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Attributable risks associated with hospital outpatient visits for mental disorders due to air pollution: A multi-city study in China

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ABSTRACT

Aim: To determine the associations between outdoor air pollution and hospital outpatient visits for mental disorders in China.
Methods: We obtained data of 111,842 hospital outpatient visits for mental disorders from the largest hospitals of 13 cities, China, between January 01, 2013 and December 31, 2015. We collected air pollutant data including particulate matter ≤2.5 µm in diameter ($PM_{2.5}$), particulate matter ≤10 µm in diameter (PM_{10}), nitrogen dioxide (NO_2), ozone (O_3) and sulphur dioxide (SO_2) from China National Environmental Monitoring Centre during the same period. We conducted a time-stratified case-crossover design with conditional logistic regression models to determine the associations.
Results: A 10 µg/m^3 increase in $PM_{2.5}$, PM_{10}, NO_2 and SO_2 was associated with a significant increase in hospital outpatient visits for mental disorders on the current day. When stratified by age, sex and season, the effects of $PM_{2.5}$ and NO_2 were robust among different subgroups at lag05 days. PM_{10} showed positive associations in males, in cold season, and in depression patients. SO_2 showed positive associations in males, in cold season, and in anxiety patients. O_3 showed positive associations in females, in warm season, and in depression patients. Nearly one sixth hospital outpatient visits for mental disorders can be attributable to NO_2.
Conclusions: Short-term increase in $PM_{2.5}$, PM_{10}, NO_2, SO_2 and O_3 concentrations was significantly associated with exacerbation of mental disorders in China as indicated by increases in hospital outpatient visits. NO_2 had more serious health threat than other pollutants in terms of mental disorders. Our findings strongly suggest a need for more strict emission control regulations to protect mental health from air pollution.

1. Introduction

Mental disorders refer to a syndromic constellation of symptoms that affect moods, thoughts, and/or behaviours (Kessler et al., 2009; World Health Organization, 2017). It is a major public health concern, manifested by affecting more than 50% of the population at least once in their lives in middle and high income countries (Trautmann et al., 2016; Zhao et al., 2020). And the cases of mental disorders in lower-income countries are going up steadily in recent years (World Health Organization, 2017). The symptoms such as depression and anxiety hang together empirically, often for unknown reasons and lead to considerable losses in health and functioning (Borsboom, 2017). Mental disorders are the leading cause of disability and major contributors to the global burden of disease, directly account for about 7.4% of disease burden worldwide (Vigoet al., 2016; Wales, 2018). In 2013, mental disorders accounted for approximately 175.3 million (22.9% of total) years lived with disability (YLDs) and 183.9 million disability-adjusted life-years (DALYs) (Wales, 2018).

Given the substantial personal and social burden of mental disorders, it is imperative to identify modifiable risk factors. Air pollution has increasingly been recognized as a risk factor of mental disorders in addition to the identified social and behavioural factors such as

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excessive pressure and smoking (Chen et al., 2018b; Power et al., 2015; Pun et al., 2016). Epidemiological studies from several countries demonstrated positive associations between air pollution exposure and the onset or worsening of mental disorders symptoms (Oudin et al., 2016; Chen et al., 2018a,b). The neurotoxicity induced by air pollutants could possibly be mediated by systemic inflammation and brain oxidative stress (Buoli et al., 2018; Madrigano et al., 2012).

China suffers from high levels of air pollution. The serious air pollution and accelerated urbanization aggravate psychiatry burden (Gong et al., 2012; Ho et al., 2014). Gao et al investigated the association between particulate matter air pollution and hospitalizations for mental disorders in Beijing. The study found that a 10 ug/m^3 increase in 0–6 days moving averages concentrations of particulate matter ≤10 μm in diameter (PM_{10}) was associated with 1.38% (95%CI: 0.52–2.23%) increase in total hospitalizations for mental disorders(Gao et al., 2017). The results were robust after adjustment for other gaseous pollutants (Gao et al., 2017).

Another study in Shanghai demonstrated that a 10 $\mu g/m^3$ increase in 2-day moving-average concentration of PM_{10} was associated with 1.27% (95%CI: 0.28%–2.26%) increase in daily hospital admissions for mental disorders. However, after adjustment for sulphur dioxide (SO_2), nitrogen dioxide (NO_2) and carbon monoxide (CO), the effect of PM_{10} became insignificant (Chen et al., 2018a). The results of these two single city studies were inconsistent in terms of whether PM_{10}'s effect was independent of gaseous pollutants. To date, there is no nation-wide study especially no hospital outpatient visits study due to the lack of routinely collected data from hospitals in the past.

In this study, we conducted a multi-city study in China to evaluate the impacts of short-term exposure to air pollutants including particulate matter ≤2.5 μm in diameter ($PM_{2.5}$), PM_{10}, NO_2, SO_2 and ozone (O_3) on hospital outpatient visits for mental disorders. Stratified analyses were performed by sex, age, and cause-specific mental disorders.

2. Methods

2.1. Data collection

Daily data on hospital outpatient visits for mental disorders were collected from the largest hospitals in 13 cities in China between January 01, 2013 and December 31, 2015. Mental disorders in this study included diagnosed “anxiety”, “depression”, “schizophrenia”, “bipolar disorder”, “obsessive-compulsive”, “attention deficit hyperactive disorder-ADHD”, “autism”. Because the cases of “anxiety” and “depression” took 89.97% of the total mental disorder cases, we analysed the association between air pollution and “anxiety”, “depression” and “other mental disorder diseases” in the cause-specific mental disorders analyses.

Data on daily air pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2 and O_3) levels in 13 cities between January 01, 2013 and December 31, 2015 were obtained from China National Environmental Monitoring Centre (CNEMC). There were on average 8 (4–11) fixed-site stations monitoring the hourly air pollutant concentrations in each city. In most of the cases we could get the daily concentrations of air pollutants. If there were missing daily air pollution data, the model will automatically treat the air pollution value as missing value “NA” .The number of air pollutant monitoring stations and size of each city is listed in supplementary material (Table S1). The daily average pollutant concentrations of the city were used to analyse with the data of hospital outpatient visits for mental disorders.

Daily mean temperature, relative humidity and wind speed data for the 13 cities were obtained from the China Meteorological Data Sharing Service System (http://data.cma.gov.cn). Meteorological data from the nearest weather station to each hospital were used in the analyses.

2.2. Statistical analysis

We conducted a time-stratified case-crossover design to evaluate the potential associations between air pollution exposure and hospital outpatient visits for mental disorders. A case-crossover design is commonly used to investigate acute health effects of ambient air pollution. It has the advantage of controlling for long-term and seasonal trend and short-term time invariant potential confounders, such as age, sex, smoking status, etc. (Peterset al., 2006).

We used conditional logistic regression models to estimate the odds ratio (OR) of hospital outpatient visits for mental disorders from 0 to 5 days after a 10 $\mu g/m^3$ increase in each air pollutant exposure (Lu et al., 2019). In this model, each case was treated as a stratum. The same day of the week in the same month of the same year and same city were selected as control days for each case. The possibility of hospital outpatient visits for mental disorders of case day was analysed with control days. Cross-basis function was used to fit the cumulative lag effects of air pollutants (Lu et al., 2019). In this study, lag1 refers to the effect of 10 $\mu g/m^3$ increase in today's air pollutant levels on tomorrow's hospital outpatient visits. Lag01 refers to the effect of 10 $\mu g/m^3$ increase in today's air pollutant levels on today and tomorrow's hospital outpatient visits. Covariates in each model included natural cubic spline function to fit the non-linear and lagged effects of daily temperature, relative humidity and wind speed with 7-day moving average for each variable and three degrees of freedom (df) (Lu et al., 2019). Public holidays were controlled as a binary variable. We used excess relative risks (ERRs) to evaluate the association between air pollution and hospital outpatient visits for mental disorders. The formula to calculate ERR was (OR-1) × 100%. Each pollutant was added separately to the model to check the effect estimates.

We performed a subgroup analysis by stratifying hospital outpatient visits for mental disorders by age (0–14, 15–34, 35–64, +65 years), sex (males and females) and season (warm season and cold season), respectively. The season division was based on the average temperature of each month. The average temperature of warm season was 22.0 °C (13.9–28.2 °C) in study cities during the study period. Cold season average temperature was 6.4 °C (−6.2 °C to 18.2 °C).

The counts of hospital outpatient visits for mental disorders attributable to air pollutants were estimated using: $ACi = Ni \cdot (ORi - 1)/ORi$. ACi is the attributable counts on day i. Ni is the average number of hospital outpatient visits for mental disorders on day i, day $i + 1$, day $i + 2$, day $i + 3$, day $i + 4$, day $i + 5$. ORi is the lag0-5 OR of each air pollutant (Gasparrini and Leone, 2014). Total attributable counts (AC) were calculated by summing the ACi of the study period. The attributable fractions (AFs) were calculated by dividing the total AC by total number of hospital outpatients.

To assess the robustness of our results, we repeated our model using different number of lag days for meteorological variables (4–9) and different df of meteorological variables (3–6). We used meta-regression to test if there were significant differences between the sensitivity analyses' results and main results. We used two-pollutant models to check whether the estimated PM associations with hospital outpatient visits for mental disorders were modified by adding different gaseous pollutants. We checked the correlations between air pollutants and meteorological variables with Pearson correlation test. We also checked the city-specific associations between air pollution and hospital outpatient visits for mental disorders.

All statistical analysis was done in R software (version 3.5.1) using “survival” to analyse the conditional logistic regression models and “dlnm” packages to analyse constrained distributed lag models, respectively.

3. Results

The daily average concentrations of air pollutants in 13 cities and daily hospital outpatient visits for mental disorders in 13 hospitals are

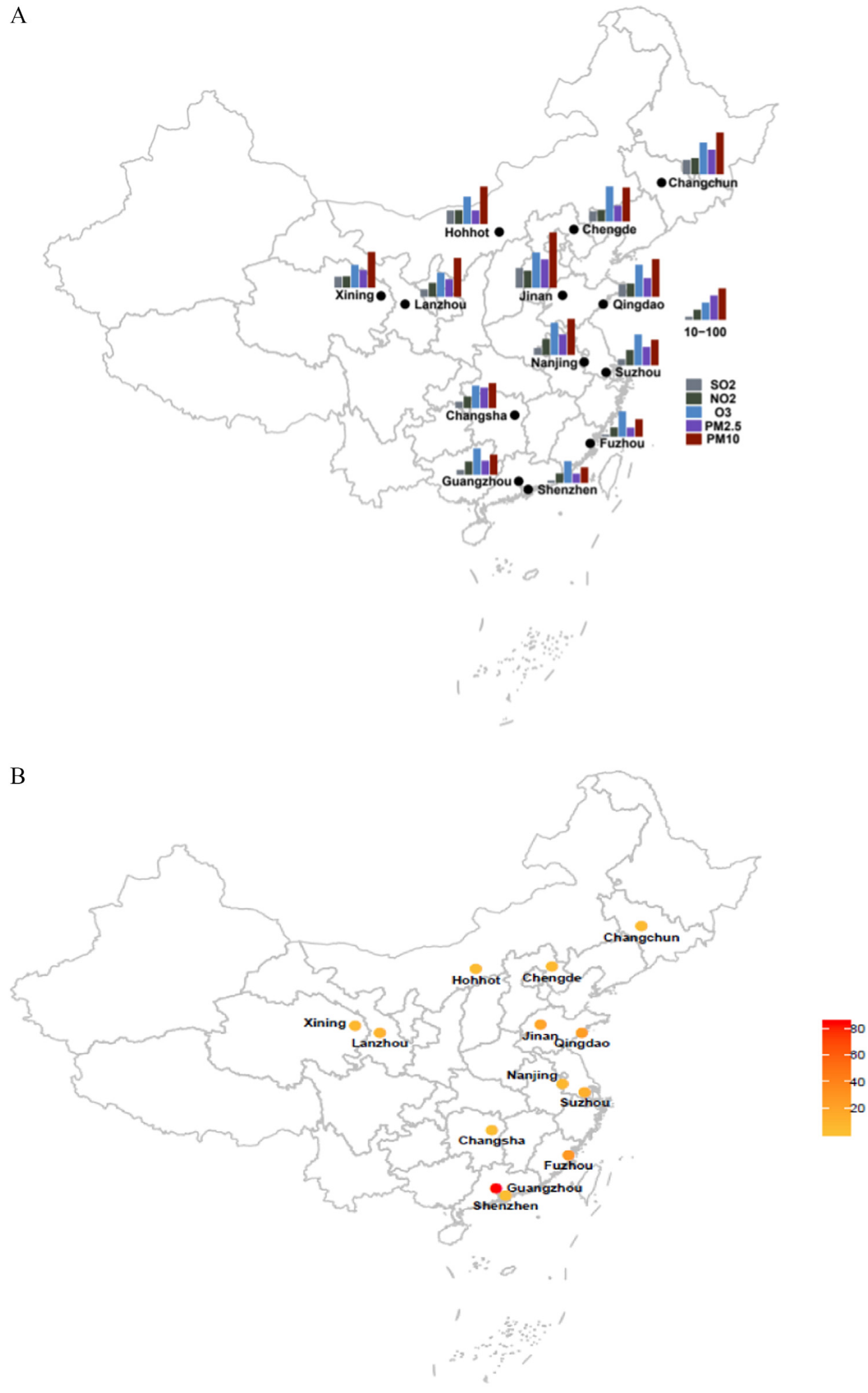

Fig. 1. (A). Location of study cities and daily average concentrations (μg/m^3) of air pollutants in 13 cities. (B). Daily average hospital outpatient visits for mental disorders in China. Note: $PM_{2.5}$: particulate matter ≤2.5 μm in diameter; PM_{10}: particulate matter ≤10 μm in diameter; NO_2: nitrogen dioxide; SO_2: sulphur dioxide; O_3: ozone.

shown in Fig. 1. Among 13 study cities, Jinan, located in north-eastern China had the highest daily average concentrations of air pollutants ($PM_{2.5}$ 88.02 μg/m^3, PM_{10} 168.98 μg/m^3, NO_2 53.23 μg/m^3, SO_2 61.52 μg/m^3, O_3 109.03 μg/m^3). Fuzhou, located in southern China had the lowest daily average concentrations of air pollutants ($PM_{2.5}$ 31.94 μg/m^3, PM_{10} 61.25 μg/m^3, NO_2 32.79 μg/m^3, SO_2 7.74 μg/m^3). The lowest daily level of O_3 (70.78 μg/m^3) appeared in Xining. In total, 111,842 hospital outpatient visits for mental disorders were collected. Nanfang Hospital of Southern Medical University in Guangzhou had the highest daily average visits for mental disorders (n = 85), while the lowest daily average visits was at the second Xiangya Hospital of Central South University located in Changsha (n = 3).

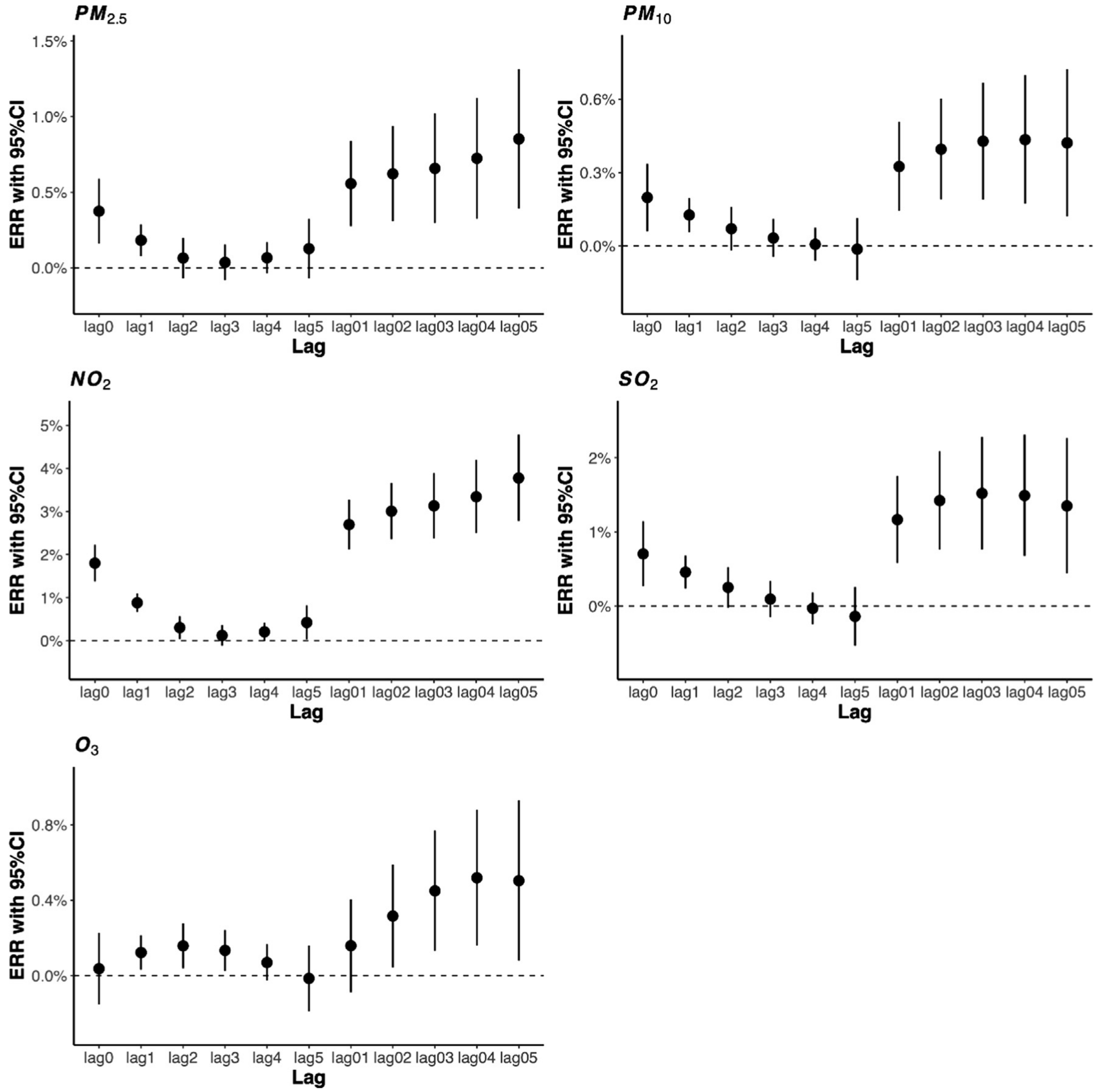

Fig. 2. Excess relative risks (and 95% confidence intervals) of hospital outpatient visits for mental disorders with a 10 μg/m^3 increase $PM_{2.5}$, PM_{10}, NO_2, SO_2 and O_3 at different lags. Note: $PM_{2.5}$: particulate matter ≤2.5 μm in diameter; PM_{10}: particulate matter ≤10 μm in diameter; NO_2: nitrogen dioxide; SO_2: sulphur dioxide; O_3: ozone.

Fig. 2 presents the lagged pattern of air pollutant effects on hospital outpatient visits for mental disorders. Statistically significant associations were observed for $PM_{2.5}$, PM_{10} and SO_2 per 10 μg/m^3 increases at lag0, lag1, lag01-lag05 days, for NO_2 at lag0, lag1, lag2, lag5, lag01-lag05 days. The effect of O_3 was delayed at lag1, lag2, lag3, lag02-lag05 days. The cumulative effects of all pollutants tended to be stable at lag05. Therefore, we only performed stratified analyses at lag05 day for all pollutants. The city-specific lagged pattern of air pollutant effects on hospital outpatient visits for mental disorders are shown in supplementary material (Fig. S1)

Table 1 shows the stratified analysis results of air pollutants at lag05 days. $PM_{2.5}$, PM_{10}, NO_2 and SO_2 demonstrated significant effects on hospital outpatient visits for mental disorders in males. The effects of $PM_{2.5}$, NO_2 and O_3 were significant in females. In 35–64 years age group, hospital outpatient visits for mental disorders were positively associated with $PM_{2.5}$ (ERR1.221%, 95%CI:0.583%,1.863%), PM_{10} (ERR0.622%, 95%CI:0.216–1.029%), NO_2 (ERR 4.006%, 95%CI:2.684–5.346%), SO_2 (ERR 1.761%, 95%CI:0.582–2.954%). In 65+ years age groups, positive associations were found with $PM_{2.5}$ (ERR 1.368%, 95%CI:0.109–2.642%), NO_2 (ERR 3.729%, 95%CI:1.063–6.465%), O_3 (ERR 1.631%, 95%CI:0.412–2.864%). In cold season, $PM_{2.5}$ (ERR 1.382%, 95%CI:0.828–1.938%), PM_{10} (ERR 0.927%, 95%CI:0.548–1.308%), NO_2 (ERR 5.812%, 95%CI:4.570–7.069%), SO_2 (ERR 1.349%, 95%CI:0.357–2.351%) were significantly associated with hospital outpatient visits for mental disorders. The effect of O_3 (ERR 0.837%, 95%CI:0.311–1.366%) was significant in warm season.

The effects of air pollutants on hospital outpatient visits for cause-specific mental disorders are shown in Table 2. At lag05, depression was significantly associated with $PM_{2.5}$ (ERR 1.039%, 95%CI:0.344–1.739%), PM_{10} (ERR 0.553%, 95%CI:0.110–0.999%), NO_2 (ERR 3.690%, 95%CI:2.239–5.160%), O_3 (ERR 0.822% 95%CI:0.182–1.467%). Anxiety was significantly associated with $PM_{2.5}$ (ERR 0.972%, 95%CI:0.350–1.597%), NO_2 (ERR 3.417%, 95%CI:2.098–4.752%), SO_2 (ERR 2.043%, 95%CI:0.839–3.261%). In addition, NO_2 (ERR 5.921%, 95%CI:2.683–9.261%) was also associated with other subtypes of mental disorders.

In two-pollutant model at lag05 days, the effects of NO_2 on hospital outpatient visits for mental disorders were robust when controlling $PM_{2.5}$ or PM_{10}. However, the effect of $PM_{2.5}$ and PM_{10} became

Table 1
Excess relative risks (%) of the association between air pollutants (per 10 μg/m^3 increase at lag05) and hospital outpatient visits for mental disorders, and effect modification by age, sex and season.

Factor		ERR and 95%CI (%)				
		$PM_{2.5}$ at lag05	PM_{10} at lag05	NO_2 at lag05	SO_2 at lag05	O_3 at lag05
	All	0.852 (0.391, 1.315) **	0.421 (0.120, 0.724) *	3.777 (2.780, 4.784) **	1.351 (0.443, 2.266) **	0.503 (0.079, 0.930) *
Sex						
	Male	0.898 (0.200, 1.600) *	0.532(0.067, 1.000) *	4.433 (2.889, 6.001) **	2.043(0.611, 3.496) **	0.169(-0.478, 0.819)
	Female	0.841(0.227, 1.458) *	0.350 (-0.046, 0.747)	3.341(2.038, 4.660) **	0.860 (-0.311, 2.045)	0.771(0.208, 1.337) **
Age						
	0–14	−0.370 (-1.739, 1.019)	−0.158(-1.175, 0.869)	−0.313(-4.554, 4.116)	0.675 (-3.649, 5.194)	−0.020(-2.066, 2.069)
	15–34	0.450 (-0.528, 1.437)	0.360 (-0.303, 1.027)	4.300(2.264, 6.376) **	0.909 (-1.170, 3.033)	0.060 (-0.758, 0.884)
	35–64	1.221(0.583, 1.863) **	0.622(0.216, 1.029) **	4.006(2.684, 5.346) **	1.761(0.582, 2.954) **	0.473 (-0.094, 1.044)
	65+	1.368(0.109, 2.642) *	0.360(-0.429, 1.155)	3.729(1.063, 6.465) **	0.546 (-1.624, 2.764%)	1.631(0.412, 2.864) **
Season						
	Cold	1.382(0.828, 1.938) **	0.927(0.548, 1.308) **	5.812(4.570, 7.069) **	1.349(0.357, 2.351) **	0.318(-0.450, 1.091)
	Warm	−0.311(-1.189, 0.575)	−0.438(-0.962, 0.088)	−1.268(-3.082, 0.579)	0.677(-1.767, 3.182)	0.837(0.311, 1.366) **

Note: $PM_{2.5}$: particulate matter ≤ 2.5 μm in diameter; PM_{10}: particulate matter ≤ 10 μm in diameter; NO_2: nitrogen dioxide; SO_2: sulphur dioxide; O_3: ozone; OR: odds ratio; 95% CI: 95% confidence interval.
*$p < 0.05$; **$p < 0.01$.

insignificant after controlling NO_2 (Supplementary Material Table S2). The correlations between air pollutants and meteorological variables are shown in Table S3 (Supplementary Material).

Table 3 presents the numbers and fractions of hospital outpatient visits for mental disorders attributable to air pollutants at lag05 days across 13 study hospitals. The attributable fractions were 4.49% (95%CI:2.1–6.8%) for $PM_{2.5}$, 3.91% (95%CI:1.14–6.59%) for PM_{10}. 14.99% (95%CI:11.34–18.47%) for NO_2, 3.34% (95%CI:1.12–5.48%) for SO_2, 4.38% (95%CI:0.7–7.9%) for O_3, respectively.

The associations between short-term increased air pollutants concentrations and hospital outpatient visits for mental disorders were robust when changing meteorological variable lag days from four to nine and df from three to six. (Supplementary Material Tables S4-5)

Table 3
Attributable counts and attributable fractions (and 95% CI) of hospital outpatient visits for mental disorders due to air pollutants at lag05.

Pollutants	Attributable counts (95% CI)	Total number	Attributable fractions (95%CI)
$PM_{2.5}$	4970 (2330,7520)	111,842	4.4% (2.1%, 6.8%)
PM_{10}	4350 (1260,7310)	111,842	3.9% (1.1%, 6.5%)
NO_2	16,600 (12600,20400)	111,842	14.9% (11.3%, 18.3%)
SO_2	3710 (1250,6060)	111,842	3.3% (1.1%, 5.4%)
O_3	4890 (786,8790)	111,842	4.4% (0.70%, 7.9%)

Note: $PM_{2.5}$: particulate matter ≤ 2.5 μm in diameter; PM_{10}: particulate matter ≤ 10 μm in diameter; NO_2: nitrogen dioxide; SO_2: sulphur dioxide; O_3: ozone; 95% CI: 95% confidence interval.

4. Discussion

To the best of our knowledge, this is the first multi-city study to investigate the association between air pollution and hospital outpatient visits for mental disorders in China. Short-term increases in $PM_{2.5}$, PM_{10}, NO_2 and SO_2 levels (per 10 μg/m^3) were associated with increased hospital outpatient visits for mental disorders on the exposure day, while the effects of O_3 started from the second day of exposure. In the subgroup analysis, the effects of $PM_{2.5}$ and NO_2 were robust among different subgroups at lag05. PM_{10} showed positive associations in male, in cold season, and in depression patients. SO_2 showed positive associations in male, in cold season, and in anxiety patients. O_3 showed positive associations in female, in warm season, and in depression patients. According to the attribute number, nearly one sixth hospital outpatient visits for mental disorders can be attributable to NO_2. Our findings confirm the adverse effect of air pollutants, especially gaseous pollutants on mental health and strongly suggest a need for stricter enforcement of emission regulations, such as traffic emission regulations.

Our results are generally consistent with previous findings (Chen et al., 2018a; Gao et al., 2017; Oudin et al., 2018). A study in Shanghai reported that 10 μg/m^3 increase in PM_{10} was associated with 1.27% (95%CI: 0.28–2.26%) increase of daily hospitalization for mental disorders at lag01 (Chen et al., 2018a). Oudin, et al. investigated the associations between PM_{10}, O_3 and NO_2 concentrations and psychiatric emergency room visits in Gothenburg, Sweden between 2012 and 2016 and found that 10 μg/m^3 increase in PM_{10} concentrations was associated with 3.5% (95%CI: 0.4–6.8%) increase in psychiatric emergency room visits at lag0 in single-pollutant model (Oudin et al., 2018). The data of hospital outpatient visits in our study is comparable to emergency room visits in most western countries, as China has a unique health care system where the regular hospital outpatient visits are unscheduled. Our results demonstrated that the effects of PM_{10} on hospital outpatient visits for mental disorders were not as strong as those city-

Table 2
Excess relative risks (%) of the association between air pollutants (per 10 μg/m^3 increase at lag05) and hospital outpatient visits for sub-categories of mental disorders.

Disease	ERR and 95%CI (%)				
	$PM_{2.5}$ at lag05	PM_{10} at lag05	NO_2 at lag05	SO_2 at lag05	O_3 at lag05
Depression	1.039(0.344, 1.739) **	0.553(0.110, 0.999) *	3.690 (2.239, 5.160) **	1.026 (-0.248, 2.316)	0.822(0.182, 1.467) *
Anxiety	0.972(0.350, 1.597) **	0.361(-0.032, 0.756)	3.417(2.098, 4.752) **	2.043(0.839, 3.261) **	0.302(-0.262, 0.869)
Others	−0.121 (-1.339, 1.111)	0.223 (-0.710, 1.164)	5.921(2.683, 9.261) **	2.222(-1.372, 5.948)	−0.002 (-1.325, 1.338)

Note: $PM_{2.5}$: particulate matter ≤ 2.5 μm in diameter; PM_{10}: particulate matter ≤ 10 μm in diameter; NO_2: nitrogen dioxide; SO_2: sulphur dioxide; O_3: ozone; OR: odds ratio; 95% CI: 95% confidence interval.
*$p < 0.05$; **$p < 0.01$.

level studies in China. Besides the adverse effects of PM, we found that NO_2 plays more important role, as indicated by the highest OR value for hospital outpatient visits for mental disorders at lag05.

Mechanisms for the neurotoxicity of air pollution remain unclear, but experimental studies indicated neuro-inflammation (Costa et al., 2017) and oxidative stress (Guerra et al., 2013) play an important role. Particulate matters could directly relocate to brain through nasal epithelium or blood-brain-barrier to activate innate immune system (Wang et al., 2017). Besides, traffic-related air pollution could alter brain-blood-barrier permeability (Oppenheim et al., 2013). Systematic inflammatory markers, such as interleukin-6 (IL-6), tumor necrosis factor α (TNF-α), induced by air pollution could subsequently increase their concentrations in central nervous system leading to structural or functional changes (Calderón-Garcidueñas et al., 2012). Air pollutants could induce oxidative stress directly (Liet al., 2016) or through epigenetic modifications (decreased methylation of oxidative response related genes) (Madrigano et al., 2012). Animal study found increased lipid peroxidation, neuro-inflammation in hippocampus and the olfactory bulb area after exposure to 250–300 $\mu g/m^3$ diesel exhaust for 6 h (Costa et al., 2017). These mechanism studies partly explain the adverse effect of air pollutant, especially traffic related air pollutant (e.g., NO_2), on mental health.

In the age stratified analysis, we found positive associations mainly with 35+ age groups. This is probably because people of 35+ age groups have more chance of exposure to air pollutants even in highly polluted days. Also, 35+ age groups tend to face more work or social pressure. Brokamp et al. analysed the effects of acute exposure to $PM_{2.5}$ on children mental disorder emergency room visits and found that a 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentrations was associated with significant increase in children psychiatric emergency department usage at 1 or 2 days after exposure (Brokamp et al., 2019). We did not find significant associations among the youth and adolescent groups. Additional researches are needed to confirm the age-specific associations.

In the sex stratified analysis, $PM_{2.5}$ and NO_2 demonstrated similar associations with males and females hospital outpatient visits for mental disorders, consistent with many previous studies (Chen et al., 2018a; Szyszkowicz et al., 2016). However, the study in Beijing demonstrated an obvious sex difference, indicated that the effect of PM_{10} is more prominent in female group (Gao et al., 2017). In this study, we found increased concentrations of O_3 were significantly associated with female hospital outpatient visits for mental disorders. Consistently, the nurse study in the United States demonstrated that O_3 was positively associated with subtypes of mental disorders' onset in the female group with hazard ratio (HR) equals 1.08 (95%CI:1.02–1.14) (Kioumourtzoglou et al., 2017). This finding warrants more attention on mental health status, especially for females during warmer seasons when O_3 concentrations are high.

Our results demonstrated obvious seasonal patterns where positive associations between increased concentrations of $PM_{2.5}$, PM_{10}, NO_2, SO_2 and hospital outpatient visits for mental disorders were found in cold season, while the effects of O_3 were more prominent in warm season. Consistent with our results, Tong et al. found positive associations between increased NO_2 concentrations and hospitalizations for mental disorders in cold season (Tong et al., 2016). Another study in Canada demonstrated that increased particulate matter concentrations were associated with increased emergency depression visits in cold season. The similar seasonal pattern is probably because the concentrations of particulate matters tend to be higher in the winter seasons than summer, when heating facilities are commonly used and produce more air pollutants. That is probably the reason that air pollutant levels in southern cities, where heating facilities are not used, are generally lower than northern cities in China. In addition to the geographic and climate features, such as coastal breeze, Fuzhou had the lowest air pollutant concentrations except O_3 during the study period. The study in Canada also found that O_3 showed positive effects in female patients in warm season (Szyszkowicz, 2007). That is probably because O_3 concentrations peak in the hot summer times.

In the cause-specific mental disorders analysis, we found $PM_{2.5}$, PM_{10}, NO_2 and O_3 were significantly associated with hospital outpatient visits for depression at lag05 days. Szyszkowicz, et al. demonstrated significant correlations of $PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3 and CO concentrations and increments in daily depression-related emergency room visits (Szyszkowicz, 2007). Further, the author enlarged sample size and used case-crossover study design indicating the significant role of NO_2 which is consistent with our findings (Szyszkowicz et al., 2009; Szyszkowicz and Tremblay, 2011). In addition, a multi-city study in Canada also found significant associations between increased concentrations of $PM_{2.5}$ and O_3 with emergency room visits for depression (Szyszkowicz et al., 2016). Studies in Korea which investigated the impact of air pollutants (PM_{10} and NO_2) on depression of susceptible population, such as elderly or people with disease also found consistent positive associations (Cho et al., 2014; Lim et al., 2012). When exposed to similar concentrations of air pollutants as in this study, another study in China demonstrated that increased $PM_{2.5}$ and PM_{10} levels were associated with hospital admissions for depression (Wang et al., 2018).

Similar as depression, significant associations between air pollutants and anxiety were also noticed. $PM_{2.5}$, NO_2 and SO_2 showed positive associations with hospital outpatient visits for anxiety at lag05. In consistent with our findings, Power et al. observed positive association between anxiety and $PM_{2.5}$, $PM_{2.5\text{-}10}$ concentrations among 71,271 women aged 57–85. The study found the odds of high anxiety symptoms were associated with higher exposure $PM_{2.5}$ concentrations, especially during the short term exposure periods (Power et al., 2015). Our results warrant more studies to explore the effect of air pollutants on the central nervous system.

In the attributable fraction analysis, nearly one sixth of hospital outpatient visits for mental disorders can be attributable to NO_2. This finding highlights the deleterious effects of traffic-related air pollution on mental health. In addition, it is necessary to notify that the effects of PM are possibly overestimated due to the collinearity with other pollutants, especially NO_2.

There are many strengths of this study. First, air pollution levels used in the study were obtained from fixed air quality monitoring system established by the Chinese government from 2013, which covers all the cities in the study. This could possibly reduce the measurement errors compared to modelled data. Second, this study has also employed validated statistical methods. The time-stratified case-crossover design can minimize autocorrelation effects and provides sufficient adjustments for confounders. Thirdly, this study provides attributable numbers of hospital outpatient visits for mental disorders due to air pollution, which offer additional evidence and significant insights for the effect of air pollutants on mental disorders in China.

Several limitations should be noted. First, the exposure data was not personal level, air pollutant concentrations were the city level average concentrations (Guo et al., 2013). In addition, we did not use high resolution spatiotemporal resolved exposure data (Di et al., 2019; Shi et al., 2016). We cannot estimate the spatial variability of air pollutant concentrations within study area. Second, limited by data-recording method, we could not separate first-time hospital outpatient visit from repeated or scheduled hospital outpatient visits for mental disorders. As we only used data from the largest hospital for each city, there might be selection bias. Consequently, it is impossible to estimate prevalence of mental disorders from this study.

5. Conclusions

We found an association between short-term increase in air pollutant concentrations and mental disorders exacerbations, manifested by increases in hospital outpatient visits in China. NO_2 had more serious health threat than other pollutants in terms of mental disorders. Our findings strongly suggest a need for more strict emission control regulations to protect mental health from air pollution.

CRediT authorship contribution statement

Peng Lu: Conceptualization, Methodology, Writing - original draft, Investigation. **Yongming Zhang:** Conceptualization, Data curation, Validation. **Guoxin Xia:** Conceptualization, Software, Visualization, Investigation, Methodology, Validation. **Wenyi Zhang:** Conceptualization, Data curation, Validation. **Rongbin Xu:** Writing - review & editing, Validation, Methodology. **Chongjian Wang:** Conceptualization, Methodology, Validation. **Yuming Guo:** Supervision, Conceptualization, Writing - review & editing, Validation. **Shanshan Li:** Supervision, Writing - review & editing, Data curation.

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.envint.2020.105906.

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