)**	3.48 (2.39, 4.58)	4.13 (0.30, 8.09)
	Female	**3.11 (1.58, 4.65)**	2.45 (1.14, 3.78)	1.92 (-2.54, 6.58)
	Age			
	<5	4.07 (2.87, 5.28)	2.88 (1.84, 3.93)	1.53 (-2.16, 5.35)
	5-14	5.59 (3.07, 8.17)	4.10 (2.39, 5.85)	6.13 (1.22, 11.28)
	Season			

	Warm	**0.08 (-1.49, 1.67)**	3.00 (1.56, 4.46)	**7.73 (2.62, 13.08)**
	Cold	**6.08 (4.42, 7.77)**	3.01 (1.51, 4.53)	**-0.30 (-4.05, 3.60)**

The bold type represents the statistically significant differences ($p < 0.05$).

Warm season: April to September; cold season: October to March.

Table 4. Counterfactual analysis on the percent of decline (95% confidence intervals) in acute lower respiratory infection outpatient visits if the level of $PM_{2.5}$, PM_c, and PM_{10} were reduced to the reference levels in Guangzhou from 2013 to 2019.

	Pneumonia	Bronchiolitis	Asthma
PM_{10}	3.89% (3.24%, 5.52%)	4.35% (3.06%, 4.82%)	5.98% (1.92%, 10.37%)
PM_c	1.42% (1.10%, 1.82%)	1.91% (1.48%, 2.36%)	1.79% (0.60%, 3.09%)
$PM_{2.5}$	4.63% (3.47%, 5.98%)	4.38% (2.68%, 5.97%)	6.07% (0.08%, 12.37%)

The references of PM_{10}, $PM_{2.5,}$ and PM_c concentration were based on the World Health Organization's Ambient Air Quality guidelines (24h mean: 50 μg/m^3 for PM_{10}, 25 μg/m^3 for PM_c, and 25 μg/m^3 for $PM_{2.5}$, respectively).

Figures

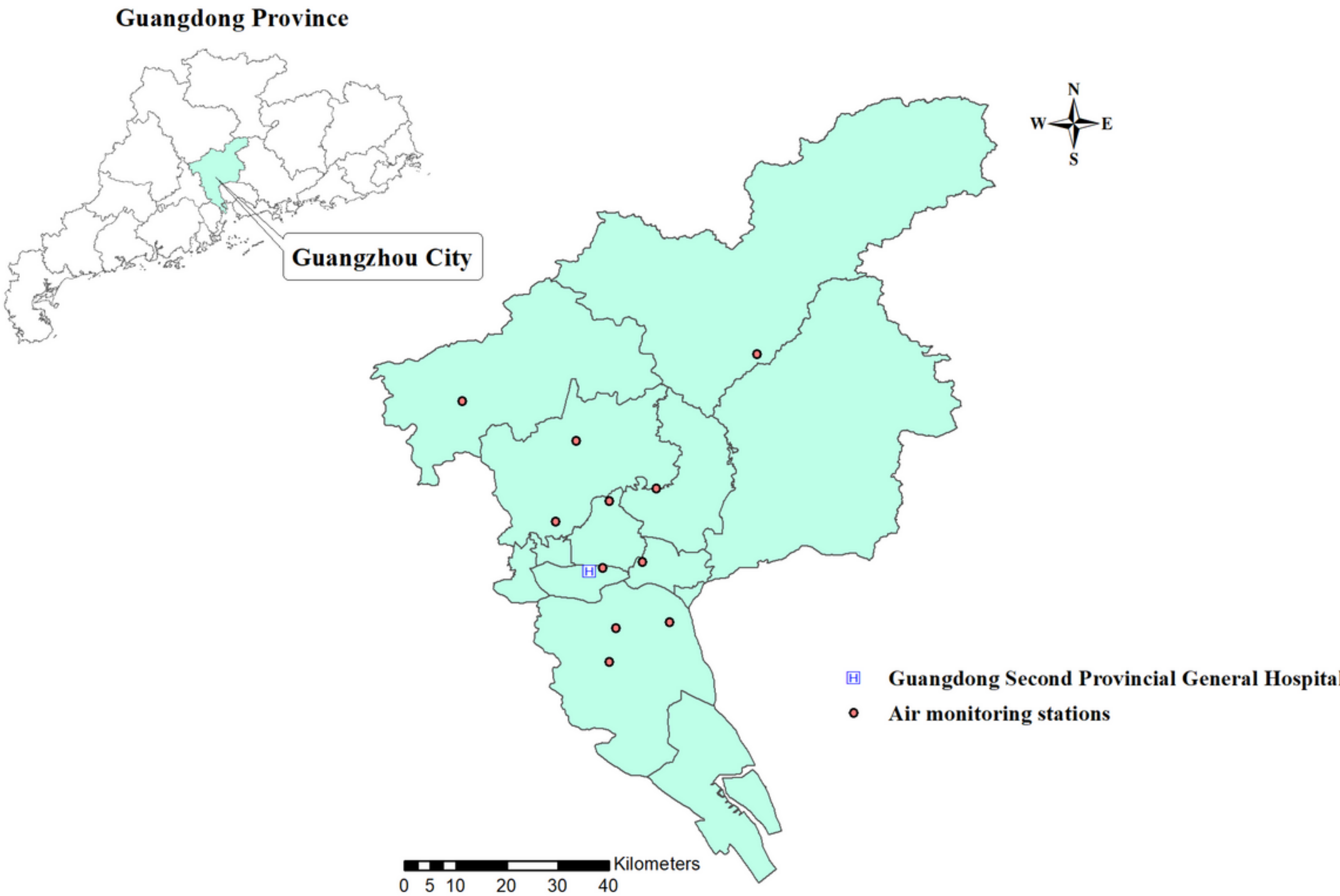

Figure 1

Geographical distribution of the sample hospitals and air monitoring stations. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area o bbnhjr of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

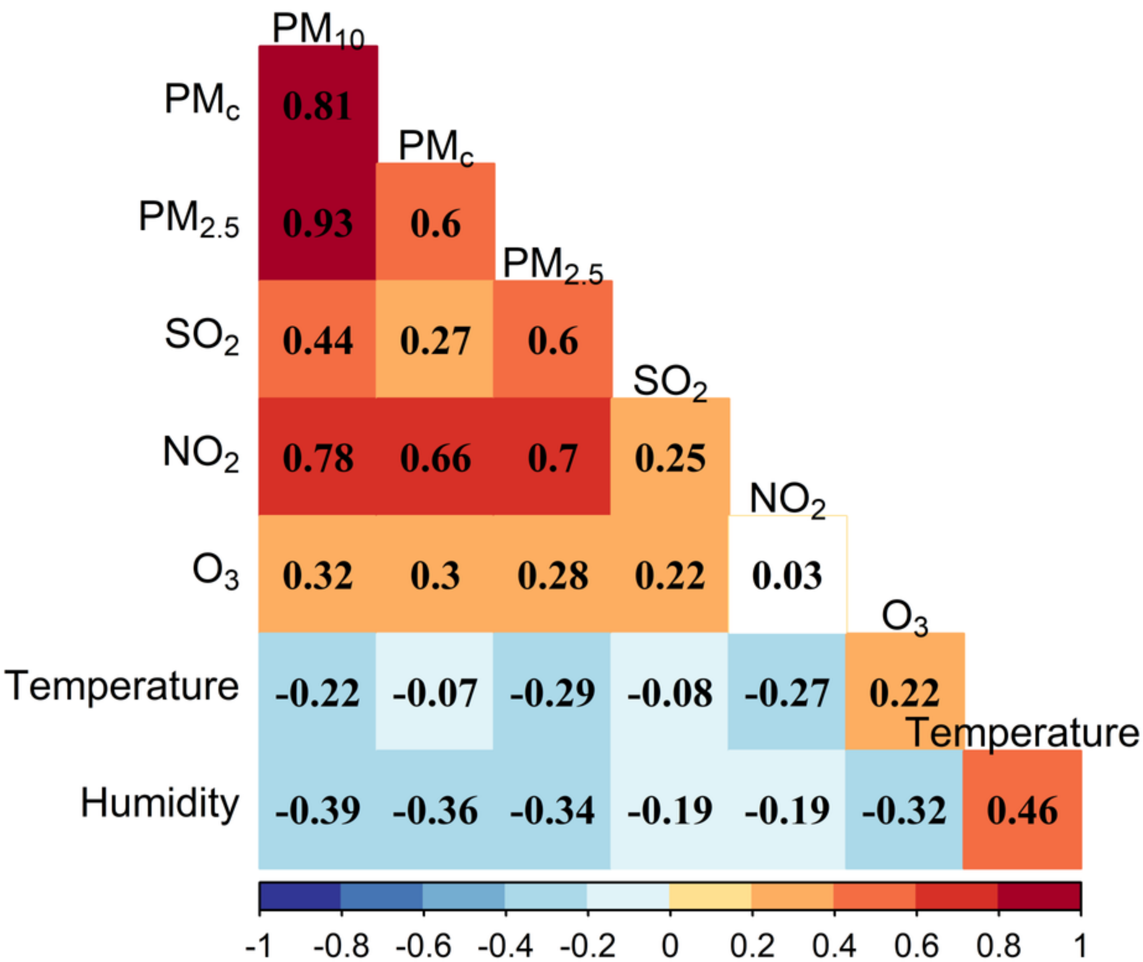

Figure 2

Correlation plot of the air pollutants and meteorological variables. The white cells indicate insignificance correlation coefficient (NO2 and O3).

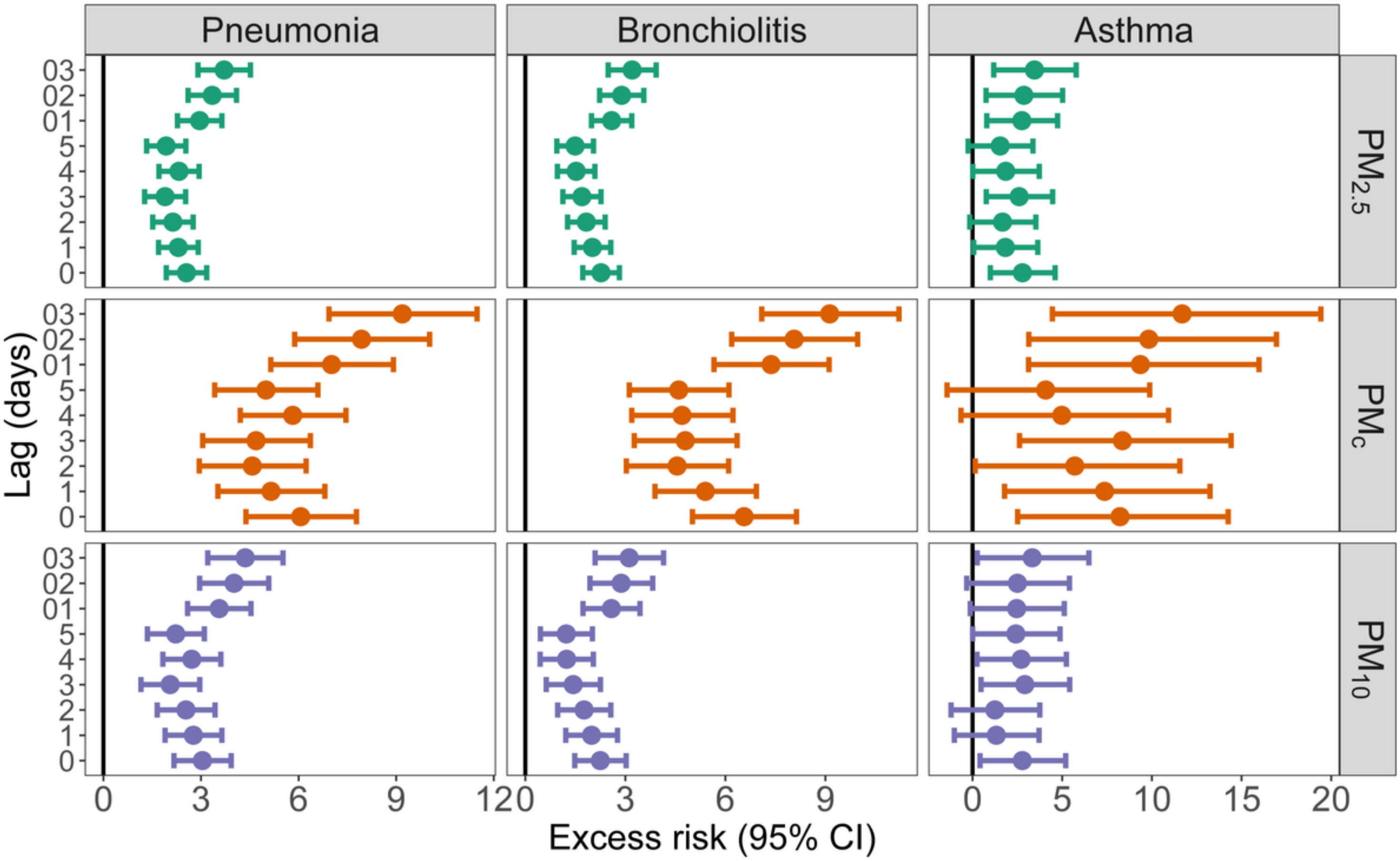

Figure 3

Excess risk (95% confidence intervals) of hospital outpatient visits associated with 10 μg/m3 increase in PM10, PMc, and PM2.5.

Supplementary Files

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