Association Between Ambient Air Pollution and Daily Hospital Admissions for Depression in 75 Chinese Cities

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Objective: Although the association between ambient air pollution and risk of depression has been investigated in several epidemiological studies, the evidence is still lacking for hospital admissions for depression, which indicates a more severe form of depressive episode. The authors used national morbidity data to investigate the association between short-term exposure to ambient air pollution and daily hospital admissions for depression.

Methods: Using data from the Chinese national medical insurance databases for urban populations, the authors conducted a two-stage time-series analysis to investigate the associations of short-term exposure to major ambient air pollutants—fine particles ($PM_{2.5}$), inhalable particles (PM_{10}), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), ozone (O_3), and carbon monoxide (CO)—and daily hospital admission risk for depression in 75 Chinese cities during the period 2013–2017.

Results: The authors identified 111,620 hospital admissions for depression in 75 cities. In the single-pollutant models, the effect estimates of all included air pollutants, with the exception of O_3, were significant at several lags within 7 days. For example, 10 $\mu g/m^3$ increases in $PM_{2.5}$, PM_{10}, and NO_2 at lag01 were associated with increases of 0.52% (95% CI=0.03, 1.01), 0.41% (95% CI=0.05, 0.78), and 1.78% (95% CI=0.73, 2.83), respectively, in daily hospital admissions for depression. Subgroup, sensitivity, and two-pollutant model analyses highlighted the robustness of the effect estimates for NO_2.

Conclusions: The study results suggest that short-term exposure to ambient air pollution is associated with an increased risk of daily hospital admission for depression in the general urban population in China, which may have important implications for improving mental wellness among the public.

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Depression, a common mental disorder, is highly prevalent worldwide and has been identified as a major contributor to global disease burden (1). The prevalence of depression has been increasing rapidly, yet effective treatments often are not easily accessible, and the etiology of the disorder is unclear (1, 2). Therefore, the task of identifying preventable risk factors for depression and developing relevant prevention strategies has drawn increasing attention. Ambient air pollution, one of the major environmental risk factors for human health, accounts for the onset and exacerbation of many multisystem diseases, including cardiovascular and pulmonary diseases (3, 4). Recently, a growing number of epidemiological studies have examined the association between increases in ambient air pollutants and risk for depression (5–11) and other mental disorders, including psychological stress (12), anxiety (8), and even suicide (13).

Several experimental studies have investigated the potential biological mechanisms between air pollution exposure and onset of depression, and increased inflammation and oxidative stress in the nervous system induced by air pollutants have been thought to be the major pathways behind the depressive symptoms after exposure (14–19). A recent meta-analysis summarized the literature on ambient particulate matter air pollution and risk of depression and found that long-term exposure but not short-term exposure to fine particles ($PM_{2.5}$, particulate matter with an aerodynamic diameter <2.5 μm) was associated with an increased risk of depression, which was defined by different methods (e.g., depressive symptoms assessed by different scales, or depression disorder diagnosis assessed by ICD codes) (20). Only one of the studies included in that meta-analysis investigated hospital admissions for depression; the authors reported positive associations between short-term exposure to ambient particulate matter and hospital admissions for depression (6). Evidence from epidemiological studies also suggests that short-term exposure to other air pollutants, such as inhalable particles (PM_{10}, particulate matter with an aerodynamic diameter <10 μm) and nitrogen dioxide (NO_2), were positively associated with risk of depression (6, 7). However, the results reported in previous studies have been inconsistent, and most of them were conducted in high-income countries with relatively low levels of ambient air

pollution. Specifically, evidence is still lacking for short-term exposure to different ambient air pollutants and hospital admission for depression, which indicates a more severe form of depression episode. Furthermore, few of these studies have investigated multiple major ambient air pollutants (including particulate matter and gaseous pollutants) simultaneously, although these pollutants may be associated with the same health conditions (21). In addition, although the concentrations of ambient air pollution and prevalence rates of depression may vary geographically, few studies have paid attention to the variation in pollutant-depression associations across different regions. Therefore, additional research evidence, especially in areas with a wide range of ambient air pollution levels, is needed to clarify these issues. The large variations in both ambient air pollution levels and depression prevalence rates across China thus provide a unique opportunity to investigate the relationship between ambient air pollution and depression in different regions.

The variation in ambient air pollution levels in China is substantial, and the urban population in China is exposed to a high-pressure lifestyle along with the rapid socioeconomic growth of recent decades. In 2015, 17% of the world's depression patients lived in China, and the prevalence rate of depression among the adult population is at a high level of 4.2% in China (22). According to clinical experience, hospital admissions for depression generally involve patients with moderate to severe depression, with neurosis symptoms and self-harm or suicidal tendencies, and these cases likely contribute a significant proportion of the disease burden (including mortality following depression, e.g., suicide) and economic burden of depression. Therefore, investigating whether the ambient air pollution may contribute to the risk of hospital admission for depression is of interest.

Using national morbidity data from social health insurance schemes in China, we conducted a two-stage time-series analysis to comprehensively investigate the association between short-term exposure to ambient air pollution and daily hospital admissions for depression during the period 2013–2017 in 75 Chinese cities.

METHODS

Study Design and Population

Our study population consisted of the urban Chinese population, through data from two major health insurance systems: the urban employee-based basic medical insurance scheme (UEBMI) and the urban resident-based basic medical insurance scheme (URBMI) (23). The former covers urban employees and those retired, and the latter covers urban residents, including children, students, elderly people without previous employment, and the unemployed (23). For this study, we extracted daily depression hospital admission data for 75 administrative divisions of prefecture-level cities and above in China from January 2013 to December 2017 from the two national urban health insurance schemes. The locations of the 75 cities are shown in Figure S1 in the online supplement. In 2017, the two databases covered 84% of all urban residents (330 million) in the 75 cities, representing more than 23% of the total general population in Mainland China.

Health Data

Daily depression hospital admission data were identified from primary discharge diagnoses that were coded as F32–F33 ICD-10 diagnoses or were consistent with the text of F32–F33. This study was exempted from institutional review board approval by the Ethics Committee of Peking University Health Science Center, Beijing, because all data used for the study were collected for administrative purposes without any individual identifiers.

Ambient Air Pollution Data

We included six international standard air pollutants that have been extensively investigated previously: fine particles ($PM_{2.5}$), inhalable particles (PM_{10}), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), ozone (O_3), and carbon monoxide (CO). Data on daily concentrations of ambient air pollutants, as a proxy for population exposure to ambient air pollution, were obtained for each city from the National Air Quality Monitoring System, in line with previous studies (24, 25). Daily mean concentrations for all ambient air pollutants in each city were calculated by averaging all valid monitoring measurements if there was more than one monitor in that city; the numbers of monitoring sites in included cities are listed in Table S1 in the online supplement. Short-term exposure indicates exposure to air pollution up to a lag of 7 days.

Covariates

To control for potential confounders, we collected data on daily mean air temperature and relative humidity for each city from the China Meteorological Data Sharing Service System. Information on the admission day of week and public holidays was also collected, and a sequence of calendar time was generated to indicate time trend. Information on the annual per capita gross domestic product (GDP) for each city was obtained from city statistical yearbooks.

Statistical Analysis

We used a two-stage analytic approach to assess the city-specific and overall associations between air pollutants and daily hospital admissions for depression.

In the first stage, we estimated city-specific associations using generalized additive models with quasi-Poisson regression (24, 25). Covariates in the models, based on several recent large national studies in China (24, 25), included a natural cubic spline of calendar time with 7 degrees of freedom per year to exclude unmeasured time trends longer than 2 months in hospital admissions for depression; an indicator variable for the admission day of week to account for possible variations over weekdays and weekends; an indicator variable for public holiday to account for possible variations in holidays; and natural cubic splines with 6 degrees of freedom for 3-day

moving average temperature and 3 degrees of freedom for 3-day moving average relative humidity to exclude potential nonlinear and delayed confounding effects of weather conditions. The time-series analysis model was as follows:

$$\log(E[Y_t]) = \alpha + \beta(\text{air pollutants}) + \text{admission day of week} + \text{holiday} + \text{ns}(\text{temperature, df}=6) + \text{ns}(\text{relative humidity, df}=3) + \text{ns}(\text{calendar time, df}=7 \text{ per year}),$$

where $E(Y_t)$ is the expected count of admissions for depression on day t; β indicates the log-relative risk of depression admissions associated with a unit increase of air pollutant levels; ns() represents the natural cubic spline function; admission day of week and holiday are indicator variables for day of week and public holidays, respectively; and temperature and relative humidity indicate 3-day moving average temperature and relative humidity with 6 degrees of freedom and 3 degrees of freedom, respectively. Air pollutant concentrations of simple lags of 0–7 days (lag0–lag7) and 1–7 days moving average (lag01–lag07; the average of the present day and previous 1–7 days), respectively, were used in the main analysis to obtain the same-day and lagged effect estimates.

In the second stage, we used a random-effects model to pool the city-specific effect estimates to obtain the overall effect estimates. Stratified analyses were conducted by pooling the city-specific effect estimates for subgroups divided by geographical regions and individual characteristics: sex, age, and insurance type. Geographical regions were classified into southern and northern regions according to the Qinling Mountains–Huai River Line (26). To exclude unstable estimates from cities with too few admission cases in subgroups, we included in subgroup analyses only cities with at least 200 admission cases in the analyzed subgroup during the study period. We compared the differences between stratified effect estimates using the z-test (27). We also investigated the possible variation in the estimated effects related to city-level characteristics, including cities' annual mean air pollutant levels, temperature, relative humidity, and GDP per capita in metaregression models (28). To elucidate the association between air pollutants and daily admission for depression at different exposure concentrations, we plotted exposure-response association curves via the approach reported by Gasparrini et al. (29).

Finally, several sensitivity analyses were conducted to evaluate the robustness of the results. First, we used different values for degrees of freedom for covariates in the time-series analysis. Second, two-pollutant model analyses were conducted for the most significant effect estimate for each air pollutant by controlling for another air pollutant at the same lag time.

We conducted all statistical analyses in R, version 3.4.2. Effect estimates were expressed as percent changes with 95% confidence intervals converted from relative risks in daily depression admissions associated with an increase of 10 $\mu g/m^3$ in $PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3 and an increase of 1 mg/m^3 in CO concentrations. A two-sided p value <0.05 was considered statistically significant.

RESULTS

From the URBMI and UEBMI insurance databases, we identified a total of 111,620 hospital admissions for depression in the period 2013–2017 in 75 Chinese cities. Among the 75 cities, 37 are located in the southern region, with 52.45% of admitted patients. Table 1 summarizes the demographic characteristics of admitted patients. Overall, 63.5% patients were female, 59.1% were in the 40- to 64-year age group, and 79.0% were identified in the UEBMI database.

Monthly variation in daily ambient air pollutant concentrations during the study period is shown in Figure S2 in the online supplement. The daily average concentrations of $PM_{2.5}$, PM_{10}, NO_2, SO_2, O_3, and CO in the 75 cities during the study period were 54.4 $\mu g/m^3$, 91.3 $\mu g/m^3$, 34.6 $\mu g/m^3$, 26.5 $\mu g/m^3$, 64.2 $\mu g/m^3$, and 1.11 mg/m^3, respectively (Table 2), and there were medium to high correlations between ambient air pollutants except O_3 and CO (see Table S2 in the online supplement).

Figure 1 shows the overall percent changes in daily hospital admissions for depression associated with increasing air pollutants at single-day lags of 0–7 days and 01–07 days moving average. Overall, the effect estimates of all included air pollutants, with the exception of O_3, were significant at several lags. At lag01, we found significant increases of 0.52% (95% CI=0.03, 1.01), 0.41% (95% CI=0.05, 0.78), and 1.78% (95% CI=0.73, 2.83) in depression hospital admission for an increase of 10 $\mu g/m^3$ in $PM_{2.5}$, PM_{10}, and NO_2, respectively. Forest plots for overall analyses of depression hospital admission associated with different air pollutants at lag01 are shown in Figures S3–S8 in the online supplement.

The associations between ambient air pollutants and depression admissions, stratified by geographical region, sex, age, and insurance type, were mostly significant at lag01, as shown in Table 3. Results at other lags are shown in Figures S9–S12 in the online supplement. The subgroup effect estimates at lag01 were generally significant for NO_2, except in the 19- to 39-year age group and those in URBMI. However, depression admissions significantly increased with increase in NO_2 concentration at lag0 among those in URBMI (see Figure S12 in the online supplement). We did not observe evidence for significant effect modification by geographical region, sex, age, and insurance type for all effect estimates at the same lag time, although the estimated effects were generally higher in the southern region, in males, in patients 65 years old or older, and in those in URBMI.

The metaregression analysis results showed no evidence for significant effect modification by mean air pollutant levels, temperature, relative humidity, and GDP per capita for air pollutants (see Table S3 in the online supplement). Figure 2 shows the exposure-response curve for the association between NO_2 concentrations (lag01) and risk for depression admission. The curve increased substantially at NO_2 concentrations above 40 $\mu g/m^3$.

In sensitivity analyses, the effect estimates of NO_2 were robust under different df values of covariates (data not shown). Results of two-pollutant models suggest that only the effect

TABLE 1. Demographic characteristics of patients admitted for depression in 75 Chinese cities, 2013–2017[a]

	Overall (N=111,620)		Northern Region (N=53,077)		Southern Region (N=58,543)	
Variable	N	%	N	%	N	%
Number of cities	75		38		37	
Sex						
Male	33,038	36.5	17,122	40.1	15,916	33.3
Female	57,471	63.5	25,614	59.9	31,857	66.7
Age (years)						
0–18	1,698	1.9	311	0.7	1,387	2.9
19–39	14,584	16.1	5,952	13.9	8,632	18.1
40–64	53,517	59.1	27,396	64.1	26,121	54.7
≥65	20,710	22.9	9,077	21.2	11,633	24.3
Insurance type						
UEBMI	88,222	79.0	44,365	83.6	43,857	74.9
URBMI	23,398	21.0	8,712	16.4	14,686	25.1

[a] Subgroups excluded admission cases without sex or age information. UEBMI=urban employee-based basic medical insurance scheme; URBMI=urban resident-based basic medical insurance scheme.

estimates of NO_2 were significant after controlling for other air pollutants at the same lag time (see Table S4 in the online supplement).

DISCUSSION

To our knowledge, this is the largest study to explore the association between short-term exposure to multiple ambient air pollutants and hospital admission for depression. After conducting the two-stage analyses, we found that short-term exposures to ambient $PM_{2.5}$, PM_{10}, NO_2, SO_2, and CO were significantly associated with increased risk for hospital admission for depression. Moreover, the effect estimates of NO_2 were generally consistent across different geographical regions and demographic characteristics, including sex, age, and insurance type, and were robust to adjustment for other air pollutants.

It is well known that exposure to ambient air pollution could cause increased respiratory and systemic inflammatory response and oxidative stress in the human body (30, 31), and several experimental studies have demonstrated that the increased inflammatory response and oxidative stress could be expanded to the central nervous system in both short-term and long-term exposure scenarios (14–19). In fact, depression is a condition of typically insidious onset and relatively long course, and both epidemiological studies (8, 10, 11) and toxicological studies (17–19) have found that long-term exposure to ambient air pollution is linked to the onset of depression. Similarly, long-term exposure to ambient air pollution has also been consistently associated with increased risk of cardiovascular and respiratory diseases, two types of chronic diseases with long courses (3, 32). However, short-term changes in ambient air pollution within short periods have also been associated with the onset of acute cardiovascular events (e.g., acute ischemic coronary events or acute decompensated heart failure) and respiratory events (e.g., exacerbation of chronic obstructive pulmonary disease) (33–35). Therefore, it is thought that short-term changes in ambient air pollution may trigger significant changes in a health condition (e.g., exacerbation of chronic obstructive pulmonary disease) on the basis of changes already induced by prior long-term exposure to ambient air pollution (e.g., respiratory disease status). Among patients with admissions for depression, it is possible that many were suffering from preexisting depressive symptoms, and short-term changes in ambient air pollution could serve as the trigger to induce moderate to severe depressive symptoms requiring hospitalization for intensive treatment.

Several epidemiological studies have investigated the association of short-term exposure to ambient air pollution with risk of depression (5–7, 9, 20, 36), but only two of them used hospital admission data (6, 36). A case-crossover study with 19,646 hospital admissions for depression (6), drawn from electronic hospitalization summary reports of tertiary A hospitals, found that short-term elevations in ambient particulate matter were associated with an increased risk of hospitalization for depression in 26 Chinese cities in 2014 and 2015, and the estimated increases in hospital admissions for depression were 3.55% and 2.92% at lag 0 for an interquartile-range increase in PM_{10} and $PM_{2.5}$ (76.9 $\mu g/m^3$ and 47.5 $\mu g/m^3$), respectively. Another study also found a significant positive association between short-term exposure to $PM_{2.5}$ and hospital admissions for depression (N=1,193) in 2015 and 2016 in Chengdu, a major city in Western China (36). In addition, other studies have reported significant positive associations between short-term exposure to ambient air pollution and emergency department visits for depression in a limited number of cities (5, 7, 9). Our study is able to expand the analyses for short-term exposure to ambient air pollution and hospital admission for depression to 75 Chinese cities, with a much larger number of admissions (N=111,620) over a period of 5 years, and is able to provide a detailed analysis for other gaseous pollutants, including NO_2, SO_2, O_3, and CO, along with ambient particulate matter. Our results support the positive associations between short-term exposures to ambient $PM_{2.5}$ and PM_{10} and hospital admission for depression and suggest that the gaseous pollutants NO_2, SO_2, and CO were also associated with an increased risk of admission for depression.

In addition to particulate matter, several previous studies have also reported associations of depression-related outcomes with other air pollutants, including NO_2 (5, 7, 9, 37), SO_2 (5, 7, 9), O_3 (5, 7, 9), and CO (5, 9), but the results have been inconsistent. For example, a recent cohort study in England

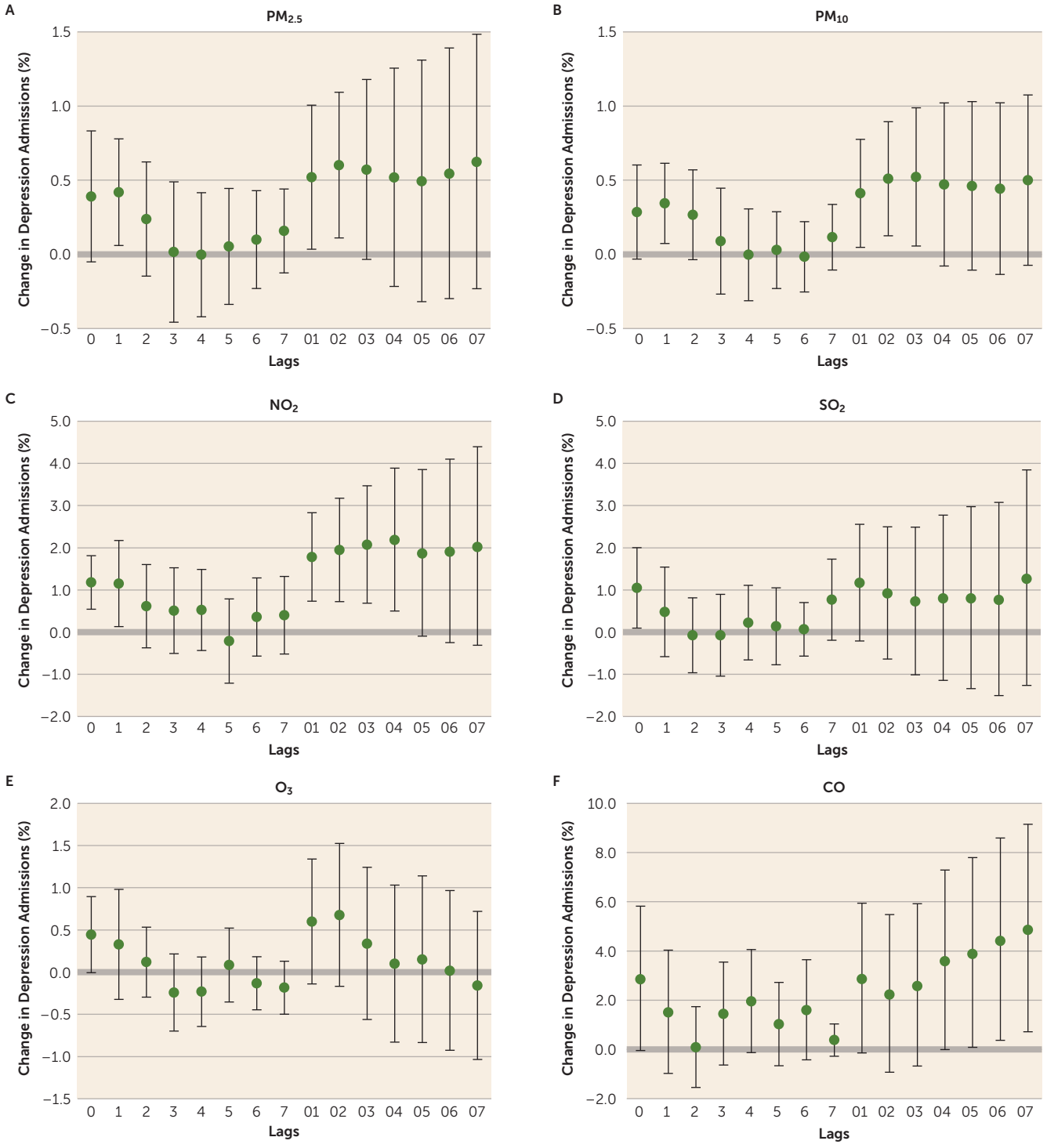
and Wales found that long-term exposure to ambient NO_2 was more strongly associated with increased adolescent psychotic experiences, a risk factor for depression, than $PM_{2.5}$ and PM_{10} (37). However, another study did not find any association for short-term exposure to NO_2 and emergency department visits for depression in Ontario's hospitals in Canada (7). Our study was able to comprehensively examine the potential effects of particulate matter and gaseous air pollutants on daily admissions for depression in a much larger population, and thus provided greater statistical power to investigate the independent impact on depression admissions for different air pollutants. Based on our study findings, we suppose that NO_2 may be the key air pollutant contributing to the increased depression risk. As mentioned earlier, increased oxidative stress may be one of the biological pathways behind the association between air pollution and depression. Specifically, oxidative stress occurs when there is an excess of free radicals over antioxidant defenses. The ambient air pollutant NO_2 functions directly as a nitrogen-centered free radical after being inhaled into the lungs, whereas other components of air pollutants mainly function as powerful oxidants to induce this pathway (38). Increased oxidative stress in the nervous system is toxic to dopaminergic neurons (15), which could contribute to the onset of depression, since depletion of dopamine in the central nervous system is one of the underlying pathophysiological mechanisms for depression (39).

TABLE 2. Summary statistics of daily ambient air pollutants and weather variables in 75 Chinese cities, 2013–2017

Measure and Region	Mean	SD	Minimum	Median	Maximum	Interquartile Range
$PM_{2.5}$ ($\mu g/m^3$)						
Total	54.4	43.3	1.0	42.7	609.8	42.4
Northern region	61.2	49.9	2.1	47.1	609.8	50.4
Southern region	46.8	32.7	1.0	38.8	543.1	35.0
PM_{10} ($\mu g/m^3$)						
Total	91.3	61.1	1.1	75.9	1305.0	69.7
Northern region	108.5	69.3	2.5	93.3	985.2	83.9
Southern region	72.8	43.9	1.1	62.5	1305.0	50.7
NO_2 ($\mu g/m^3$)						
Total	34.6	19.1	1.0	31.0	286.6	24.3
Northern region	37.5	20.2	1.3	34.1	209.3	26.2
Southern region	31.5	17.3	1.0	28.1	286.6	21.9
SO_2 ($\mu g/m^3$)						
Total	26.5	26.9	0.5	17.8	446.7	21.2
Northern region	34.4	33.4	0.5	23.7	446.7	32.0
Southern region	18.0	12.7	1.0	14.7	234.0	12.7
O_3 ($\mu g/m^3$)						
Total	64.2	41.7	1.2	57.7	338.4	45.8
Northern region	66.2	37.9	2.4	61.0	335.8	47.8
Southern region	62.6	37.9	1.2	54.8	338.4	42.9
CO (mg/m^3)						
Total	1.11	0.67	0.05	0.96	18.92	0.62
Northern region	1.37	0.80	0.10	1.10	18.92	0.82
Southern region	0.95	0.42	0.05	0.88	12.94	0.43
Temperature (°C)						
Total	14.5	10.7	−28.9	16.1	36.5	15.7
Northern region	12.3	11.5	−28.9	12.6	35.4	19.0
Southern region	18.0	8.2	−11.1	18.9	36.5	13.1
Relative humidity (%)						
Total	67.9	18.0	7.0	71.0	100.0	26.0
Northern region	71.3	18.6	7.0	62.0	100.0	29.0
Southern region	77.8	14.0	12.0	77.0	100.0	20.0

Results of subgroup analyses could offer insights into susceptible populations and suggest implications for research and public health promotion. Our subgroup study showed that the positive associations between NO_2 and hospital admission risk for depression were the most robust among the investigated air pollutants. In addition, the effect estimates were not modified by the mean air pollutant levels, city-specific levels of temperature, relative humidity, and GDP per capita. We found, too, that effect estimates of NO_2 appeared higher for males than for females at the same lag time, which is consistent with findings from a previous study (5). We also found that the effect estimates of NO_2 in the age 65 or older group were all higher than in other age groups, which may be due to the potential high sensitivity of older people to air pollution effects (6). The higher effect estimates of NO_2 found in URBMI compared with UEBMI may be related to the "healthy worker effect" (40), which usually appears as a minor reduction of morbidity in occupational cohorts compared with the general population. Moreover, although the differences were statistically insignificant, we found that NO_2 and CO were more strongly associated with hospital admission risk for depression in the southern region compared with the northern region, potentially because of the variation of major air pollutant components between these regions as a result of China's Huai River Policy, which provided free winter heating via the provision of coal for boilers to the northern cities but not to the southern cities. Northern cities generally have a higher proportion of air pollutants from the combustion of coal, such as total suspended particulates and SO_2, whereas air pollutants in southern cities are more closely associated with vehicle exhaust emissions, especially of NO_2 and CO (26). Furthermore, doors and windows of buildings in the southern region are poorly sealed compared with those in the northern region, and gaseous

FIGURE 1. Overall percent changes in daily hospital admissions for depression per 10 μg/m^3 increases in $PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3 and 1 mg/m^3 increase in CO at different lag days in 75 Chinese cities[a]



[a] Error bars indicate 95% confidence intervals.

pollutants are more likely to penetrate indoors, which may be one of the reasons why the estimated health effects in the southern region were more significant.

Our study has several strengths. Most previous studies have been restricted to a single city or region, or to large hospitals, and thus have limited representativeness and power to investigate the question of interest among the general population. This study investigated the short-term association between major ambient air pollutants and hospital admission risk for depression in a large number of cities

TABLE 3. Overall percent changes in daily hospital admissions for depression per 10 μg/m^3 increases in $PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3 and 1 mg/m^3 increase in CO at lag01 in 75 Chinese cities, stratified by geographical region, sex, age, and insurance type[a]

	$PM_{2.5}$		PM_{10}		NO_2		SO_2		O_3		CO	
Characteristic	Percent Change	95% CI	Percent Change	95% CI	Percent Change	95% CI	Percent Change	95% CI	Percent Change	95% CI	Percent Change	95% CI
Geographical region[b]												
Northern region	0.32	−0.27, 0.91	0.25	−0.17, 0.67	1.40*	0.32, 2.50	0.08	−1.18, 1.36	0.68	−0.27, 1.65	1.67	−1.31, 4.74
Southern region	0.72	−0.16, 1.60	0.62	−0.06, 1.30	2.20*	0.30, 4.13	3.50	−0.09, 7.22	0.41	−0.77, 1.60	4.87	−3.94, 14.50
Z-test, p value	0.459		0.364		0.479		0.079		0.725		0.512	
Sex												
Male	0.51	−0.11, 1.13	0.44	−0.04, 0.93	2.86**	1.24, 4.52	1.85	−0.39, 4.14	0.45	−0.60, 1.50	9.54**	2.69, 16.85
Female	0.51	−0.03, 1.06	0.42*	0.01, 0.84	2.09**	0.52, 3.68	2.45*	0.55, 4.39	0.33	−0.65, 1.32	3.98*	0.23, 7.88
Z-test, p value	0.998		0.946		0.507		0.692		0.878		0.170	
Age range[c]												
19–39 years	0.76	−0.31, 1.84	0.58	−0.22, 1.39	1.66	−0.76, 4.14	0.91	−1.62, 3.51	1.30	−0.19, 2.81	2.76	−7.20, 13.80
40–64 years	0.49	−0.17, 1.16	0.37	−0.11, 0.86	2.38**	0.78, 4.02	2.06*	0.32, 3.84	0.47	−0.51, 1.46	7.04**	2.42, 11.87
Z-test, p value	0.675		0.667		0.630		0.469		0.364		0.472	
≥65	0.64	−0.16, 1.44	0.65*	0.07, 1.24	4.19**	2.07, 6.35	3.08*	0.21, 6.04	0.00	−1.26, 1.28	4.36	−4.73, 14.31
Z-test, p value	0.862		0.887		0.129		0.272		0.194		0.825	
Insurance type												
UEBMI	0.22	−0.28, 0.71	0.34	−0.02, 0.70	1.30*	0.13, 2.48	0.67	−0.66, 2.02	0.78*	0.02, 1.55	2.40	−0.62, 5.52
URBMI	0.60	−0.16, 1.36	0.41	−0.16, 0.97	1.23	−0.57, 3.05	2.79	−0.31, 5.99	−0.59	−1.96, 0.81	1.15	−5.35, 8.10
Z-test, p value	0.404		0.839		0.948		0.220		0.091		0.741	
Total	0.52*	0.03, 1.01	0.41*	0.05, 0.78	1.78**	0.73, 2.83	1.16	−0.21, 2.56	0.60	−0.14, 1.34	2.85	−0.14, 5.94

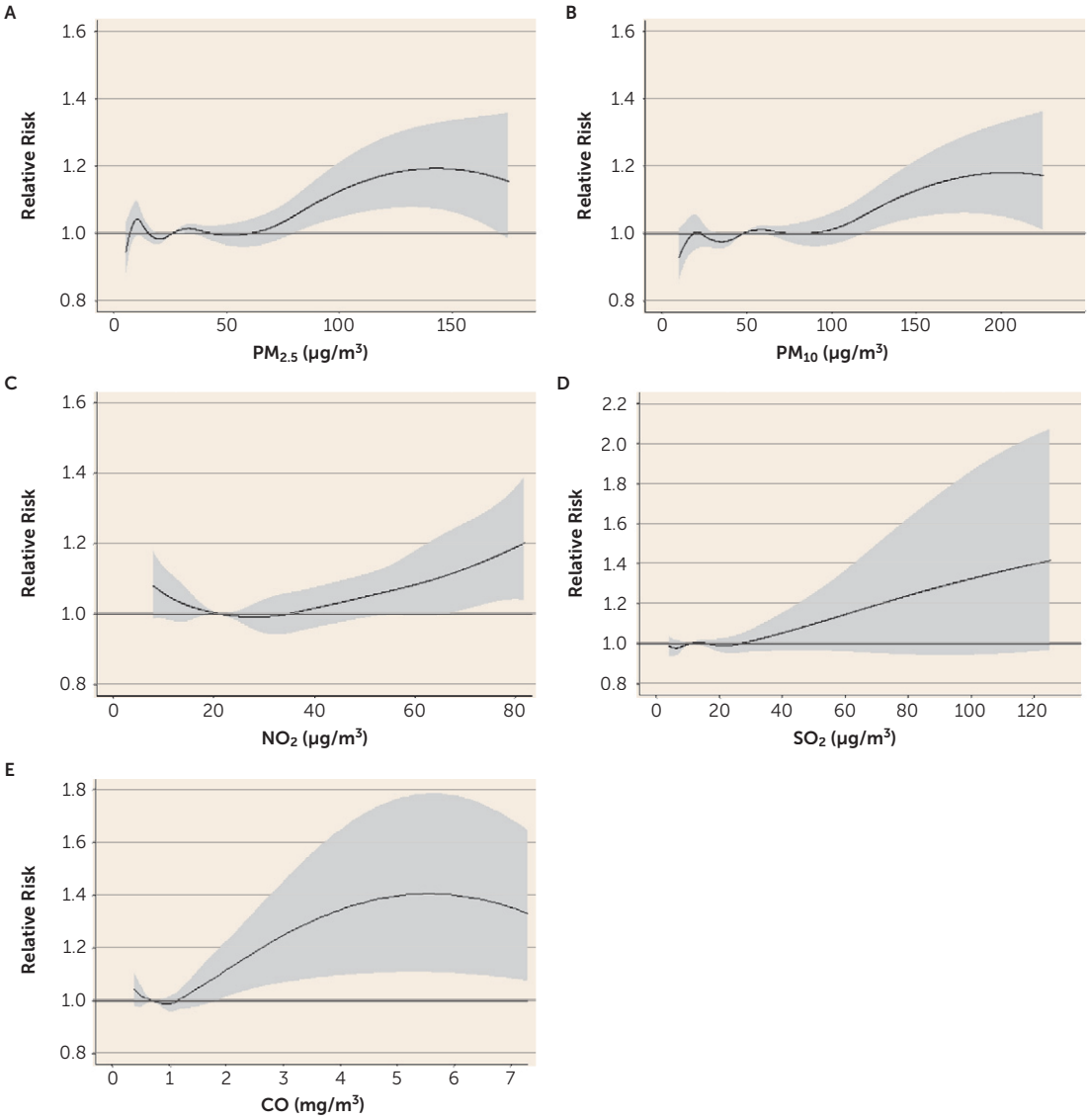
[a] Admission cases without sex or age information were excluded from the subgroup analyses. UEBMI=urban employee-based basic medical insurance scheme; URBMI=urban resident-based basic medical insurance scheme.
[b] The 75 cities included in the study were classified into the southern and northern region categories according to the Qinling Mountains–Huai River Line.
[c] Analyses for the 0- to 18-year age group were not conducted because the number of depression admission cases in that age range exceeded 200 in only one of the 75 cities during the 2013–2017 period.
*p<0.05. **p<0.01.

in China by using national medical insurance data covering a large proportion of the general urban population, and thus has fair representativeness. Moreover, our investigation, based on multiple high-heterogeneity cities, provides research evidence for the potential modification effects of geographical region, weather conditions, air pollution levels, and socioeconomic status on the estimated risk of hospital admission for depression associated with air pollution.

Our study also has several limitations, which are similar to those of other studies using the same analytic method (24, 25). First, ecological bias is inherent to the time-series analysis method. For example, we did not have specific individual diagnostic data to allow classification of depression admission cases into subgroups according to the severity of their symptoms, or as initial or recurrent admission for depression, a limitation that may affect the interpretation of the results into clinical practice. Second, since no specific exposure data were obtained for individual subjects, exposure measurement errors would occur from using ambient air pollution data at the city level instead of at the individual level or at the level of smaller geographical units. Nevertheless, previous studies have shown that fixed-site air monitoring measurements could reflect ambient air pollution levels of the urban background to a certain extent (41), and the monitoring data have been commonly used as a proxy for population exposure to ambient air pollution in previous time-series analyses (25, 42). Third, potential misclassification of depression diagnosis in insurance data should also be considered, although these possible errors would be expected to bias the risk estimates toward null (43). Fourth, the collinearity among ambient air pollutants limit the interpretation of the effect estimates of single air pollutants in the two-pollutant models. Fifth, studies have shown that other factors, such as noise (44), psychological stress (45), poverty (46), and population density (47), may also influence the risk of depression, but related data were not available in this study. Although we considered the impact of GDP per capita on the results and no significant effect modification of the exposure-health associations by GDP per capita was found, future studies would benefit from investigating the potential confounding effects of these factors in the context of ambient air pollution. Finally, subgroup analyses for patients age 18 and under were not conducted because few cities met our inclusion criterion (≥200 admission cases) for subgroup analysis for patients in that age range. Because the brain and respiratory system are still developing in children and teenagers and are considered more vulnerable to ambient air pollution, future studies should also pay more attention to individuals in this age group.

In summary, our findings suggest that increases in short-term exposure to ambient air pollution are associated with increased risk of daily hospital admission for depression among the general urban population in China. Targeted strategies such as more stringent air pollution guidelines and air quality control measures may be helpful for promoting public mental health. Further studies are needed to confirm our findings and to investigate the underlying mechanisms for the reported associations.

FIGURE 2. Exposure-response curves for the association between ambient air pollutant concentrations (lag01) and risk for daily hospital admissions for depression in 75 Chinese cities[a]



[a] We did not include the exposure-response curve for O_3 because no significant association between O_3 and hospital admissions for depression was found in the main analysis. Shaded areas indicate 95% confidence intervals.

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