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Causal effect of PM_1 on morbidity of cause-specific respiratory diseases based on a negative control exposure

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ABSTRACT

Background: Extensive studies have linked $PM_{2.5}$ and PM_{10} with respiratory diseases (RD). However, few is known about causal association between PM_1 and morbidity of RD. We aimed to assess the causal effects of PM_1 on cause-specific RD.

Methods: Hospital admission data were obtained for RD during 2014 and 2019 in Beijing, China. Negative control exposure and extreme gradient boosting with SHapley Additive exPlanation was used to explore the causality and contribution between PM_1 and RD. Stratified analysis by gender, age, and season was conducted.

Results: A total of 1,183,591 admissions for RD were recorded. Per interquartile range (28 $\mu g/m^3$) uptick in concentration of PM_1 corresponded to a 3.08% [95% confidence interval (CI): 1.66%–4.52%] increment in morbidity of total RD. And that was 4.47% (95% CI: 2.46%–6.52%) and 0.15% (95% CI: 1.44%-1.78%), for COPD and asthma, respectively. Significantly positive causal associations were observed for PM_1 with total RD and COPD. Females and the elderly had higher effects on total RD, COPD, and asthma only in the warm months ($Z = 3.03$, $P = 0.002$; $Z = 4.01$, $P < 0.001$; $Z = 3.92$, $P < 0.001$; $Z = 2.11$, $P = 0.035$; $Z = 2.44$, $P = 0.015$). Contribution of PM_1 ranked first, second and second for total RD, COPD, and asthma among air pollutants.

Conclusion: PM_1 was causally associated with increased morbidity of total RD and COPD, but not causally associated with asthma. Females and the elderly were more vulnerable to PM_1-associated effects on RD.

1. Introduction

Respiratory diseases (RD) are major public health issues, as well as the second cause of death, contributing to more than 9.5 million deaths worldwide (Collaborators, 2020a; Organization, 2019). By 2040, deaths attributable to RD were forecasted to be 11.6 million globally (Foreman et al., 2018). As one of the most common RD, chronic obstructive pulmonary diseases (COPD) and asthma have affected around 3.9% and 3.6% of people worldwide (Collaborators, 2020a; Collaborators, 2020b). In China, approximately 8.6% and 4.2% of adults suffered from COPD and asthma, of which disability-adjusted life-years ranked third globally (Huang et al., 2019; Wang et al., 2018a; Zhou et al., 2019a). The prevalence of COPD was 15.7% in Beijing, which at the top within China

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Abbreviations

RD	respiratory diseases
COPD	acute exacerbation of chronic obstructive pulmonary disease
PM	particulate matter
$PM_{2.5}$	particulate matter with an aerodynamic diameter ≤2.5 μm
PM_{10}	particulate matter with an aerodynamic diameter ≤10 μm
PM_1	particulate matter with an aerodynamic diameter ≤1 μm
XGBoost	eXtreme Gradient Boosting
SHAP	SHapley Additive exPlanation
GAM	generalized additive model
df	degrees of freedom
E-R	exposure-response
PC	percentage change
IQR	interquartile range
95% CI	95% confidence interval
SO_2	sulfur dioxide
NO_2	nitrogen dioxide
CO	carbon monoxide
O_3	ozone

(Wang et al., 2020). Given the substantial disease burden, it is essential to identify risk factors of COPD and asthma, particularly in Beijing, China.

Emerging evidence has indicated that particle matter (PM) is a risk factor for RD (Shin et al., 2022; So et al., 2022). Due to the adsorption capacity, PM becomes the carrier of toxic substances (Wang et al., 2022). $PM_{2.5}$ (particulate matter with an aerodynamic diameter ≤2.5 μm) and PM_{10} (particulate matter with an aerodynamic diameter ≤10 μm) may affect RD such as COPD and asthma when they are inhaled into the lungs (Bo et al., 2021; Odo et al., 2022; Wei et al., 2022b). Toxicology suggested that the particle size were smaller, and the toxicity were greater, as well as the higher risk to health (Wang et al., 2021a). And epidemiologic investigation reported that effect size of PM_1 (particulate matter with an aerodynamic diameter ≤1 μm) may be larger than $PM_{2.5}$ and PM_{10} (Yang et al., 2022). Whereas, exact contribution of PM_1 for RD remains vague, and there are challenges in comparing synthesized effect estimates because of the interaction of all air pollutants.

Recently, causal inference method has been applied in environmental epidemiologic studies, such as instrumental variable, difference-in-difference, and regression discontinuity design (Knittel et al., 2016; Streeter et al., 2017; Williams et al., 2019). Negative control exposure can reduce residual confounding, which has been certified the ability of unbiased causal effect estimation (Li et al., 2022; Wei et al., 2022a). But less is recognized about causal associations between PM_1 and morbidity of RD (Hu et al., 2022; Wang et al., 2021b). Furthermore, it is difficult to obtain an unbiased causal estimation due to the strict assumptions, but negative control exposure can exactly evaluate causal effects, which compares the impacts of post and pre-outcome exposures on outcome (Yu et al., 2021).

In this study, a negative control exposure was used to evaluate the causal effect of PM_1 concentrations on morbidity of cause-specific RD. In addition, PM_1 contributions on cause-specific RD were identified by eXtreme Gradient Boosting (XGBoost) method with SHapley Additive exPlanation (SHAP). And subgroup analyses of gender, age, and season were taken, which explore the susceptible subpopulations or season.

2. Materials and methods

2.1. Study population

In this study, daily counts of hospital admissions for RD were obtained from Beijing Municipal Health Big Data and Policy Research Center (http://www.phic.org.cn/) between January 1, 2014 and December 31, 2019, which is a government agency that gathers and consolidates hospital information. The agency gathers approximately 95% of permanent residents in Beijing, and thus can highly represent the overall population of Beijing (Li et al., 2018). The code of RD was in terms of the International Classification of Diseases, the 10th Revision, which total RD was code as J00-J99, COPD was code as J44, and asthma was code as J45-J46. And admissions for RD were subdivided by gender and age (≤60 and > 60 years). The study was approved by the Institutional Review Board of Capital Medical University (No. IRB00009511). Informed consent was not required because we did not use personal data.

2.2. Air pollutants and meteorological data

The PM_1 data were collected from the ChinaHighAirPollutants dataset (CHAP, https://weijing-rs.github.io/product.html), which was generated by machine learning algorithm, and was characterized by high-resolution and high-quality via cross-validation (Wei et al., 2019). We gathered $PM_{2.5}$ and PM_{10} data from ChinaHighAirPollutants dataset as well (Wei et al., 2020, Wei et al., 2021a, Wei et al., 2021b). Daily mean concentrations of other air pollutants (SO_2, NO_2, O_3, CO) were gained from Beijing Environmental Protection Bureau (http://www.bjepb.gov.cn/). Meteorological data were gained from China Meteorological Data Service Center (http://data.cma.cn/).

2.3. Statistical analysis

2.3.1. Generalized additive model

A generalized additive model (GAM) was conducted to explore the effects of PM_1 concentration on admissions for RD, which was with quasi-Poisson regression (Wang et al., 2018b). A penalized cubic spline was adopted to adjust potential long-term trend with 7 degrees of freedom (*df*) per year (Meng et al., 2021). The day of the week (DOW) was controlled by adding an indicator variable in the model accounting for possible variations in a week. The spline functions with 3 *df* for moving average temperature of 14 days and 3 *df* for current relative humidity were used to exclude lagged and nonlinear confounding effects (Rahman et al., 2022). The model is specified as:

$$logE(Yt) = \alpha + \beta Zt + s(time) + s(Temp) + s(RH) + factor(DOWt) + factor(holiday)$$

Where: *E(Yt)* is the expectation of admissions on day *t*, α is the intercept; β is the coefficients calculated from the regression model; *s()* indicates the smoother based on the penalized cubic spline; *time* represents long-term trend; *Temp* and *RH* are moving average temperature of 14 days and current relative humidity on day *t*, respectively; *DOW* is the day of the week on day *t* and *holiday* is to avoid impact of public holidays.

The effects of PM_1 are usually not observed instantly but are delayed. Hence, to explore the delayed effects of PM_1, we assessed the effects both in single-day lags and moving-day lags. For example, lag 0 represented that the PM_1 concentration and the number of admissions were on the same day. And lag 01 represented that the exposure was mean of the previous and intraday concentration. Given that the study focused on the short-term effects, the maximum lag in this study was 7 days (Li et al., 2021c). Exposure-response (E-R) curves between PM_1 and RD were estimated to inspect the linearity. If E-R curves showed that it was not right to treat PM_1 as linear variable among all concentrations, a change point was chosen where the slope changed to gain the

appropriate concentrations assessing the effects of PM_1 on RD (Barrio et al., 2013; Knight et al., 2020).

2.3.2. Negative control exposure

A negative control exposure may reduce unmarked confounding bias, which could be used in time-series studies as well (Lipsitch et al., 2010; Yu et al., 2021). Negative control exposure is defined as a variable that is associated with an unobserved confounding factor but has no causal association with outcome (Tchetgen Tchetgen, 2014). Causal association between environmental exposure and disease was determined by comparing the effect of post-outcome exposure and pre-outcome exposures on outcome (Magen-Molho et al., 2021). We used the exposure before the outcome to calculate the causal effect of PM_1 on RD and the exposure after the outcome on corresponding day was used as the negative control exposure, with the maximum lag of 7 days. It should be noticed that lag 02 represented the average concentration of the previous two days, which was different from the association effect estimation.

2.3.3. EXtreme gradient boosting model

An XGBoost model with SHAP value was employed to calculate the magnitude of PM_1 to admissions of RD compared with other air pollutants. XGBoost based on decision trees was an optimized and enhanced ensemble model, which can provide better performance to deal with both continuous and categorical data. It avoids many drawbacks, which has been reported, such as over-fitting, handling missing values, and training efficiency (Zhou et al., 2019b). The SHAP method is preferred over other explain ability methods in the literature because it shows the impact of each feature and indicates how much a given feature altered the prediction (Štrumbelj et al., 2014). In our study, we put air pollutants (PM_1, $PM_{2.5}$, PM_{10}, SO_2, NO_2, O_3, CO) and other confounding into the model at the same time. After calculating the SHAP value of each observation, the mean SHAP values were ranked to determine the magnitude of PM_1 among air pollutants, which were averaged by absolute value.

2.3.4. Outcome indicator and sensitivity analyses

The percentage change (PC) for RD per interquartile range (IQR) uptick in PM_1 concentration was calculated as follows: $percentage\ change = [exp\ (\beta * IQR) - 1] * 100$, where β referred to the coefficient of PM_1 from GAM, *IQR* was the per interquartile range uptick in PM_1 concentration. The confidence intervals (CI) of were percentage change reported as well. The Z values and corresponding *P* values across subgroups were calculated to check for statistical differences (Altman and Bland, 2003). Stratification analyses were conducted to find potentially susceptible gender and age populations. The stratification of season was carried out: cold season (November to April) and warm season (May to October).

Additionally, we developed two-pollutant model, which were modified by gaseous pollutants, to check the robustness. We also changed the *df* of meteorological (2–7 *df*) and time variables (5–10 *df*). Data were analyzed by R software (version 4.0.5) using the *mgcv*, *NCETS*, and *xgboost* packages. The statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

3. Results

3.1. Descriptive statistics

A total of 1,183,591 admissions were recorded during the study period, corresponding to a daily average of 89 for total RD (Table 1). On average, there were 84 and 14 daily admissions for COPD and asthma. All admissions were more reported in the elderly than in younger patients, with the elderly constituting more than 62.54% of total cases. There were more admissions in the cold season (53.81%).

During the study, mean everyday concentration of PM_1 was 35.9 ± 26.2 μg/m^3, ranging from 3.9 to 204.6 μg/m^3 (Table 2). Daily PM_1concentration was higher in the cold season (41.8 ± 30.7 μg/m^3) than in the warm season (29.6 ± 18.3 μg/m^3). Generally, PM_1 was positively related with SO_2, NO_2, and CO, weakly related with relative humidity, and negatively related with temperature and O_3 (Fig. S1).

Table 1
Characteristics of respiratory diseases in Beijing, 2014–2019.

	N	Mean ± SD	Min	P_{25}	P_{50}	P_{75}	Max	IQR
Total	1,183,591	540 ± 203	174	330	574	687	1192	357
Cause-specific								
COPD	184,533	84 ± 34	16	52	86	105	217	53
Asthma	30,311	14 ± 7	0	8	14	18	56	10
Gender								
Man	713,317	326 ± 121	96	192	353	415	687	223
Woman	470,266	215 ± 84	59	139	219	274	542	135
Age group								
≤60 years	442,140	202 ± 73	57	138	205	253	494	115
≥61 years	740,201	338 ± 134	94	191	363	437	775	246
Season								
Cold season	636,941	586 ± 214	184	365	629	746	1192	381
Warm season	546,650	495 ± 181	174	293	537	642	961	349

Note: N: total admission during the study period; SD: standard deviation; Min: minimum daily admission; P_{25}: the 25th percentile; P_{50}: the 50th percentile; P_{75}: the 75th percentile; Max: maximum daily admission; IQR: interquartile range; COPD: chronic obstructive pulmonary disease; Cold season: November to April; Warm season: May to October.

3.2. Association between PM_1 and morbidity of RD

Percentage changes (%) and 95% CI associated with per IQR increase in PM_1 for RD were present in Fig. 1. As the relationships between PM_1 and RD as well as COPD were nonlinear, the concentrations of ≤60 μg/

Table 2
Summary distributions of air pollutants and meteorological factors.

	Mean ± SD	Min	P_{25}	P_{50}	P_{75}	Max	IQR
PM_1, μg/m^3	35.9 ± 26.2	3.9	17.7	28.6	45.8	204.6	28.2
$PM_{2.5}$, μg/m^3	54.8 ± 38.6	7.4	28.2	44.5	69.4	276.6	41.2
PM_{10}, μg/m^3	94.9 ± 53.5	20.6	58.1	82.9	117.4	816.7	59.3
SO_2, μg/m^3	9.2 ± 9.8	2.0	3.2	5.8	10.9	78.1	7.7
NO_2, μg/m^3	42.9 ± 19.8	8.6	29.1	38.7	52.6	141.7	23.5
CO, mg/m^3	1.0 ± 0.8	0.2	0.5	0.8	1.1	7.6	0.6
O_3, μg/m^3	60.8 ± 37.0	3.1	31.8	55.4	83.3	77.6	51.6
Temperature, °C	12.5 ± 11.3	−16.9	1.3	13.9	22.8	31.4	21.5
Relative humidity, %	53.6 ± 19.0	11.2	38.2	53.4	69.5	95.3	31.4

Note: SD: standard deviation; Min: minimum daily admission; P_{25}: the 25th percentile; P_{50}: the 50th percentile; P_{75}: the 75th percentile; Max: maximum daily admission; IQR: interquartile range; PM_1: particulate matter with aerodynamic diameter ≤1 μm; $PM_{2.5}$: particulate matter with aerodynamic diameter ≤2.5 μm; PM_{10}: particulate matter with aerodynamic diameter ≤10 μm; SO_2: sulfur dioxide; NO_2: nitrogen dioxide; CO: carbon monoxide; O_3: ozone.

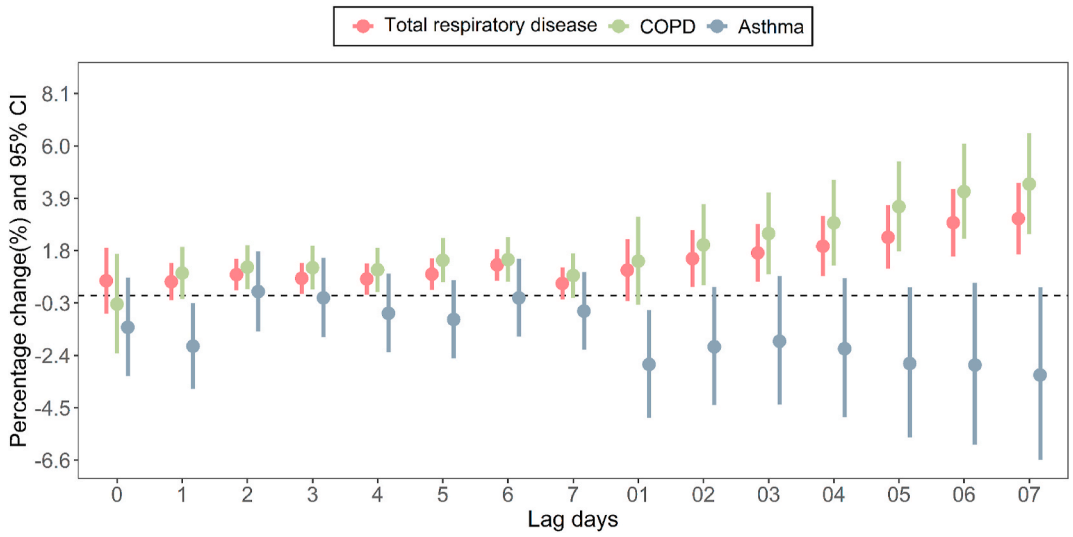

Fig. 1. Percentage changes (%) and 95% CI for respiratory diseases per IQR increment in PM_1 concentration. Note: COPD: chronic obstructive pulmonary disease; CI: confidence intervals; IQR: interquartile range; PM_1: particulate matter with aerodynamic diameter ≤1 μm.

m^3 were used to assess the effects of PM_1 on total RD and COPD. Significant associations were observed between PM_1 with total RD and COPD. Per IQR (28 μg/m^3) uptick of PM_1 concentration corresponded to a 3.08% (95% CI: 1.66%–4.52%), 4.47% (95% CI: 2.46%–6.52%), and 0.15% (95% CI: 1.44%-1.78%) increase in morbidity of total RD, COPD, and asthma, respectively, at lag 07 days, lag07 days, and lag2 days. The effects of PM_1 increased when adjusting for SO_2, NO_2, and O_3, and declined a bit when adjusting for CO, but all associations remained statistically significant (Fig. S2).

3.3. Causal effect estimation of PM_1 on RD

Fig. 2 showed the causal effect estimation and 95% CI for PM_1 and RD using a negative control exposure. Significantly positive causal associations were observed for PM_1 with total RD at lag6, lag 06, and lag07, corresponding to 0.55 (95%CI: 0.05–1.05), 1.03 (95%CI: 0.15–1.91), and 1.08 (95%CI: 0.13–2.03) causal effect estimator. And that for COPD was at lag2, lag 3, lag6 and lag02 to lag07 with highest causal effect estimator of 0.20 (95%CI: 0.04–0.35). But PM_1 had no significantly causal effect on asthma.

3.4. Stratification analyses

The effects of PM_1 on RD were slightly larger for females and the elderly than males and younger individuals, but there was no statistical difference on total RD, COPD, or asthma (Fig. 3).

We also stratified by gender and age during cold and warm season (Fig. 4). In the warm season, the PM_1-related total RD increment in female was slightly higher than in male [4.12% (95% CI: 1.71%–6.58%) vs. 3.29% (95% CI: 0.36%–6.30%), Z = 3.03, P = 0.002]; and the PM_1-related COPD increment in females was much higher than in males [7.47% (95% CI: 1.04%–14.31%) vs. 5.59% (95% CI:2.27%–9.03%), Z = 2.02, P = 0.044]; and the PM_1-related asthma increments in females and the elderly were statistically significantly higher than in males and younger adults [4.41% (95% CI: 0.21%-9.25%) vs. 2.71% (95% CI: 2.39%-8.07%), Z = 2.11, P = 0.035; 5.70% (95% CI: 2.53%-14.63%) vs. 3.63% (95% CI: 1.30%-8.81%, Z = 2.44, P = 0.015). No statistics difference was found in the connections of PM_1 and subgroups of participants with seasonal stratified analysis (Table S1).

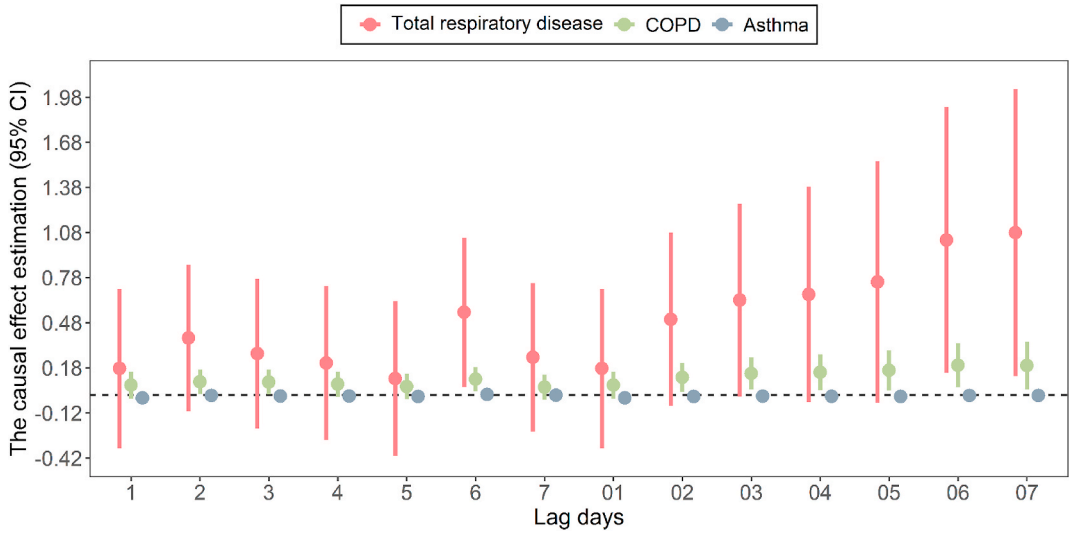

Fig. 2. The causal effect estimation for respiratory diseases with PM_1. Note: COPD: chronic obstructive pulmonary disease; CI: confidence intervals; PM_1: particulate matter with aerodynamic diameter ≤1 μm.

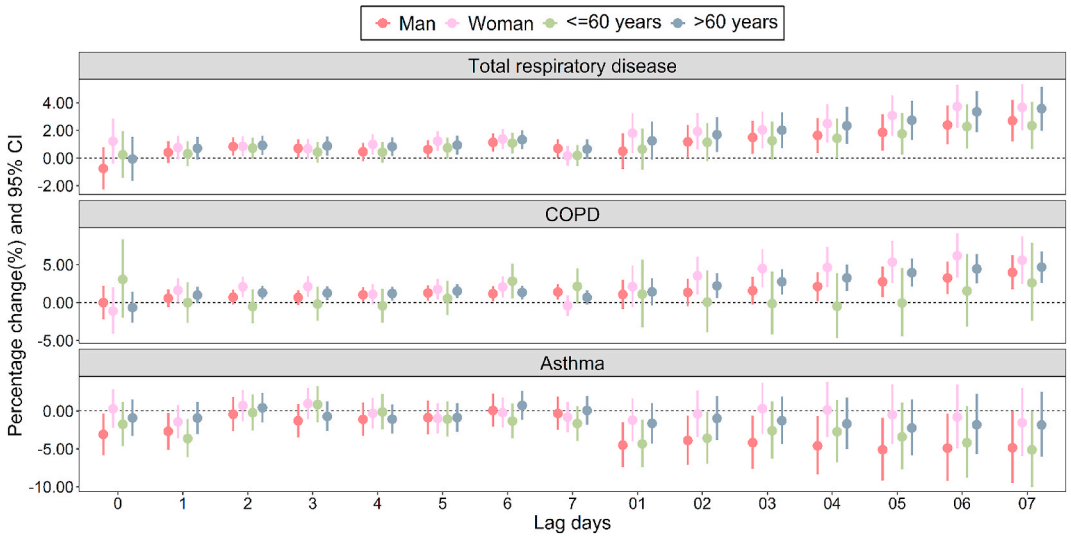

Fig. 3. Percentage changes (%) for respiratory diseases stratified by sex and age associated with per IQR increment in PM_1. Note: COPD: chronic obstructive pulmonary disease; CI: confidence intervals; IQR: interquartile range; PM_1: particulate matter with aerodynamic diameter ≤1 μm.

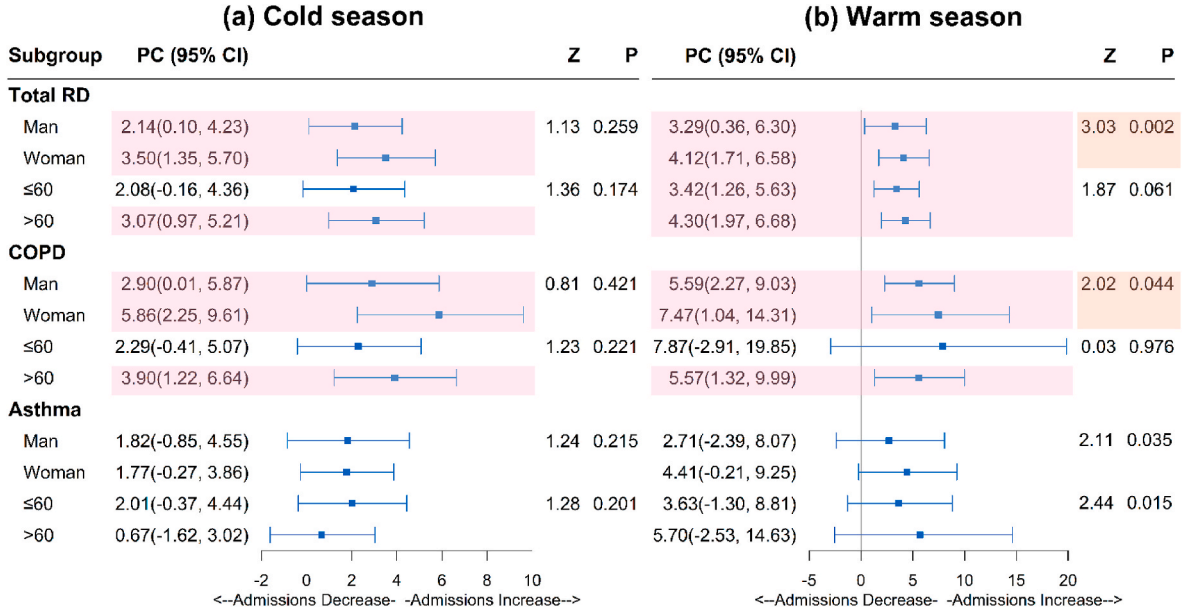

Fig. 4. Percentage changes for respiratory diseases stratified by sex and age during cold and warm seasons associated with per IQR increment in PM_1. Note: CI: confidence intervals; IQR: interquartile range; PM_1: particulate matter with an aerodynamic diameter ≤1 μm; PC: percentage change; RD: respiratory disease; COPD: chronic obstructive pulmonary disease. Pink indicated statistically significant effect estimates, and yellow indicated $P < 0.05$. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3.5. Rank of contribution of PM_1 to RD

Fig. 5 showed the contribution of PM_1 in the XGBoost model which took all air pollutants into account. Taking the average absolute values of SHAP for every variable was to compare the contribution of each variable to RD. From this plot, it can be inferred that contribution of PM_1 ranked first for total RD with the SHAP value of 8.991, and second for COPD (2.132) and asthma (0.294), in which air pollutants was ordered by the mean SHAP values. Moreover, the effect of PM_1 was much larger than $PM_{2.5}$ and PM_{10}, regardless of total RD, COPD, or asthma.

3.6. Exposure-response curve

The E-R curves between PM_1 and RD were shown in Fig. 6. For total RD, the E-R curve increased slightly at low concentrations and then became plateauing. For COPD, the E-R curve was almost inverted U-shaped with an inflection point at 60 $\mu g/m^3$. The E-R curve of asthma showed a generally linear increasing trend. Stratification analysis was also done for E-R curves (Fig. S3 and Fig. S4). The E-R curve for PM_1 for total RD changed to an inverted U-shaped in subgroups. The E-R curve of younger adults (age ≤60 years) for asthma was generally linear with a descending trend.

4. Discussion

To the best of our knowledge, this is the first study to assess causal effects between PM1 and morbidity of cause-specific RD in Beijing. In our study, exposure to PM1 had causal impact on incident COPD. Female and the elderly were more vulnerable to PM1-associated effects. PM1 contributed greater to RD, especially compared with other particulate

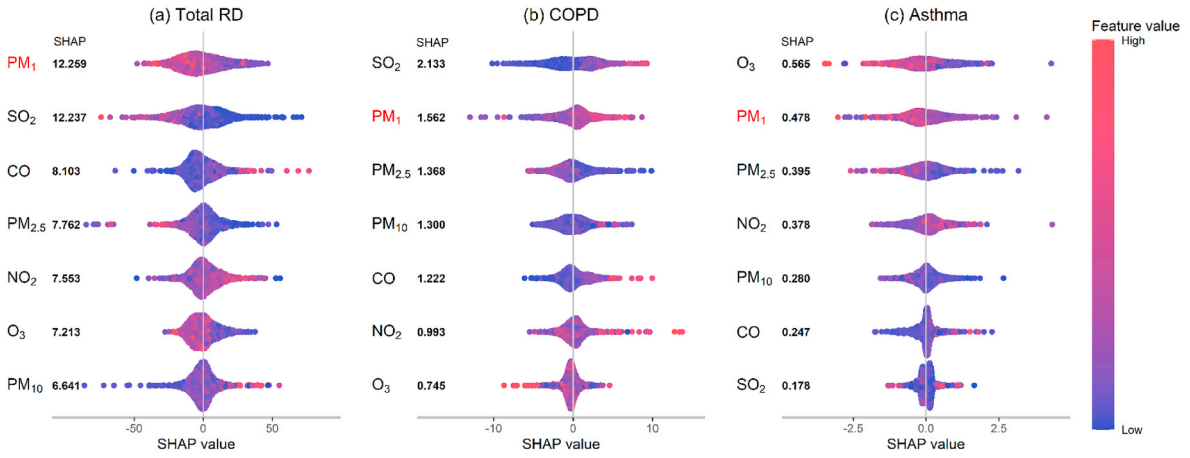

Fig. 5. SHAP summary plot of PM_1 ranked by global feature importance in XGBoost model: (a) for total respiratory diseases; (b) for COPD; (c) for asthma. Note: PM_1: particulate matter with aerodynamic diameter ≤1 μm; 1 μm; SO_2: sulfur dioxide: CO: carbon monoxide; $PM_{2.5}$: particulate matter with aerodynamic diameter ≤2.5 μm; NO_2: nitrogen dioxide; O_3: ozone; PM_{10}: particulate matter with aerodynamic diameter ≤10 μm; SHAP: SHapley Additive exPlanation; XGBoost: eXtreme Gradient Boosting; COPD: chronic obstructive pulmonary disease.

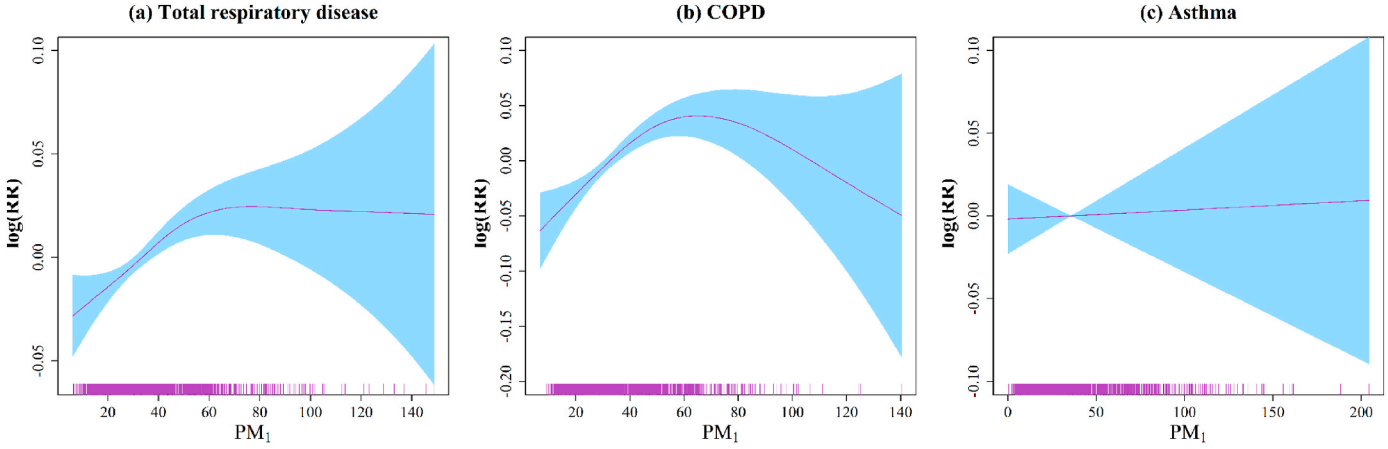

Fig. 6. Exposure-response relationships between PM_1 and respiratory diseases. Note: PM_1: particulate matter with aerodynamic diameter ≤1 μm; COPD: chronic obstructive pulmonary disease.

matters. Non-linear exposure-response relationships were observed between PM1 with total RD and COPD. Our findings added evidence for PM1-induced adverse effects on RD in China.

In our study, positive causal effects were observed between PM_1 and total RD and COPD, but no significant effect was observed on asthma. Consistent with our findings, Yazdi et al. reported that there was causally effect between PM2.5 and increased admissions of RD using a difference-in-difference approach, another causal inference method (Yazdi et al., 2022). Most of previous studies reported non-causal associations of PM with morbidity for RD (Lin et al., 2018; Zhang et al., 2020). Several research stated that it was long-term, instead of short-term exposure to PM_1, had a positive association with asthma, which was roughly corresponding to our result (Hu et al., 2022). Potential mechanisms underlying the causal association may be biologically credible: PM could induce airway reactivity by triggering oxidative stress and inflammation, and then weakening immune defense and aggravating existing or ongoing RD (Jheng et al., 2021; Pan et al., 2021; Riggs et al., 2020; Yee et al., 2021).

It is crucial to identify susceptible populations to public health. We found that females and the elderly were more susceptible to PM_1 associated COPD and asthma, and there was a much greater impact in warm season than cold season, which were in conformity to previous research (Peng et al., 2022; Priyankara et al., 2021; Wang et al., 2019). A two-year panel study in Shanghai, China showed that elderly female subjects were susceptible to PM_1-associated COPD and asthma (Chen et al., 2021). The difference between sex groups may be related to socioeconomic, behavioral, and psychological factors. Possibly, it is the smaller lungs and narrower airways in females that may aggravate airway reactivity and increase particle deposition (Bennett et al., 1996). The elderly are susceptible to PM_1 partially because of their inability to regulate pro-inflammatory and anti-inflammatory mediators (Glencross et al., 2020). Compared to cold season, people have more chances to do outdoor activity in warm season. Meanwhile, there were more ultrafine particulate matters penetrating from outdoor to indoor in warm season, resulting in increased exposure (Zauli-Sajani et al., 2018).

We found PM1 had a greater contribution to RD, particularly in particulate matters based on SHAP value of XGBoost model. Some studies have determined the smaller particles can lead to worse adverse health effects (Zhu et al., 2021). A study from 652 cities worldwide supported that impacts of PM2.5 was larger than PM10, regardless of country-specific or pooled estimates (Liu et al., 2019). Similarly, the effect of PM1 was slightly larger than that of PM2.5 on RD with a 1.91% increment in our study (Liu et al., 2021). The greater contribution of PM1 may be supported by ample evidence that smaller particles can carry more toxics and permeate deeper (Kim et al., 2015). The greater contribution of SO2 on COPD can be explained by the irritant and bronchoconstrictor characteristic (Li et al., 2021a). And the inhalation of O3 can increase more asthma admissions by impairing treatment

responsiveness in asthmatic patients and eliciting more severe symptoms (Flayer et al., 2020).

The E-R curves were seemed to flatten at high daily mean PM_1 concentrations for total RD, curvilinear for COPD and approximately linear for asthma in our study, which were partially in line with previous studies (Dong et al., 2021). The threshold can be explained that people living in cities, which are at high levels of PM_1 such as Beijing, are possibly adaptive to PM1 (Liu et al., 2019). However, a study from five typical Chinese cities reported different city-specific trends between particles and RD (Li et al., 2021b). The heterogeneity in the E-R curves could be roughly explained by the varying population susceptibility, data quality, and unique source and chemical composition of PM_1 in different cities, which could affect its toxicity immensely (Niu et al., 2022; Tao et al., 2021). Organic aerosol from primary sources was the major component of PM_1, particularly traffic organic aerosol and coal combustion organic aerosol, which indicated that traffic distribution and the composition of coal could alter the health effect of PM_1 (Niu et al., 2021). As a major chemical composition of PM_1, polycyclic aromatic hydrocarbons especially carcinogenic polycyclic aromatic hydrocarbons had respective effects on RD (Agudelo-Castañeda et al., 2017; Insian et al., 2022).

There are several strengths that should be encompassed. First, this was the first study to estimate causal effects of PM_1 and cause-specific RD, including COPD and asthma. The implications of our findings extend to causal inference through a negative control exposure, which has been verified that it could reduce residual confounding and obtain unbiased estimates by using post-outcome exposures as negative control exposures. Second, SHAP value derived from XGBoost was implemented to rank the contribution of PM_1 among air pollutants on RD. XGBoost has been identified better performance than other machine learning methods, which does a second-order Taylor expansion and then is more accurate in handing segmentation point and missing data (Nam et al., 2022). And SHAP value is an intuitive and theoretically reliable way to determine the contribution in machine learning, which shows how estimation changes after each variable is removed (Scavuzzo et al., 2022). Third, the air pollutant in this study was focused on PM_1 of which adverse effect was higher than $PM_{2.5}$ and PM_{10}. Smaller particles may absorb more toxic components and filter deeper into the lungs. Fourth, the study was conducted for a relatively long time from 2014 to 2019, and the data had been proven to be highly reliable. Therefore, the results in our study could reflect the authentic impacts of PM_1 on RD in Beijing.

Some limitations also should be acknowledged. First, exposure misclassification may be inevitable due to the exposure estimates are based on site rather than personal monitoring. Second, as a single-city study, we were unable to extrapolate our findings to other cities or regions. Third, the effects may be underestimated, because the standard of hospital admission is stricter due to the heavy medical burden in prosperous areas. Fourth, due to data issue, we cannot identify the impacts of each composition of PM_1, which warranted further study. Fifth, it may be inaccurate for the E-R curves in high concentration due to the limited data, which was adjusted in the model to evaluate effects.

5. Conclusion

Exposure to PM_1 was causally associated with incident COPD. Females and the elderly were identified as susceptible, particularly in the warm season. PM1 contributed greater to RD among air pollutants, especially in particulates. Our findings added to evidence of COPD attributable to PM_1 pollution.

Author contributions

Shiyun Lv: Writing original draft, Data curation, Methodology, Visualization. **Xiangtong Liu**: Writing - review & editing, Supervision. **Zhiwei Li**: Software, Visualization. **Feng Lu**: Data curation. **Moning Guo**: Data collection. **Mengmeng Liu**: Methodology. **Jing Wei**: Data curation. **Zhiyuan Wu**: Writing - review & editing, Supervision. **Siqi Yu**: Methodology. **Shihong Li**: Methodology, Supervision. **Xia Li**: Writing - review & editing. **Wenkang Gao**: Data collection. **Lixin Tao**: Writing - review & editing. **Wei Wang**: Methodology, Visualization. **Jinyuan Xin**: Writing - review & editing, Data collection and cleaning, Methodology. **Xiuhua Guo**: Writing - review & editing, Conceptualization, Project administration, Supervision.

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Ethical approval

Informed consent was not required because we did not use personal data identifiers.

Consent for publication

Not applicable.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that has been used is confidential.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2022.114746.

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