



Health and economic impacts of particulate matter pollution on hospital admissions for mental disorders in Chengdu, Southwestern China

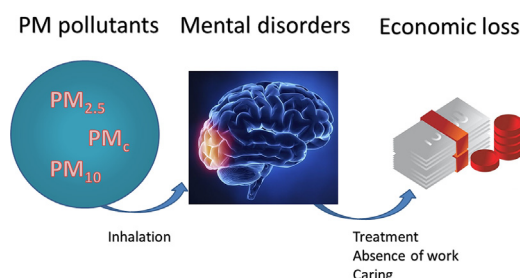
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HIGHLIGHTS

- This study assessed both the health and economic impacts of PM pollution on hospital admissions for mental disorders.
- Short-term exposure to PM is positively associated with increased hospital admissions for mental disorders.
- Economic burden of mental disorders hospitalization due to PM exposure accounted for 0.026% of local GDP in 2013–2017.

GRAPHICAL ABSTRACT



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ABSTRACT

The evidence for adverse effects of ambient particulate matter (PM) pollution on mental disorders (MDs) is limited, especially in developing countries. This study aimed to quantify both PM related health impacts and corresponding economic losses for overall and specific MDs in southwestern China. Data regarding 134,292 hospital admissions for MDs were collected from local Compulsory Medical Insurance Database in 2013–2017. A generalized additive model (GAM) was applied to estimate the exposure-response effects of PM pollution on hospital admissions for MDs. And the cost of illness method (COI) was adopted to further assess corresponding hospitalization costs and productivity losses. It was showed that PM pollution was significantly related to hospital admissions for overall and specific MDs. Each $10 \mu\text{g}/\text{m}^3$ increase in concentrations of PM_{10} (particles with an aerodynamic diameters $\leq 10 \mu\text{m}$), $\text{PM}_{2.5}$ ($\leq 2.5 \mu\text{m}$) and PM_c ($2.5 \mu\text{m} < c < 10 \mu\text{m}$) at the cumulative lag03 day would be responsible for 3.25% (95%CI: 2.34–4.16%), 6.38% (95%CI: 4.79–7.97%), and 3.81% (95%CI: 2.13–5.50%) increments in daily hospital admissions for MDs, respectively. Stronger associations were observed in males, cool season and people over 45 years. During the study period, PM pollution brought 1453.18 million Yuan economic losses for overall MDs, accounting for 0.026% of local GDP. This study suggested that short-term exposure to PM pollution, especially to $\text{PM}_{2.5}$, was associated with increased hospital admissions for MDs in southwestern China. In addition, potential benefits of lowering PM concentrations are considerable.

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1. Introduction

Ambient air pollution is one of the most concerned issues around the world. Over 91% population worldwide are living in places where air quality exceeds WHO guideline limits, resulting in 4.2 million premature deaths each year (Organization, W. H, 2016). Air pollution,

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especially particulate matter (PM), has not only been well proved to be a pathogenic factor on respiratory and cardiovascular diseases biologically and epidemiologically (Mirabelli et al., 2018; Requia et al., 2018; al, 2014), but recently, associated with mental disorders (MDs) via toxicological studies (Block and Calderon-Garciduenas, 2009; Calderon-Garciduenas et al., 2008; Dooley et al., 2018).

Biological evidence points that air pollution had adverse effects on nervous system (Felger et al., 2015; Levesque et al., 2011; Kelly, 2003), suggesting a possible link between air pollution and MDs. The adverse health effects of air pollution partly result from inflammation and oxidative stress in exposed organ systems (al, 2014; Coccaro et al., 2014), while inflammatory processes have been demonstrated to play a crucial role in the etiology of a wide range of MDs (Dooley et al., 2018; Felger et al., 2015; Coccaro et al., 2014). Besides, several experimental studies have explored that air pollutants, particularly PM, are capable of crossing the blood-brain-barrier and triggering neuroinflammation (Calderon-Garciduenas et al., 2008; Levesque et al., 2011). Animal experiments have stated that PM can activate microglia, then microglia-generated oxidant species and pro-inflammatory cytokines such as IL-6 would cause neuronal toxicity, which increased the risk of MDs (Attademo et al., 2017; Block et al., 2004). Moreover, human experiments have also demonstrated that short-term exposure to air pollution has adverse effects on human health. A study in Europe found that even 30min exposure to diesel exhaust would lead to a significant increase in people's median power frequency of electroencephalography (Cruts et al., 2008). A study in Beijing displayed that the PM_{2.5} exposure promoted the secretion of glucocorticoid in blood, which can exacerbate brain damage (Jia et al., 2018). A comprehensive understanding of risk factors is key to prevent and curb MDs. Thus, apart from the conventional factors, such as drug abuse, maternal infection, physical inactivity, and so on (Arango et al., 2018; Kim and Kim, 2017), clarifying the role of air pollution may provide new ideas for the control of MDs.

Over the past decade, many epidemiology studies have provided consistent evidence that exposure to air pollution could augment the burden of MDs from emergency department visits (Szyszkowicz et al., 2010; Oudin et al., 2018; Bernardini et al., 2019) and hospital admissions (Wang et al., 2018; Bai et al., 2019; Tao et al., 2014). These studies mainly provided evidence for the short-term impacts of air pollution on depression (Szyszkowicz, 2007; Wang et al., 2014), schizophrenia (Attademo and Bernardini, 2017; Duan et al., 2018), dementia (Attademo and Bernardini, 2017; Chen et al., 2017a) and suicide (Guo and Barnett, 2015; Min et al., 2018). For example, studies in Canada investigated the association between air pollution and emergency department visits for depression, demonstrating the adverse effects of ozone (O₃), nitrogen dioxide (NO₂), particles with aerodynamic diameters $\leq 2.5 \mu\text{m}$ (PM_{2.5}), particles with aerodynamic diameters $\leq 10 \mu\text{m}$ (PM₁₀), carbon monoxide (CO), and sulfur dioxide (SO₂) on depression (Szyszkowicz, 2007; Szyszkowicz et al., 2016; Szyszkowicz, 2010; Szyszkowicz et al., 2009). Besides, there are also some studies focusing on the long-term impacts (Min et al., 2018; Vert et al., 2017). For example, a cohort study in Korea demonstrated that long-term exposure to PM_{2.5} would increase major depressive disorder (Kim et al., 2016).

However, existing findings regarding the association between air pollution and MDs comes largely from developed areas (Charlson et al., 2018; Organization, W. H. n.d.), although people in underdeveloped areas suffer more from MDs than their counterparts in developed ones (Organization, W. H. n.d.; Livingston et al., 2017; Zhou et al., 2019a; Naslund et al., 2017). According to the Global Burden of Diseases, Injuries, and Risk Factors Study 2017 (GBD 2017), over 970 million people worldwide suffered from MDs, placing it among the major causes of illness and disability (Zhou et al., 2019a). In China, MDs is the second cause of years lived with disability (YLDs) during 1990–2017 with significant impacts on health and economic consequences in the society (Zhou et al., 2019b). In India, one in seven people were affected by MDs of varying severity in 2017, with the proportional contribution of MDs to the total disease burden doubled since 1990 (Sagar et al., 2019).

In addition, even though epidemical researches have provided evidence about health impacts of air pollution on MDs, the corresponding economic losses remain unanswered. The monetary measurement of productivity losses and hospital expenditure due to ailments attributing to air pollution may throw a light on attaching more importance to air pollution from societal perspective, as being of comparability across disease burden and other social sectors.

This study, therefore, aimed to quantify 1) the association between short-term exposure to PM pollutants and hospital admissions of overall and specific MDs (schizophrenia, dementia, and depression), and 2) the corresponding hospitalization economic losses of MDs caused by PM pollution.

2. Materials and methods

2.1. Study area and population

Chengdu, located in southwestern China (latitude 30°05′–31°26′ N and longitude 102°54′–104°53′ E), is the largest and most densely populated city lying in Sichuan Basin which is in a typical subtropical climate area with four distinct seasons. By the end of 2017, Chengdu had a population of 14.35 million in an area of 14,335km². Due to its large population, unfavorable atmospheric diffusion conditions, and relatively high humidity (Li et al., 2017), local air pollution problem, especially PM pollution, is becoming a health threat increasingly. As one of the most PM polluted cities in China (Ning et al., 2018), the annual average concentration of PM_{2.5} in Chengdu during the study period (70.88 $\mu\text{g}/\text{m}^3$) is almost three times higher compared to the WHO air quality guidelines level of 25 $\mu\text{g}/\text{m}^3$ ³⁴⁵.

2.2. Data collection

2.2.1. Hospital admission and related costs data

Data of hospital admissions and related costs for MDs of Chengdu were obtained from local Compulsory Medical Insurance Databases (CMIDs) between January 1, 2013 and October 15, 2017, which included 134,292 official MDs records in 1161 hospitals in study area. CMIDs are composed of two types of compulsory medical insurance system. One is Urban Employee Essential Medical Insurance (UEEMI), which is compulsory for those people working in all kinds of entities, such as companies and factories. The other is Urban-Rural Residency Essential Medical Insurance (URREMI) which covers the population out of UEEMI. In Chengdu, around 16.5 million people are covered by CMIDs, which accounting for >95% of local population. CMIDs incorporates hospital admissions through hospital entry records. In this study, MDs were defined according to the International Classification of Diseases tenth version (ICD-10), with codes F00–F99. Besides, we also took three specific subtypes of MDs into account, including dementia (F00–F03), schizophrenia (F20–F21) and depression (F32–F33). We selected these three specific MDs because of their large numbers of hospital admissions during the study period and existing evidence regarding associations between them and air pollution. In this study, we used the first diagnose as the driving factor of hospitalization, to recognize our subjects of study. Those with the same MD diagnose and readmitted within 30 days were excluded.

2.2.2. Pollution data

Daily data of PM₁₀, PM_{2.5}, PM_C (2.5 μm < particles with an aerodynamic diameters <10 μm), NO₂, O₃, and SO₂ were collected from the China National Environmental Monitoring Center (<http://www.cnemc.cn/>). We averaged the 24-hour mean values from 12 environmental monitoring stations in Chengdu. The average and the maximum distances between the environmental monitoring stations in Chengdu are 23.00 km and 67.56 km, respectively. Since PM_C was not monitored, we calculated its concentrations by subtracting concentrations of PM_{2.5} from PM₁₀ (Qiu et al., 2019; Chen et al., 2018a). There were about 0.3%

missing values for pollutant data, which were interpolated by using the mean value of previous and the next days' values.

2.2.3. Meteorological data

To control the confounding factors, we also collected the meteorological data. Data on daily average temperature (in Celsius) and relative humidity (%) during the study period were obtained from China Meteorological Data Sharing Service System (<http://www.nmic.cn/>).

2.2.4. Local GDP

We collected the annual GDP data of Chengdu during 2013–2017 from National Bureau of Statistics (<http://www.stats.gov.cn/>).

2.3. Modeling

The statistical analysis includes three steps: estimating exposure-response function, calculating the number of hospital admissions for MDs due to PM pollution, and evaluating corresponding economic losses due to hospitalization.

2.3.1. Estimating exposure-response function

We applied a generalized additive model (GAM) to analyze the association between PM pollution and hospital admissions of MDs (Chen et al., 2018a; Song et al., 2018). In our model, quasi-Poisson was used as the linked function because daily hospital admissions typically followed an over-dispersed Poisson distribution. Natural spline functions were used to control the influence of temperature, relative humidity and long-term trends. According to previous studies (Tao et al., 2014; Feng et al., 2019; Liu et al., 2017), we chose 3 as the *df* of temperature and relative humidity, and set the *df* of calendar time to 7 per year. The model formula is as follows:

$$Y \sim \text{quasiPoisson}(\mu)$$

$$\mu = \alpha + \beta Z + \text{NS}(\text{Temp}, df = 3) + \text{NS}(\text{RH}, df = 3) + \text{NS}(\text{Time}, df = 7 * 5) + \text{Dow} \quad (1)$$

Y: daily hospital admissions of MDs;
 μ : the estimator of *Y*;
 α : the intercept;
 β : the coefficient;
Z: the concentration of PM pollutant;
NS: the natural spline function;
df: the degree of freedom;
Temp: daily mean temperature;
RH: daily mean relative humidity;
Time: calendar time, to control long-term temporal trends;
Dow: day of week, a dummy variable to control the systematic variation within a week.

We incorporated both single-day lag (from current day to 6 days before: lag0-lag6) and multi-day moving average (from lag01 to lag06), fitting separate models with the same parameter settings as in the main model. After analyzing the overall effects of PM pollution on hospital admissions of MDs, we explored whether the effects were modified by gender, age, and season. The results were illustrated as percentage changes and corresponding confidence intervals (CI) of hospital admissions for every 10 $\mu\text{g}/\text{m}^3$ increase in PM pollutant concentrations. Furthermore, the differences between each two subgroups were tested by $(Q1 - Q2) \pm 1.96 \sqrt{SE_1^2 + SE_2^2}$, where *Q1*, *Q2* represented effect estimates of the two subgroups, *SE1*, *SE2* are the standard errors (Zhong et al., 2018).

In sensitivity analysis, we examined potential influence of *df* by changing the *df* value for calendar time (*df* = 4–10). Then we built two-pollutant models to test the stability of the effects after adjustment for other air pollutants (NO_2 , O_3 , and SO_2). All analyses were completed

in R software version 3.6.1, using “mgcv” package. Statistical tests were 2-sided, and a *P* value < .05 was considered statistically significant.

2.3.2. Calculating the number of hospital admissions for MDs due to PM pollution

Based on the exposure-response coefficients obtained by GAM, we further calculated the number of hospital admissions for MDs related to PM pollution according to the methods for attributable risk (Qiu et al., 2019; Chen et al., 2017b). In this part we set the reference concentrations for all PM pollutants according to the WHO's standards (50 $\mu\text{g}/\text{m}^3$ for PM_{10} , 25 $\mu\text{g}/\text{m}^3$ for $\text{PM}_{2.5}$, and 25 $\mu\text{g}/\text{m}^3$ for $\text{PM}_{10-2.5}$) (Organization, W. H., 2005). Because only impacts on lag0 to lag3 were significant, the coefficient β_j equaled to the sum of the coefficients of lag0 to lag3 obtained from the first analysis step (Chen et al., 2017b; Leone, 2014; Qu et al., 2019). The formula is as follows:

$$AR_{ij} = 1 - \exp(-\beta_j * (x_{ij} - x_{0j}))$$

$$AN = \sum_{j=1}^3 \sum_{i=1}^{1749} (AR_{ij} * n_{ij}) \quad (2)$$

i: day number of the study period (from 1 to 1749);
j: PM pollutants, PM_{10} , $\text{PM}_{2.5}$, and $\text{PM}_{10-2.5}$;
 AR_{ij} : attributable risk;
 β_j : the exposure-response coefficient;
 x_{ij} : daily concentration of PM pollutants;
 x_{0j} : the reference concentration;
 n_{ij} : the number of daily hospital admissions of MDs;
AN: the total attributable number of MDs.

2.3.3. Evaluating the corresponding hospitalization economic losses

We adopted cost of illness method (COI) when evaluating PM-related hospitalization economic burden of MDs (Jo, 2014; Kennelly, 2017). The COI method took both the medical expenses incurred when a person is ill (the direct costs of illness) and the loss in productivity when a person is in hospital (the indirect costs of illness) into account. Because we could not obtain the income information of each hospital admission, we collected the regional daily GDP per capita to calculate productivity loss. The economic losses were obtained according to the following calculation steps:

$$\text{meanC} = C_h + d\text{GDP}_p \times \text{meanT}_h \quad (3)$$

$$\Delta C = AN \times \text{meanC}$$

meanC: average total economic costs per hospital admission;
 C_h : the mean treatment cost per hospital admission calculated according to our data in Chengdu in 2013–2017;
 $d\text{GDP}_p$: daily GDP per capita;
 meanT_h : mean hospitalization days per hospital admission;
 ΔC : the total economic lose due to PM pollution during the study period.

3. Results

Table 1 summarized the descriptive statistics for MDs hospitalization, air pollutant concentrations and meteorological variables in Chengdu from 2013 to 2017. A total of 134,292 cases of hospital admissions for overall MDs were collected during the 1749 study days, with a daily average of 77 cases. There are 77,183 and 57,109 cases for male and female, respectively. The young (<45) and the elderly (>64) patients accounted for 37.7% and 20.9%, respectively. The number of hospital admissions in warm season (From March to September: 70964 hospital admissions) was a little bit larger than that in cool season (From October to February: 63328 hospital admissions). For the three specific MDs we concentrated on, there were 74,294 hospital

Table 1
Descriptive statistics for MDs hospitalization, air pollutants concentrations and meteorological variables in Chengdu from 2013 to 2017.

Variables	Total number	Descriptive statistics for daily data					
		Mean ± SD	Min	P ₂₅	M	P ₇₅	Max
Mental disorders	134,292	76.78 ± 171.16	5	35	52	75	3659
Schizophrenia	74,294	42.48 ± 129.50	1	13	22	35	2725
Depression	7127	4.54 ± 2.84	0	2	4	6	20
Dementia	5020	3.67 ± 8.29	0	1	2	4	189
Gender							
Male	77,183	44.13 ± 117.95	2	17	27	40	2629
Female	57,109	32.65 ± 54.68	1	16	25	35	1030
Age							
<45	50,623	28.94 ± 66.53	1	13	20	29	1413
45–64	55,578	31.78 ± 74.61	1	13	20	31	1643
>64	28,091	16.12 ± 37.04	1	6	10	16	603
Season							
Warm	70,964	77.56 ± 111.44	10	40	59	81.5	1476
Cool	63,328	75.93 ± 218.75	5	30	46	64	3659
Air pollutants							
PM ₁₀ (μg/m ³)	–	114.74 ± 77.96	16	61	93	146.3	862
PM _{2.5} (μg/m ³)	–	70.88 ± 51.03	6	36	55	90	427
PMc(μg/m ³)	–	43.76 ± 34.72	4	23	35	56	592
NO ₂ (μg/m ³)	–	55.93 ± 18.32	15	43	53	66	144
SO ₂ (μg/m ³)	–	18.16 ± 12.30	4	11	14	21	96
O ₃ (μg/m ³)	–	90.25 ± 53.12	4	49	80	129	301
Meteorological data							
Relative humidity (%)	–	80.51 ± 8.57	42	76	81	87	98
Mean temperature (°C)	–	16.91 ± 7.25	–1.9	10.3	18	23.1	29.8

PM₁₀: particulate matter ≤10 μm in aerodynamic diameter; PM_{2.5}: particulate matter ≤2.5 μm in aerodynamic diameter; PMc: 2.5 μm < particulate matter <10 μm in aerodynamic diameter; P₂₅: the 25th percentile; M: median, the 50th percentile; P₇₅: the 75th percentile.

admissions for schizophrenia, 7127 hospital admissions for depression, and 5020 hospital admissions for dementia during the study period. Daily mean concentrations of air pollutants were 114.74 μg/m³, 70.88 μg/m³, 43.76 μg/m³, 55.93 μg/m³, 18.16 μg/m³, and 90.25 μg/m³ for PM₁₀, PM_{2.5}, PMc, NO₂, SO₂, and O₃, respectively. Spearman's correlations between daily air pollutant concentrations and meteorological variables were displayed in Table S1. There were strong correlations among air pollutants excepting ozone. Daily mean temperature and relative humidity were 16.91 °C and 80.51%, respectively.

Fig. 1 showed the percentage changes of MDs hospital admissions in single-pollutant models using different lag days. Overall, there were obvious associations of PM₁₀, PM_{2.5}, and PMc with hospital admissions of

MDs. The associations were statistically significant at lag 0–3 days and all the cumulative lag days, with the largest effects at cumulative lag 3 day. Per 10 μg/m³ increase in concentrations of PM₁₀, PM_{2.5}, and PMc were associated with 3.25% (95%CI: 2.34–4.16%), 6.38% (95%CI: 4.79–7.97%), and 3.81% (95%CI: 2.13–5.50%) increments in daily hospital admissions for MDs at cumulative lag 3 day, respectively. In addition, there was also a negative association between PM pollution and admission at lag 6 day. It means that PM pollution showed a protect effect on MDs at lag 6 day. The results of percentage changes of admission and betas on different lag period were presented in Table S2, Table S3.

Fig. 2 illustrated the results of subgroup analyses of gender, age, and seasons. The impacts of PM pollution on hospital admissions of MDs

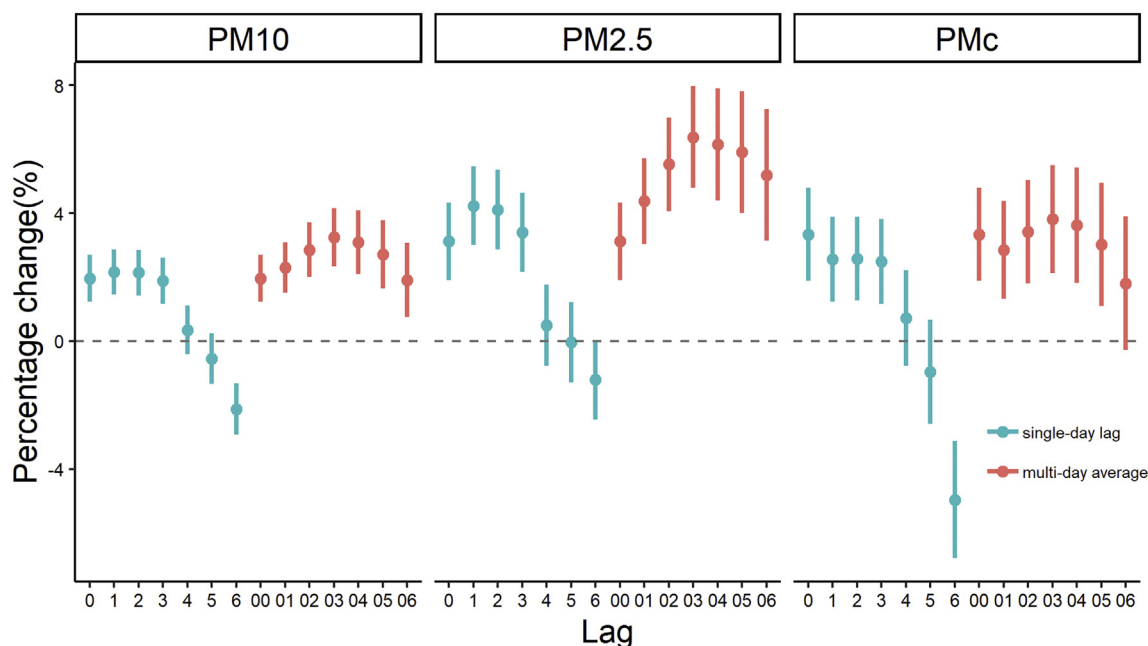


Fig. 1. Percentage changes of MD hospitals on different single-day lags and multi-moving averages affected by PM₁₀, PM_{2.5} and PMc, respectively

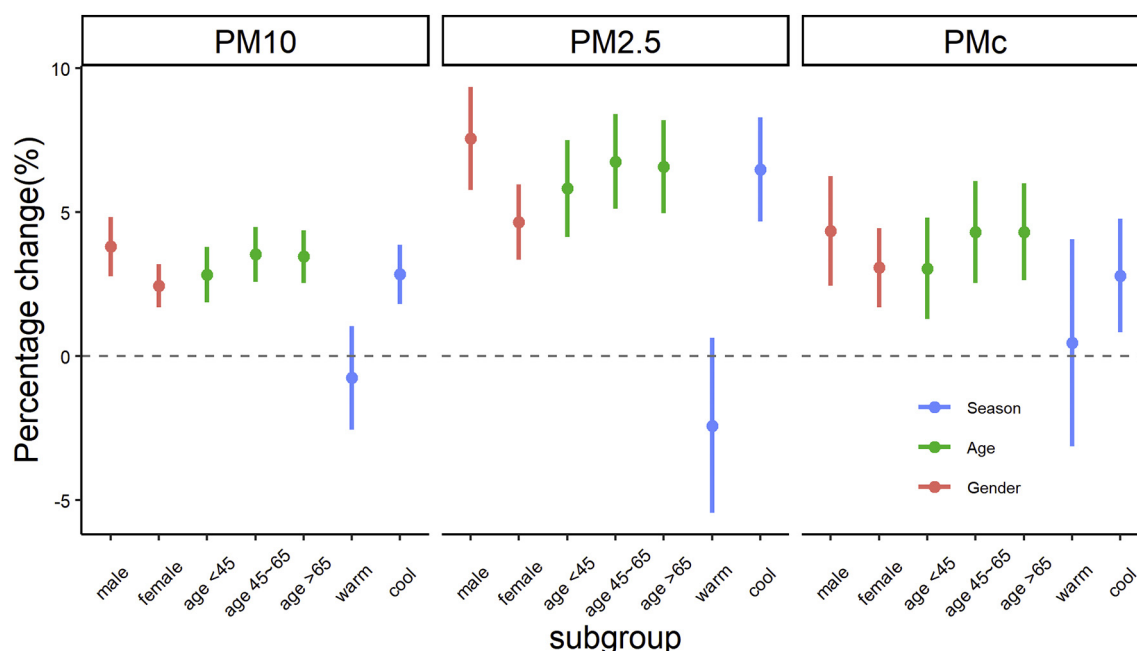


Fig. 2. Percentage changes of MD hospitals across gender, age and season affected by PM₁₀, PM_{2.5} and PMc, respectively

were negative and significant at lag03 day in all the subgroups except in warm-season. In gender-specific analysis, the effects were generally more pronounced in male. In age-specific analysis, it was shown that PM pollution was more harmful to people over 45 years. As for season-specific analysis, the results in this part suggested an adverse impact only in cool season. Noteworthily, only the discrepancy of the impact of PM_{2.5} across warm and cool season was significant among all these subgroups. Corresponding results in tabular form were displayed in Table S4.

Table 2 was the percentage changes of hospital admissions for MDs with a 10 $\mu\text{g}/\text{m}^3$ increase in PM pollutants at lag03 using single and two-pollutant models. It was showed that the effects of PM pollution on MDs were still significant after adjustment for NO₂, O₃ and SO₂. Table S5 displayed the percentage changes of hospital admissions for MDs with a 10 $\mu\text{g}/\text{m}^3$ increase in PM pollutants at lag03 under varying degrees of freedom for the smooth function of time trend. The results remained robust after adjustment of smoothness of time (4–10 *df* per year).

Fig. 3 depicted the effects of PM pollution on hospital admissions of specific MDs. For schizophrenia, the effects of PM pollution were significant at lag0 to lag3 and all the cumulative lag days. And for dementia, the harmful effects were significant at lag2 and lag02–04 for PM₁₀, at lag2 and lag02–06 for PM_{2.5}, and at lag2 for PMc. However, for depression, we found that PMc had a harmful effect at lag0 and lag00, while PM₁₀ and PM_{2.5} showed no adverse effect.

Table 3 showed the attributable number (AN), attributable risk (AR) and economic costs of hospital admissions for MDs related to PM pollution using WHO's air quality guidelines as reference in Chengdu in 2013–2017. During the study period, the total economic costs of hospital admissions for overall MDs, schizophrenia, depression, and dementia

due to PM pollution were 1453.18, 987.55, 68.48, and 37.62 million Yuan, respectively. In terms of different pollutants, the greatest economic burden came from PM_{2.5}, which reached 657.92 million Yuan for overall MDs, then followed by PM₁₀, and PMc.

4. Discussion

To our knowledge, this study is one of the few studies to investigate the association between PM and MDs in a developing country. In this time-series study, short-term exposure to ambient PM pollution (PM₁₀, PM_{2.5}, and PMc) was partially responsible for increase of hospital admissions for overall and specific MDs after adjusting temperature, relative humidity, long-term trend, and day of week. Besides, it was showed that PM pollution entailed heavy economic burden for MDs hospitalization to the society, which was 1453.18 million Yuan, accounting for approximately 0.026% of local GDP during the study period 2013–2017. These results would enrich evidence about the links between air pollution and MDs in heavily polluted areas of developing countries.

Consistent with some existing evidence, we found positive associations between PM pollutants (PM₁₀, PM_{2.5}, and PMc) and hospital admissions of MDs at different lag patterns (Song et al., 2018; Chen et al., 2018b; Xue et al., 2019; Buoli et al., 2018). The mechanisms of this association were probably because of increased inflammation in some brain areas such as hippocampus, which had been demonstrated to be one potential biological pathway in animals exposed to air pollution (Guo et al., 2012; Guo et al., 2015). Recently a study in China further stated that this association may be partially mediated by physical activity, neighborly reciprocity, and sunlight (Wang et al., 2019). On the other hand, several studies concluded in opposite. Two epidemiological

Table 2

Percentage increases of hospital admissions for MDs with a 10 $\mu\text{g}/\text{m}^3$ increase in PM pollutants at lag03 using single and two-pollutant models.

Model	PM ₁₀	PM _{2.5}	PMc
None	3.48 (2.56,4.40)	6.39 (4.90,7.88)	4.58 (2.67,6.50)
+NO ₂	3.45 (2.62,4.29)	7.15(5.71,8.6)	3.94 (2.33,5.56)

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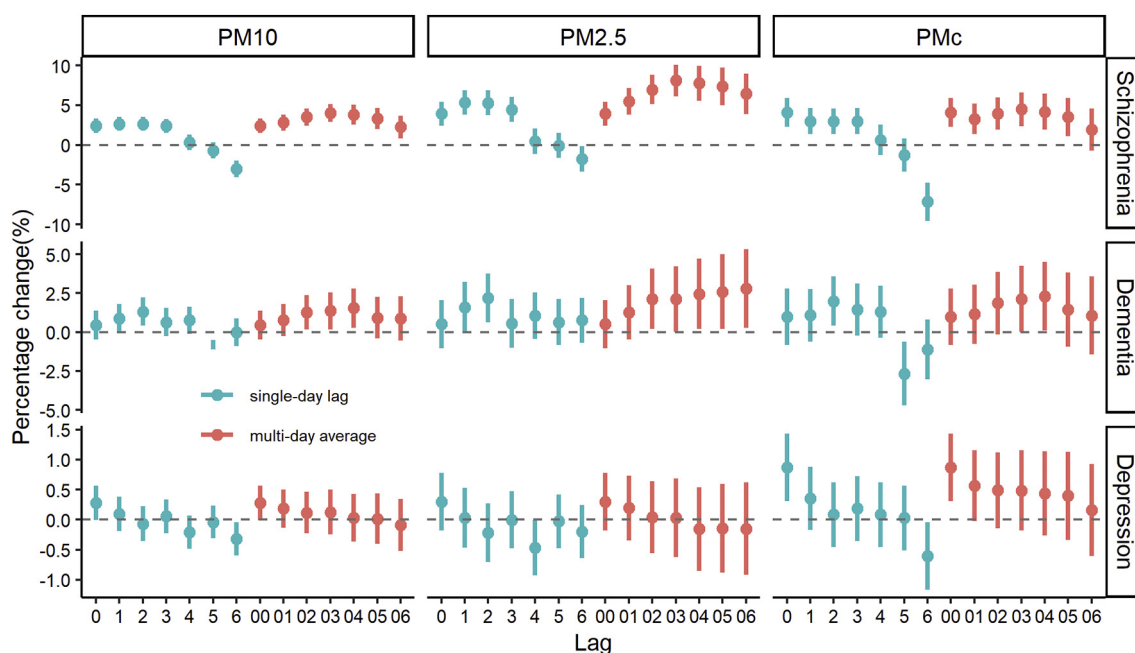


Fig. 3. Percentage changes of three specific MDs hospitals on different lag days and multi-day averaging affected by PM₁₀, PM_{2.5} and PMc, respectively

studies from Shanghai and Beijing demonstrated that PM_{2.5} had no adverse effects on MDs (Chen et al., 2018a; Gao et al., 2017). This divergence may be caused by the difference in the composition of PM pollutants, because different emission sources and weather conditions across areas can greatly affect the composition of PM_{2.5}, which would obviously influence the association between PM pollution and MDs (Yang et al., 2019; Morakinyo et al., 2016). In addition, it is worth noting that we also found the so-called “harvest” phenomenon at lag6 (6 days after exposure) when exploring the effects of PM pollution on MDs. The possible reason for this phenomenon was MDs’ symptom will occur sooner in fragile people who are much more sensitive to PM pollution than counterparts, leaving limited numbers of susceptible subjects at risk later on (Zhang et al., 2017). The overall hazard, therefore seemed to be reduced at lag6.

In terms of gender, we found that the effect of PM pollution was stronger for males. For example, an increase of 10 µg/m³ in PM_{2.5} would result in 7.56% (95% CI: 5.77–9.35%) rising of MDs hospital admissions in males, compared with 4.66% (95%CI: 3.35–5.96%) in females. This result was in line with previous studies (Qiu et al., 2019; Song et al., 2018) and may be explained by more physical activities and inspiratory capacity in males (Duan et al., 2018; Xue et al., 2019). As for age, the harmful effects were most pronounced for people over 45 years. Studies in North China and South Korea showed similar trends with ours (Song et al., 2018; Lee et al., 2019). As far as seasons were concerned, it should be noted that the hazards of PM pollution were only significant in cool season. This result may be due to more severe PM

pollution in cool season in Chengdu (Li et al., 2017). Another possible reason was the different temperature in warm and cool seasons, which played an important role in determining emission, transport, dilution and chemical transformation of air pollutants (Macdonald et al., 2005).

With regard to three specific MDs, schizophrenia is a psychiatric syndrome characterized by psychotic symptoms of hallucinations, delusions, and disorganized speech, by negative symptoms such as decreased motivation and diminished expressiveness, and by cognitive deficits involving impaired executive functions, memory, and speed of mental processing (Marder and Cannon, 2019). Findings in this study showed that all PM pollutants (PM₁₀, PM_{2.5}, and PMc) were significantly related to hospital admissions for schizophrenia at lag0 to lag3 and all the cumulative lag days, with the strongest effects peaked at lag03 day. This result was in line with studies conducted in Tongling, Xi’an, China and Osaka (Duan et al., 2018; Liang et al., 2019; Eguchi et al., 2018). It suggested that the effects of PM pollutants on schizophrenia may be acute and cumulative. The behind reasons were not clear and could be complex, but evidences had pointed out that 15-day exposure to PM₁₀ would induce inflammation and endothelial dysfunction in rat brain (Guo et al., 2012). Another study found that PM₁₀ can activate microglia, then microglia-generated oxidant species and pro-inflammatory cytokines such as IL-6 would cause neuronal toxicity, which increased the risk of schizophrenia (Attademo et al., 2017). Schizophrenia is among the top 10 global causes of disability (Fleischacker et al., 2014). In China, the prevalence of schizophrenia

Table 3
The attributable number, attributable fraction and economic costs (million Yuan) of hospital admissions related to PM pollution using WHO’s air quality guidelines in Chengdu 2013–2017.

	PM ₁₀			PM _{2.5}			PMc			Total costs
	AN	AR	Costs	AN	AR	Costs	AN	AR	Costs	
MDs	21,840	0.13(0.09,0.16)	519.67	27,650	0.16(0.13,0.21)	657.92	11,582	0.06(0.04,0.09)	275.59	1453.18
Sch	12,687	0.29(0.10,0.17)	353.14	15,985	0.22(0.13,0.22)	444.94	6807	0.07(0.04,0.09)	189.47	987.55
Dm	1024	0.11(0.08,0.14)	24.39	1317	0.15(0.15,0.18)	31.37	534	0.18(0.03,0.07)	12.72	68.48
Dp	723	0.11(0.08,0.14)	13.48	929	0.19(0.11,0.19)	17.32	366	0.05(0.05,0.07)	6.82	37.62

AN: attributable number; AR: attributable risk; AN and AR were calculated based on the largest effect estimated in single pollutant models; MDs: mental disorders; Sch: Schizophrenia; Dp: depression; Dm: dementia.

increased 132% between 1990 and 2010 (Liang et al., 2019). More studies are needed to test these mechanisms, and if confirmed, more efficient environmental protection policies should be formulated to ease the burden of schizophrenia.

Dementia, a major neurocognitive clinical syndrome of acquired intellectual disturbances produced by brain dysfunction (Livingston et al., 2017), has been reported to be positively related to PM pollution (Attademo and Bernardini, 2017; Chen et al., 2017c). In this study, we reconfirmed this conclusion and found that per $10\text{ }\mu\text{g}/\text{m}^3$ increase of PM_{10} , $\text{PM}_{2.5}$, and PMc led to 1.37% (95%CI: 0.18–2.56%), 2.12% (95%CI: 0.01–4.23%), and 2.13% (95%CI: 0.02–4.25%) up of dementia hospitalization in Chengdu, respectively. Compared to results of prior studies, these associations were quite modest. One possible reason for this may be differences from pollutants levels and composition. For example, Hong Chen and his colleagues analyzed the impacts of ambient air pollution on incidence of dementia in Ontario, Canada, where the concentrations of pollutants were among the lowest in the world (Chen et al., 2017a). Besides, the differing effect size may also be attributable to differences in population characteristics. But existing evidence is limited, it remains to be demonstrated by more dementia related studies worldwide. In addition, more consideration should be given to global current aging problem when analyzing the results of this type. Alzheimer's disease (AD) is the most common type of dementia, which affects substantial number of older adults. According to our data, 89.4% of dementia patients are over 65 years. As the proportion of the elderly keeps increasing in China, dementia would bring heavier burden to the society in the future. It is urgent to elucidate the pathogenesis of dementia and take corresponding preventive measures.

Contrary to existing evidence, we found no relationship between PM_{10} , $\text{PM}_{2.5}$ and depression. While for PMc , it showed a modest harmful effect on depression only on the day of the exposure. So far, studies about the associations between air pollution and depression predominantly have been conducted in Canada and South Korea (Szyszkowicz, 2007; Szyszkowicz et al., 2009; Kim et al., 2016). Findings of these studies confirmed that increased concentrations of $\text{PM}_{2.5}$, especially if for prolonged in time, may be related to a new onset of depression (Vert et al., 2017; Kim et al., 2016). The difference between ours and those results may come from distinct study designs and modeling strategies, as we explored short-term effects of PM pollution while these studies concentrated on long-term impacts. The findings in this study that air pollution was not related to depression were consistent with two prior study undertaken in the United States and Europe (Wang et al., 2014; Zijlema et al., 2016). It suggested that the effects of PM on depression may take a long-term rather than a short-term period. Due to the heterogeneous outcomes, further studies with a larger and more representative study population are needed.

When it comes to economic losses, the total economic burden of hospital admissions for overall MDs was 1453.18 million Yuan in 2013–2017, accounting for 0.026% of local GDP during the same period. As for different pollutants, $\text{PM}_{2.5}$ brought the predominant economic burden of hospital admissions for MDs. It may be because $\text{PM}_{2.5}$ is smaller, which make it easier to cross the blood–brain barrier, thus it is liable to damage the neurological system through introducing neuro-inflammation, neuronal signaling dysfunction, and immune responses (Jia et al., 2018). In China, the total annual costs of MDs increased from \$1094.8 in 2005 to \$3665.4 in 2013 for individual patients, and from \$21.0 billion to \$88.8 billion for the whole society (Xu et al., 2016). MDs took a heavy toll on the patient, the patient's close relatives, and society. To date, no study has assessed the economic burden of hospital admissions for MDs due to PM pollution, yet studies related to this topic would be of great value on diseases comparing and policy making in societal perspective. In light of results in this part, similarly to what happens for respiratory and cardiovascular diseases, it is conceivable that a reduction in levels of PM pollution, especially $\text{PM}_{2.5}$, can efficiently reduce the costs of MDs.

Our study has some limitations. First, we assumed that residents in Chengdu shared the same level of PM pollution, because information on specific residence for each hospital admission was scarce. This assumption did not consider spatial heterogeneity of PM pollution and people's time-activity patterns, may lead to underestimation of the association between short-term exposure to PM pollution and hospital admissions of MDs. Secondly, PM is made up of many kinds of components, and the composition and size of PM vary substantially according to emission sources and prevailing weather conditions (Institute, H. E., 2002). But we only explored the overall impacts of PM pollution on MDs, ignoring the effects of its subcomponents. Thirdly, the economic burden calculated in this study included the costs due to hospitalization and productivity loss, but did not take into consideration costs attributed to transportation, care-giving and so on. Finally, due to the limitation of our claim data, we failed to access the age of onset and reasons for hospitalization this time. Analyses considering more factors should be conducted in the future.

Despite the limitations, this study still has some strengths. It involved >95% of the city's whole population. This huge database avoided selection bias and guaranteed enough statistical power to reveal the association between PM pollution and hospital admissions of MDs. In addition, this study considered both overall and specific MDs when analyzing the impacts of PM pollution, which can provide more comprehensive results about the association. Last but not least, this study assessed hospitalization economic losses of MDs attributable to short-term exposure to PM pollution. The results in monetary form can not only help to raise people's attention to MDs, but also provide direct scientific basis for decision-makers to allocate social resources for air pollution control.

5. Conclusion

This study demonstrated that short-term exposure to PM pollution (PM_{10} , $\text{PM}_{2.5}$, and PMc) was associated with increasing hospital admissions of overall MDs, schizophrenia and dementia in Chengdu, southwestern China. Male and elderly individuals were more sensitive to particulate matter pollution. Furthermore, compared with warm season, MD are apt to occur during cold circumstances. In addition, PM-related hospital admissions for MDs inevitably imposed heavy economic burden on the society. It is strongly suggested that further studies from both epidemiological and physiological perspective should be put in agenda to confirm the causal relationship between PM pollution and MDs.

Credit authorship contribution statement

Pei Zhang: Methodology, Software, Writing - original draft.
Xiaoyuan Zhou: Conceptualization, Methodology, Supervision, Writing - review & editing.

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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2020.139114>.

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