

# Urban air pollution and emergency admissions for cerebrovascular diseases in Taipei, Taiwan

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## KEYWORDS

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Stroke;  
Air pollution;  
Carbon monoxide;  
Particulate matters;  
Epidemiology

**Aims** This study was designed to evaluate the association between urban air pollutants and emergency admissions for cerebrovascular diseases.

**Methods and results** Daily emergency admissions for cerebrovascular diseases (ICD-9-CM, 430–437) to the National Taiwan University Hospital were regressed against daily concentrations of carbon monoxide (CO), nitrogen dioxide (NO<sub>2</sub>), sulphur dioxide (SO<sub>2</sub>), ozone (O<sub>3</sub>), and particulate matters with aerodynamic diameter <2.5 (PM<sub>2.5</sub>) and 10 µm (PM<sub>10</sub>) from 12 April 1997 to 31 December 2002 in Taipei metropolitan areas by the Poisson regression models adjusting for meteorological conditions and temporal trends. Single-pollutant models showed O<sub>3</sub> lagged 0 day, CO lagged 2 days, and PM<sub>2.5</sub> and PM<sub>10</sub> lagged 3 days were significantly associated with increasing emergency admissions for cerebrovascular diseases and CO lagged 2 days was significantly associated with increasing emergency admissions for strokes (ICD-9-CM, 430–434). Such association remained significant for O<sub>3</sub>, CO, and cerebrovascular admissions after adjusting for PM<sub>2.5</sub> and PM<sub>10</sub> in two-pollutant models. The odds ratios were 1.021–1.022 per 31.3 ppb O<sub>3</sub> and 1.023–1.031 per 0.8 ppm CO, respectively. However, only CO was significantly associated with emergency admissions for stroke in the three-pollutant models with CO, O<sub>3</sub>, and PM<sub>2.5</sub> or PM<sub>10</sub>.

**Conclusion** Emergency admissions for cerebrovascular diseases among adults were positively associated with increasing urban air pollution levels of O<sub>3</sub> lagged 0 day and CO lagged 2 days in Taipei.

## Introduction

Studies on associating air pollution with cerebrovascular mortality have been conducted in several countries. In a study in the Netherlands, short-term exposure to sulphur dioxide (SO<sub>2</sub>), carbon monoxide (CO), and ozone (O<sub>3</sub>) was found to be significantly associated with cerebrovascular mortality [International Classification of Disease, 9th revision (ICD-9), 430–436].<sup>1</sup> Two studies conducted in Seoul, Korea reported that acute effects of air pollutants including particulate matter with diameter <10 µm (PM<sub>10</sub>), nitrogen dioxide (NO<sub>2</sub>), SO<sub>2</sub>, CO, and O<sub>3</sub> were all significantly associated with haemorrhagic and ischaemic deaths (431 and 434 by ICD-9 and 161 and 163 by ICD-10)<sup>2</sup> and stroke mortality (160–169 by ICD-10).<sup>3</sup> One study in Shanghai, China showed that PM<sub>10</sub> and NO<sub>2</sub> were significantly associated with acute stroke mortality (ICD-9, 430–438).<sup>4</sup> However, one study in Hong Kong found no association between air pollution and cerebrovascular mortality (ICD-9, 430–438).<sup>5</sup>

In addition to the mortality studies on the association between air pollution and cerebrovascular diseases, several recent studies were also performed to associate

hospital admissions for cerebrovascular diseases with urban air pollution in USA, European, and Asian countries. One study conducted in nine US cities showed that acute exposure to PM<sub>10</sub>, CO, NO<sub>2</sub>, and SO<sub>2</sub> was significantly associated with hospital admission for ischaemic stroke [International Classification of Disease, 9th revision-Clinical Modification (ICD-9-CM, 434)].<sup>6</sup> Three studies in Europe showed that cerebrovascular admissions [ICD-9, 430–438; ICD-9, 430–436; and 160–169 by the International Classification of Diseases, 10th revision (ICD-10)] were significantly associated with short-term effects of NO<sub>2</sub>,<sup>7,8</sup> and PM<sub>10</sub>.<sup>9</sup> One study in Asia reported significant associations between acute exposure to PM<sub>10</sub>, NO<sub>2</sub>, SO<sub>2</sub>, CO, and O<sub>3</sub> and both primary intracerebral haemorrhage (ICD-9, 431–432) and ischaemic stroke (ICD-9, 433–435) admissions.<sup>10</sup> However, some other studies failed to identify significant associations between air pollution and cerebrovascular admissions (ICD-9, 430–438).<sup>11,12</sup>

Apparently, the association between air pollution and mortality and hospital admissions for cerebrovascular diseases and strokes remained inconclusive because there were no consistent findings on their associations in previous studies. To shed light on this unanswered question, we conducted this study to investigate whether air pollution was associated with hospital admissions for cerebrovascular

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diseases (ICD-9-CM, 430–437) in general and strokes (ICD-9-CM, 430–434) in particular among adults aged above 50 over the 6-year period from 1997 to 2002 in Taipei, Taiwan.

## Methods

### Emergency admissions for cerebrovascular diseases

Our emergency admission data were collected from the National Taiwan University Hospital (NTUH), which is a major medical centre with 2000 beds in Taipei metropolitan areas and serves as a major emergency care centre for all residents in the areas. The population in Taipei metropolitan area, which is situated in northern Taiwan and covers an area of about 1050 km<sup>2</sup>, was approximately 5.91–6.10 millions from 1997 to 2002.<sup>13</sup> Our outcome variables in this study include admissions for cerebrovascular diseases (ICD-9-CM, 430–437), strokes (ICD-9-CM, 430–434), haemorrhagic stroke (ICD-9-CM, 430–432), and ischaemic stroke (ICD-9-CM, 433–434). We obtained all electronic medical records of daily emergency admissions for cerebrovascular diseases from 12 April 1997 to 31 December 2002 to match with the available air pollution data in the same period for further analysis. Each medical record included a patient's admission date, age, sex, and address in addition to discharge diagnoses and diagnostic code of cerebrovascular admissions from ICD-9. Our study population was limited to adults aged above 50 during their admissions because they have been reported to have higher incidence of cerebrovascular diseases than younger population aged below 50 in Taiwan.<sup>14</sup> All haemorrhagic and ischaemic stroke cases admitted to the NTUH were evaluated by the standardized diagnostic criteria, i.e. the National Institute of Health Stroke Scale (NIHSS) score,<sup>15</sup> computed tomography, and/or magnetic resonance tomography, before they were given ICD-9 codes. Such a procedure improved the accuracy of coding different types of stroke by the ICD-9 system in the NTUH.

### Environmental data

Sixteen monitoring stations operated by the Taiwan Environmental Protection Agency spread around the Taipei Metropolitan area and measure hourly data of air pollution and temperature. Five air pollutants, including NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub>, CO, and PM<sub>10</sub>, are measured to track trend of air quality in Taipei in all 16 monitoring stations. Two of these 16 stations measure particulate matter with aerodynamic diameter <2.5 μm (PM<sub>2.5</sub>) since 12 April 1997. Accordingly, our study period was limited to 2090 days from 12 April 1997 to 31 December 2002 when the air pollution data of all six pollutants were available. The measured environmental data were used to represent average ambient concentrations in the region using the following procedures. Daily environmental data were summarized by 24 h arithmetic averages (noon-to-noon) of temperature, temperature range, dew point temperature, PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, and SO<sub>2</sub> concentrations, and maximum values of 8 h CO concentrations and 1 h O<sub>3</sub> concentrations for each monitoring station. These environmental data in each monitoring station were then averaged across all 16 monitoring stations to represent daily air pollution situations in the entire Taipei metropolitan areas.

### Modelling approach

Because emergency admissions to hospital for any diseases were naturally rare events, we chose the Poisson models as an appropriate approach to perform data analysis in our study. We first constructed a base model with potential confounders,<sup>16</sup> including three time-trend variables, which were year, month, and day-of-week, and three temperature variables, which were daily temperature, daily temperature difference between minimum and maximum temperatures, and dew point temperature, to predict daily emergency admissions for cerebrovascular diseases. Generalized additive models (GAMs) were used to adjust for

non-linear relation between confounders and emergency admissions.<sup>17</sup> Smooth function in GAM was used to control temperature effects and time-trend variables in our models. The general form of our base model is  $\log(E(Y_t)) = \alpha I_t + \beta X_t$ .  $Y_t$ , which obeys Poisson distribution with parameter  $\mu = E(Y_t)$ , represents hospital emergency admissions on day  $t$  in the equation.  $I_t$  is a matrix containing the time function of year, month, and day-of-week.  $X_t$  is the temperature covariate matrix containing three temperature variables. The matrices of  $\alpha$  and  $\beta$  are coefficients for covariate matrices  $I_t$  and  $X_t$ , respectively. We then built single-pollutant models by adding to the base model, one by one, data regarding air pollution levels for each of six air pollutants lagged 0 to 3 days. As previous study indicated that the increased mortality or hospital admissions were associated with high air pollution levels on the same day or the previous 2 days,<sup>18</sup> we used the cumulative lag up to 3 days in our models. The assumption of the linearity between the log of emergency admissions and air pollution was graphically analysed by using the locally weighted running-line smoother (loess) for smoothing function.<sup>19</sup> The air pollutants, whose odds ratios (ORs) and 95% confidence intervals (CIs) for interquartile range (IQR) change in pollution levels less than a significance level of 0.05 in the single-pollutant models, were considered for further analyses in our multi-pollutant models. When there were several significant ORs at different day lags for one specific air pollutant, we used only the one with the maximum OR and combined the air pollutants with the same or shorter time lags together in our multi-pollutant models. A significance level of 0.05 with two-sided distribution was used to determine statistical significance in our models. Finally, we examined residuals plots to check the residuals' autoregressive effects and determine whether autoregressive terms should be added to remove serial correlations between the repeated daily measures in all single-pollutant and multi-pollutant Poisson models. The selection criterion of goodness-of-fit was assessed using Akaike's information criterion.<sup>20</sup>

## Results

There were 8582 cerebrovascular admissions in NTUH between 12 April 1997 and 31 December 2002. Among them, there were 7341 cerebrovascular patients aged above 50 (mean age 69.7, standard deviation 9.9, and range 50–100 years), which accounted for 85% of total cerebrovascular admissions. Among the 7341 adult cerebrovascular patients, there were 690 cases of haemorrhagic stroke and 1494 cases of ischaemic stroke. The gender ratio of cerebrovascular patients between male and female was 3/2. As shown in *Table 1*, daily emergency admissions in NTUH averaged at 3.5 cerebrovascular admissions, 1.0 stroke admission, 0.3 haemorrhagic stroke admission, and 0.7 ischaemic stroke admission for adults aged above 50 during the study period. Daily ambient temperatures and air pollution levels also varied significantly during this period in Taipei. During the 2090 days of our study period, daily temperatures fluctuated between 7.9 and 33.5°C, and ambient air pollution levels differed by nine times for CO, 20 times for O<sub>3</sub>, 15 times for PM<sub>2.5</sub>, 10 times for PM<sub>10</sub>, and 40 times for SO<sub>2</sub>. The IQRs of these environmental data, which were used for calculating ORs in the Poisson regression models, were 8.1°C for daily temperature, 4.2°C for daily difference in temperature, 6.8°C for dew point, 0.8 ppm for CO, 31.3 ppb for O<sub>3</sub>, 19.7 μg/m<sup>3</sup> for PM<sub>2.5</sub>, 25.4 μg/m<sup>3</sup> for PM<sub>10</sub>, 9.6 ppb for NO<sub>2</sub>, and 3.1 ppb for SO<sub>2</sub>, respectively. Pearson correlation between CO, O<sub>3</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> showed no significant correlation between these four air pollutants except PM<sub>10</sub> and PM<sub>2.5</sub> ( $r = 0.61$ ) (*Table 2*).

**Table 1** Summary of daily emergency admissions for cerebrovascular diseases and stroke in the NTUH and environmental conditions in Taipei between 12 April 1997 and 31 December 2002

Variables	No.	Mean	SD	Minimum	Maximum	IQR
Emergency admissions						
Cerebrovascular diseases (ICD-9-CM, 430–437) <sup>a</sup>	2090	3.5	2.0	0	11	3
Strokes (ICD-9-CM, 430–434)	2090	1.0	1.4	0	8	2
Haemorrhagic stroke (ICD, 430–432)	2090	0.3	0.6	0	4	1
Ischaemic stroke (ICD-9-CM, 433–434)	2090	0.7	1.1	0	6	1
Temperature						
Daily (°C)	2090	23.9	5.1	7.9	33.5	8.1
Daily Difference (°C)	2090	6.3	2.7	0.6	16.5	4.2
Dew point (°C)	2090	18.7	4.6	1.0	26.4	6.8
Air pollution						
O <sub>3</sub> (ppb), 1 h maximum	2090	50.9	26.4	7.4	150.3	31.3
CO (ppm), 8 h average	2090	1.7	0.6	0.6	4.4	0.8
SO <sub>2</sub> (ppb), 24 h average	2090	4.3	2.4	0.4	17.1	3.1
NO <sub>2</sub> (ppb), 24 h average	2090	29.9	8.4	8.3	77.1	9.6
PM <sub>2.5</sub> (µg/m <sup>3</sup> ), 24 h average	2090	31.5	16.0	15.6	200.6	19.7
PM <sub>10</sub> (µg/m <sup>3</sup> ), 24 h average	2090	50.2	22.1	16.0	325.4	25.4

SD, standard deviation.

<sup>a</sup>Subarachnoid haemorrhage [International Classification of Disease, 9th revision-Clinical Modification (ICD-9-CM) 430]; other intracerebral haemorrhage (ICD-9-CM, 431); other and unspecified intracranial haemorrhage (ICD-9-CM, 432); occlusion and stenosis of pre-cerebral arteries (ICD-9-CM, 433); occlusion of cerebral arteries (ICD-9-CM, 434); transient cerebral ischaemia (ICD-9-CM, 435); acute, but ill-defined cerebrovascular disease (ICD-9-CM, 436); and other and ill-defined cerebrovascular disease (ICD-9-CM, 437).

**Table 2** Pearson correlation coefficients for air pollutants in Taipei during 1997–2002

Pearson correlation coefficients	O <sub>3</sub>	CO	SO <sub>2</sub>	NO <sub>2</sub>	PM <sub>2.5</sub>	PM <sub>10</sub>
O <sub>3</sub>	1.00					
CO	0.30	1.00				
SO <sub>2</sub>	0.51	0.63	1.00			
NO <sub>2</sub>	0.43	0.77	0.64	1.00		
PM <sub>2.5</sub>	0.33	0.44	0.51	0.50	1.00	
PM <sub>10</sub>	0.43	0.47	0.59	0.64	0.61	1.00

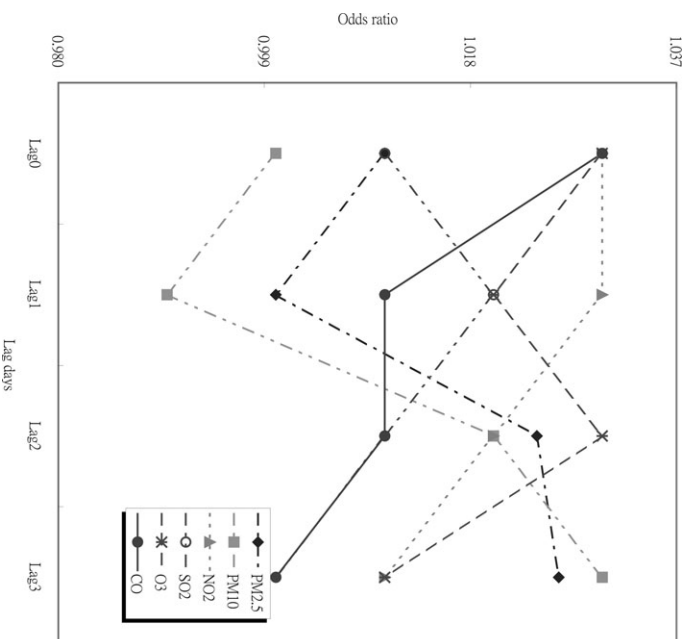
Our base model without air pollutants contained only four key factors, including long-term trend of year and month, short-term temporal variation of day-of-week, and 1-day lagged daily averaging temperatures. By adding individual air pollutants at 0-day to 3-day lags to our single-pollutant models, we found only O<sub>3</sub>, CO, PM<sub>2.5</sub>, and PM<sub>10</sub> at certain day lags were associated with emergency admissions for cerebrovascular diseases among 72 single-pollutant models. There were positive trends in the emergency admissions for cerebrovascular diseases and NO<sub>2</sub> and SO<sub>2</sub> concentrations, although their associations were not statistically significant. As shown in *Table 3*, O<sub>3</sub> lagged 0 day, CO lagged 2 days, PM<sub>2.5</sub> lagged 3 days, and PM<sub>10</sub> lagged 3 days were significantly associated with cerebrovascular admissions, whereas CO lagged 2 days was significantly associated with admissions for strokes. None of the air pollutants was associated with emergency admissions for either ischaemic stroke or haemorrhagic stroke in single-pollutant models. Although the ORs for ischaemic and haemorrhagic strokes were not significant, it is apparent that all ORs for ischaemic stroke were greater than 1, with relatively few ORs for haemorrhagic stroke being greater than 1.

As shown in *Figure 1*, the highest ORs for each IQR increase in these four air pollutants were O<sub>3</sub> lagged 0 day (OR = 1.031; 95% CI = 1.008–1.054), CO lagged 2 days (OR = 1.033; 95% CI = 1.010–1.056), PM<sub>2.5</sub> lagged 3 days (OR = 1.021; 95% CI = 1.005–1.037), and PM<sub>10</sub> lagged 3 days (OR = 1.030; 95% CI = 1.011–1.049). These four air pollutants at specific day lags were then combined together to construct to our multi-pollutant models. Neither NO<sub>2</sub> nor SO<sub>2</sub> was considered in our multi-pollutant models because none of them was significantly associated with emergency admissions for cerebrovascular diseases.

To avoid collinearity due to high correlation, PM<sub>10</sub> and PM<sub>2.5</sub> were fitted separately to our multi-pollutant models. The ORs of emergency admissions for cerebrovascular diseases per IQR change in CO, O<sub>3</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> by two-pollutant and three-pollutant models were summarized in *Table 4*. CO lagged 2 days remained the strongest association with emergency admissions for cerebrovascular diseases among the four air pollutants after controlling other pollutants in multi-pollutant models. The OR was about 1.031 per IQR change in CO concentrations in both two-pollutant and three-pollutant models. The association between O<sub>3</sub> lagged 0 day and emergency admissions for cerebrovascular diseases was significant in two-pollutant models, but marginally significant in three-pollutant models. Both PM<sub>2.5</sub> lagged 3 days and PM<sub>10</sub> lagged 3 days became marginally associated with emergency admissions for cerebrovascular diseases in two-pollutant model, but not in three-pollutant model. As expected, low temperature was significantly associated with increase in emergency admissions for cerebrovascular diseases. The ORs per IQR change in temperature were approximately 0.927 in both two-pollutant and three-pollutant models. We did not apply two-pollutant or three-pollutant models to analyse emergency admissions for haemorrhagic or ischaemic stroke in this study, because no air pollutant was significantly associated with outcomes in single-pollutant models.

**Table 3** ORs of emergency admissions for cerebrovascular diseases, strokes, ischaemic stroke, and haemorrhagic stroke by IQR changes of air pollution levels at the same day, 1-day lag, 2-day lag, and 3-day lag

		O <sub>3</sub>	CO	SO <sub>2</sub>	NO <sub>2</sub>	PM <sub>2.5</sub>	PM <sub>10</sub>
Cerebrovascular diseases	Lag 0	1.031 (1.008, 1.054)	1.029 (0.995, 1.063)	1.008 (0.969, 1.047)	1.032 (0.991, 1.074)	1.006 (0.993, 1.019)	1.001 (0.969, 1.033)
	Lag 1	1.012 (0.969, 1.056)	1.024 (0.994, 1.054)	1.023 (0.994, 1.052)	1.027 (0.997, 1.057)	1.002 (0.990, 1.014)	0.999 (0.978, 1.020)
	Lag 2	1.009 (0.967, 1.054)	1.033 (1.010, 1.056)	1.014 (0.971, 1.058)	1.018 (0.998, 1.038)	1.015 (0.978, 1.052)	1.023 (0.989, 1.057)
	Lag 3	1.000 (0.992, 1.008)	1.007 (0.967, 1.047)	1.001 (0.981, 1.021)	1.006 (0.972, 1.040)	1.021 (1.005, 1.037)	1.030 (1.011, 1.049)
Stroke	Lag 0	1.021 (0.992, 1.050)	1.022 (0.993, 1.051)	0.991 (0.916, 1.066)	0.994 (0.914, 1.074)	0.931 (0.831, 1.031)	0.969 (0.897, 1.041)
	Lag 1	0.984 (0.934, 1.033)	1.024 (0.994, 1.054)	1.014 (0.971, 1.058)	1.013 (0.971, 1.056)	0.936 (0.845, 1.027)	0.992 (0.918, 1.066)
	Lag 2	0.973 (0.913, 1.033)	1.032 (1.009, 1.055)	0.982 (0.942, 1.022)	1.014 (0.975, 1.053)	0.931 (0.820, 1.042)	1.004 (0.993, 1.015)
	Lag 3	0.989 (0.929, 1.049)	1.006 (0.964, 1.051)	0.969 (0.929, 1.010)	1.011 (0.966, 1.056)	0.991 (0.969, 1.013)	1.009 (0.988, 1.030)
Ischaemic stroke	Lag 0	1.046 (0.981, 1.111)	1.055 (0.985, 1.126)	1.044 (0.966, 1.125)	1.025 (0.956, 1.094)	0.981 (0.907, 1.055)	0.984 (0.932, 1.036)
	Lag 1	1.043 (0.961, 1.125)	1.071 (0.994, 1.148)	1.051 (0.969, 1.133)	1.029 (0.955, 1.103)	0.994 (0.920, 1.078)	0.993 (0.939, 1.047)
	Lag 2	1.019 (0.990, 1.048)	1.051 (0.978, 1.124)	1.000 (0.922, 1.078)	1.035 (0.993, 1.078)	0.960 (0.885, 1.035)	0.989 (0.927, 1.041)
	Lag 3	1.087 (0.993, 1.181)	1.064 (0.993, 1.135)	1.039 (0.961, 1.117)	1.051 (0.972, 1.130)	1.059 (0.984, 1.134)	1.042 (0.981, 1.103)
Haemorrhagic stroke	Lag 0	0.989 (0.877, 1.101)	0.982 (0.883, 1.081)	0.918 (0.815, 1.021)	0.963 (0.884, 1.042)	0.870 (0.740, 1.010)	0.966 (0.884, 1.048)
	Lag 1	0.921 (0.799, 1.043)	1.000 (0.895, 1.105)	0.981 (0.876, 1.086)	0.994 (0.907, 1.081)	0.882 (0.761, 1.003)	0.990 (0.908, 1.072)
	Lag 2	0.950 (0.826, 1.074)	0.973 (0.862, 1.084)	0.974 (0.867, 1.081)	1.011 (0.921, 1.101)	0.909 (0.810, 1.008)	1.002 (0.920, 1.084)
	Lag 3	0.882 (0.763, 1.001)	0.992 (0.881, 1.103)	0.910 (0.803, 1.017)	0.980 (0.901, 1.060)	0.921 (0.830, 1.012)	0.974 (0.902, 1.046)

**Figure 1** ORs of hospital emergency admissions for cerebrovascular diseases attributable to IQR changes in air pollutant levels for different lag models with a maximum lag of 3 days.

## Discussion

In general, our results suggested that urban air pollution with mixtures of both gaseous and particulate air pollutants was associated with emergency admissions for cerebrovascular diseases. The three air pollutants responsible for cerebrovascular admissions in our single-pollutant models, i.e. PM<sub>10</sub>, O<sub>3</sub>, and CO, were generally consistent with the air pollutants reported in previous studies on cerebrovascular morbidity (Table 5). For example, hospital admissions for cerebrovascular diseases were reported to be associated with PM<sub>10</sub> in Birmingham of UK and Kaohsiung of Taiwan,<sup>9,10</sup> with CO in Valencia of Spain and Kaohsiung of Taiwan,<sup>7,10</sup> and with O<sub>3</sub> in Kaohsiung of Taiwan,<sup>10</sup> PM<sub>2.5</sub>, which has not yet been reported in previous studies, was found to be associated with cerebrovascular admissions in our study. In contrast, NO<sub>2</sub>, which was associated with cerebrovascular admissions in several previous studies,<sup>7,8,10</sup> was not significantly associated with the cerebrovascular admissions in our study. The reason for the absence of an association with NO<sub>2</sub> with cerebrovascular diseases in this study is probably that NO<sub>2</sub> is highly correlated with PM<sub>10</sub> ( $r = 0.64$ ) and CO ( $r = 0.77$ ) in Taipei during the study period.

In particular, our two-pollutant models showed that two gaseous air pollutants, i.e. O<sub>3</sub> and CO, were more significantly associated with cerebrovascular admissions than two particulate pollutants, PM<sub>10</sub> and PM<sub>2.5</sub>. In our study, three-pollutant models indicated that cerebrovascular admissions were more consistently associated with CO. Our models also suggested a clear time course of pollution effects on cerebrovascular admissions by different air pollutants. There were 0-day lag for O<sub>3</sub>, 2-day lag for CO, and 3-day lag for particulate matters. Our results indicated

**Table 4** ORs of cerebrovascular emergency admissions for IQR changes of air pollution levels by two-pollutant and three-pollutant models

	Lag	ORs	CIs
<b>Two-pollutant model</b>			
<b>O<sub>3</sub> + CO</b>			
O <sub>3</sub>	Lag 0	1.022	1.001, 1.043
CO	Lag 2	1.033	1.011, 1.056
Temperature	Lag 1	0.921	0.882, 0.960
<b>O<sub>3</sub> + PM<sub>2.5</sub></b>			
O <sub>3</sub>	Lag 0	1.021	1.002, 1.040
PM <sub>2.5</sub>	Lag 3	1.009	0.987, 1.031
Temperature	Lag 1	0.923	0.884, 0.962
<b>O<sub>3</sub> + PM<sub>10</sub></b>			
O <sub>3</sub>	Lag 0	1.022	1.001, 1.043
PM <sub>10</sub>	Lag 3	1.018	0.987, 1.049
Temperature	Lag 1	0.931	0.890, 0.972
<b>CO + PM<sub>2.5</sub></b>			
CO	Lag 2	1.023	1.002, 1.044
PM <sub>2.5</sub>	Lag 3	1.014	0.993, 1.035
Temperature	Lag 1	0.929	0.888, 0.970
<b>CO + PM<sub>10</sub></b>			
CO	Lag 2	1.031	1.009, 1.053
PM <sub>10</sub>	Lag 3	1.019	0.988, 1.050
Temperature	Lag 1	0.931	0.888, 0.974
<b>Three-pollutant model</b>			
<b>O<sub>3</sub> + CO + PM<sub>2.5</sub></b>			
O <sub>3</sub>	Lag 0	1.021	0.989, 1.053
CO	Lag 2	1.034	1.001, 1.067
PM <sub>2.5</sub>	Lag 3	1.009	0.987, 1.031
Temperature	Lag 1	0.922	0.883, 0.961
<b>O<sub>3</sub> + CO + PM<sub>10</sub></b>			
O <sub>3</sub>	Lag 0	1.030	0.988, 1.072
CO	Lag 2	1.032	1.013, 1.052
PM <sub>10</sub>	Lag 3	1.015	0.985, 1.045
Temperature	Lag 1	0.933	0.890, 0.976

that gaseous air pollutants related to vehicle emissions and photochemical formation were more significantly associated with cerebrovascular admissions than other particulate air pollutants in the urban environments of Taipei.

It has been proposed that air pollution can induce alveolar inflammation, leading to exacerbation of pre-existing lung disease, increased blood coagulability, and an associated increased risk of cardiovascular events.<sup>21</sup> Such biological plausibility may also be applied to the association between air pollution and cerebrovascular diseases. Studies have shown that exposures to concentrated ambient PM and O<sub>3</sub> would produce an inflammatory response in humans,<sup>22,23</sup> animal models,<sup>24,25</sup> and *in vitro* cellular models.<sup>26,27</sup> It has been reported that high concentrations of CO, as carboxyhaemoglobin (COHb) in blood, could produce signs and symptoms of headache, dilation of the cutaneous blood vessels, and dyspnoea in exposed subjects when their COHb concentrations were over 10%.<sup>28</sup> An *in vivo* study also showed that high concentrations of CO could also impair pigeons' cardiovascular system by damaging their arterial walls.<sup>29</sup> However, no current study is available to explain whether such a physiological response to high CO concentrations can also occur at comparatively low ambient concentrations. There are other important effects such as systemic oxidant stress and inflammation that are

likely to contribute to altered endothelial function and atherosclerotic plaque instability.<sup>21</sup> These effects are quite possibly present in the cerebrovascular system, although at this time there is no proof.

It should be noted that emergency admissions for haemorrhagic and ischaemic strokes were not associated with any air pollutants in single-pollutant models in this study. Given that there are only 690 and 1494 cases from haemorrhagic and ischaemic stroke admissions, respectively, over the 2090 study days, we believe that insufficient sample size is possibly the reason why no air pollutants were significantly associated emergency admissions for either haemorrhagic or ischaemic stroke in our study. Apparently, no differences in pollution effects on ischaemic vs. haemorrhagic stroke were found in single-pollutant models because the CIs for many of these estimates included 1. However, 100% of the ORs for gaseous pollutants were 1 or above for ischaemic stroke, whereas only 31% (5/16) of the ORs were above 1 for haemorrhagic stroke in *Table 3*, which indicated air pollution could have more marked effects on ischaemic stroke than on haemorrhagic stroke. These findings partially provide additional support to the study showing that elevation in PM<sub>10</sub>, CO, NO<sub>2</sub> and SO<sub>2</sub> may increase the risk of ischaemic stroke, but not haemorrhagic stroke.<sup>6</sup>

Previous studies on cerebrovascular mortality and morbidity have reported seasonal and temperature effects on cerebrovascular mortality and morbidity.<sup>30-33</sup> We believe that the association between urban air pollution and cerebrovascular admissions in this study was not confounded by either seasonal or temperature effects because we have adjusted long-term trend in years and months and short-term temporal variation in day-of-week, as well as daily averaging temperatures in our models. Our results also confirmed that low ambient temperature was associated with the increase in cerebrovascular morbidity reported in one previous study,<sup>33</sup> because ambient temperature was negatively associated with emergency admissions for cerebrovascular diseases in this study. Although a U-shaped relation between temperature and cerebrovascular mortality was reported in a previous study,<sup>34</sup> we have not observed such kind of relation between temperature and cerebrovascular admissions in our data.

Because we used the number of cases rather than rates of occurrence of cerebrovascular diseases to estimate the association between air pollution and cerebrovascular admissions, the model-determined association could possibly be confounded by an ageing population or by population change over the 6-year period from 1997 to 2002. However, such a confounding effect was likely to be limited because we found no significant changes in population rates (18.2-17.5%) for residents aged above 50 in Taipei over the study period.

We used air pollution levels from air monitoring stations to represent individuals' exposures. Therefore, we could not avoid the measurement error of misclassifying our subjects' exposures to air pollutants, especially PM<sub>2.5</sub> measured only by two air monitoring stations in Taipei. Such exposure misclassification can bias our outcomes towards either null or positive results, as reported in previous studies.<sup>35,36</sup> It is likely that NO<sub>2</sub> and PM<sub>10</sub> measured at the air monitoring station may not properly represent our subjects' actual air pollution exposures. Furthermore, it is the older people who get most of the cerebrovascular diseases, and many of

**Table 5** Epidemiological studies on air pollution and cerebrovascular diseases and stroke worldwide

Reference	Diseases definition <sup>a</sup>	Outcome	City	Time period	Pollutants examined	Main findings
Ponka <i>et al.</i> <sup>8</sup>	Cerebrovascular diseases: ICD-9 codes 430–438	Emergency room admissions	Helsinki	1987–89	SO <sub>2</sub> , NO <sub>2</sub> , NO, O <sub>3</sub> , TSP	Cerebrovascular admissions were associated with NO <sub>2</sub>
Poloniecki <i>et al.</i> <sup>11</sup>	Cerebrovascular diseases: ICD-9 codes 430–438	Hospital admissions	London	1987–94	SO <sub>2</sub> , NO <sub>2</sub> , CO, O <sub>3</sub> , black smoke	No association was observed
Wordley <i>et al.</i> <sup>9</sup>	Cerebrovascular diseases: ICD-9 codes 430–436	Hospital admissions	Birmingham	1992–94	SO <sub>2</sub> , NO <sub>2</sub> , nitrogen oxides, CO, O <sub>3</sub> , PM <sub>10</sub>	Cerebrovascular admissions were associated with PM <sub>10</sub>
Ballester <i>et al.</i> <sup>7</sup>	Cerebrovascular diseases: ICD-9 codes 430–438	Hospital admissions	Valencia	1994–96	SO <sub>2</sub> , NO <sub>2</sub> , CO, O <sub>3</sub> , black smoke	Cerebrovascular admissions were associated with NO <sub>2</sub>
Hoek <i>et al.</i> <sup>1</sup>	Cerebrovascular diseases: ICD-9 codes 430–436	Mortality	The Netherlands	1986–94	SO <sub>2</sub> , NO <sub>2</sub> , CO, O <sub>3</sub> , PM <sub>10</sub> , black smoke	Cerebrovascular deaths were associated with SO <sub>2</sub> , O <sub>3</sub> , CO, and black smoke
Hong <i>et al.</i> <sup>2</sup>	Stroke: ICD-10 codes 160–169	Mortality	Seoul	1995–98	SO <sub>2</sub> , NO <sub>2</sub> , CO, O <sub>3</sub> , PM <sub>10</sub>	Cerebrovascular deaths were associated with all pollutants
Le Tertre <i>et al.</i> <sup>12</sup>	Stroke: ICD-9 codes 430–438	Hospital admissions	Barcelona, Birmingham, London, Milan, The Netherlands, Paris, Rome, Stockholm	1992–94	SO <sub>2</sub> , NO <sub>2</sub> , CO, O <sub>3</sub> , PM <sub>10</sub> , black smoke	No association was observed
Wong <i>et al.</i> <sup>5</sup>	Cerebrovascular diseases: ICD-9 codes 430–438	Mortality	Hong Kong	1995–98	SO <sub>2</sub> , NO <sub>2</sub> , O <sub>3</sub> , PM <sub>10</sub>	No association was observed
Kan <i>et al.</i> <sup>4</sup>	Stroke: ICD-9 codes 430–438	Mortality	Shanghai	2001–02	SO <sub>2</sub> , NO <sub>2</sub> , PM <sub>10</sub>	Cerebrovascular deaths were associated with PM <sub>10</sub> and NO <sub>2</sub>
Tsai <i>et al.</i> <sup>10</sup>	PIH: ICD-9 codes 431–432 IS: ICD-9 codes 433–435	Hospital admissions	Kaohsiung	1997–2000	SO <sub>2</sub> , NO <sub>2</sub> , CO, O <sub>3</sub> , PM <sub>10</sub>	IS admissions were associated with all pollutants. PIH admissions were associated with NO <sub>2</sub> , CO, O <sub>3</sub> , and PM <sub>10</sub>
Wellenius <i>et al.</i> <sup>6</sup>	HS: ICD-9-CM code 431 IS: ICD-9-CM code 434	Hospital admissions	Birmingham, Chicago, Cleveland, Detroit, Minneapolis, New Haven, Pittsburgh, Salt Lake City, Seattle	1986–99	SO <sub>2</sub> , NO <sub>2</sub> , CO, PM <sub>10</sub>	IS admissions were associated with all pollutants

IS, ischaemic stroke; HS, haemorrhagic stroke; PIH, primary intracerebral haemorrhage; TSP, total suspended particulates.

<sup>a</sup>Diseases defined by original authors in their studies.

them are disabled and may stay most of their time indoors. Therefore, we still cannot entirely rule out the effects of other air pollutants, such as PM<sub>10</sub> and PM<sub>2.5</sub>, on increasing emergency admissions for cerebrovascular diseases in this study. It should also be noted that Taipei is a subtropical city; therefore, our findings may not be readily extrapolated to other locations with different population characteristics, environmental, and meteorological conditions.

Regardless the limitation, we conclude that urban air pollution can increase emergency admissions for cerebrovascular diseases among adults aged above 50 in Taipei. Among the measured air pollutants in Taipei, we conclude that CO and O<sub>3</sub> are stronger predictors of cerebrovascular admissions than other pollutants. However, epidemiological studies and more direct measure of vehicular traffic, such as black carbon or particle number, are still needed to confirm the contribution of different components in urban air pollution to increase emergency admissions for cerebrovascular diseases in Taipei. Further toxicological studies are also recommended to elucidate the biological mechanisms and pathogenetic processes in the cerebrovascular system induced by urban air pollution.

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