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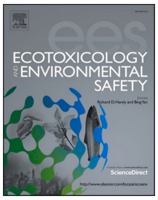

Acute effect of particulate matter pollution on hospital admissions for cause-specific respiratory diseases among patients with and without type 2 diabetes in Beijing, China, from 2014 to 2020

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ABSTRACT

Background: Scientific studies have identified various adverse effects of particulate matter (PM) on respiratory disease (RD) and type 2 diabetes (T2D). However, whether short-term exposure to PM triggers the onset of RD with T2D, compared with RD without T2D, has not been elucidated.

Methods: A two-stage time-series study was conducted to evaluate the acute adverse effects of PM on admission for RD and for RD with and without T2D in Beijing, China, from 2014 to 2020. District-specific effects of $PM_{2.5}$ and PM_{10} were estimated using the over-dispersed Poisson generalized addictive model after adjusting for weather conditions, day of the week, and long-term and seasonal trends. Meta-analyses were applied to pool the overall effects on overall and cause-specific RD, while the exposure-response (E-R) curves were evaluated using a cubic regression spline.

Results: A total of 1550,154 admission records for RD were retrieved during the study period. Meta-analysis suggested that per interquartile range upticks in the concentration of $PM_{2.5}$ corresponded to 1.91% (95% CI: 1.33–2.49%), 2.16% (95% CI: 1.08–3.25%), and 1.92% (95% CI: 1.46–2.39%) increments in admission for RD, RD with T2D, and RD without T2D, respectively, at lag 0–8 days, lag 8 days, and lag 8 days. The effect size of $PM_{2.5}$ was statistically significantly higher in the T2D group than in the group without T2D ($z = 3.98$, $P < 0.01$). The effect sizes of PM_{10} were 3.86% (95% CI: 2.48–5.27%), 3.73% (95% CI: 1.72–5.79%), and 3.92% (95% CI: 2.65–5.21%), respectively, at lag 0–13 days, lag 13 days, and lag 13 days, respectively, and no statistically significant difference was observed between T2D groups ($z = 0.24$, $P = 0.81$). Significant difference was not observed between T2D groups for the associations of PM and different RD and could be found between three groups for effects of PM_{10} on RD without T2D. The E-R curves varied by sex, age and T2D condition subgroups for the associations between PM and daily RD admissions.

Conclusions: Short-term PM exposure was associated with increased RD admission with and without T2D, and the effect size of $PM_{2.5}$ was higher in patients with T2D than those without T2D.

Abbreviations: RD, respiratory disease; T2D, type 2 diabetes; COPD, chronic obstructive pulmonary disease; PM, particle matters; $PM_{2.5}$, fine particulate matter with an aerodynamic diameter ≤ 2.5 μm; PM_{10}, inhalable particulate matter with an aerodynamic diameter ≤ 10 μm; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; O_3, ozone; CO, carbon monoxide; BMHCIC, the Beijing Municipal Health Commission Information Centre; ICD-10, International Classification of Diseases, 10th Revision; URI, upper respiratory tract infection; LRI, lower respiratory tract infection (preclude pneumonia); GAM, generalized additive model; RR, relative risk; IQR, interquartile range; df, degrees of freedom; E-R curves, exposure-response curves; 95% CI, 95% confidence interval; SD, standard deviation.

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1. Introduction

Respiratory disease (RD) is the leading cause of morbidity and mortality worldwide (Collaborators, 2020; Gunasekaran et al., 2021; Zhang et al., 2021). Type 2 diabetes (T2D) is one of most common comorbidities in patients with RD. Recent estimates indicate that 116.4 million people in the Chinese adult population had T2D, ranking first in the world (Saeedi et al., 2019). About one fifth of patients suffering from chronic obstructive pulmonary disease (COPD) is comorbid with T2D, leading to poor prognosis (Castañ-Abad et al., 2020).

Compared with those without T2D, adults with T2D have 1.54-fold increased risk of COPD-related severe exacerbation and death (Castañ-Abad et al., 2020). Diabetes-related respiratory complications, especially COPD and asthma, are mainly responsible for the disability and premature death associated with T2D (Peters et al., 2020; Wang et al., 2020). Given the substantial prevalence of comorbidities of T2D and RD, it is essential to determine modifiable risk factors, particularly in middle-income countries.

Air pollutants are common modifiable risk factors for RD and T2D (Paul et al., 2020; Shao et al., 2021). Existing study has evaluated the association between particulate matter (PM) and RD (Li et al., 2021). Recently, the effect of air pollution on T2D has attracted increasing attention (Bo et al., 2021; Wu et al., 2021). Globally, ambient fine particulate matter contributes to approximately 3.2 million incident cases of T2D, and approximately 8.2 million disability-adjusted life years are caused by diabetes (Bowe et al., 2018). Epidemiological studies suggest that people with T2D may be more susceptible to respiratory health effects associated with air pollution, with lower vascular reactivity and stronger respiratory inflammatory responses (Castañ-Abad et al., 2020; Hao et al., 2017; Rayner et al., 2018). However, few studies have focused on the adverse effects of air pollution on the morbidity of RD among people with T2D in the real world.

Most previous studies focus on whether the effects of air pollution on lung function are associated with diabetes mellitus (Chen et al., 2020a; Hao et al., 2017; Khafaie et al., 2017). To the best of our knowledge, despite the significant comorbidity burden, only two related studies have reported the stratified analysis of air pollution on RD by diabetes status (Abramson et al., 2020; Chen et al., 2020). However, the short-term effect of ambient particulate matter exposure on cause-specific RD admissions among patients complicated with or without T2D remains unknown in China. These associations have not been comprehensively reported at the city-specific level, especially in Beijing.

Hence, a time series analysis was employed to elucidate the district-specific association between PM and cause-specific RD morbidity among patients complicated with or without T2D in Beijing. Stratified analyses by sex and age were also conducted to explore the associations in these susceptible subpopulations.

2. Materials and methods

2.1. Data preparation

According to time-series study design, we collected the following three types of daily data from January 1, 2014 to December 31, 2020: air pollution, meteorological conditions, and hospital admission data. Hourly concentrations of ambient $PM_{2.5}$ (particles with an aerodynamic diameter $\leq$2.5 μm), PM_{10} (particles with an aerodynamic diameter $\leq$10 μm), NO_2 (nitrogen dioxide), SO_2 (sulfur dioxide), O_3 (ozone) and CO (carbon monoxide) from 35 stations in 16 districts in Beijing were retrieved from the Beijing Environmental Protection Bureau (http://www.bjepb.gov.cn/) during the same period. The locations of the 16 districts are illustrated in the Supplementary Materials (Fig. S1). In this study, we averaged $PM_{2.5}$ and PM_{10} data from stations in each district as district-specific daily levels. Given that meteorological parameters may alter the associations between PM exposure and RD (Zhang et al., 2020), hourly data of temperature (℃) and relative humidity (%) of 18 meteorological monitoring stations in Beijing were obtained from online China Meteorological Data Sharing Service System online (https://data.cma.cn/en) over the same period. We averaged the temperature and relative humidity data from stations in each district as district-specific daily levels to prepare for subsequent modeling.

RD hospital admission records between Jan 1, 2014, and Dec 31, 2020, were extracted from the Beijing Municipal Health Commission Information Centre (BMHCIC) (http://www.phic.org.cn/). The BMHCIC is a government agency that administers governmental hospitals in Beijing. Computerized records of hospital admissions are maintained at each hospital and sent to the BMHCIC through an internal computer network. The geographic locations of the 258 hospitals included in this study have been described elsewhere (Li et al., 2018). To implement the integration of health information resources in Beijing, hospitals under the BMHCIC cover approximately 90% of permanent residents' medical services and, thus, may be highly representative of the Beijing population. The data recording system in the study area has been proven to be of high validity (Aklilu et al., 2020; Li et al., 2018; Liu et al., 2021).

The study population was divided into two populations according to whether an RD inpatient was simultaneously diagnosed with T2D. According to the 10th revision of the International Classification of Diseases (ICD-10), T2D was coded as E12, which was defined as fasting blood glucose $\geq$7.1 mmol/L, and/or current treatment of diabetes with antidiabetic medication before admission. Respiratory diseases were coded as J00–J99. Selected disease subcategories included acute exacerbation of COPD (ICD-10: J44.0-J44.1), asthma (ICD-10: J45-J46), pneumonia (ICD-10: J12-J18), upper respiratory infections (URI, ICD-10: J02-J06), and lower respiratory infections (LRI, ICD-10: J19-J22). Daily hospital admissions were further categorized by sex, age ($\leq$60; $>$60 years of age), and marriage status. This study only included RD admissions of residents living in Beijing.

2.2. Ethical clearance

The study was approved by the Institutional Review Board of Capital Medical University (No. IRB00009511). Informed consent was not specifically required since personal identifiers were not collected.

2.3. Statistical analysis

A two-stage analysis was applied to estimate the effects of $PM_{2.5}$ and PM_{10} on daily inpatient visits according to previous studies (Chen et al., 2017; Gasparrini et al., 2012). As the daily counts on hospital admissions usually followed a Poisson distribution, the district-specific effects of $PM_{2.5}$ and PM_{10} on RD hospital admissions were investigated separately using an over-dispersed generalized additive model (GAM) in the first stage, as follows:

$$\log[E(Yt)] = intercept + \beta Z_t + s(time, 7) + s(temp, 3) + s(RH, 3) + DOW_t + Holiday_t$$

where $E(Yt)$ represents the number of RD cases on day t; Zt is the concentration on day t; β represents the log-relative risk (RR) of RD hospitalization associated with an interquartile range (IQR) increase in each

Table 1
Descriptive statistics for the daily hospital admission for respiratory disease (n = 1,550,154), air pollution concentrations, and weather conditions in Beijing, 2014–2020.

Variables	Mean ± SD	Minimum	Percentile			Maximum	IQR
			25th	50th	75th		
Daily hospital admission							
RD	655 ± 251	200	393	695	838	1444	445
RD with T2D	115 ± 49	23	65	121	151	272	86
RD without T2D	540 ± 203	174	330	574	687	1192	357
Air pollutants							
$PM_{2.5}$ ($\mu g/m^3$)	61.86 ± 59.94	1.75	22.24	43.96	79.86	607.33	57.62
PM_{10} ($\mu g/m^3$)	92.21 ± 73.13	2.00	44.73	73.57	116.74	1300.42	72.01
NO_2 ($\mu g/m^3$)	40.78 ± 23.77	1.75	23.25	36.29	53.42	197.69	30.17
SO_2 ($\mu g/m^3$)	8.40 ± 10.16	1.00	2.70	4.59	9.67	196.40	6.97
O_3($\mu g/m^3$)	60.71 ± 38.16	1.79	31.82	55.17	83.32	230.35	51.50
CO (mg/m^3)	0.94 ± 0.81	0.10	0.48	0.73	1.08	13.40	0.60
Meteorological variables							
Temperature (°C)	12.4 ± 11.34	-19.46	1.46	13.66	22.82	33.14	21.36
Relative humidity (%)	53.57 ± 19.46	9.80	37.80	53.50	69.60	99.00	31.80

Note: RD: respiratory disease; T2D: type 2 diabetes. SD: standard deviation; IQR: inter-quartile range; $PM_{2.5}$: particles with an aerodynamic diameter ≤2.5 μm; PM_{10}: particles with an aerodynamic diameter ≤10 μm; NO_2: nitrogen dioxide; SO_2: sulfur dioxide; O_3: ozone; CO: carbon monoxide.

pollutant mean concentration; *s*() indicates a natural spline function to filter out long-term trends and seasonal patterns in daily RD admissions; temp is the daily mean temperature (℃); RH is the relative humidity (%); DOW_t is the day of the week; and DOW_t and $Holiday_t$ were included as categorical variables. Considering that a nonlinear relationship has been shown between temperature, relative humidity and hospitalizations for RD in the previous studies, a natural cubic spline with 3 degrees of freedom (*df*) was used for each weather condition variable (Liu et al., 2017; Tian et al., 2018; Wang et al., 2021).

Then, after obtaining the effects from each district, we conducted a meta-analysis to pool the district-specific and overall estimates in the second stage. We plotted the exposure-response (ER) curves between PM and RD admissions of patients. In brief, a natural spline function with 3 *df* was added into the abovementioned model. Given the uncertainty in determining the best lag days for estimation, we used multiple lag structures, including single-day lags from 0 to 14 and moving average

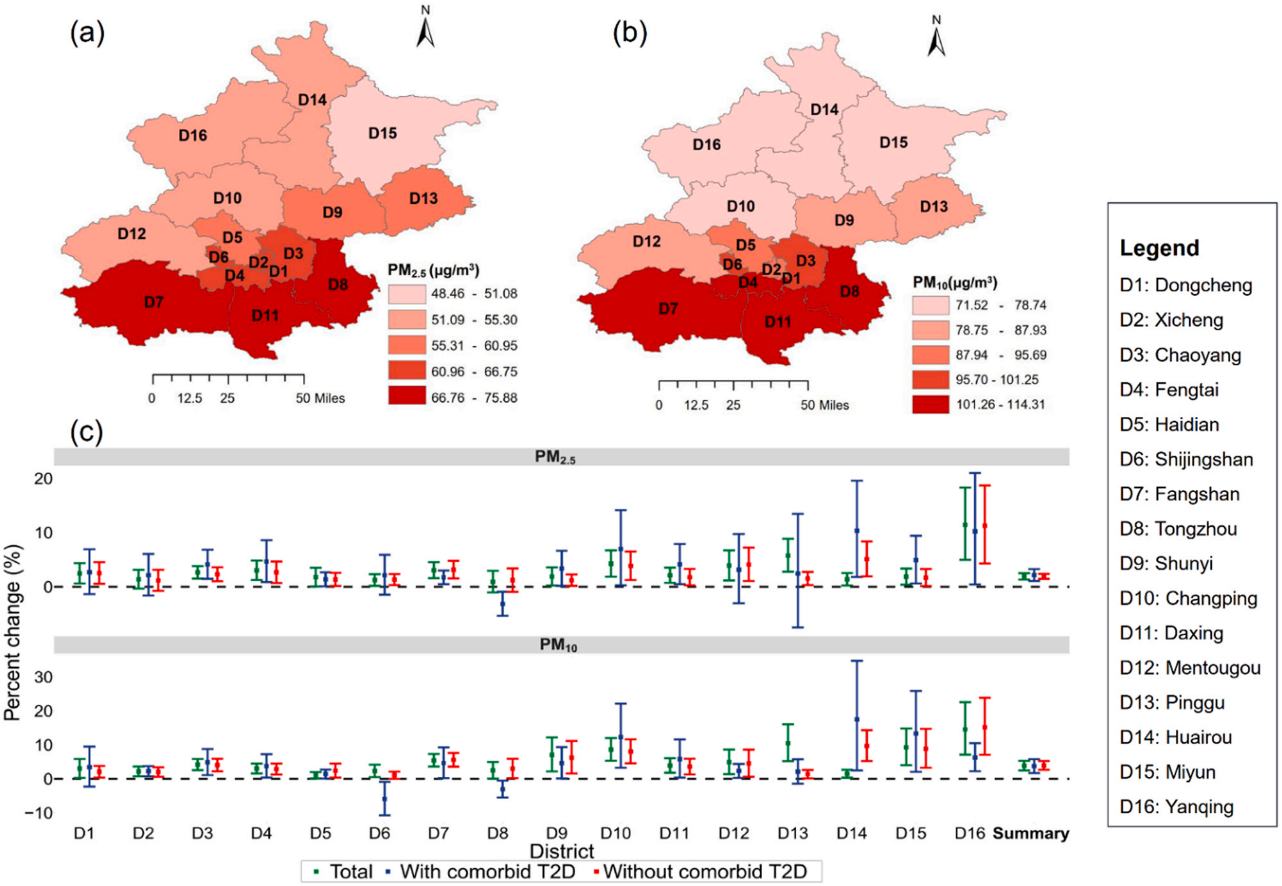

Fig. 1. Map of average concentrations of $PM_{2.5}$ (a) and PM_{10} (b) of each district during 2014–2020 in Beijing, and their associations with admissions for total respiratory diseases and respiratory diseases with and without T2D (c). Note: $PM_{2.5}$: particles with an aerodynamic diameter ≤2.5 μm; PM_{10}: particles with an aerodynamic diameter ≤10 μm; T2D: type 2 diabetes.

Table 2
Percent changes in respiratory diseases admissions associated with per IQR increase in $PM_{2.5}$ and PM_{10} concentrations for different lag structures in multi-pollutant generalized additive model according to T2D comorbid conditions.

Lag days	$PM_{2.5}$					PM_{10}				
	Total RD	RD with T2D	RD without T2D	*z*	*P*	Total RD	RD with T2D	RD without T2D	*z*	*P*
1	0.30 (−0.02, 0.62)	0.17 (−0.78, 1.13)	0.29 (−0.15, 0.74)	0.44	0.66	**0.70 (0.44, 0.97)**	**1.17 (0.24, 2.12)**	**0.72 (0.30, 1.13)**	0.23	0.82
2	**0.74 (0.55, 0.93)**	0.62 (−0.18, 1.42)	**0.51 (0.08, 0.93)**	0.25	0.80	**0.88 (0.62, 1.14)**	**1.43 (0.62, 2.24)**	**1.13 (0.76, 1.50)**	0.90	0.37
3	**0.59 (0.38, 0.80)**	**1.33 (0.58, 2.09)**	**0.99 (0.64, 1.34)**	1.98	0.05	**0.79 (0.52, 1.07)**	**1.62 (0.87, 2.38)**	**1.29 (0.83, 1.75)**	0.30	0.77
4	**0.56 (0.38, 0.75)**	**1.53 (0.75, 2.32)**	**1.19 (0.83, 1.55)**	2.54	0.01	**0.78 (0.55, 1.01)**	**1.88 (1.03, 2.74)**	**1.53 (1.12, 1.94)**	0.20	0.84
5	**0.52 (0.30, 0.74)**	**1.85 (1.02, 2.69)**	**1.34 (0.95, 1.72)**	3.01	<0.01	**0.74 (0.51, 0.97)**	**2.25 (1.27, 3.23)**	**1.88 (1.40, 2.37)**	0.16	0.87
6	**0.55 (0.25, 0.85)**	**2.04 (1.15, 2.94)**	**1.57 (1.16, 1.98)**	3.03	<0.01	**0.81 (0.48, 1.15)**	**2.45 (1.15, 3.78)**	**2.01 (1.46, 2.56)**	0.13	0.90
7	0.20 (0.00, 0.41)	**2.12 (1.17, 3.08)**	**1.86 (1.42, 2.30)**	3.85	<0.01	**0.51 (0.31, 0.72)**	**2.52 (1.07, 4.00)**	**2.25 (1.62, 2.89)**	0.91	0.36
8	-0.08 (−0.28, 0.13)	***2.16 (1.08, 3.25)***	***1.92 (1.46, 2.39)***	3.98	<0.01	0.18 (−0.02, 0.38)	**2.64 (0.91, 4.39)**	**2.38 (1.61, 3.16)**	0.24	0.81
9	-0.13 (−0.41, 0.15)	**2.03 (0.87, 3.19)**	**1.83 (1.33, 2.33)**	3.63	<0.01	-0.01 (−0.30, 0.27)	**2.59 (0.78, 4.43)**	**2.52 (1.60, 3.44)**	0.66	0.51
10	0.03 (−0.29, 0.35)	**1.93 (0.79, 3.07)**	**1.69 (1.11, 2.27)**	3.11	<0.01	0.14 (−0.17, 0.45)	**2.65 (0.94, 4.38)**	**2.76 (1.74, 3.79)**	0.50	0.61
11	0.12 (−0.14, 0.38)	**1.87 (0.67, 3.08)**	**1.70 (0.95, 2.46)**	2.80	0.01	**0.44 (0.16, 0.72)**	**2.99 (1.23, 4.78)**	**3.24 (2.19, 4.29)**	0.33	0.74
12	0.03 (−0.27, 0.34)	**1.89 (0.63, 3.16)**	**1.69 (0.89, 2.49)**	2.84	<0.01	-0.02 (−0.33, 0.29)	**3.48 (1.56, 5.44)**	**3.87 (2.71, 5.04)**	0.07	0.94
13	**0.21 (0.01, 0.40)**	**1.66 (0.27, 3.08)**	**1.58 (0.72, 2.45)**	1.96	0.05	0.08 (−0.11, 0.28)	***3.73 (1.72, 5.79)***	***3.92 (2.65, 5.21)***	0.92	0.36
14	**0.39 (0.17, 0.60)**	1.39 (−0.11, 2.90)	**1.60 (0.65, 2.57)**	1.26	0.21	**0.43 (0.16, 0.71)**	**3.46 (1.53, 5.43)**	**3.84 (2.51, 5.20)**	1.04	0.30
0–1	-0.20 (−0.75, 0.35)	**0.53 (0.01, 1.04)**	**0.39 (0.13, 0.66)**	0.67	0.50	**0.52 (0.12, 0.92)**	**0.87 (0.37, 1.36)**	**0.80 (0.57, 1.04)**	0.88	0.38
0–2	0.23 (−0.31, 0.77)	**1.02 (0.57, 1.46)**	**0.72 (0.52, 0.93)**	1.62	0.11	**1.03 (0.60, 1.47)**	**1.14 (0.69, 1.59)**	**0.91 (0.68, 1.14)**	0.67	0.50
0–3	**0.88 (0.50, 1.26)**	**0.66 (0.10, 1.22)**	**0.54 (0.34, 0.74)**	0.99	0.32	**1.25 (0.74, 1.76)**	**0.90 (0.25, 1.55)**	**0.80 (0.58, 1.01)**	0.74	0.46
0–4	**1.13 (0.80, 1.46)**	**0.72 (0.22, 1.23)**	**0.49 (0.28, 0.69)**	1.48	0.14	**1.49 (1.02, 1.96)**	**0.82 (0.16, 1.49)**	**0.75 (0.54, 0.97)**	0.72	0.47
0–5	**1.33 (0.98, 1.68)**	0.34 (−0.15, 0.85)	**0.54 (0.33, 0.74)**	3.09	<0.01	**1.83 (1.29, 2.38)**	**0.81 (0.19, 1.44)**	**0.76 (0.56, 0.96)**	0.65	0.51
0–6	**1.58 (1.20, 1.96)**	0.33 (−0.26, 0.92)	**0.61 (0.35, 0.87)**	3.36	<0.01	**1.97 (1.30, 2.65)**	**0.80 (0.34, 1.26)**	**0.83 (0.52, 1.15)**	0.62	0.54
0–7	**1.83 (1.34, 2.32)**	0.06 (−0.38, 0.49)	**0.22 (0.02, 0.42)**	5.68	<0.01	**2.23 (1.45, 3.01)**	0.28 (−0.26, 0.81)	**0.54 (0.33, 0.75)**	0.33	0.74
0–8	***1.91 (1.33, 2.49)***	-0.08 (−0.52, 0.36)	-0.07 (−0.27, 0.14)	6.13	<0.01	**2.38 (1.44, 3.33)**	0.13 (−0.33, 0.59)	0.19 (−0.02, 0.41)	0.26	0.79
0–9	**1.79 (1.17, 2.41)**	0.01 (−0.43, 0.45)	-0.16 (−0.44, 0.12)	5.34	<0.01	**2.44 (1.38, 3.52)**	0.17 (−0.34, 0.67)	-0.02 (−0.29, 0.24)	0.07	0.95
0–10	**1.65 (0.99, 2.31)**	-0.14 (−0.58, 0.30)	0.06 (−0.26, 0.38)	4.93	<0.01	**2.60 (1.45, 3.76)**	0.02 (−0.44, 0.49)	0.17 (−0.14, 0.48)	0.11	0.91
0–11	**1.68 (0.89, 2.48)**	-0.04 (−0.56, 0.49)	0.13 (−0.11, 0.37)	3.72	<0.01	**3.07 (1.89, 4.26)**	**0.51 (0.05, 0.97)**	**0.42 (0.16, 0.68)**	0.24	0.81
0–12	**1.69 (0.81, 2.57)**	-0.08 (−0.62, 0.46)	0.02 (−0.25, 0.30)	3.60	<0.01	**3.67 (2.39, 4.97)**	-0.04 (−0.52, 0.45)	-0.06 (−0.33, 0.22)	0.34	0.74
0–13	**1.60 (0.65, 2.55)**	0.02 (−0.41, 0.46)	**0.25 (0.05, 0.45)**	3.17	<0.01	***3.86 (2.48, 5.27)***	-0.10 (−0.55, 0.35)	0.13 (−0.07, 0.34)	0.15	0.88
0–14	**1.58 (0.55, 2.63)**	0.31 (−0.12, 0.75)	**0.42 (0.22, 0.62)**	2.41	<0.01	**3.85 (2.45, 5.27)**	0.22 (−0.24, 0.69)	0.51 (0.24, 0.77)	0.31	0.75

Note: Statistically positive significant results are indicated in bold ($P < 0.05$); the maximum significant effect is indicated in bold and italics. RD: respiratory disease; T2D: type 2 diabetes; $PM_{2.5}$: particles with an aerodynamic diameter ≤2.5 μm; PM_{10}: particles with an aerodynamic diameter ≤10 μm.

exposures from multiple days.

The data were also classified according to sex, age, marriage, T2D comorbid conditions and cause specificity. Patients were classified into two age groups: younger (≤60 years) and elderly (>60 years). A *z* value was calculated to test the statistical significance of subgroup differences as follows: $z = (\beta_1 - \beta_2)/\sqrt{SE_1^2 + SE_2^2}$, where β_1 and β_2 were the effect estimates for the two categories (e.g., males and females) and SE_1 and SE_2 were the corresponding standard errors (Altman and Bland, 2003). Then, a *P* value could be obtained from the standard normal distribution based on the *z* value.

Sensitivity analysis was conducted to check the stability of the model. First, we checked the *df* values of the time variable from 4 to 10 per year. Second, to investigate the independent effects of particulate matter, principal component analysis was employed. Principal component analysis is a good approach to address collinearity among air pollutants (Yang et al., 2013), and the details have been described in the Supplementary Materials.

Spearman's correlation coefficients were calculated to assess the degrees of correlation between air pollutants and meteorological variables. The statistical tests were two-sided, and associations with $P < 0.05$ were considered statistically significant. The effects are described as the percent change and 95% confidence intervals (CIs) in daily counts of admissions for RD per IQR increase in $PM_{2.5}$ and PM_{10} among patients with or without T2D. All statistical models were run in R software (version 4.0.2) using the ***mgcv*** and ***meta*** packages.

3. Results

3.1. Descriptive analyses

In total, 1,550,154 admissions for RD were included in this study during the period from 2014 to 2020, of which 275,383 patients had comorbid T2D (accounting for 17.76%). Table S1 summarizes the descriptive statistics of daily total and cause-specific RD admissions, stratified by sex, age, marriage and T2D comorbid conditions. Table 1 presents the summary statistics of daily RD admissions (counts per day), air pollutants and meteorological conditions in Beijing during the study period. On average, there were 655 admissions for RD per day with a maximum of 1444 admissions.

The annual average values of daily mean concentrations of air pollutants were 61.86 μg/m³ for $PM_{2.5}$ and 92.21 μg/m³ for PM_{10}, which exceeded the national secondary standard. The annual average values were 12.40 °C for temperature and 53.57% for relative humidity. Fig. S2 shows pairwise Spearman correlation coefficients between air pollutants and weather conditions. Air pollutants except O_3 were strongly correlated with each other (Spearman's correlation coefficients distributed from 0.55 to 0.86) and were moderately correlated with weather conditions (−0.57 to 0.51).

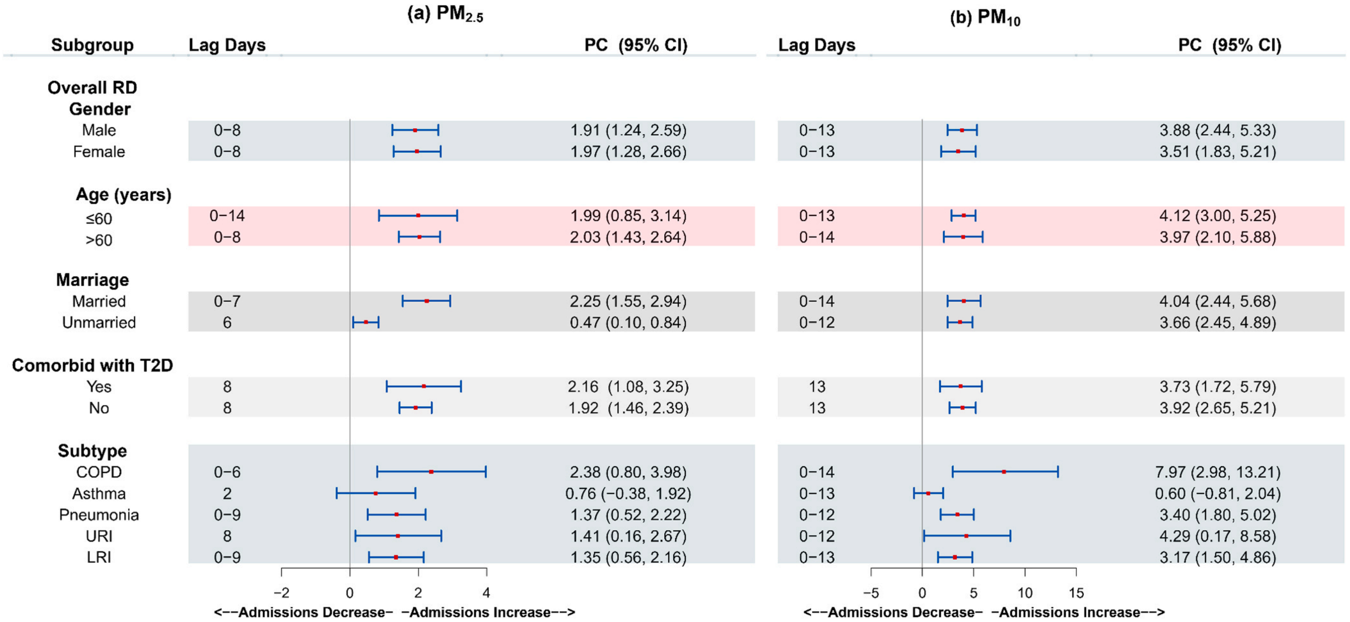

Fig. 2. Results from meta-analysis: percent change in respiratory diseases admissions stratified by gender, age, marriage, and subtype associated with per interquartile range increase in $PM_{2.5}$ and PM_{10} in Beijing, 2014–2020. Note: PC: percent change; CI: confidence interval; $PM_{2.5}$: particles with an aerodynamic diameter ≤2.5 μm; PM_{10}: particles with an aerodynamic diameter ≤10 μm; RD: respiratory disease; T2D: type 2 diabetes; COPD: chronic obstructive pulmonary disease; URI: upper respiratory tract infection; LRI: lower respiratory tract infection (preclude pneumonia).

3.2. *District-specific associations between PM and RD admissions*

Fig. 1 depicts the district-specific associations between $PM_{2.5}$ and PM_{10} concentrations and admissions for total RD and RD with and without T2D.

The effect size of $PM_{2.5}$ on overall RD was the highest in Yanqing district [11.43% (95% CI: 4.97, 18.29%)] and the lowest in Tongzhou district [0.91% (95% CI: −1.06, 2.93%)], and the difference was statistically significant ($z = 3.09$, $P = 0.002$). The effect sizes of $PM_{2.5}$ on admissions for RD with T2D ranged from −3.17 to 10.22% at the district-specific level ($z = 2.65$, $P = 0.008$), and a negative effect was found in Tongzhou district [−3.17% (95% CI: −5.37, −0.92%)]. The effect sizes of $PM_{2.5}$ on admissions for RD without T2D ranged from 1.16% to 11.25% at the district-specific level ($z = 2.77$, $P = 0.006$). There was no statistically significant difference between individuals with and without T2D for all districts except Tongzhou district ($z = 2.77$, $P = 0.01$).

The effect size of PM_{10} on the overall RD was the highest in Yanqing district [14.56% (95% CI: 7.10–22.54%)] and the lowest in Haidian district [1.03% (95% CI: 0.11–1.96%)], and the difference was statistically significant ($z = 3.65$, $P < 0.05$). The PM_{10}-related RD with comorbid T2D effects for each district ranged from −5.93 to 17.48% ($z = 2.97$, $P = 0.003$). Negative effects were found in Shijingshan district [−5.93% (95% CI: −10.75, −0.86%)] and Tongzhou district [−3.06% (95% CI: −5.49, −0.56%)]. The PM_{10}-related RD without T2D effects for each district ranged from 1.07% to 15.15% ($z = 3.48$, $P = 0.001$). The adverse effects of PM_{10} were not statistically significant between RD with and without T2D for all districts except Tongzhou district ($z = 3.17$, $P < 0.05$).

3.3. *Pooled association between PM and RD admissions*

Table 2 shows a pooled analysis of the effect estimates of $PM_{2.5}$ and PM_{10} concentrations on daily RD admissions using different lag structures in multipollutant models according to T2D comorbid conditions.

The effect estimates of $PM_{2.5}$ and PM_{10} using moving average lags were much higher than those using single-day lags for patients with RD. Per IQR uptake in the concentration of $PM_{2.5}$ corresponded to 1.91% (95% CI: 1.33–2.49%), 2.16% (95% CI: 1.08–3.25%), and 1.92% (95% CI: 1.46–2.39%) increments in admission for RD, RD with T2D, and RD without T2D, respectively, at lag 0–8 days, lag 8 days, and lag 8 days, and the effect size was statistically significantly higher in T2D group than that in group without T2D ($z = 3.98$, $P < 0.01$). For the comparison of estimates with the same lag periods, the effect of $PM_{2.5}$ was statistically significantly higher in patients with T2D than in patients without T2D from lag 4 to lag 12 days ($P < 0.05$) (Table 2). The effect sizes of PM_{10} were 3.86% (95% CI: 2.48–5.27%), 3.73% (95% CI: 1.72–5.79%), and 3.92% (95% CI: 2.65–5.21%) for RD, RD with T2D and RD without T2D, respectively, at lag 0–13 days, lag 13 days and lag 13 days, and the difference between T2D groups was not statistically significant ($z = 0.37$, $P = 0.84$). No statistically significant difference was observed between T2D groups for the association between PM_{10} and RD over the same lag period ($P > 0.05$).

3.4. *Stratification analyses*

According to the results of the stratification analyses, the effect estimate of the $PM_{2.5}$ on RD was slightly higher for elderly adults (>60 years) than for younger adults ($z = -0.34$, $P < 0.05$), and the maximum effect value appeared earlier (Fig. 2a). The $PM_{2.5}$-related RD increment in patients with T2D was 2.16% (95% CI: 1.08–3.25%), which was much higher than the 1.92% (95% CI: 1.46–2.39%) in patients without T2D ($z = 3.98$, $P < 0.05$). The effect estimates of PM_{10} were higher for males ($z = -3.61$, $P < 0.05$) and the ≤60-years-old group ($z = -2.44$, $P < 0.05$) (Fig. 2b). The PM_{10}-related RD increment in patients without T2D was 3.92% (95% CI: 2.65–5.21%), which was slightly higher than the 3.73% (95% CI: 1.72–5.79%) in patients with T2D ($z = 0.24$, $P = 0.81$) (Fig. 2b). No significant difference was found between groups with and without T2D in the associations of PM and RD subtypes (Fig. 3). There was no significant difference in the associations of PM on hospital admissions for different RD (Tables S2 & S3). Significant difference could be found between three groups (COPD vs. Asthma, Pneumonia vs. URI, Pneumonia vs. LRI) ($\alpha' = 0.005$) for effects of PM_{10} on RD without T2D (Table. S3).

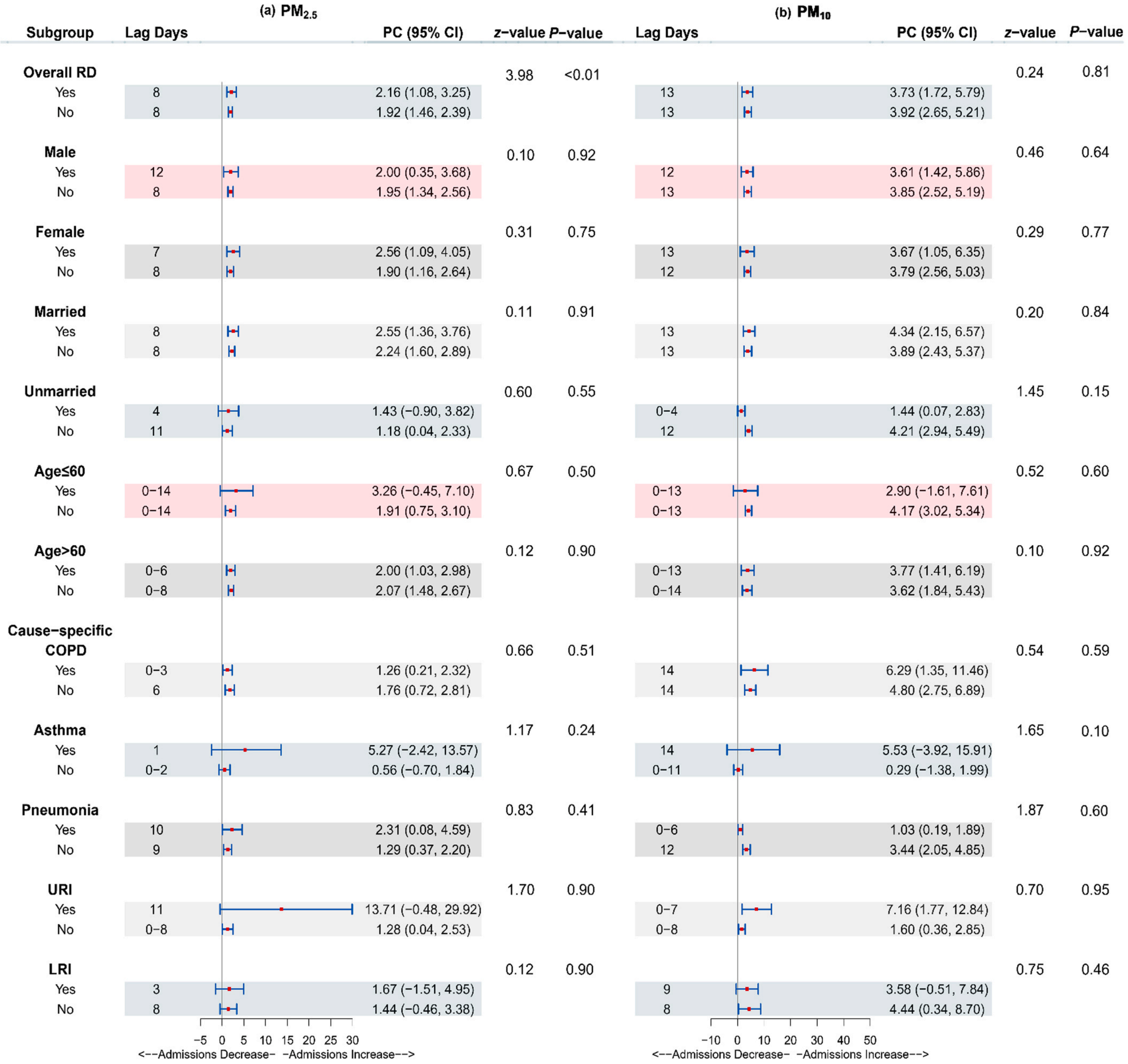

Fig. 3. Results from meta-analysis: percent change in subtype respiratory diseases admissions stratified by T2D conditions associated with per interquartile range increase in $PM_{2.5}$ and PM_{10} in Beijing, 2014–2020. Note: PC: percent change; CI: confidence interval; $PM_{2.5}$: particles with an aerodynamic diameter $\leq$ 2.5 μm; PM_{10}: particles with an aerodynamic diameter $\leq$10 μm; RD: respiratory disease; T2D: type 2 diabetes; COPD: chronic obstructive pulmonary disease; URI: upper respiratory tract infection; LRI: lower respiratory tract infection (preclude pneumonia).

3.5. E-R curves

The ER curves for the associations between $PM_{2.5}$ and PM_{10} and daily RD admissions varied by sex, age and subtype (Fig. 4 and Fig. 5). For $PM_{2.5}$, the ER curves of total RD, younger adults (age $\leq$60 years) and subgroups with T2D slightly increased at low concentrations and then showed flat slopes at concentrations $\geq$200 μg/m^3, 200 μg/m^3 and 100 μg/m^3, respectively. The concentration response curves of females appeared to be generally linear, with an increasing trend observed. For $PM_{10,}$ the ER curves for the total RD and males were almost J-shaped, rising sharply at approximately 300 μg/m^3. The ER curve for PM_{10} in elderly adults (>60 years) slightly increased at low concentrations and then showed flat slopes at concentrations $\geq$300 μg/m^3.

4. Discussion

To our knowledge, our study is the first attempt to demonstrate associations between PM and cause-specific RD admissions in patients with and without T2D in China. We found that short-term exposures to PM were associated with increased admissions for RD and for RD with and without T2D. Moreover, the effect of $PM_{2.5}$ on RD admissions was significantly higher in patients with T2D than those without T2D. No difference was observed between T2D groups for the associations of PM and selected cause-specific RD. The E-R curves of $PM_{2.5}$ and PM_{10} on RD varied by sex, age and cause, which were robust when adjusted for co-pollutants using PCA in multipollutant models. This study enriched the limited evidence of the health effects of PM pollution in populations with comorbidities in developing countries.

During our study period, the annual average concentration of both

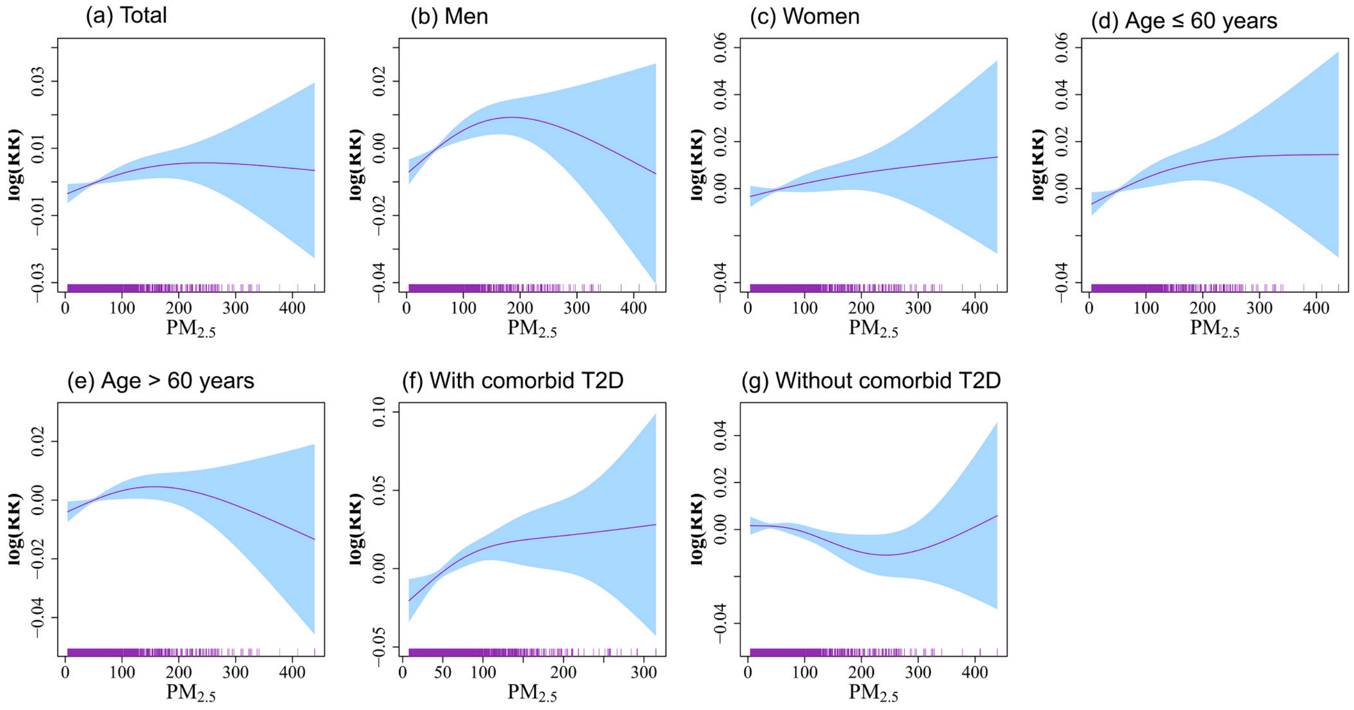

Fig. 4. Exposure-response curves between $PM_{2.5}$ and respiratory diseases admissions in Beijing, 2014–2020 using multi-pollutant model, after adjusted for day of week and public holidays, temperature, and relative humidity. Note: $PM_{2.5}$: particles with an aerodynamic diameter ≤2.5 μm; T2D: type 2 diabetes.

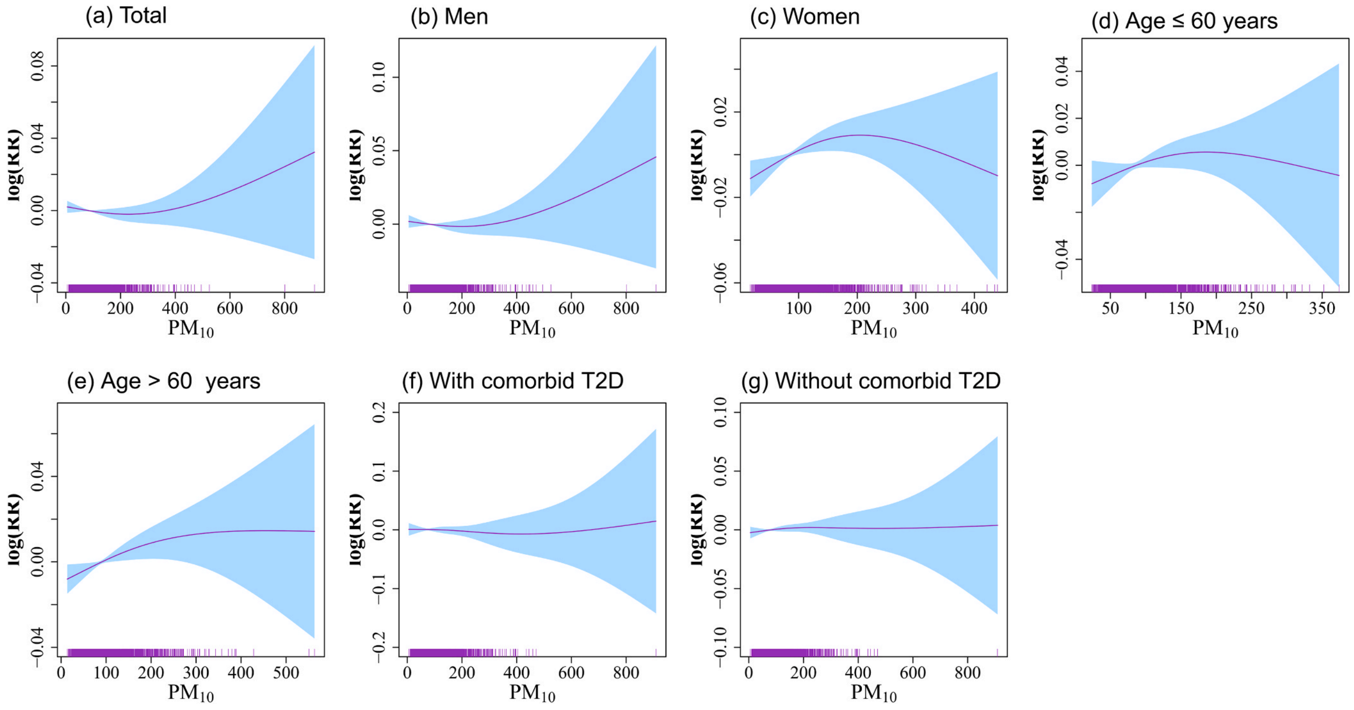

Fig. 5. Dose-response relationship between PM_{10} and respiratory diseases admissions in Beijing, 2014–2020 using multi-pollutant model, after adjusted for day of week and public holidays, temperature, and relative humidity. Note: PM_{10}: particles with an aerodynamic diameter ≤10 μm; T2D: type 2 diabetes.

$PM_{2.5}$ and PM_{10} in Beijing all exceeded the national secondary standard. Thus, the air pollution in Beijing remains serious and needs to be improved. Even if the adverse effect attributable to exposure to PM pollution in an individual might be small, the overall attributable risk might be considerably higher, given the higher pollutant concentrations and large proportion of the population with T2D in China (Maji et al., 2017, 2018). We found adverse effects of $PM_{2.5}$ and PM_{10} on total RD, RD with and without T2D, which varied by districts in Beijing. Such disparities might be caused by the combined effects of health care resources, population characteristics, and PM sources (Zhang et al., 2020).

In our study, positive associations were observed between short-term exposure to PM and respiratory diseases, which is consistent with existing studies (Phosri et al., 2020; Szyszkowicz et al., 2018). And the effect size in Beijing is much larger than Shenzhen (Jiao et al., 2020), but lower than that in Thailand (Phosri et al., 2020). Similarly, a meta-analysis of five cities in China reported that each 10 μg/m^3 increase in $PM_{2.5}$ and PM_{10} concentrations at lag 07 days was associated with 1.39% (95% CI: 0.38%, 2.40%) and 1.10% (95% CI: 0.38%, 1.83%) increases in total RD, showing that the acute effects of PM on RD might be prolonged over a much longer period (Li et al., 2021).

Our study indicated that the effect size of $PM_{2.5}$ on RD was much higher in patients with T2D than those without T2D. Compared with those without T2D, patients with T2D might be more vulnerable to air pollutant exposure (Yang et al., 2020). Respiratory inflammation is a critical step in the biological mechanism underlying the cardiorespiratory effects of $PM_{2.5}$. Respiratory inflammation in individuals with diabetes may be related to enhanced susceptibility to particle-associated health effect. Several studies have shown that exposure to $PM_{2.5}$ could reduce lung function in T2D patients (Chen et al., 2020a, 2020b; Khafaie et al., 2019). No significant difference was observed between T2D groups for the association between PM_{10} and RD in our study. Another study indicated that PM_{10}-related reduction of lung function was independent of T2D status (Khafaie et al., 2017), which is roughly consistent with what we found.

No significant difference can be found in the associations of PM on hospital admissions for different RD. The mechanisms of PM on the comorbidity of cause-specific RD and type 2 diabetes have not been described.

Subgroup analysis of age showed that elderly population were more susceptible to $PM_{2.5}$ than younger adults. In consistent with our findings, Jo and colleagues found that elderly individuals were vulnerable to air pollution and extreme environmental conditions in terms of morbidity and mortality (Jo et al., 2017). However, fluctuations in PM_{10} appeared to impact males and younger adults, those who tend to participate in more outdoor activities but have lower personal protective intentions, resulting in higher exposure to PM_{10}. Some studies show that increased concentration of PM_{10} is associated with the increase of respiratory hospitalization in all age groups, with the most significant impact on the population between 16 and 59 years old (Agudelo-Castañeda et al., 2019).

Evidence for the E-R relationships between air pollutants and hospital admissions for respiratory disease was limited. In the current study, the curves for $PM_{2.5}$ were nonlinear association with total RD, age ≤ 60 and T2D group, which was consistent with those of previous studies showing that the thresholds for associations between $PM_{2.5}$ and respiratory hospital admissions (Dong et al., 2021). Curves for PM_{10} indicated almost linear association with total RD and male. Saturation effects on the elderly were evident when the concentrations of PM_{10} at high concentration in our study. This phenomenon could be supported by observation that patients vulnerable to PM have developed respiratory symptoms requiring healthcare before PM reached high concentrations (Tian et al., 2019).

There are some limitations inherent in our study. First, we used fixed-site monitor measurements as a proxy for personal exposure, which may result in exposure errors and underestimation of the associations between ambient air pollution and diseases. However, measuring every participant's exposure directly is not feasible in such a large epidemiologic study. Second, owing to the limitation of the available data, we did not collect data on the relationships between patients. However, there might be a few family-cluster cases, which may affect population sensitivity (Yang et al., 2018). Third, the generalizability of our results might be limited, as the study collected data from only one highly polluted city. Fourth, since the date of diagnosis is not available, the accuracy of the occurrence of RD and T2D cannot be differentiated. Fifth, owing to the availability of data, we could not remove the influence of planned admissions.

5. Conclusions

Short-term PM exposure was associated with increased RD admission with and without T2D. $PM_{2.5}$ had a higher effect on RD in patients with T2D than in those without T2D. Our study indicates that the prevention and control for RD should be given more attention on people with T2D, suggesting that more efforts may be required to mitigate $PM_{2.5}$ pollution in Beijing, China.

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CRediT authorship contribution statement

Mengmeng Liu: Writing - original draft, Data collection and cleaning, Methodology, Visualization. **Zhiwei Li:** Data collection and cleaning, Methodology, Software. **Feng Lu:** Data collection and analysis. **Moning Guo:** data collection and analysis. **Lixin Tao:** Manuscript review and editing. **Mengyang Liu:** Data collection, Methodology. **Yue Liu:** Data collection, Methodology. **Aklilu Deginet:** Data collection, Methodology. **Yaoyu Hu:** Data collection and cleaning. **Yutong Li:** Data collection and cleaning. **Mengqiu Wu:** Data collection and cleaning. **Yanxia Luo:** Writing - review & editing. **Xiaonan Wang:** Writing - review & editing. **Xinghua Yang:** Writing - review & editing. **Bo Gao:** Writing review & editing. **Xiuhua Guo:** Writing - review & editing, Project administration, Supervision. **Xiangtong Liu:** Writing - review & editing, Conceptualization, Project administration, Supervision.

Declaration of Competing Interest

The authors declare that they have no competing interests.

Availability of data and materials

The data can be accessed from the Beijing Municipal Health Commission Information Center with permission via direct request.

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Ethics approval

In this study, informed consent was not specifically required because we did not use personal data identifiers.

Consent for publication

Not applicable.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2021.112794.

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