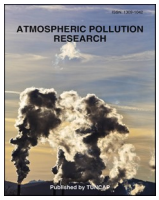
Atmospheric Pollution Research 15 (2024) 102308

Contents lists available at ScienceDirect

Atmospheric Pollution Research

journal homepage: www.elsevier.com/locate/apr



Ambient air pollution and stroke risk among different accumulation patterns of comorbidities: Casual inference study based on marginal 'between-within' model

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ARTICLE INFO

Keywords:
Ambient air pollution
Comorbidity
Stroke
Case-crossover study
Causal inference

ABSTRACT

Previous studies showed that ambient air pollution is a risk factor for stroke. But its effects on patients with different comorbidity accumulation patterns and the causal relationship remain unclear. Hospitalization data were collected from the Beijing Municipal Health Commission Information Center. Pollutant data, including particulate matter ($PM_{2.5}$, PM_{10}, PM_1, $PM_{1\text{-}2.5}$), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3) from 2014 to 2017, were obtained from the widely-used ChinaHighAirPollutants dataset. An individual-level case-crossover design was employed to identify case days and control days. The exposure-response association was estimated by fitting conditional logistic regression models. The newly proposed marginal 'between-within' models were used to estimate counterfactual hospitalization probability. In a total of 237 487 stroke patients, 211 741 diagnosed with ischemic stroke (IS) and 25 641 with hemorrhagic stroke (HS). Except for SO_2, the seven pollutants were associated with higher risk of overall stroke and IS. Particulate matter showed larger estimated effects in patients with hypertension and diabetes but without hyperlipidemia. NO_2 and CO showed larger estimated effects in patients with hypertension but without diabetes. O_3 showed larger estimated effects in patients with hypertension, diabetes, and hyperlipidemia. PM_1, PM_{10}, NO_2, and CO had statistically significant and persistent causal relationships with stroke risk during the lag periods. This study highlighted the need for targeted interventions of air pollution. Prioritizing control measures for PM_1, PM_{10}, NO_2, and CO is particularly crucial in stroke prevention efforts.

1. Introduction

Ambient air pollution is considered as a significant risk factor for human health. According to a systematic analysis for the Global Burden of Disease Study, ambient air pollution was one of the top five risk factors that contributed to attributable deaths in 2019 (Collaborators, 2020). Cardiovascular diseases including stroke accounted for the majority of deaths attributed to ambient air pollution (Collaborators,

Abbreviations: IS, ischemic stroke; HS, hemorrhagic stroke; PM_1, particulate matter with aerodynamic diameter ≤1 μm; $PM_{2.5}$, particulate matter with aerodynamic diameter ≤2.5 μm; NO_2, nitrogen dioxide; FCMD, first cardiometabolic disease; CMM, cardiometabolic multimorbidity; ICD-10, International Classification of Diseases 10th Revision codes; PM_{10}, particulate matter with aerodynamic diameter ≤10 μm; $PM_{1\text{-}2.5}$, particulate matter with aerodynamic diameter between 10 μm and 2.5 μm; SO_2, sulfur dioxide; CO, carbon monoxide; O_3, ozone; CHAP, the ChinaHighAirPollutants; *df*, dataset, degrees of freedom; ER, excess risk; IQR, interquartile range; PM, particulate matters; OR, odd risk; CVDs, cardiovascular diseases; HR, hazard ratio.

Peer review under responsibility of Turkish National Committee for Air Pollution Research and Control.

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https://doi.org/10.1016/j.apr.2024.102308
Received 25 November 2023; Received in revised form 10 September 2024; Accepted 11 September 2024
Available online 12 September 2024

2020). China bears heavy disease burden of stroke, and the burden is likely to increase because of the aged tendency of population and the incremental risk factors (Wang et al., 2017; Wang et al., 2022; Wu et al., 2019). Increasing evidence over the past few years has indicated that there is a link between air pollution exposure and the risk of ischemic stroke (IS) (Chen et al., 2021; Ho et al., 2022; Tian et al., 2018; Verhoeven et al., 2021), but air pollution does not appear to be associated with the risk of hemorrhagic stroke (HS). Besides, PM_1 (particulate matter with aerodynamic diameter $\leq$1 μm) was suggested to be more harmful than $PM_{2.5}$ (particulate matter with aerodynamic diameter $\leq$2.5 μm) (Wu et al., 2022a). Casual inference studies tried to explore the health impact of ambient air pollution within a counterfactual framework. The study utilized various research methods, including difference-in-differences study (Kioumourtzoglou et al., 2016; Li et al., 2021; Renzi et al., 2019; Wang et al., 2016), generalized propensity score (Wei et al., 2020; Wu et al., 2020), instrumental variable approach (Bae et al., 2020; Ju et al., 2022; Schwartz et al., 2017), negative control approach (Schwartz et al., 2023; Yu et al., 2021), and inverse probability weighting (Wei et al., 2021c). The majority of these studies focused on mortality as the primary health outcome. Until now, there is no study specifically examined the causal relationship of ambient air pollution and the risk of stroke.

It has recently become more important to understand the association between pre-existing cardiovascular conditions and environmental air pollution. The principal motivation is to characterize how the influence of ambient air pollution may vary among different comorbidities. A previous study indicated that exposure to $PM_{2.5}$ was associated with a greater risk of hospital admission for stroke in patients with hypertension (Chang et al., 2022). While comorbidity generated greater susceptibility to ambient air pollution in some studies (Chang et al., 2022; Li et al., 2019), there were researches reported smaller risks of health outcomes in comorbidity patients than in those without comorbidity (Chen et al., 2020a; Seposo et al., 2020). White et al. (2020) found that both air pollution and comorbidity score contributed to in-hospital mortality, but they did not find evidence of interaction (White et al., 2020).To some extent, these results from cross-sectional studies were consistent with a prospective study. Luo et al. (2022) found that $PM_{2.5}$ and nitrogen dioxide (NO_2) increased the risks of transitions from baseline to the first cardiometabolic disease (FCMD), from FCMD to cardiometabolic multimorbidity (CMM), from baseline to death, but $PM_{2.5}$ did not increase the risk of transition from FCMD or CMM to death, NO_2 did not increase the risk of transition from CMM to death (Luo et al., 2022). Thus, it appears that ambient air pollution increased the risks of health outcomes but not in all the stages of disease development. There might be a sensitive window or sensitive comorbidity accumulation pattern. However, the limited study examined the acute effect of air pollutants in patients with different numbers or accumulation patterns of comorbidities. Ambient air pollution contributed to the accumulation of comorbidities, resulting in additional burdens for health, society and the economy(Arias de la Torre et al., 2023). The research considering the role of ambient air pollution in patients with different comorbidities could strengthen our understanding on the health effect of ambient air pollution and broaden the way of stroke management.

Our team has been focusing on the patients with comorbid conditions to analyze the harmful effects of air pollutants on stroke hospital admissions (Liu et al., 2021, 2022b; Zhao et al., 2022b, 2023) We found that high level of air pollutants could be a risk factor for stroke among those with hypertension and diabetes. However, the previous studies of our team only considered a single comorbidity in each study population, and none of the study explored the causal link. Thus, as a further exploration based on our previous studies, and with an objective of exploring the impact of air pollution in a perspective of disease accumulation, we undertook this research among patients with various comorbidities to investigate the correlation between short-term exposure to 8 air pollutants and the risk of being hospitalized for stroke. In this study, we evaluated personal exposure based on a high-quality air pollution database. We also accounted for varying comorbidity numbers and patterns of accumulation. In the vulnerable population, we examined the causal relationship within a counterfactual framework.

2. Data and methods

2.1. Hospitalization data

We collected medical record from the Beijing Municipal Health Commission Information Center. The dataset contained the front sheet of medical record of patients who were admitted for cerebrovascular disease to the secondary and above-level hospitals in Beijing. Our study period was from January 1st, 2014 to December 31st, 2017. Information including gender, age, home address, admission date, principal diagnosis, and secondary diagnosis were collected. The principal diagnosis was used to screen patients who were admitted for stroke. Based on the International Classification of Diseases 10th Revision codes (ICD-10), we identified overall stroke and the subtypes: overall stroke (I60-I64), IS (I63) and HS (I60-I62). The secondary diagnosis was used to confirm the patients' comorbidities. In this study, we mainly focused on 3 comorbidities: hypertension (I10, Essential (primary) hypertension), diabetes (E10-E14, Diabetes mellitus), hyperlipidemia (E78, Disorders of lipoprotein metabolism and other lipidaemia). A total of 346 915 stroke patients were admitted to secondary and tertiary hospitals in Beijing from 2014 to 2017. Of these, 109 280 patients had missing or unidentifiable home addresses, 137 patients were younger than 18 years old, and 11 patients had missing gender information. A total of 237 487 stroke patients were included in the analysis. The subject flowchart is shown in Fig. 1.

2.2. Exposure assessment

This study examined the acute effect of 8 air pollutants: $PM_{2.5}$, particulate matter with aerodynamic diameter $\leq$10 μm (PM_{10}), PM_1, particulate matter with aerodynamic diameter between 10 μm and 2.5 μm ($PM_{1\text{-}2.5}$), sulfur dioxide (SO_2), NO_2, carbon monoxide (CO), and ozone (O_3), which were collected from the ChinaHighAirPollutants (CHAP) dataset (Wei et al., 2019, 2021a, 2021b, 2022a, 2022b, 2023). The CHAP is the series of long-term, high-resolution, high quality, and full-coverage datasets of ground-level air pollutants in China. Combined

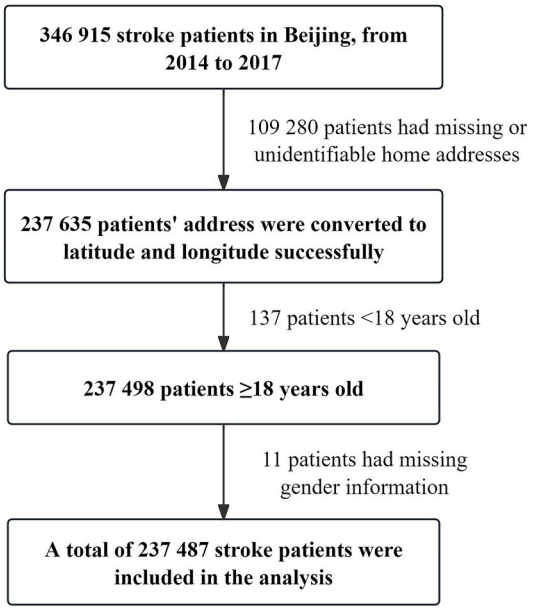

Fig. 1. Subject flowchart of this study.

with the dig data of ground-based measurements, atmospheric reanalysis, satellite remote sensing products, and model simulations, the concentrations of particulate matter at 1 km resolution and the concentrations of gaseous pollutants at 10 km resolution were estimated using the proposed Space-Time Extra-Trees (STET) model. The CHAP datasets yielded a higher data quality and outperformed most of the previous models. The 10-fold cross-validation R^2 was 0.92 for $PM_{2.5}$, 0.90 for PM_{10}, 0.83 for PM_1, 0.84 for SO_2, 0.84 for NO_2, 0.80 for CO, 0.87 for O_3. We collected the daily 24-h average concentration of $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and daily maximum 8-h average of O_3. The concentration of $PM_{1\text{-}2.5}$ was calculated by subtracting PM_1 from $PM_{2.5}$.

Following methods widely used in previous studies (Liu et al., 2022a), we estimated the air pollutant exposure for hospitalized patients based on their home addresses. Specifically, we obtained the home address of each hospitalized patient from their medical records. Then, we used the "baidumap" package in R-4.0.5 and the "pandas json" package in Python to convert these home addresses into latitude and longitude coordinates. Using these coordinates, we extracted the pollutant concentrations from the CHAP database. The CHAP dataset provides gridded data, and we employed the "Extract Multi Values to Points" tool in ArcGIS to retrieve the pollutant concentrations corresponding to each set of coordinates. According to the latitude and longitude of each patient, we extracted the personal exposure of the 8 pollutants on both the case day and the control days, and at 5 lag days (Lag 01- Lag 05).

2.3. Meteorological factors assessment

The data of relative humidity, wind speed, air pressure, and daily temperature were collected from the China Meteorological Administration. The ordinary kriging method was used to interpolate the meteorological factors in Beijing, and personal value was extracted according to patients' geographical coordinates.

2.4. Individual-level case-crossover study design

We employed an individual-level case-crossover study design to examine the acute effects of ambient air pollution on hospitalization risk of stroke. The case-crossover study was an appealing design in environmental epidemiology and was widely used to analyze the acute health effects of environmental factors. In case-crossover study, each subject serves as his or her own control, which allows the researcher to compare relevant exposures on the day of the event and the days before or after the event so as to account for individual-level characteristics and temporally constant confounders. The case-crossover study can be based on ecologic cluster data or individual data. When individual data are available, it allows better control of unmeasured confounders and enables subsequent study of characteristics pertaining to individuals. In the current study, the time-stratified method, which was the most frequently used design, was employed to select control days. The hospitalization date of a patient was considered as the case day; the days that were in the same year, the same month and the same day of the week were considered as the control days. A total of 237 487 case days and 807 233 control days were chosen.

2.5. Analysis of comorbidity patterns

We did a series of analyses to clarify the effects of ambient air pollution on stroke among different comorbidity accumulation patterns and to detect the vulnerable population. In the current study, we focused on three comorbidities, hypertension, diabetes, and hyperlipidemia, which were considered to be dominant risk factors for stroke. First, we classified the patients into 4 groups based on the number of comorbidities. The 4 groups are as follows: 1) Patients without hypertension, diabetes and hyperlipidemia; 2) patients with one of the following comorbidities: hypertension, diabetes, or dyslipidemia; 3) patients with two of the following comorbidities: hypertension, diabetes, or dyslipidemia; 4) patients with all of the following comorbidities: hypertension, diabetes, or dyslipidemia. The main models and lag-effect models were fitted in each group. Second, we divided the patients according to comorbidity accumulation pattern. The accumulation of comorbidities in this study started from hypertension, the major risk factor of stroke. The effect estimates of hypertension patients were compared with non-hypertension patients. Then the effects of patients with hypertension and diabetes were compared with patients with hypertension but without diabetes. Eventually, the effects of patients with hypertension, diabetes, and hyperlipidemia were compared with patients with hypertension, diabetes but without hyperlipidemia.

2.6. Statistical methods

2.6.1. Conditional logistic regression

We fitted conditional logistic regression models to estimate the odds of being hospitalized for stroke. Each of the air pollutants was included in the model as a continuous variable separately. We divided the concentration of each pollutant by the its interquartile range (IQR), so that we could obtain the risk associated with an increase of one IQR in pollutant concentration. Meteorological factors, including air pressure, wind speed, relative humidity, and daily temperature were introduced to the model by natural cubic spline functions of 3 degrees of freedom (*df*). We chose df = 3 for meteorological factors to capture the non-linear relationships between these factors and health outcomes while avoiding overfitting, consistent with the approach used in most previous studies (Chen et al., 2020b; Cui et al., 2022; Li et al., 2023). To account for the 'holiday effect', we also introduced a dummy variable indicating whether the specific day was a public holiday. In order to depict the lag structures, we calculated the moving average of 0–5 lag days of each pollutant: Lag 0 denoted the exposure on the case day or the control day, Lag 01 denoted the arithmetic mean exposure on the day and the previous 1 day, Lag 02 denoted the arithmetic mean exposure on the day and previous 2 days, and so on in a similar fashion. The selection of Lag 01 to Lag 05 days was based on prior research and the physiological understanding that the effects of air pollution on health outcomes can have short-term lagged impacts (Toubasi and Al-Sayegh, 2023). For each of the 8 pollutants, we fitted a lag-effect model in which exposure of different lag days (from Lag 01 to Lag 05) was taken as the independent variable.

Among the patients, subgroups were classified according to their gender and age (age <65, age ≥ 65), and subgroup analysis was performed to determine whether age and gender modify the association. Sensitivity analyses were performed in the vulnerable population detected by the analysis of comorbidity patterns to test the robustness of the results: (1) We adjusted *df* of the meteorological factors from 2 to 5. (2) We constructed multi-pollutant models in which the pollutants with Spearman rank correlation coefficient less than 0.7 were adjusted.

2.6.2. Marginal 'between-within' (BW) model

Case-crossover study design has a good capacity to control for unmeasured confounders because it utilizes clusters (a patient's own case and control days). Typically, fixed-effects models find application in the examination of clustered data, where they incorporate all consistent confounding variables related to the clusters into specific intercepts corresponding to each cluster (Sjölander, 2021). However, for binary outcomes, conditional logistic regression models cannot be used to predict risks or estimate marginal counterfactual means (Sjölander, 2021). Recently, Arvid Sjolander proposed the marginal BW model as an improved method of the logistic BW model (Neuhaus and Kalbfleisch, 1998; Neuhaus and Mcculloch, 2006), which utilizes clustered design to estimate marginal causal effects. The simulation study showed that by fitting a marginal BW model and utilizing regression standardization, counterfactual risks of a binary outcome could be estimated for a specific exposure level and could be contrasted to present marginal causal

effects.

In the current study, we employed the marginal BW model and regression standardization to estimate the causal effects of ambient air pollution in a counterfactual framework. Patients were considered as independent clusters. Each cluster consisted of personal air pollutant exposure of the same patient at case and control days, as well as the corresponding outcome. The cluster-constant confounders were a group of unmeasured factors, including individual-level characteristics and temporal trends. The cluster-varying confounders were meteorological factors and an indicator of a public holiday. In our marginal BW models, the response variable was the binary hospitalization outcome and the independent variables were the personal exposure to air pollutant; the covariates were the other pollutants with Spearman rank correlation coefficient less than 0.7, meteorological factors, and the holiday indicator. The mean exposure level of the pollutants and meteorological factors in each cluster were added to the model to control for unmeasured cluster-constant confounders. Meteorological factors were introduced in the models with natural cubic spline functions of 3 degrees of freedom (*df*). After the marginal BW model was fitted, we used regression standardization to estimate the counterfactual probability of hospitalization risk if all patients were exposed to mild pollution (25th percentile of concentration, P_{25}), severe pollution (75th percentile of concentration, P_{75}), and extremely severe pollution (99th percentile of concentration, P_{99}). The regression standardization method was described elsewhere (Sjölander, 2016, 2018). Briefly, the fitted model is used to estimate hospitalization risk for specific concentrations of pollutants for each observed level of measured confounders, and the estimates are averaged. We estimated the causal effects of ambient air pollution on hospitalization risk in the vulnerable population identified by the analysis of comorbidity patterns.

All calculations, statistical analyses, and statistical graph were performed using R 4.0.5. 'survival' package was utilized to fit conditional logistic models. 'stdReg' package was utilized to perform the regression standardization based on the fitted marginal BW models. We reported the estimated effects of the conditional logistic models by excess risk (ER) associated with every IQR increase of each pollutant ($ER = \left(e^{IQR\times\beta} - 1\right) \times 100\%$) (Wang et al., 2019). In this formula, "*e*" represents the base of the natural logarithm, β represents the regression coefficient for each pollutant, and *IQR* denotes the interquartile range of the concentration for each pollutant. The significance level is 0.05.

3. Results

3.1. Statistical description and Spearman's correlation

Among the identified 237 487 stroke admission cases from 2014 to 2017 in Beijing, 89.16% were IS and 10.80% were HS. The mean age was 68.23. Patients ≥65 accounted for 60.31%, and males accounted for 62.07%. 76.26% of patients had a history of hypertension, 36.75% had a history of diabetes, and 62.44% had a history of hyperlipidemia. 21.02% of patients had all of the three comorbidities (Table 1). Table 2 displays the dispersion of ambient air pollution for both the days of cases and of controls. Fig. 2 illustrates the outcomes derived from conducting Spearman rank correlation analysis between the pollutants and the meteorological factors.

3.2. Association in the total population

The estimated effects at the exposure day are shown in Table 3. There were significant positive associations between $PM_{2.5}$, PM_{10}, PM_1, $PM_{1\text{-}2.5}$, NO_2, CO, and O_3 and the risk of being hospitalized for overall stroke and IS. In terms of particulate matters (PM), $PM_{2.5}$ exhibited the highest effect estimate, with an ER (%) of 1.184% (95% CI: 0.487%–1.885%) for overall stroke and 1.353% (95% CI: 0.612%–2.099%) for IS. In terms of gaseous pollutants, O_3 exhibited the highest effect estimate, with an ER (%) of 1.742% (95% CI: 0.258%–3.248%) for overall stroke and 1.944% (95% CI: 0.377%–3.536%) for IS. The estimated effects of SO_2 were not found to be significant. Fig. 3 illustrates the lag effect patterns. The positive association of PM_{10}, PM_1, CO, and O_3 was observed throughout the entire lag period from Lag 0 to Lag 05. However, the lag effects of $PM_{1\text{-}2.5}$ appeared relatively late, specifically at Lag 04. As shown in the supplementary materials, Table S1, Table S2, and Table S3 present the results of subgroup analysis, which revealed more significant effect estimates among patients aged ≥65 and males.

Table 1
Characteristics of the study population in terms of demographics.

Characteristics	n
Overall stroke (%)	
Ischemic stroke	211 741 (89.16)
Hemorrhagic stroke	25 641 (10.80)
Unclassified	105 (0.04)
Age (mean ± SD)	68.23 ± 12.86
<65 (%)	94 249 (39.69)
≥65 (%)	143 238 (60.31)
Gender (%)	
Male	147 404 (62.07)
Female	90 083 (37.93)
History of comorbidities (%)	
Hypertension	181 117 (76.26)
Diabetes	87 288 (36.75)
Hyperlipidemia	148 277 (62.44)
Number of comorbidities (%)	
0	19 695 (8.29)
1	68 823 (28.98)
2	99 048 (41.71)
3	49 921 (21.02)
Accumulation pattern of comorbidities (%)	
Hypertension, and diabetes	71 563 (30.13)
Hypertension, but no diabetes	109 554 (46.13)
Hypertension, diabetes, and hyperlipidemia	49 921 (21.02)
Hypertension, diabetes, but no hyperlipidemia	21 642 (9.11)

Table 2
Exposure levels at case days and control days.

Ambient air pollution	Mean	SD	Percentile			
			25th	50th	75th	99th
Case days (n = 237 487)						
$PM_{2.5}$ (μg/m^3)	72.03	58.68	31.70	57.10	92.10	295.50
PM_{10} (μg/m^3)	113.93	73.44	64.10	98.10	141.50	383.40
PM_1 (μg/m^3)	41.45	36.10	16.84	31.07	52.33	175.91
$PM_{1\text{-}2.5}$ (μg/m^3)	30.58	25.89	13.85	24.51	38.69	137.33
SO_2 (μg/m^3)	15.68	16.99	5.06	9.65	19.37	83.26
NO_2 (μg/m^3)	49.47	24.34	32.41	43.84	60.66	127.33
CO (mg/m^3)	1.22	0.94	0.68	0.95	1.39	5.02
O_3 (μg/m^3)	95.91	59.24	51.03	85.02	133.84	247.03
Control days (n = 807 233)						
$PM_{2.5}$ (μg/m^3)	71.86	57.76	32.00	57.10	92.30	291.50
PM_{10} (μg/m^3)	113.77	71.85	64.70	98.30	141.70	377.00
PM_1 (μg/m^3)	41.38	35.57	17.00	31.24	52.45	174.14
$PM_{1\text{-}2.5}$ (μg/m^3)	30.49	25.42	13.98	24.48	38.71	136.10
SO_2 (μg/m^3)	15.64	16.91	5.03	9.63	19.46	83.22
NO_2 (μg/m^3)	49.23	23.96	32.44	43.77	60.35	125.97
CO (mg/m^3)	1.21	0.92	0.68	0.95	1.38	4.92
O_3 (μg/m^3)	96.20	58.95	51.18	86.05	134.64	245.77

3.3. Effects in different comorbidity accumulation patterns

Fig. 4, Fig. S1, and Fig. S2 (Supplementary materials) presents the comparison of the estimated effects when focused on single comorbidity. For overall stroke and IS, the associations were estimated to be stronger among patients with hypertension or diabetes compared to those without these comorbidities, while the associations were similar between patients with hyperlipidemia and those without. For HS, we noticed significant positive associations between NO_2 and CO with the

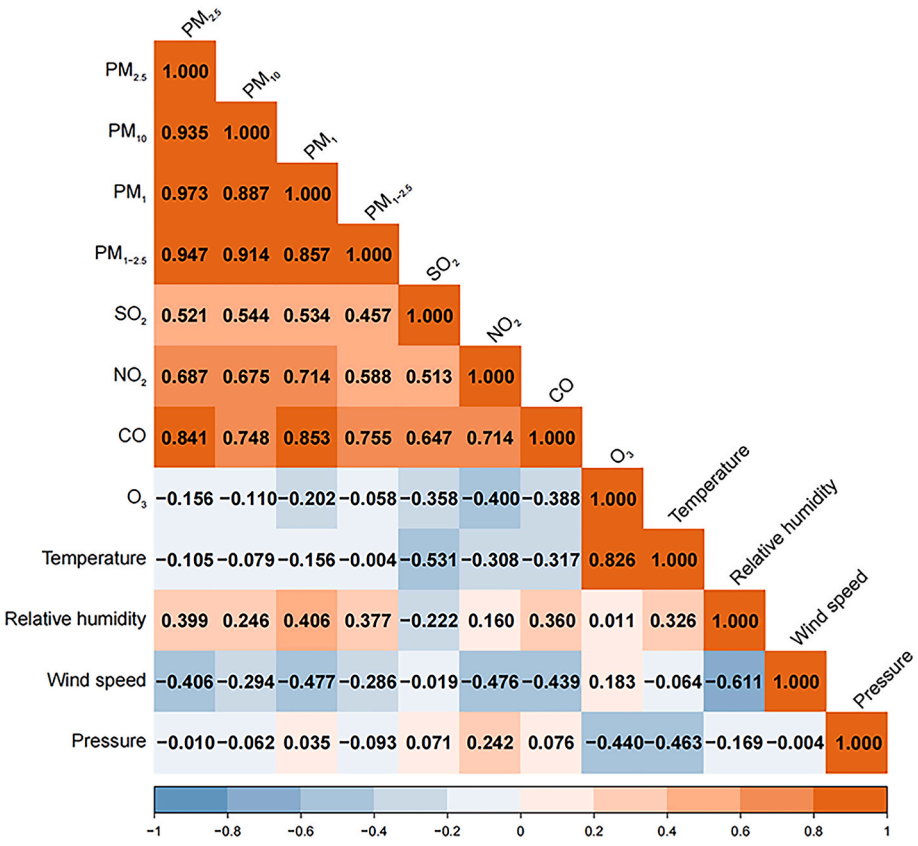

Fig. 2. Spearman rank correlation coefficients. Note: All correlations were statistically significant.

Table 3
Estimated excess risk (%) of hospital admission for stroke at the exposure day (per interquartile range increase).

Pollutant	IQR	Excess risk (%)		
		Overall stroke	Ischemic stroke	Hemorrhagic stroke
$PM_{2.5}$	60.30 μg/m^3	1.184 (0.487, 1.885)[a]	1.353 (0.612, 2.099)[a]	−0.011 (−2.049, 2.069)
PM_{10}	77.10 μg/m^3	0.965 (0.310, 1.625)[a]	1.082 (0.386, 1.783)[a]	0.171 (−1.758, 2.138)
PM_1	35.45 μg/m^3	1.115 (0.416, 1.819)[a]	1.200 (0.458, 1.948)[a]	0.546 (−1.525, 2.661)
$PM_{1\text{-}2.5}$	24.76 μg/m^3	0.873 (0.303, 1.446)[a]	1.067 (0.462, 1.677)[a]	0.594 (−1.003, 2.218)
SO_2	14.40 μg/m^3	−0.436 (−1.153, 0.285)	−0.244 (−1.007, 0.524)	−1.650 (−3.729, 0.473)
NO_2	27.97 μg/m^3	1.422 (0.491, 2.362)[a]	1.586 (0.597, 2.584)[a]	0.377 (−2.372, 3.204)
CO	0.70 mg/m^3	1.228 (0.692, 1.768)[a]	1.318 (0.748, 1.891)[a]	0.594 (−1.003, 2.218)
O_3	83.30 μg/m^3	1.742 (0.258, 3.248)[a]	1.944 (0.377, 3.536)[a]	−0.141 (−4.683, 4.617)

Note.
[a] $P < 0.05$.

risk of hospital admission among patients with hyperlipidemia, a significant positive association of NO_2 among patients without diabetes, and a significant negative association of O_3 and SO_2.

Fig. 3–5 present the associations between ambient air pollution and the risk of being hospitalized for overall stroke, IS, and HS in patients with different numbers of the comorbidities. We noticed significant positive associations between exposure to $PM_{2.5}$, PM_{10}, PM_1, $PM_{1\text{-}2.5}$, NO_2, and CO, mainly in patients with 2 comorbidities. For O_3, the association was stronger and more significant in patients with 3 comorbidities. Moreover, as the lag period extended, the association for $PM_{2.5}$, PM_{10}, and $PM_{1\text{-}2.5}$ in patients with 3 comorbidities also became significant, observed at Lag 05. Additionally, we observed a negative association of SO_2 at some lag days. The effect estimates of HS were predominantly insignificant and had relatively larger confidence intervals.

Fig. 6, Fig. S5, and Fig. S6 (Supplementary materials) present the effect estimates for overall stroke, IS, and HS in patients with different accumulation patterns of the comorbidities. In general, when exposed to PM, the patients with hypertension, and diabetes, but without hyperlipidemia had larger and more significant estimated ER (%) for overall stroke and IS. For the patients with all three comorbidities, the associations between $PM_{2.5}$, PM_{10}, and $PM_{1\text{-}2.5}$ with the risks of overall stroke and IS were not statistically significant until Lag 05. The negative association of SO_2 with IS observed in the whole study population disappeared. When exposed to NO_2 and CO, patients with hypertension but without diabetes had larger and more significant estimated ER (%). When exposed to O_3, patients with hypertension, diabetes, and hyperlipidemia had larger and more significant estimated ER (%). Hospital admissions for HS were mainly unrelated to ambient air pollution exposure.

3.4. Sensitivity analysis

When we adjusted the *df* of the meteorologic factors from 2 to 5, the estimated ER (%) remained almost the same (Supplementary materials, Fig. S7). The estimated ER (%) from the single-pollutant model and multi-pollutant model of each pollutant were roughly similar. The positive association between NO_2 and hospitalization for overall stroke and IS became significant in the multi-pollutant models at some lag days. The association of $PM_{2.5}$, PM_{10}, and $PM_{1\text{-}2.5}$ and hospitalization for IS became insignificant at some lag days (Supplementary materials, Fig. S8).

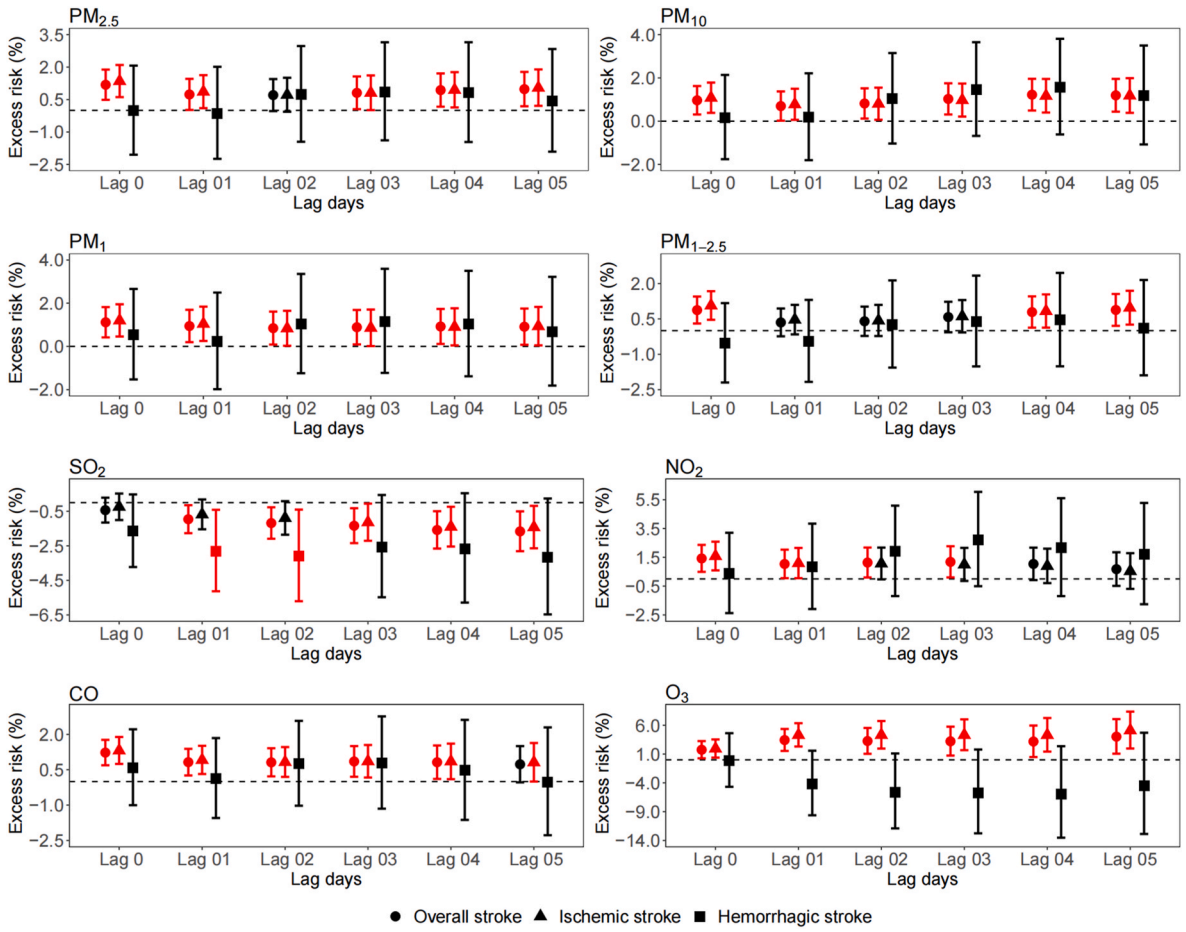

Fig. 3. Lag effects of air pollutants on the risk of hospitalization for stroke. Note: Excess risks of statistical significance were indicated in red.

3.5. Causal relationship

Based on the results obtained from the conditional logistic models, we have identified the following pollutant-specific vulnerable population: patients with hypertension and diabetes but without hyperlipidemia were found to be vulnerable to PM, patients with hypertension but without diabetes were found to be vulnerable to NO_2 and CO, and patients with comorbidities of hypertension, diabetes, and hyperlipidemia were found to be vulnerable to O_3. The estimated counterfactual risk and odd risk (OR) of the vulnerable population were presented in Table 4 and Table S4 (Supplementary materials). For the estimated causal effects of $PM_{2.5}$, PM_{10}, PM_1, $PM_{1\text{-}2.5}$, NO_2, and CO on overall stroke, we observed statistically significant OR of exposure to severe pollution (P_{75}) and extremely severe pollution (P_{99}) compared with mild pollution (P_{25}). For the causal effect of O_3 on overall stroke, we only observed statistically significant OR of exposure to extremely severe pollution (P_{99}) compared with mild pollution (P_{25}) at lag 05. For the causal effects of ambient air pollution on IS, we observed statistically significant OR of exposure to severe pollution (P_{75}) and extremely severe pollution (P_{99}) of PM_{10}, PM_1, NO_2, CO, and statistically significant OR of exposure to severe pollution (P_{75}) of O_3 at lag 05. Statistical significance was not observed in the estimated causal effects of $PM_{2.5}$ and $PM_{1\text{-}2.5}$.

4. Discussion

In this particular investigation utilizing the case-crossover approach, conducted at an individual level with a substantial sample size, we sought to investigate the short-term effects of eight ambient air pollutants on the risk of hospital admission for stroke in patients with various comorbidity patterns. With the exception of SO_2, we observed a positive association between the increase of the other seven air pollutants and the risk of overall stroke and IS. The effects of ambient air pollutants varied among patients with different comorbidity patterns. We identified vulnerable comorbidity accumulation patterns for each of the seven pollutants. The causal effects estimated within a causal framework were more conservative compared to those estimated using traditional regression models. The causal effects were predominantly observed for PM_{10}, PM_1, NO_2, and CO.

In the past few years, mounting evidence indicated that short-term exposure to ambient air pollution could increase the risk of cerebrovascular diseases, including stroke (de Bont et al., 2022; Hahad et al., 2020; Verhoeven et al., 2021). Wu et al. (2022) analyzed the association between county-level $PM_{2.5}$, PM_{10}, and PM_1 and the incidence of stroke in Shandong Province. They observed significantly positive associations between PM with overall stroke and IS, but not with HS (Wu et al., 2022b). They reported that the attributable fractions of total stroke were 6.9% (95%CI: 5.1%, 8.5%), 5.6% (95%CI: 4.2%, 6.8%) and 5.6% (95% CI: 3.9%, 7.1%) for PM_1, $PM_{2.5}$, and PM_{10}, respectively (Wu et al., 2022b). Another study demonstrated that the relative risks on IS per 10 $\mu g/m^3$ increase in PM_1, $PM_{2.5}$, and PM_{10} were 1.014 (95%CI: 1.005, 1.0023), 1.007 (95%CI: 1.000, 1.014) and 1.005 (95%CI: 1.001, 1.009), respectively (Chen et al., 2020b). In addition, the gaseous pollutants were also found to be risk factors of stroke (Cui et al., 2022; Czernych et al., 2023). Our results were roughly in line with these studies. But we also found that short-term exposure to SO_2 was negatively associated with stroke admission risk at some lag days. This finding is consistent with previous research by Cui M et al., who reported negative associations between NO_2 at a 3-day lag and SO_2 at a 7-day lag with the risk of

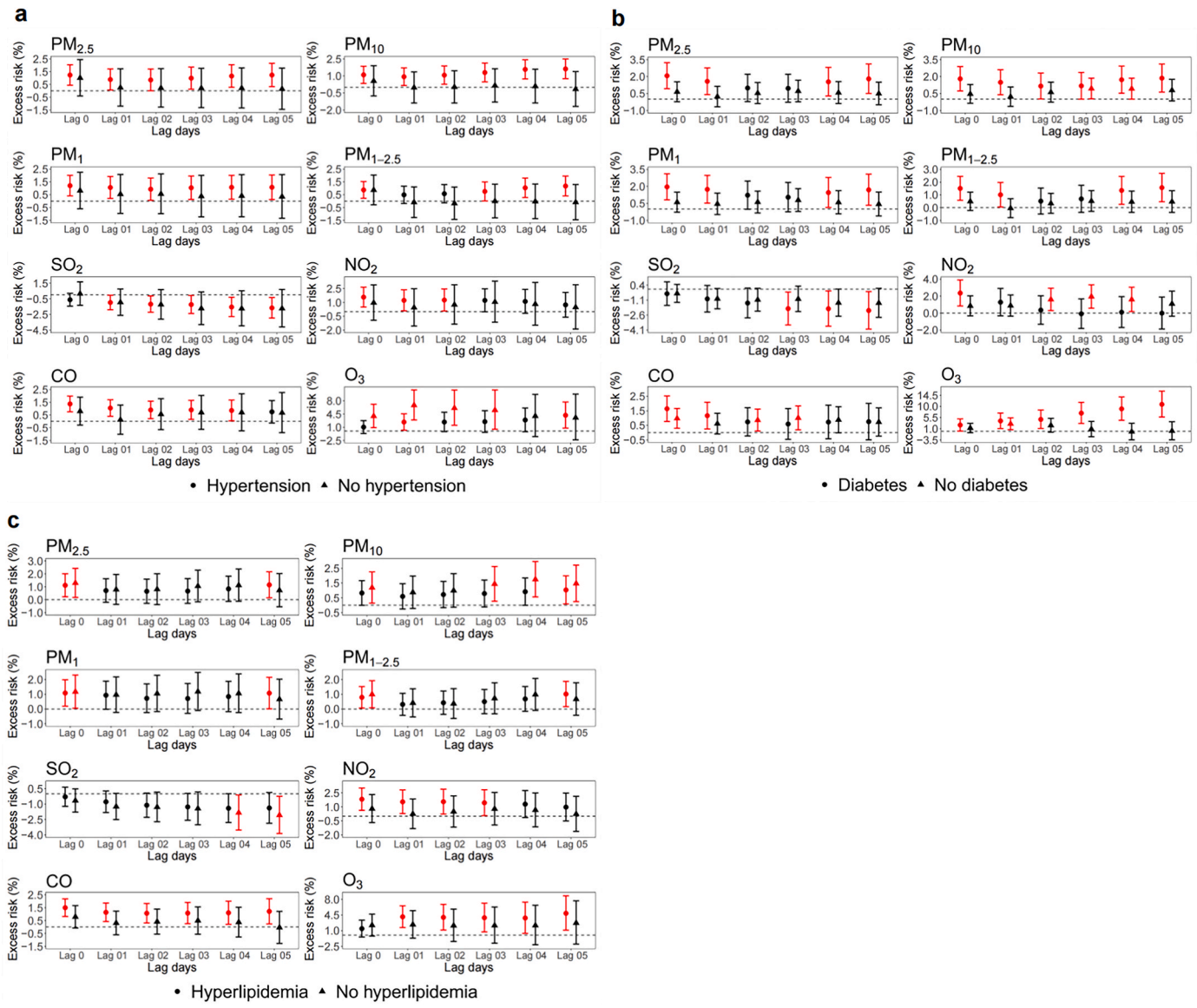

Fig. 4. Effect estimates of the pollutants on the risk of being hospitalized for overall stroke in patients with different comorbidities. Note: Statistically significant excess risks were indicated in red. a: the association in patients with hypertension and without hypertension. b: the association in patients with diabetes and without diabetes. c: the association in patients with hyperlipidemia and without hyperlipidemia.

IS admission (Cui et al., 2022). We hypothesize that the negative association observed for SO_2 might be attributed to a potential "harvesting" effect caused by other pollutants (Smith, 2003). Specifically, increased concentrations of other pollutants could lead to a higher incidence of stroke among susceptible individuals, resulting in their hospitalization. Consequently, this might lead to a temporary reduction in stroke incidence observed later. Given these complexities, we could not conclude that SO_2 has a protective effect on stroke risk based on our findings alone. Further research is needed to better understand the impact of SO_2 on the risk of cerebrovascular diseases.

The main focus of our study was to investigate whether the effects of pollutants vary among different comorbidity patients, among patients with different numbers of comorbidities, and with different comorbidity accumulation patterns, as well as to identify the vulnerable population. The comorbidities of interest in the current study were hypertension, diabetes, and hyperlipidemia. It has been reported that ambient air pollution might increase the burden of multimorbidity (Arias de la Torre et al., 2023; Ronaldson et al., 2022; Su et al., 2023). Hu et al. (2022) explored the link between $PM_{2.5}$ and the accumulation of multimorbidity in a longitudinal study design. Their findings suggested that long-term exposure to $PM_{2.5}$ was associated with a higher risk as well as faster accumulation of cardio-metabolic and respiratory multimorbidity (Hu et al., 2022). Yuan et al. (2023) demonstrated a significant synergistic effect between atherosclerotic cardiovascular disease risk and long-term $PM_{2.5}$ exposure(Yuan et al., 2023). Previous studies on the relation of ambient air pollution and stroke risk have primarily focused on examining the differences in effect estimates among individuals with a single comorbidity (Chang et al., 2022; Chen et al., 2020a; Ho et al., 2018; Tang et al., 2021). In consistent with the previous studies, we found that patients with pre-existing hypertension and diabetes had a higher risk when exposed to ambient air pollution. For the first time, we took the number of comorbidities and accumulation patterns into consideration. The aim was to probe the harmful effects of ambient air pollution in a perspective of disease progress. Except for O_3, the larger and more significant estimated effects were not observed among patients with all three comorbidities. For PM, a larger effect size was observed among patients with hypertension and diabetes but without hyperlipidemia. For NO_2 and CO, a larger effect size was

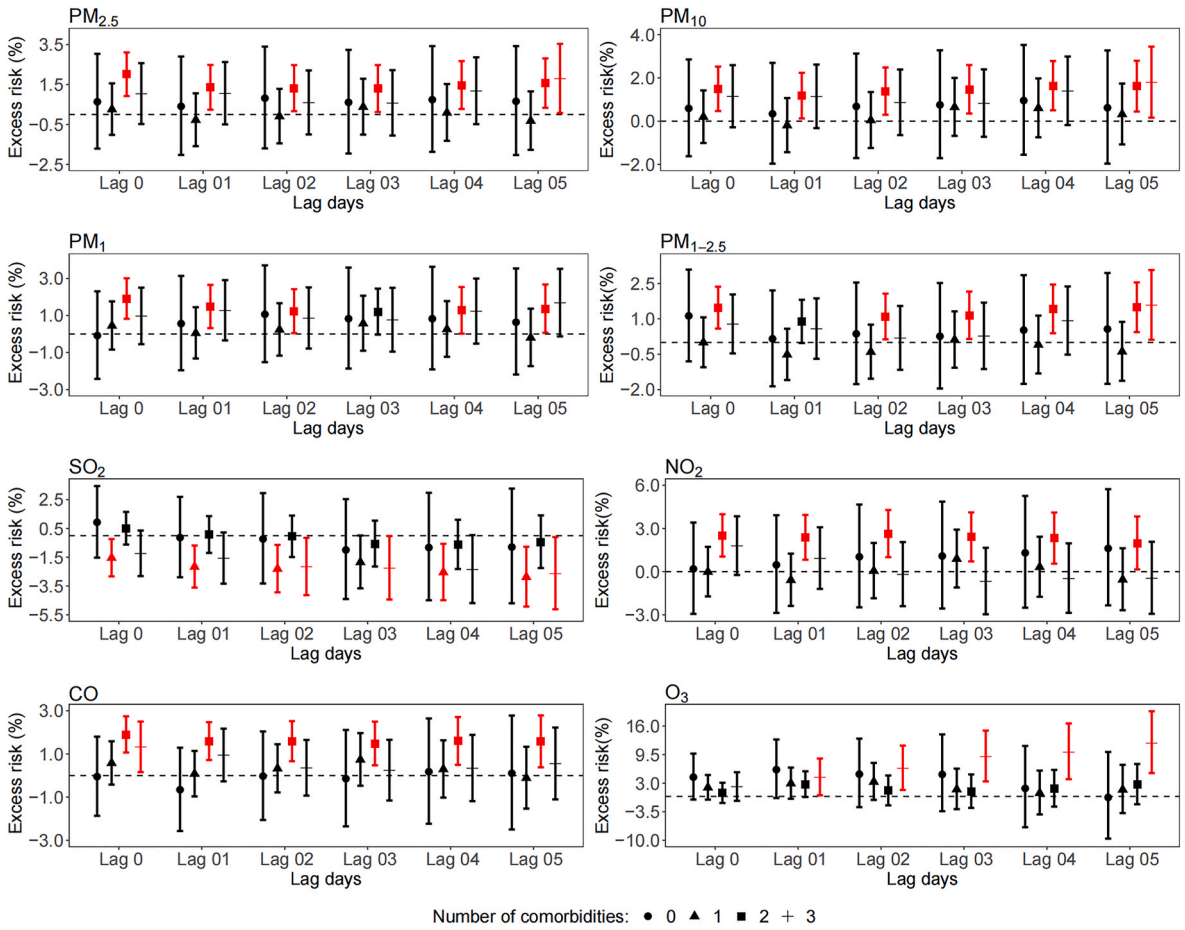

Fig. 5. Effect estimates of the pollutants on the risk of being hospitalized for overall stroke in patients with different numbers of comorbidities. Note: Statistically significant excess risks were indicated in red.

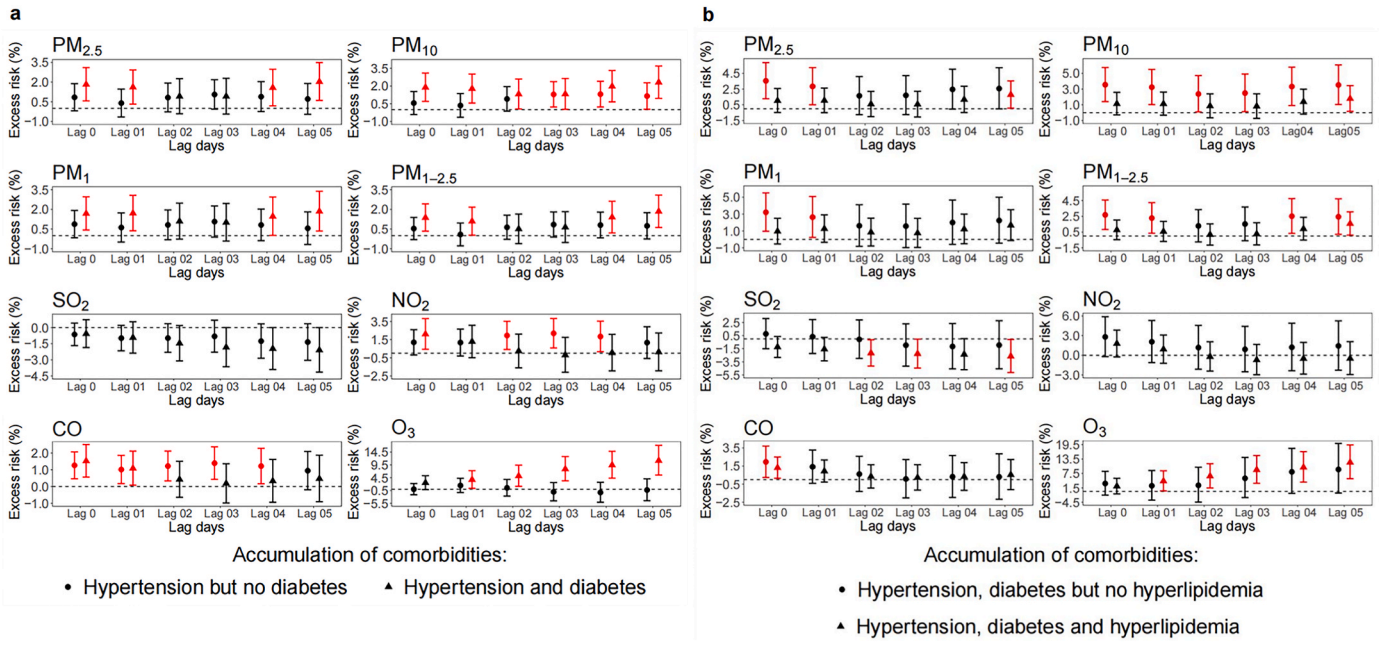

Fig. 6. Effect estimates of the pollutants on the risk of being hospitalized for overall stroke in patients with different accumulation patterns of comorbidities. Note: Statistically significant excess risks were indicated in red. a: The association in patients with hypertension but without diabetes and in patients with hypertension and diabetes. b: The association in patients with hypertension, diabetes but without hyperlipidemia and in patients with hypertension, diabetes, and hyperlipidemia.

Table 4
Counterfactual probability of hospitalization risk and odd risk for overall stroke among the vulnerable population.

Pollutant	Counterfactual risk			Odd risk (OR)	
	P_{25}	P_{75}	P_{99}	$OR_{75/25}$	$OR_{99/25}$
$PM_{2.5}$					
Lag 0	0.222 (0.217, 0.227)	0.230 (0.226, 0.233)	0.255 (0.229, 0.281)	1.043 (1.004, 1.082)[a]	1.200 (1.007, 1.393)[a]
Lag 01	0.223 (0.217, 0.229)	0.229 (0.226, 0.233)	0.250 (0.219, 0.281)	1.035 (0.989, 1.082)	1.161 (0.935, 1.386)
Lag 02	0.226 (0.219, 0.233)	0.228 (0.224, 0.232)	0.234 (0.200, 0.268)	1.011 (0.958, 1.063)	1.048 (0.812, 1.283)
Lag 03	0.225 (0.217, 0.232)	0.229 (0.224, 0.233)	0.242 (0.204, 0.281)	1.023 (0.964, 1.082)	1.104 (0.828, 1.380)
Lag 04	0.221 (0.213, 0.229)	0.230 (0.226, 0.235)	0.262 (0.218, 0.306)	1.054 (0.988, 1.119)	1.254 (0.917, 1.591)
Lag 05	0.220 (0.212, 0.228)	0.231 (0.226, 0.235)	0.267 (0.219, 0.315)	1.061 (0.990, 1.131)	1.290 (0.918, 1.663)
PM_{10}					
Lag 0	0.223 (0.218, 0.227)	0.230 (0.226, 0.233)	0.253 (0.232, 0.274)	1.042 (1.008, 1.075)[a]	1.181 (1.027, 1.334)[a]
Lag 01	0.223 (0.218, 0.228)	0.230 (0.226, 0.233)	0.252 (0.227, 0.277)	1.040 (1.000, 1.080)	1.173 (0.990, 1.357)
Lag 02	0.224 (0.219, 0.230)	0.229 (0.225, 0.233)	0.243 (0.215, 0.271)	1.026 (0.981, 1.072)	1.112 (0.911, 1.313)
Lag 03	0.223 (0.217, 0.229)	0.230 (0.226, 0.234)	0.252 (0.220, 0.284)	1.041 (0.989, 1.092)	1.176 (0.939, 1.414)
Lag 04	0.219 (0.213, 0.226)	0.232 (0.227, 0.236)	0.273 (0.237, 0.308)	1.073 (1.018, 1.129)[a]	1.334 (1.052, 1.617)[a]
Lag 05	0.218 (0.212, 0.225)	0.232 (0.228, 0.237)	0.279 (0.241, 0.317)	1.083 (1.024, 1.143)[a]	1.386 (1.076, 1.696)[a]
PM_{1}					
Lag 0	0.221 (0.217, 0.225)	0.230 (0.227, 0.233)	0.262 (0.240, 0.284)	1.052 (1.021, 1.083)[a]	1.252 (1.086, 1.418)[a]
Lag 01	0.221 (0.216, 0.226)	0.230 (0.227, 0.233)	0.262 (0.236, 0.288)	1.052 (1.015, 1.089)[a]	1.252 (1.054, 1.449)[a]
Lag 02	0.223 (0.217, 0.228)	0.229 (0.226, 0.233)	0.253 (0.225, 0.281)	1.039 (0.997, 1.080)	1.184 (0.974, 1.393)
Lag 03	0.221 (0.215, 0.227)	0.230 (0.226, 0.233)	0.261 (0.230, 0.293)	1.051 (1.006, 1.096)[a]	1.246 (1.008, 1.485)[a]
Lag 04	0.219 (0.213, 0.225)	0.231 (0.227, 0.234)	0.272 (0.238, 0.306)	1.066 (1.017, 1.116)[a]	1.331 (1.059, 1.603)[a]
Lag 05	0.218 (0.212, 0.224)	0.231 (0.227, 0.235)	0.281 (0.244, 0.318)	1.079 (1.026, 1.132)[a]	1.401 (1.095, 1.707)[a]
$PM_{1\text{-}2.5}$					
Lag 0	0.224 (0.220, 0.228)	0.229 (0.226, 0.232)	0.249 (0.228, 0.270)	1.029 (1.002, 1.055)[a]	1.151 (1.004, 1.298)[a]
Lag 01	0.225 (0.220, 0.229)	0.229 (0.225, 0.232)	0.244 (0.218, 0.270)	1.022 (0.989, 1.055)	1.114 (0.936, 1.293)
Lag 02	0.227 (0.222, 0.232)	0.227 (0.224, 0.231)	0.229 (0.200, 0.259)	1.003 (0.964, 1.041)	1.014 (0.821, 1.207)
Lag 03	0.225 (0.220, 0.231)	0.228 (0.224, 0.232)	0.239 (0.205, 0.273)	1.015 (0.971, 1.060)	1.078 (0.843, 1.312)
Lag 04	0.222 (0.216, 0.228)	0.230 (0.226, 0.234)	0.264 (0.224, 0.303)	1.047 (0.997, 1.097)	1.256 (0.959, 1.552)
Lag 05	0.222 (0.215, 0.228)	0.230 (0.226, 0.234)	0.264 (0.221, 0.307)	1.048 (0.994, 1.101)	1.259 (0.939, 1.579)
NO_2					
Lag 0	0.222 (0.220, 0.225)	0.231 (0.229, 0.233)	0.252 (0.241, 0.263)	1.050 (1.028, 1.071)[a]	1.177 (1.096, 1.258)[a]
Lag 01	0.222 (0.216, 0.228)	0.230 (0.226, 0.235)	0.252 (0.225, 0.279)	1.051 (0.996, 1.106)	1.183 (0.974, 1.391)
Lag 02	0.218 (0.215, 0.221)	0.234 (0.232, 0.237)	0.277 (0.261, 0.293)	1.099 (1.068, 1.130)[a]	1.376 (1.245, 1.506)[a]
Lag 03	0.217 (0.214, 0.220)	0.235 (0.232, 0.238)	0.281 (0.264, 0.299)	1.108 (1.073, 1.143)[a]	1.413 (1.264, 1.563)[a]
Lag 04	0.217 (0.214, 0.221)	0.235 (0.232, 0.238)	0.280 (0.261, 0.300)	1.106 (1.068, 1.144)[a]	1.404 (1.242, 1.566)[a]
Lag 05	0.218 (0.215, 0.222)	0.234 (0.231, 0.237)	0.273 (0.253, 0.293)	1.092 (1.052, 1.132)[a]	1.343 (1.178, 1.509)[a]
CO					
Lag 0	0.223 (0.221, 0.224)	0.229 (0.227, 0.23)	0.262 (0.251, 0.273)	1.036 (1.025, 1.047)[a]	1.241 (1.160, 1.321)[a]
Lag 01	0.223 (0.221, 0.225)	0.229 (0.227, 0.23)	0.259 (0.247, 0.272)	1.033 (1.021, 1.046)[a]	1.220 (1.129, 1.311)[a]
Lag 02	0.222 (0.220, 0.224)	0.229 (0.227, 0.23)	0.264 (0.250, 0.278)	1.038 (1.024, 1.052)[a]	1.252 (1.150, 1.355)[a]
Lag 03	0.222 (0.220, 0.224)	0.229 (0.228, 0.23)	0.269 (0.253, 0.284)	1.043 (1.027, 1.058)[a]	1.289 (1.174, 1.403)[a]
Lag 04	0.222 (0.219, 0.224)	0.229 (0.228, 0.23)	0.270 (0.253, 0.286)	1.044 (1.027, 1.060)[a]	1.296 (1.171, 1.422)[a]
Lag 05	0.221 (0.219, 0.224)	0.229 (0.228, 0.23)	0.271 (0.253, 0.289)	1.045 (1.027, 1.063)[a]	1.306 (1.168, 1.443)[a]
O_3					
Lag 0	0.226 (0.222, 0.230)	0.229 (0.225, 0.232)	0.232 (0.220, 0.244)	1.014 (0.978, 1.051)	1.034 (0.946, 1.122)
Lag 01	0.226 (0.221, 0.230)	0.229 (0.225, 0.233)	0.233 (0.219, 0.248)	1.018 (0.973, 1.064)	1.044 (0.934, 1.153)
Lag 02	0.225 (0.220, 0.231)	0.229 (0.225, 0.234)	0.234 (0.218, 0.251)	1.022 (0.970, 1.075)	1.053 (0.926, 1.179)
Lag 03	0.223 (0.217, 0.229)	0.231 (0.226, 0.236)	0.242 (0.223, 0.261)	1.047 (0.988, 1.107)	1.114 (0.966, 1.263)
Lag 04	0.222 (0.216, 0.228)	0.232 (0.226, 0.237)	0.245 (0.224, 0.266)	1.056 (0.991, 1.121)	1.136 (0.972, 1.300)
Lag 05	0.221 (0.215, 0.227)	0.233 (0.227, 0.239)	0.250 (0.228, 0.273)	1.072 (1.001, 1.143)[a]	1.176 (0.994, 1.358)

Note: Counterfactual risk and odd risk were estimated by marginal BW model and regression standardization.
[a] $P < 0.05$.

observed among patients with hypertension but without diabetes. This could be attributed to medication treatment or improved lifestyle habits the patients might have during their exposure to ambient air pollution, which has also been discussed in some previous studies (Lavigne et al., 2016; Seposo et al., 2020). With an increasing number of comorbidities, patients had higher usage of vascular protective medications and

adopted changes in lifestyle habits, resulting in a diminished significance of the effects of gaseous pollutants. However, despite potentially using more cardiovascular protective medications, the harmful impact of PM, which is more prevalent and severe in China (Cui et al., 2022; Hu et al., 2015; Song et al., 2021), remained evident in patients with two comorbidities. As the lag period extended to 5 days, the cumulative effects of PM among patients with all three comorbidities also reached statistical significance. This indicates that patients with more than two comorbidities are also susceptible to air pollution, albeit with a longer lag period. Another potential explanation for the less significant association among patients with all three comorbidities is that ambient air pollution may have a greater impact on the progression of cardiovascular diseases (CVDs) in the early stages. In a previous trajectory analysis of the UK Biobank cohort with a 12-year follow-up, Zhang et al. (2023) observed that $PM_{2.5}$ and oxynitride were associated with an increased likelihood of transitioning from pre-hypertension to CVDs, but the association was not statistically significant for the transition from hypertension to CVDs (Zhang et al., 2023).

We also aimed to investigate the influence of air pollution within a counterfactual framework. Based on the individual-level case-crossover design (Carracedo-Martinez et al., 2010), we estimated the marginal causal effects by employing the marginal BW model and regression standardization (Sjölander, 2016, 2018, 2021). Recently, several studies have emerged utilizing causal inference research designs or statistical methods to investigate the causal relationship between air pollution and health outcomes. However, the majority of studies have primarily focused on mortality outcomes (Bae et al., 2020; Chen et al., 2023; Renzi et al., 2019; Wang et al., 2016), with limited research investigating the causal relationship between a variety of air pollutants and stroke. Chen et al. (2023) assessed the potential causal links of PM and cerebrovascular mortality by using the marginal structural Cox model. The adjusted hazard ratio (HR) of cerebrovascular mortality were 1.041 (95% CI: 1.034 to 1.049) and 1.032 (95% CI: 1.026 to 1.038) for 1 $\mu g/m^3$ increase in $PM_{2.5}$, and PM_{10}, respectively (Chen et al., 2023). Another study conducted in New Jersey employed a variant of the difference-in-differences approach and reported that an interquartile IQR increase in annual $PM_{2.5}$ was causally associated with a 3.0% (95% CI: 0.2%–5.9%) increase in all-cause mortality (Wang et al., 2016). In contrast, Bae et al. (2020) observed a significant negative causal relationship between daily O_3 and mortality (Bae et al., 2020). Within a causal framework, we observed statistically significant OR for overall stroke associated with exposure to all seven pollutants. Among the different particle sizes, significant lag effects were primarily found for PM_{10} and PM_1. We also found that only PM_{10}, PM_1, NO_2, and CO had a causal link with the risk of hospital admission for IS. These results further indicated the significance of the prevention and control of PM_1, which has also been suggested in a previous study (Wu et al., 2022a). It is important to note that while O_3 showed relatively larger estimated effects in our traditional regression model, its significance diminished in our marginal BW model. This could potentially be attributed to the neuroprotective effects of O_3 (Masan et al., 2021; Resitoglu et al., 2018), and the inverse relationship between O_3 and other pollutants. From our findings, we speculate that the heterogeneity of O_3 effects observed in previous epidemiological studies may have been induced by unobserved confounding factors (Chen et al., 2019; Cui et al., 2022; Tian et al., 2018; Zhao et al., 2022a).

In comparison to previous case-crossover studies that utilized ecologic cluster data, our study collected individual-level data and extracted personal exposure to air pollutants from the CHAP dataset, using the patients' residential addresses. Therefore, we anticipated that our approach would allow for a more precise estimation of the association. Unlike previous research, which often focused solely on whether stroke patients had a specific comorbidity, our study conducted detailed subgroup analyses among different comorbidity populations. We aimed to explore whether there are differences in susceptibility to air pollutants among individuals with different comorbidities and various comorbidity accumulation patterns. Additionally, we were the first to attempt using the marginal BW model proposed by Arvid Sjolander within a time-stratified case-crossover design (Sjölander, 2021). This innovative approach was used to explore potential causal relationships between air pollutants and the risk of stroke admission. These aspects of our study represent significant advancements in understanding the complex interactions between air pollution and stroke, and we hope they contribute meaningfully to the existing body of research.

We acknowledge several limitations in our study. Firstly, the estimation of personal exposure relied on geographical coordinates, leading to the exclusion of patients with unidentifiable residential addresses. This potential selection bias could be minimized as these patients were randomly distributed in the population and would not significantly impact our main conclusions. The other limitation of our study is the inability to account for the activity patterns of the participants, such as the time spent in different locations throughout the day. While we estimated air pollutant exposure based on the patients' home addresses, this approach assumes that individuals spend most of their time at home, which may not accurately reflect their true exposure. This limitation is consistent with many previous studies in the field, where detailed activity patterns were also not considered due to data availability constraints. Consequently, there may be some degree of exposure misclassification, which could affect the robustness of our findings. Future studies should aim to incorporate more detailed personal exposure data, including time-activity patterns, to enhance the accuracy of air pollution exposure assessments. Thirdly, as an observational study, there is the possibility of unmeasured confounding factors introducing uncertainty in the results. However, the case-crossover design used in our study provides an advantage in controlling for confounding factors that remain constant at the case and control days, such as life styles, daily activities, occupational history, genetics, and so on. Thus, it can be assumed that the reference exposure time window represents the counterfactual exposure level the patient would have had if he or she had not been admitted to the hospital (Carracedo-Martinez et al., 2010).

5. Conclusion

Benefiting from an expanded sample size and an extended study duration, this case-crossover study at an individual level offers substantial substantiation concerning the link between eight air pollutants and the susceptibility to stroke-related hospitalization. Notably, we investigated the impact of these pollutants among patients with different patterns of comorbidity accumulation, thereby identifying specific vulnerable populations for each pollutant. Moreover, we established a causal link between ambient air pollution and stroke risk within a counterfactual framework. These results underscore the noteworthy impact of outdoor air pollution on stroke occurrence and carry significant implications for the management and mitigation of cerebrovascular conditions.

Funding

This work was supported by the National Natural Science Foundation of China [grant number 81773512], Scientific Research Common Program of Beijing Municipal Commission of Education [grant number KM201810025008] and "Practical Training Plan" of Beijing Municipal Education Commission.

Compliance with ethical standards

Disclosure of potential conflicts of interest.

The authors have no relevant financial or non-financial interests to disclose.

Research involving human participants and/or animals

This is an observational study. Because this study used secondary data and did not involve human subjects directly, informed consent was not obtained from the patients. The medical record data is sourced from the Beijing Municipal Health Commission Information Center. During the data utilization process, we rigorously uphold the privacy of hospitalized patients by concealing any personally identifiable information that is unrelated to the research objectives.

Informed consent

This is an observational study. The study protocol was approved by the institutional review boards of the Ethics Committee of Capital Medical University. The Committee has confirmed that no ethical approval is required.

Data availability

The hospitalization data used in this study is confidential. Ambient air pollution data can be obtained by accessing the CHAP dataset website (https://weijing-rs.github.io/product.html) and applying to the author of CHAP dataset.

CRediT authorship contribution statement

Zemeng Zhao: Writing – review & editing, Writing – original draft, Software, Methodology. **Moning Guo:** Writing – review & editing, Resources, Data curation. **Peng Tan:** Writing – review & editing, Data curation, Conceptualization. **Xue Tian:** Writing – review & editing, Formal analysis. **Lili Luo:** Writing – review & editing. **Hui Luo:** Writing – review & editing. **Xiaonan Wang:** Writing – review & editing, Supervision, Conceptualization. **Xiangtong Liu:** Writing – review & editing, Supervision. **Xiuhua Guo:** Writing – review & editing, Supervision. **Jing Wei:** Writing – review & editing, Validation, Methodology, Data curation, Conceptualization. **Yanxia Luo:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization.

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.

Acknowledgements

We would like to express our gratitude to the Beijing Municipal Health Commission Information Center, the Beijing Air Pollution and Metrological Data Center, and the authors of the CHAP datasets for their valuable contributions. We sincerely thank all authors who critically revised this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.apr.2024.102308.

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