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Short-term attributable risk and economic burden of hospital admissions for anxiety disorders due to air pollution: a multicity time-stratified case-crossover study

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Abstract

Background Anxiety disorders are a leading cause of severe quality of life impairment and are among the most common mental disorders globally. However, few studies have investigated the association between exposure to high levels of air pollution and an increased risk of developing anxiety disorders. This study aimed to investigate the relationship between air pollutants and hospitalisation for anxiety disorders and the associated economic burden of these hospitalisations in Sichuan, China.

Methods We collected 7,282 records of anxiety disorder hospitalisation from medical institutions across nine cities between January 1, 2017, and December 31, 2018. Concurrent meteorological and air pollution data, including temperature, humidity, $PM_{2.5}$, PM_{10}, SO_2, and CO, were obtained from 183 monitoring stations in Sichuan Province. After controlling for long-term trends, day of the week, and meteorological factors, we employed a time-stratified case-crossover design based on conditional logistic regression to assess the association between concentrations of the four pollutants ($PM_{2.5}$, PM_{10}, SO_2, and CO) and hospital admissions for anxiety disorders, with stratified analysis by age, sex, and season. The cost of hospitalisation was evaluated using the cost-of-illness method.

Results The finding indicated a positive correlation between short-term exposure to air pollutants and hospitalization rates of anxiety disorders. The effect of each 10 μg/m^3 increase in airborne particulate matter (PM) and SO_2 on hospital admissions for people with anxiety disorders peaked with a lag of 5 days, and each 1 mg/m^3 increase in CO had the greatest effect on the 0–7 day moving average lag, with OR values of $PM_{2.5}$:1.002 (95% CI: 1.001,1.004), PM_{10}:1.001 (95% CI: 1.000,1.002), SO_2:1.034 (95% CI: 1.020,1.047), and CO: 1.614 (95% CI: 1.247, 2.089). Air pollution increases the chances of anxiety disorders during the cold season. Furthermore, the elderly are particularly susceptible to these pollutants, which may contribute to an increased hospitalization rates of anxiety disorders ($P < 0.05$). The total economic cost of hospitalisation for anxiety disorders due to particulate matter pollution was ¥ 966,319 during the study period.

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Conclusion Short-term exposure to $PM_{2.5}$, PM_{10}, $SO_{2,}$ and CO may increase the risk of hospital admissions for anxiety disorders and impose significant financial burdens.

Keywords Anxiety disorders, Air pollution, Short-term effects, Temporal stratification, Economic costs

Introduction

Anxiety disorders are the most common mental disorders, characterised by persistent psychogenic anxiety, somatic anxiety, and sleep disturbances [1]. Anxiety disorders were among the top 25 leading causes of disability worldwide in 2019. In 2020, the global prevalence of anxiety disorders increased to 4802.4 cases per 100,000 population, equivalent to 374 million people [2]. In 2019, anxiety disorders remained the most prevalent of all major mental disorders in China, exceeding that of depression, especially among adults. The lifetime prevalence of any of the anxiety disorders is approximately 7.6%, and an annual prevalence of approximately 4.98% [3]. In 2017, the lifetime cost of perinatal depression and anxiety disorders in Brazil amounted to $4.86 billion [4]. Understanding the risk factors that predispose individuals to anxiety disorders is important to reduce the prevalence of these conditions, as they can significantly reduce the quality of life of individuals.

Anxiety disorders can be precipitated by various factors. In addition to genetic predisposition, environmental risk factors may contribute to the onset or exacerbation of anxiety disorders. Experimental studies have demonstrated that airborne particulate matter (PM) pollution is a significant source of environmentally induced inflammation and oxidative stress. Furthermore, oxidative stress and inflammation in the brain lead to abnormal brain function, which results in the development of anxiety disorders-like symptoms [5]. A number of studies have demonstrated a correlation between acute exposure to air pollutants and the hospitalization rates due to anxiety disorders [6–8]. A hospital case-crossover study conducted in southern China using a single-pollutant model demonstrated that each 10 μg/m³ increase in $PM_{2.5}$ exposure correlates with a significant increase in outpatient hospitalisations for anxiety disorders, with an estimated increase of 3.14%. The associations mentioned earlier demonstrated stability in the two-pollutant model [9]. A study of children in Cincinnati, USA, demonstrated a significant correlation between exposure to traffic-related elemental carbon at birth (ECAT) and child-reported anxiety disorders. Specifically, a 0.25 μg/m³ increase in ECAT concentration was associated with a 2.3-point increase in the Spencer Children's Anxiety Scale score [10]. Another observational cohort study demonstrated that the prevalence of severe anxiety disorder symptoms was 15% within the sample, with the odds of increased anxiety disorder symptoms significantly increasing with longer exposure to fine PM ($PM_{2.5}$) over multiple averaging periods. Models that included multiple exposure windows demonstrated that short-term averaging periods were more relevant than long-term averaging periods [11].

China is among the most polluted countries globally [12], and air pollution has worsened with the accelerated development of heavy industry in recent decades. Sichuan, now one of the most polluted regions in China regarding air quality, is characterised by a high concentration of air pollution, attributed to the extensive industrial development and geographical conditions that impede the dispersion of air pollutants [13]. Similarly, limited studies have been conducted to assess overall exposure to air pollutants in various regions of Sichuan Province [14]. Given the substantial public health and economic impact of anxiety disorders, it is imperative to ascertain whether there is an association between common air pollutants and an increased risk of hospitalisation for anxiety disorders. This would offer essential theoretical support for decision-making regarding primary prevention and targeted interventions. This study collected data on hospitalised cases of anxiety disorders in nine cities in Sichuan between 2017 and 2018 and utilised a time-stratified case-crossover study design to investigate the potential association between four air pollutants (PM_{10}, $PM_{2.5}$, CO, and SO_2) and hospitalisation for anxiety disorders. Furthermore, stratified analyses were performed according to sex, age, and season. The economic burden of disease attributable to exposure to air pollutants was evaluated.

Methods

Study population

We selected nine cities: Chengdu, Zigong, Luzhou, Mianyang, Nanchong, Meishan, Yibin, Guang'an, and Liangshan Yi Autonomous Prefecture. Eight of these cities are located in the Sichuan Basin and are situated in the Western Sichuan Plateau, collectively representing the diverse conditions of the entire Sichuan Province across various populations. Herein, we collected data on hospitalised cases of anxiety disorders from hospitals in nine cities between January 1, 2017, and December 31, 2018. According to the International Classification of Diseases, Tenth Revision (ICD-10) codes, patients diagnosed with F40 (phobic anxiety disorders) and F41 (other anxiety disorders) in ICD-10 were included in this study. We extracted 7282 valid anxiety disorder cases from the data collected for the study. The data set comprised age, sex, residential address, date of admission, date of discharge, disease diagnosis, disease code (ICD-10), and total cost of hospitalisation.

Air pollution and meteorological data

The data regarding sulfur dioxide (SO_2), carbon monoxide (CO), and respirable particulate matter (PM_{10}, $PM_{2.5}$) for the period between January 1, 2017, and December 31, 2018, were obtained from the Sichuan Environmental Monitoring Station(http://www.scdata.net.cn/). Daily meteorological data on temperature and humidity for the specified period were obtained from the Sichuan Meteorological Bureau. Average daily temperature and relative humidity data were included in the analysis to account for the potential influence of meteorological conditions on anxiety disorder hospitalisation. Hourly data from monitoring stations were used to calculate the average daily exposure to air pollutants and meteorological variables.Meanwhile, the locations of all monitoring stations and the home addresses of hospitalized anxiety patients were geo-coded using the Gaode Map API (https://lbs.amap.com/). The inverse distance (1/distance^2) weighted average of the concentrations from all monitoring stations was then used to assess air pollutant exposure during a specific hospitalization period, including single-day lag exposure (lag0–lag7) and multi-day moving average lag exposure (lag01–lag07).

Study design

We used a time-stratified case-crossover design study in which cases served as their controls to investigate the possible association between ambient air pollutant concentrations and hospitalisations for anxiety disorders. This approach allowed for the adjustment of time-invariant characteristics, including age and sex, thereby ensuring unbiased estimates from conditional logistic regression and avoiding time-trend bias. The exposure of each patient to ambient air pollutants on the day of admission was compared with exposure on three or four reference days for each case of anxiety disorder. The reference days were selected to correspond to the same days of the week, within the same year, month, and admission day. This controls the effects of the day of the week, long-term trends, and individual somatic differences (genetics).

Statistical analysis

Association between air pollution and the admissions for anxiety disorders

In this study, a time-stratified case-crossover design was employed. The general and clinical characteristics of all 7,282 cases were described, and Spearman's correlation analysis was employed to assess the associations between exposure variables. Conditional logistic regression was employed to investigate the correlation between air pollutant concentrations and anxiety disorder hospitalisations on each specific lag day. Since meteorological factors may affect hospitalization rates, temperature was introduced as a control variable in the model. To examine the short-term association between air pollution concentrations and anxiety disorders, different lag structures were fitted to the model, ranging from the day of hospitalization (lag 0 days) to 7 lag days (lag 7 days). In light of the possibility that single-day lag models may underestimate the effects of air pollution [15]. Additionally, we assessed the association between the concentrations of the four air pollutants with the multi-day moving average day (from lag 01 to 07), representing the cumulative average from the current day (lag 0) to the lag day.

The two-pollutant models with first-order interactions were used in sensitivity analyses to examine the effects of four air pollutants on anxiety disorders, including various crossover levels of other pollutants, including SO_2 and CO [16]. A z-test was used to create stratified models to assess potential effect modifications by age (divided into three categories: <18 years, 18–65 years, and ≥65 years) and sex. The 18–64 years age group was selected as the reference group for the age-stratified analyses. We divided the admission time of the study patients according to the cold season (October–March) and the warm season (April–September).The following formula was used to assess whether the differences between subgroups were statistically significant: $(\widehat{Q}_1 - \widehat{Q}_2)/\sqrt{(S\widehat{E}_1)^2 + (S\widehat{E}_2)^2}$

In the formula, $\widehat{Q}_1$ and $\widehat{Q}_2$ are the estimates of different categories in each stratified subgroup, while $S\widehat{E}_1$ and $S\widehat{E}_2$ represent the respective standard error for each estimated value.

The results are presented as a percentage increase in air pollutant concentrations and 95% confidence intervals (CIs) for the daily admissions for anxiety disorders per interquartile range (IQR = 75th percentile of air pollutants – 25th percentile). The R software (version 4.3.3) and Statistical Package for the Social Sciences software (version 27)were used for all statistical analyses. All statistical tests were performed using a two-tailed hypothesis with a significance level of 0.05.

Economic costs of hospitalisation for anxiety disorders due to exposure to air pollution

Single-pollutant modelling results were used to identify pollutants with significant effects, and attributable risk equations were used to calculate the number of hospitalisations for anxiety disorders resulting from exposure to each selected pollutant. The World Health Organization (WHO) air quality guidelines were used as a reference point for the analysis, with the following concentrations taken as the basis for comparison: 15 μg/m^3 for $PM_{2.5}$, 45 μg/m^3 for PM_{10}, 40 μg/m^3 for SO_2 and 4 mg/m^3 for

Table 1 Demographic characteristics of patients hospitalised for anxiety in nine Sichuan cities during 2017–2018

Variable	Individual Anxiety Admissions
Total (n)	7282
Sex	
Male (%)	2363 (32.4)
Female (%)	4919 (67.6)
Age (year) (mean ± SD)	52.94 ± 16.08
< 18 (%)	156 (2.1)
18–65 (%)	5346 (73.4)
≥ 65 (%)	1780 (24.5)
Season	
Cold (%)	3438 (47.2)
Warm (%)	3844 (52.8)

Abbreviations: SD = Standard deviation

CO over 24 h [17]. Attribution Eqs. (1)–(3) are presented below [18–19]:

$$AN_i = [(\exp(\beta * \Delta AP_i) - 1)/\exp(\beta * \Delta AP_i)] * N_i \quad (1)$$

$$meanC = C_h + \text{dPCDI} \times meanT_h \quad (2)$$

$$\Delta C = AN \times meanC \quad (3)$$

In these formulae, i represents the days within the study period.AN_i represents the admissions on day i due to exposure to pollutants,$\triangle AP_i$ indicates the difference between the average pollutant concentration on the day i and the reference concentration, N_i represents the number of hospital admissions due to anxiety disorders on day i, β is the exposure-response coefficient (coef value) correlating pollutants with the number of admissions for anxiety disorders, and the term meanC represents the mean total economic cost per hospital admission. Ch denotes the mean total cost of each hospitalisation throughout the study period. Additionally, dPCDI signifies the per capita disposable income per day in Sichuan Province over the same period. meanTh denotes the mean number of days spent in the hospital per admission. ΔC denotes the total economic cost caused by air pollution.

Sensitivity analysis

We performed a two-pollutant model analysis to evaluate the robustness of the association between specific air pollutants and anxiety disorders, controlling for the effects of other pollutants to ascertain the reliability of these findings. To avoid collinearity, air pollutants with correlation coefficients $r > 0.60$ were removed from the model.

Results

We screened 7,282 patients admitted with anxiety disorders with valid information (mean age of patients: 52.94 ± 16.08 years; 32.4% male, 67.6% female) in nine cities of Sichuan Province in 2017–2018. Of these 7282 patients, 2.1% were adolescents (mean age: 14.67 ± 3.35 years), and 24.5% were older adults (mean age: 72.73 ± 6.25 years). Furthermore, 47.2% of the patients were admitted during the cold season, and 52.8% were admitted during the warm season (Table 1).The detailed basic information of participants from each city is presented in table A of the supplementary material.

Table 2 presents the descriptive statistics of air pollutants and meteorological measurements in the sampled cities for case days and control days in this study.

Table 2 Summary statistics for air pollutant concentrations and meteorological variables

Variables	Air pollutants and meteorology						
	Mean ± SD	Min	P25	Median	P75	Max	IQR
Pollutants (Lag 0 day)							
$PM_{2.5}$ (μg/m^3)	46.73 ± 33.84	8.09	2.91	36.39	60.35	258.53	57.44
PM_{10} (μg/m^3)	72.00 ± 45.90	15.34	38.30	59.04	93.61	366.96	55.31
SO_2 (μg/m^3)	11.86 ± 3.52	2.63	9.55	11.10	13.73	33.42	4.18
CO (mg/m^3)	0.80 ± 0.01	0.35	0.64	0.75	0.91	1.84	0.27
Meteorology (Lag 0 day)							
Temperature (℃)	17.67 ± 7.34	2.91	10.90	17.70	23.92	34.41	13.02
Relative humidity (%)	76.94 ± 10.11	44.00	70.26	77.86	84.20	98.86	13.94
Pollutants (control days)							
$PM_{2.5}$ (μg/m^3)	47.04 ± 33.11	7.00	22.95	36.42	62.73	212.03	39.78
PM_{10} (μg/m^3)	72.41 ± 44.62	16.04	38.07	59.29	97.49	268.03	59.42
SO_2 (μg/m^3)	11.91 ± 3.67	3.821	9.35	11.20	13.61	38.11	4.26
CO (mg/m^3)	0.80 ± 0.24	0.34	0.63	0.75	0.91	1.93	0.28
Meteorology (control days)							
Temperature (℃)	17.63 ± 7.35	2.06	10.70	17.80	23.86	31.87	13.16
Relative humidity (%)	76.88 ± 10.12	43.61	69.91	77.37	85.23	96.73	15.32

a P25, the 25th percentile; median, the 50th percentile; P75, the 75th percentile; IQR = Interquartile

On case days, the daily average concentrations ($\bar{x}$ ± sd) of $PM_{2.5}$, PM_{10}, SO_2, and CO were 46.73 ± 33.84 μg/m³, 72.00 ± 45.90 μg/m³, 11.86 ± 3.52 μg/m³, and 0.80 ± 0.01 mg/m³, respectively. The daily average temperature and relative humidity were 17.67 ± 7.34 °C and 76.94 ± 10.11%, respectively. On control days, the daily average concentrations ($\bar{x}$ ± sd) of $PM_{2.5}$, PM_{10}, SO_2, and CO were 47.04 ± 33.11 μg/m³, 72.41 ± 44.62 μg/m³, 11.91 ± 3.67 μg/m³, and 0.80 ± 0.24 mg/m³, respectively. The daily average temperature and relative humidity on control days were 17.63 ± 7.35 °C and 76.88 ± 10.12%, respectively.$PM_{2.5}$ concentrations were significantly and positively correlated with PM_{10} concentrations ($r = 0.97$, $P < 0.05$). Additionally, $PM_{2.5}$ and PM_{10} concentrations were positively correlated with SO_2 and CO concentrations ($r = 0.58–0.77$, $P < 0.05$). Additionally, SO_2 and CO concentrations were positively correlated ($r = 0.46$, $P < 0.05$) (Figs. 1 and 2). However, all pollutant concentrations exhibited a general negative correlation with temperature and humidity.

Figure 2 depicts a summary of the single-pollutant model results for anxiety disorder admissions, intending to elucidate the relationship between environmental factors and mental health. The data has been adjusted for external influences, including temperature, relative humidity, and holidays, for enhanced clarity. Our results show that, depending on the lag structure considered, the admissions for anxiety disorders increases for every 10μg/m³ increase in $PM_{2.5}$, PM_{10}, and SO_2 concentrations, or every 1 mg/m³ increase in CO. A positive correlation exists between $PM_{2.5}$ and PM_{10} concentrations and the number of anxiety disorder admissions, particularly at lag 2 and lag 4 to lag 6 days and lag 02 days. Additionally, at lag 7 days, $PM_{2.5}$ concentrations exhibited a positive correlation with the incidence of admissions for anxiety disorders. Except at lag 3 days, CO concentrations exhibited a positive correlation with anxiety disorder admissions. At lag 2, lag 4 to lag 6, lag 02, lag 04 to lag 07, SO_2 concentrations were positively associated with anxiety disorder admissions.

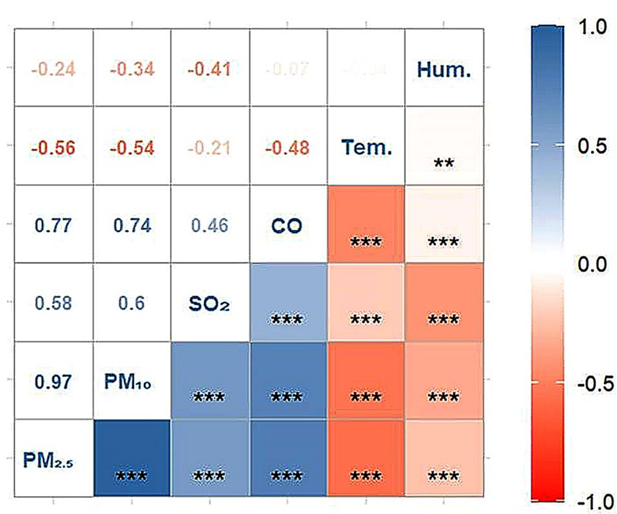

Fig. 1 Spearman's correlation coefficients between air pollutants and meteorological factors. The correlation strength is expressed by colour intensity in the graph: a greater correlation corresponds to a darker colour, while a correlation closer to 0 results in a lighter shade. *$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$

The peak effect estimates for all three pollutants occurred with a 5-day lag, except for CO, which peaked at day 07. Each 10 μg/m³ increase in $PM_{2.5}$ corresponded to a 1.002-fold increase in anxiety disorder admissions (95% CI: 1.001, 1.004). Each 10 μg/m³ increase in PM_{10} was associated with a 1.001-fold (95% CI: 1.000, 1.002) increase in anxiety disorder admissions. The maximum effect estimates for CO occurred at 07 days. This corresponds to a 1.614-fold (95% CI: 1.247, 2.089) increase in hospital admissions for anxiety disorders for each 1 mg/m³ increase in CO at 07 days, thereby demonstrating that the impact of short-term exposure to CO is considerable. Furthermore, a 10 μg/m³ increase in SO_2 is associated with an increase in anxiety disorder admissions of 1.034 (95% CI: 1.020, 1.047).

Table 3 presents the findings of the two-pollutant model. After adjusting for $PM_{2.5}$ and CO, the association between anxiety disorder hospitalizations and PM_{10} (lag 5 days) was found to be statistically non-significant. In contrast, after adjusting for PM_{10}, the estimated effect of CO (lag 07 days) increased to 1.877 (95% CI: 1.323, 2.661). Furthermore, after adjusting for $PM_{2.5}$, the association between anxiety disorder hospitalizations and CO (lag 5 days) significantly increased and remained statistically significant. However, CO attenuated the effect of $PM_{2.5}$ (lag 5 days), rendering it non-significant.

The analysis of the different subgroups (Fig. 3) revealed that the association between $PM_{2.5}$/PM_{10} and anxiety disorders was most pronounced among the older adult cohort compared to the younger cohort ($P < 0.05$). For each 10 μg/m³ increase in $PM_{2.5}$ and PM_{10} concentrations at 07 days, the odds ratios were 1.006 (95% CI: 1.002, 1.009) and 1.004 (95% CI: 1.001, 1.007), respectively, for the older adult group. Additionally, SO_2 exposure increased the risk of being hospitalized for anxiety disorders during the cold season ($P < 0.05$), with a lag of 1.029 (95% CI: 1.002, 1.057) in the cold season and 0.994 (95% CI: 0.967, 1.021) in the warm season at day 5. However, with a lag of 2 and 5 days, the effects of CO_2 exposure on hospitalisation rates for anxiety disorders were greater during the cold season ($P < 0.05$). No seasonal differences were observed in the effects of other pollutants on anxiety disorders. However, the effects by sex were not significantly different in this study.The results of the Z-test are presented in the Table B of the supplementary material

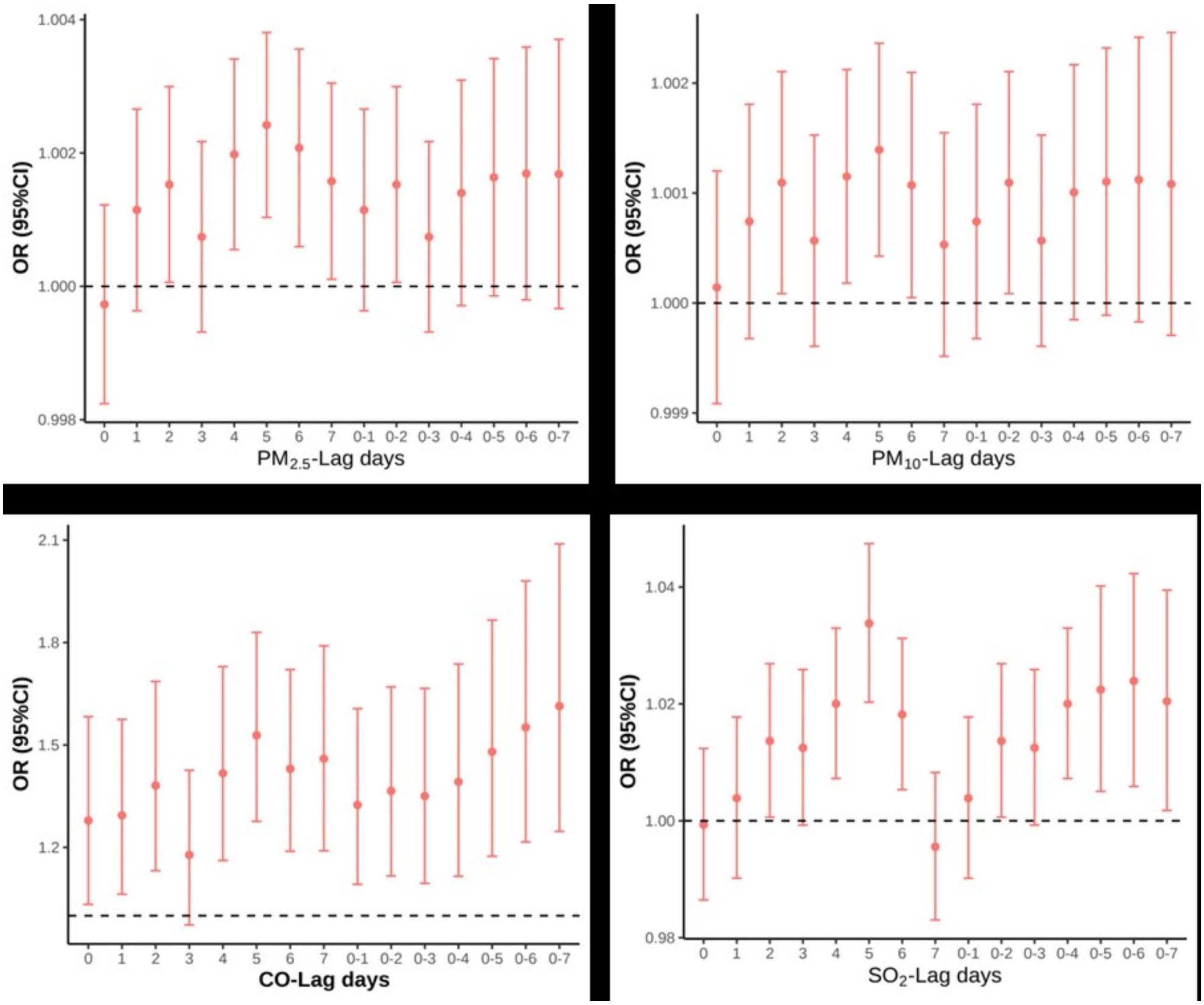

Fig. 2 Associations between pollutant concentrations and anxiety disorders in a single pollutant model in Sichuan, 2017–2018

Table 3 Odds ratio (OR) and 95% confidence intervals for anxiety disorder hospitalisation in single- and two-pollutant models

	Two-pollutant models	OR (95% CI)[a]	Lag days
$PM_{2.5}$	—[b]	1.002 (1.001, 1.004)	Lag 5
	Adjusted for CO	1.000 (0.998, 1.002)	Lag 5
PM_{10}	—[b]	1.001 (1.000, 1.002)	Lag 5
	Adjusted for CO	1.000 (0.998, 1.001)	Lag 5
CO	—[b]	1.613 (1.247, 2.089)	Lag07
	Adjusted for $PM_{2.5}$	1.924 (1.336, 2.769)	Lag07
	Adjusted for PM_{10}	1.877 (1.323, 2.661)	Lag07

a Unit: Calculated for Odds ratio of pollutants and controlled for temperature and humidity

b Unit: Single-pollutant model

We used WHO air quality standards as reference concentrations to assess the number of hospital admissions for anxiety disorders due to air pollution exposure and the associated economic costs. Based on the analysis of the results in the single- and two-pollutant models, we selected respirable PM ($PM_{2.5}$ and PM_{10}), which provided more reliable results and measured attributable health risks and economic costs due to air pollution. The study revealed that 0.71% of anxiety disorder hospitalisations (52 of 7282) were attributable to $PM_{2.5}$, and 0.34% of anxiety disorder hospitalisations (25 of 7282) were attributable to PM_{10}. The economic costs of health hazards due to exposure to PM ($PM_{2.5}$, PM_{10}) were ¥ 966,319. The economic costs associated with $PM_{2.5}$ were the highest at ¥648,509 (Table 4)

Discussions

This study investigated the correlation between ambient air pollutants and hospitalisation for anxiety disorders across nine cities in Sichuan, China. The study demonstrated that short-term exposure to elevated concentrations of $PM_{2.5}$, PM_{10}, SO_2, and CO increased the risk of

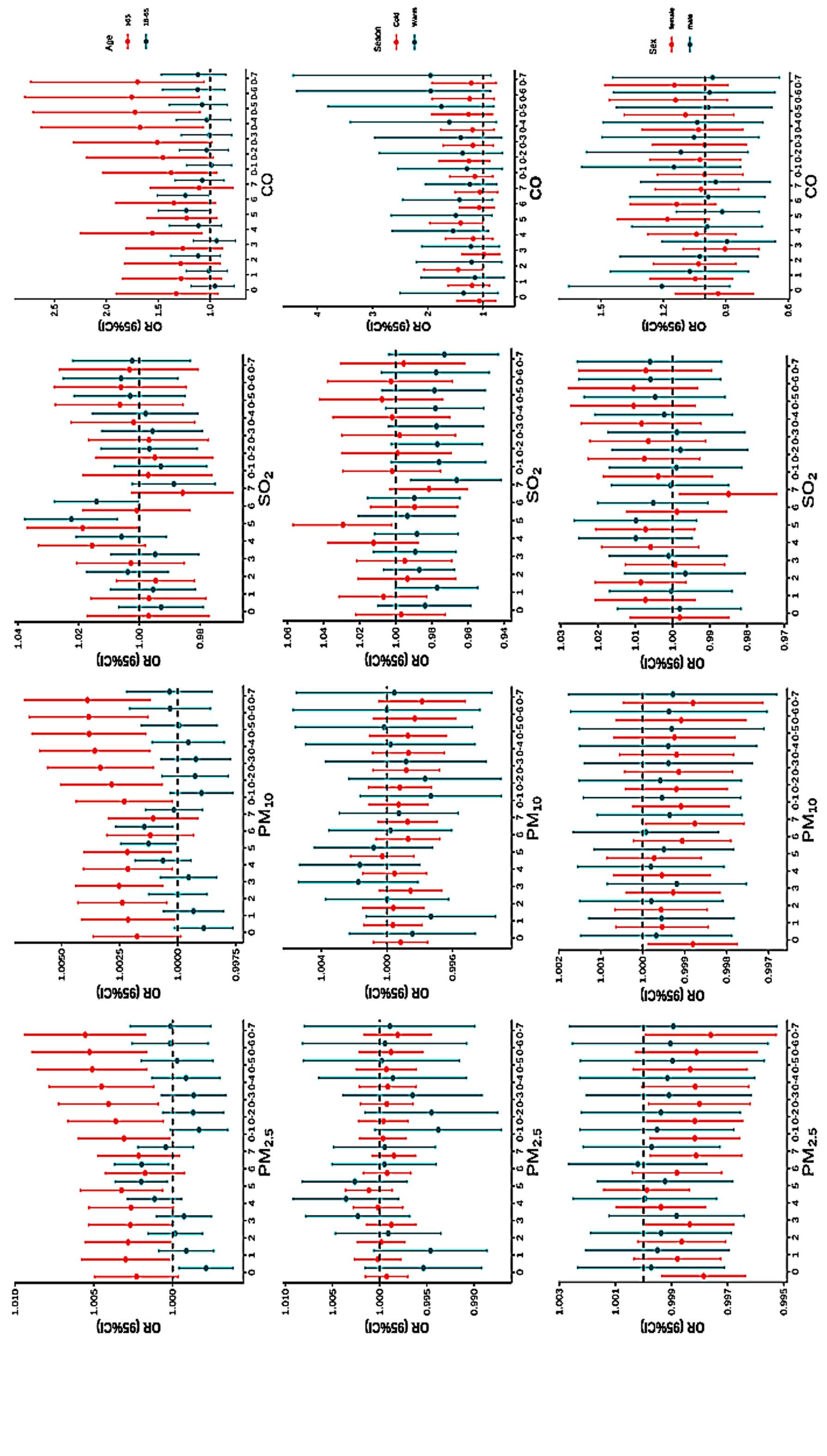

Fig. 3 OR (95% CI) of stratified analyses for each air pollutant in the single-pollutant model in the Sichuan Province, China, during 2017–2018

Table 4 The AN, AR, and economic costs of hospital admissions related to air pollution 2017–2018

	$PM_{2.5}$	PM_{10}
Lag days	Lag 5	Lag 5
AN	52	25
AR	0.074 (0.032–0.113)	0.037 (0.012–0.062)
Costs (yuan)	648,509	317,810

AN = attributable number; AR = attributable risk

hospitalisation for anxiety disorders and imposed a significant economic burden. The economic cost of anxiety disorders attributable to respirable particles was estimated at ¥ 966,319 during the study period

A previous study has demonstrated that short-term exposure to air pollutants correlates with the onset of anxiety disorder symptoms [20]. One possible explanation for this association is that oxidative stress and inflammatory responses induced by air pollution exposure are implicated in the pathogenesis of depression [21]. Ehsanifar et al. reported that exposure of mice to diesel exhaust particles induced oxidative stress and inflammatory responses in the mouse brain, resulting in abnormalities in brain function and anxiety-depression-like behavioural changes [22]. In an animal study, male C3H/HeNHsd mice with intact melatonin secretion were used to mimic humans exposed to dLAN and polluted air. The study simultaneously exposed four groups of mice to elevated ambient concentrations of $PM_{2.5}$ or FA and/or dLAN or LD. Following the exposure period, the mice were subjected to behavioural assessments. These studies demonstrated that $PM_{2.5}$ may contribute to depression and anxiety disorders [23]

Our study found some lag effect of air pollution exposure, consistent with the findings of existing studies [24]. One potential explanation is that patients regard anxiety as a common and acceptable condition, resulting in insufficient self-recognition of the illness. Consequently, even in times of distress, individuals may refrain from pursuing prompt hospital evaluation and treatment, potentially leading to delayed diagnosis and treatment of anxiety disorders [25]. Regarding the potential pathways through which air pollutants may gain access to the central nervous system (CNS), the observed delay in the onset of effects associated with PM may be attributed to the transmission route, which could involve the direct transport of particles to the CNS or the onset of a systemic inflammatory response following the initial recruitment of immune cells into the lung tissue [26]. Suppose it is the onset of a systemic inflammatory response. In that case, particles may enter the circulation and reach the alveolar region through the lungs via a transitional process (where they are most likely to be absorbed by phagocytes and translocated from the lung tissues), thereby prolonging the time to reaction [27]. Consequently, gaseous pollutants may remain dissolved in the bloodstream after entering the body, resulting in a longer window before hospitalisation for patients with anxiety disorders

The higher hospitalization rates of anxiety disorders among women relative to men may be attributed to the heightened susceptibility of women to anxiety disorders, which may be exacerbated by the stressors they encounter on a daily basis, particularly those related to family life and appearance [28]. Herein, there was no evidence that air pollution exposure increased the odds of anxiety disorders in women. It is unclear whether the observed findings are due to sex-related biological differences (hormone levels and body size) or differences in how sex affects the biotransport of environmental chemicals, life stage, co-exposure, or other factors [29–31]. Another potential explanation is the comparatively small sample size of this study. Future studies should include more extensive sample sizes to validate these findings. For women or men, the results of this study did not indicate that exposure to air pollutants increased the risk of anxiety disorders, possibly attributable to the provision of adequate health care services and family education services for Chinese women, resulting in enhanced health awareness and improved health outcomes [32]. Age modelling indicates that older adults are significantly susceptible to air pollutants. This finding may be corroborated by the detrimental effects observed in the results of a Belgian panel study of healthy older adults. Each 10 μg/m^3 increase in NO_2 concentration was associated with a 1.3-point decrease (95% CI: -2.49, -0.17) in a positive mood and a 0.11-point increase (95% CI: 0.02, 0.20) in a negative mood. These results suggest that short-term exposure to air pollution may induce non-pathological changes in mood in a healthy older adult population [33]. Nevertheless, fewer epidemiological studies have indicated that individuals aged ≥ 65 years are more vulnerable to airborne pollutants. For instance, the findings of a multi-city case-crossover study demonstrated that age was a non-significant moderating factor in the observed effect [24], and an observational cohort study demonstrated little support for differences in these associations by the age factor [11]. Furthermore, a previous study demonstrated that the 18–60 age group, or those < 65 years old are more sensitive to air pollutants [20]. The transition from cold to warm seasons may be associated with anxiety disorders. During the cold season, people are more prone to anxiety [34]. The possible reason is that during the cold season, people are less likely to exercise outdoors and instead move around in a single warm environment, which may lead to decreased physical activity and increased anxiety levels [35]. Therefore, further research is needed to examine whether the cold and warm seasons affect this association

In examining the economic costs of hospitalisation for anxiety disorders, we utilised a methodology that considered the health effects of PM, resulting in more accurate outcomes for the attribution analysis. The attributable risk was higher for $PM_{2.5}$ than for PM_{10}. Because $PM_{2.5}$ particles are smaller, they are more likely to cross the blood-brain barrier, activate inflammatory responses in the hippocampus, and induce various emotionally related behavioural disorders, leading to an increase in hospitalisation for anxiety disorders and the associated economic costs. The Malaysian economy was projected to lose RM14–46 billion in 2018 due to workplace mental health issues, including anxiety disorders [36]. In addition, in the study by Xi Gao et al., it was found that the total economic cost of hospitalization caused by exposure to particulate matter ($PM_{2.5}$, PM_{10}) was US$ 8.36 million. Meanwhile, Biao Yang et al. found that the total economic costs of hospitalization due to IS caused by $PM_{2.5}$ and PM_{10} pollution during the study period were US$ 67.96 million and US$ 48.1 million, respectively [37–38]. Although the diseases studied in their research differ from ours, comparing these results reflects that the economic burden of anxiety disorders caused by air pollution is similarly significant as that of other frequently studied diseases, proving the importance of implementing effective air quality policies

This study has some limitations. First, the concentrations of air pollutants at the monitoring stations in the study area were considered as individual exposure levels. However, this might have resulted in measurement errors due to the potential for intercity migration of patients. Second, the risk factors analysed in our model were limited to air pollutants and meteorological factors. Consequently, this study did not consider other factors that could influence this association (for instance, concomitant diseases, including asthma). Furthermore, this study was unable to differentiate between sudden anxiety disorder-related hospitalisations and those scheduled for other reasons, complicating the determination of the relationship between exposure to pollutants and the emergence of anxiety disorder symptoms. In estimating economic costs, only those who presented to the hospital were included, and those unable to afford hospital fees or lacked time for treatment were excluded. This might have led to an underestimation of economic losses. The duration of hospitalisation was used to estimate costs, excluding costs of missed work, transportation, and similar factors. This might have led to underestimating the economic costs of air pollution exposure

Conclusions

Short-term exposure to high concentrations of $PM_{2.5}$, PM_{10}, CO, and SO_2 is associated with an increased risk of hospitalisation among individuals with anxiety disorders. We observed changes in the effects of age and season, revealing increased vulnerability to air pollutants for older age groups and an increased risk of anxiety disorders among individuals exposed to air pollutants during the cold season; however, no gender-related effects were observed. The findings of this study indicate that the reduction of air pollution could be a cost-effective strategy for alleviating the significant burden of disease associated with anxiety disorders. Future studies need more extensive study populations and designs to validate and complement the findings of this study

Agreement

We declare that this manuscript is original, has not been previously published, and is not being considered for publication elsewhere. We confirm that the manuscript has been read and no other persons who satisfied the criteria for authorship was not listed. We further confirm that all of us have approved the order of authors listed in the manuscript. We understand that the corresponding author is the sole contact for the editorial process. She is responsible for communicating with the other authors about progress, submissions of revisions, and final approval of proofs

Supplementary Information

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Supplementary Material 1

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Author contributions

FP developed the idea for this study and was responsible for writing the original manuscript. jW developed the formal analyses and software. tXY and SY were involved in data collation. yL was involved in reviewing and editing the manuscript and designed the study idea. All authors revised the manuscript based on reviewers' comments and approved the final report. All authors read and approved the final manuscript.

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Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

Competing interests

The authors declare no competing interests.

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