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# Risk and economic cost of hospitalization due to atrial fibrillation caused by air pollution: a multi-city time series analysis

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## Abstract

**Background** Atrial fibrillation (AF) is the most common arrhythmia, resulting in serious cardiovascular diseases. Air pollution may cause heart rate disturbance, but there is no clear or consistent evidence that short-term exposure to air pollution leads to an increased risk of hospitalisation for symptomatic episodes of AF. This study aimed to assess the impact of short-term exposure to air pollution on inpatient numbers.

**Methods** The inpatient records of AF cases in nine cities of the Sichuan Province, China and air pollution and meteorological data from 183 monitoring stations from 2017 to 2018 were collected. The impact of short-term exposure to air pollution on AF inpatients was evaluated using a time-stratified crossover case study design. The economic burden of AF attributable to air pollution was also estimated.

**Results** A total of 5,958 patients with AF from 123 medical institutions were included in the analysis. Air pollutants had a significant impact on the number of patients with AF. The number increased by 2.5% (95% confidence interval [CI] = 1.006 to 1.044) and 1.8% (95% CI = 1.003–1.033) for every 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$ ,  $\text{PM}_{10}$ , concentration, respectively. Moreover, the number increased by 12.7% (95% CI = 1.006 to 1.262) for every 10  $\mu\text{g}/\text{m}^3$  increase of  $\text{SO}_2$  concentration. For every 0.1  $\mu\text{g}/\text{m}^3$  increase in CO concentration, the number of inpatients with AF increased by 3.9% (95% CI = 1.010–1.070). People aged 65 years or older and women were more likely to be affected by air pollutants. The AF in 430 and 209 inpatients were attributable to  $\text{PM}_{2.5}$  and  $\text{PM}_{10}$ , respectively. The total hospitalization expenses attributed to excessive exposure to  $\text{PM}_{2.5}$  and  $\text{PM}_{10}$  were 13.98 million CNY and 6.68 million CNY, respectively. Furthermore, the out-of-pocket expenses were 6.81 million CNY and 3.28 million CNY, respectively.

**Conclusions** This study showed a strong correlation between air pollution and AF. Hence, there is a need to reduce air pollution to control health risks.

**Keywords** Attributable risk, Hospital admission, Air pollution, Atrial fibrillation

## Background

Atrial fibrillation (AF) is the most common arrhythmia and has a complex etiology. AF can lead to increased morbidity and mortality due to stroke, heart failure, and other heart diseases [1, 2]. It is estimated that 2–4% of adults worldwide are affected by AF [3]. The prevalence of AF in Europe and the USA is approximately 1–4%, while the prevalence in Asia is significantly lower (0.5–1.9%) [4]. Although the burden of AF is smaller in low- and middle-income countries compared to developed

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countries, this gap is gradually narrowing [5]. China, as a developing country, is also trending toward a developed country in terms of AF prevalence. According to a national survey from 2017 to 2021, the total prevalence of AF in Chinese adults was 1.60% [6], which increased by 0.56% compared with the results of Wang et al. in 2015–2017 [7]. AF is an important risk factor for Cerebral Ischemic Stroke (CIS). The risk of CIS in patients with AF is 5–6 times higher than that in the general population [8]. China has one of the highest disease burdens related to stroke in the world. In 2018, 3.01 million patients were admitted to 1,853 large hospitals for stroke. Of these, 2.47 million (81.9%) were patients with CIS [9]. This disease burden cannot be ignored.

The etiology of AF is diverse. In general, the risk factors are divided into modifiable factors (e.g., environment, sedentary, smoking, alcohol consumption, hypertension, diabetes) and non-modifiable factors (e.g., age, gender, race, and genetics) [10]. Previous epidemiological studies showed that air pollution has association with AF, and exposure to a certain level of air pollutants may significantly affect the incidence of AF [11, 12]. A 16-year study in the US found an association between exposure to air pollution and increased incidence of AF [13]. A study in Swedish, found a positive correlation between the increase in  $PM_{2.5}$  concentration and AF morbidity [14]. A study in Rome suggests an association between air pollutant exposure and emergency room visits for atrial fibrillation [15]. A UK study conducted using three national databases revealed that  $NO_2$  was related to the occurrence of AF, and  $PM_{2.5}$  was related to the increased mortality associated with AF [16]. A study in Beijing, China found that the risk of AF increased by 3.8% and 2.7% for every  $10 \mu g/m^3$  increase in  $PM_{2.5}$  and  $PM_{10}$  concentration, respectively [17]. A study in Taiwan also found that AF was significantly associated with an increase in  $PM_{2.5}$  concentration [18]. These studies confirmed the association between air pollution and AF. However, most of these studies focused on the impact of PM on AF only. Few analyzed the impacts of other major air pollutants on AF in the general population. Moreover, most previous studies were conducted in developed countries or regions, while countries or regions with different economic strengths often have different levels of air pollution. This factor may affect the research results. Finally, previous studies have focused on specific populations, such as the elderly and special patients with implantable cardioverter defibrillators (ICD) or pacemakers [19]. The investigation results of specific study populations may not be applicable to the general population because of the likely probability of co-developing heart failure and coronary heart disease.

Contrarily, other studies found that there was no significant association between the number of inpatients with AF and short-term exposures to air pollution. For example, a study in Utah, USA, showed that the hospitalization rate of AF did not increase with the short-term increase in PM exposure [20]. However, this study was conducted in developed countries, where there are differences in economic levels, demographics and lifestyle habits between developed and developing countries, and the results may not be applicable to developing countries. Therefore, more studies are needed to analyze whether air pollutants increase the risk of AF.

Sichuan Province is located in the southwest of China and covers 2.7% of China's geographical area. By the end of 2021, Sichuan's total GDP ranked sixth in China, with its per capita GDP at 18th in China and less than more than 50% of the provinces in China. These confirmed that Sichuan is an economically underdeveloped province. However, Sichuan is more polluted than developed areas with its anthropogenic emissions of  $PM_{2.5}$ ,  $PM_{10}$ ,  $SO_2$ , and  $NO_x$  accounting for 6.4%, 5.7%, 8.2%, and 4.2% of China's total emissions, respectively [21]. These numbers all exceed Sichuan's geographical area in proportion to China's total area. Due to the topography of the basin, air pollutant concentrations in Sichuan Province are consistently higher compared to other areas of China with high air pollution [22]. Therefore, Sichuan was selected as an example of an economically underdeveloped and heavily polluted region to conduct a time series study of cross-over cases. The impact of major air pollutants on the number of inpatients with AF was analyzed. Longer lag structures and potential confounding factors were also explored.

## Materials and methods

### Hospitalization data

The hospitalization data of AF cases from 2017 to 2018 were collected from 123 medical institutions in nine cities and prefectures of the Sichuan Province, including Chengdu, Guang'an, Luzhou, Liangshan Yi Autonomous Prefecture, Mianyang, Meishan, Nanchong, Yibin, and Zigong. Medical institutions are all types of hospitals in the area, including general hospitals, Chinese medicine hospitals, specialist hospitals and private hospitals, but we have excluded some lower rated hospitals. The collected data included age, sex, home address, date of admission, disease diagnosis, comorbid diagnosis, treatment cost, and disease code of the patient. The study population was drawn from our database of collected hospitalisations, defined as patients admitted to hospital for an episode of AF, whose admission diagnosis was completed by a clinician. After excluding invalid cases with missing personal information, inaccurate diagnosis,

living outside the study area, and no cost information, the data from 5,958 inpatients with AF and the ICD-10 code I48 according to the criteria of the International Classification of Diseases were analyzed to determine the impact of air pollutants on the number of inpatients with AF and the economic burden attributable to the disease.

**Pollutants and meteorological data**

The air pollutant data came from 183 provincial-level air quality monitoring stations, covering 21 cities and prefectures in the Sichuan Province. The data included the daily average concentrations of PM<sub>2.5</sub> with an average aerodynamic diameter of less than 2.5 μm, PM<sub>10</sub> with an average aerodynamic diameter of less than 10 μm, nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>), ozone (O<sub>3</sub>), and carbon monoxide (CO). The air pollutant monitoring in each station was conducted strictly according to the air pollution monitoring standard procedure promulgated by China. The meteorological data came from the same source as the air pollutant data, including 24-h mean temperature (°C) and relative humidity (%).

Notably, the pollutant concentration data obtained from fixed air quality monitors do not reflect the actual exposure level of individuals and cannot compensate for the missing data. However, the spatial models can effectively account for these errors. Spatial interpolation is a commonly used modeling method [23]. The spatial interpolation method can make use of the existing monitoring stations’ data to estimate the values of the measured points and generate a high-precision spatial surface model, which can effectively repair the missing observation data and obtain precise individual exposure levels. The inverse distance weighted interpolation (IDW), a commonly used spatial interpolation method, was used in this study to estimate the exposure levels among the patients using the patients’ most recent monitoring station data and supplement the missing data that could not be obtained from the monitoring stations. The interpolation resolution was 0.05° × 0.05°.

**Statistical analysis**

The daily hospitalized cases of AF generally follow Poisson’s distribution. The conditional Poisson regression linear model and the time-stratified crossover case design are mature methods used to study the correlation between air pollutants and diseases [24]. The time-stratified crossover case design is similar to the time-stratified case–control study. Janes et al. found through their statistical simulation that the time-stratified crossover case study can simultaneously control confounding factors, such as seasonal and “day of the week” effects, eliminate temporal trend bias, and obtain an unbiased estimation

of parameters with conditional logistic regression [25]. In this study, the admission date of the AF patients was taken as the case date. The control day was selected as the same day of the week in the same month and the same year by the time stratification method. The air pollutant concentration on the admission day was compared with that on the control day. Then, the correlation between the daily number of inpatients with AF and the air pollutants was analyzed using conditional logistic regression. Moreover, meteorological factors may affect the number of AF cases. Therefore, the daily ambient temperature and the relative humidity were introduced into the model as control variables to estimate the odds ratio (OR) and the 95% confidence interval (CI) of the number of inpatients with AF when the concentration unit of the air pollutant changes.

Previous studies showed that air pollution has a lag effect on health [26, 27]. To fully study the lag pattern of the correlation between AF and various air pollutants, a lag structure was constructed from the day of admission (lag0) to 7 days before admission (lag7) to evaluate the 1-day lag effect. The cumulative impact of the pollutants on AF was assessed by fitting the air pollutants’ concentrations and calculating the moving average from the day of admission to 7 days before admission (i.e., from lg01 to lg07). Then, a stratified analysis was conducted by age (less than 65 years, greater than or equal to 65 years), gender (male, female), and season (cold season: November to April; warm season: May to October) to further explore the impact of air pollutants on the number of inpatients with AF. The test formula for possible differences between different subgroups is shown in Eq. (1):

$$D(95\%) = (\hat{Q}_1 - \hat{Q}_2) \pm 1.96 \sqrt{(\hat{SE}_1)^2 + (\hat{SE}_2)^2} \tag{1}$$

where Q<sub>1</sub> and Q<sub>2</sub> are the estimated values of the effects of different categories of people affected by air pollutants between different layers. SE<sub>1</sub> and SE<sub>2</sub> are their corresponding standard deviations.

Based on the attribution risk analysis, the number of AF inpatients and the related economic cost attributable to air pollution was estimated[28]. The reference concentration was based on the World Health Organization (WHO) air quality guidelines (i.e., 24 h mean of 15 μg/m<sup>3</sup> for PM<sub>2.5</sub>; 24 h mean of 45 μg/m<sup>3</sup> for PM<sub>10</sub>)[29]. The calculation formulae are shown in Eqs. (2)–(4):

$$AN_i = HAs_i * (1 - \exp(-\beta * \Delta CP_{i-t})) \tag{2}$$

$$AC_{ytotal} = AN_y * Cost_{ytotal} * Cpl_y \tag{3}$$

$$AC_{ypocket} = AN_y * Cost_{ypocket} * Cpl_y \tag{4}$$

where  $AN_i$  is the number of AF inpatients attributed to exposure to air pollutants on the  $i$ th day.  $\beta$  is the exposure-response coefficient between air pollutants and the number of AF inpatients.  $\Delta CP_{i-t}$  is the difference between the observed concentration and the reference concentration of the air pollutants on the  $i$ th day.  $HA_{si}$  is the number of the AF inpatients on the  $i$ th day.  $AC_{ytotal}$  and  $AC_{ypocket}$  represent the total hospitalization cost and the out-of-pocket cost caused by excessive exposure to air pollutants for  $y$  years.  $AN_y$  is the sum of  $y$  years.  $Cost_{ytotal}$  and  $Cost_{ypocket}$  represent the average total hospitalization cost and the average out-of-pocket cost per case of  $y$  years, respectively.  $Cpl_y$  is the consumer price index from year of  $y + 1$  to 2018. The concentration standard proposed by the WHO is the theoretical minimum threshold level, below which the air pollutants have no impact on health.

### Robustness analysis

We estimated the robustness of the results by adding another pollutant to the primary model of each pollutant to construct a two-pollutant model. Moreover, to eliminate the pollutant concentration error caused by the excessive remote distance between the patient’s residence and the air monitoring station, the “Distance to the nearest hub” and the “Distance matrix” kits in the QGIS software were used to eliminate the patients whose residence is outside a 50 km range of an air monitoring station. The daily average exposure of air pollutants was recalculated and substituted into the model. The daily average temperature and humidity were also controlled in the same manner. Sensitivity analysis was conducted again to further verify the stability of the results [30].

All the analyses were performed using the statistical software R (version 4.0.1, R Core Team, 2019, <https://www.R-project.org>). The statistical test was two-tailed and  $P < 0.05$  means statistically significant.

**Table 1** Descriptive statistics of inpatients characteristics, air pollutants, and meteorological factors from 2017 to 2018

Variable	Total	Min	Mean	SD	Max	Percentile		
						25th	50th	75th
Atrial fibrillation	5958.00	1.00	8.19	4.14	24.00	5.00	8.00	11.00
Age								
< 65 years	2061.00	1.00	3.00	2.05	12.00	1.00	3.00	4.00
≥ 65 years	3897.00	1.00	5.43	2.80	16.00	3.00	5.00	7.00
Gender								
Male	2856.00	1.00	4.00	2.44	15.00	2.00	4.00	5.00
Female	3102.00	1.00	4.00	2.40	18.00	3.00	4.00	6.00
Season								
Warm	3089.00	1.00	8.42	4.22	23.00	5.00	8.00	11.00
Cold	2869.00	1.00	7.00	4.02	24.00	5.00	7.00	10.00
Medical expense								
Total expense	19,222.17	0.01	3.23	3.67	27.52	0.54	1.02	6.14
Out-of-pocket health payment	9353.13	0.00	1.57	2.38	19.25	0.17	0.41	2.23
Air pollutant								
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	–	3.03	42.80	32.32	264.62	20.50	33.50	54.22
PM <sub>10</sub> (µg/m <sup>3</sup> )	–	4.13	66.57	43.54	441.48	35.53	55.05	85.89
NO <sub>2</sub> (µg/m <sup>3</sup> )	–	2.03	29.80	15.47	127.10	18.40	26.40	38.00
O <sub>3</sub> (µg/m <sup>3</sup> )	–	3.93	83.42	42.23	299.50	52.54	75.41	109.21
CO (µg/m <sup>3</sup> )	–	0.06	0.76	0.27	2.47	0.59	0.72	0.90
SO <sub>2</sub> (µg/m <sup>3</sup> )	–	1.04	10.62	5.39	77.28	7.05	9.57	12.83
Meteorological	–							
Temperature (°C)	–	– 9.51	17.63	7.38	34.39	10.76	17.98	23.90
Humidity (%)	–	15.31	77.46	11.89	99.98	70.15	78.77	86.45

Unit: million Chinese Yuan (CNY). The annual economic costs were measured with a fixed price in 2018

Min Minimum, Max Maximum, SD Standard deviation, PM<sub>2.5</sub> an average aerodynamic diameter of less than 2.5 µm, PM<sub>10</sub> an average aerodynamic diameter of less than 10 µm, NO<sub>2</sub> nitrogen dioxide, O<sub>3</sub> ozone, CO carbon monoxide, SO<sub>2</sub> sulfur dioxide

## Results

### Data description

Descriptive results are shown in Table 1. A total of 5,958 patients with AF from 123 hospitals in nine cities and prefectures of the Sichuan Province from 2017 to 2018 were included in this study. There were 3102 females (52.06% of the total), which was slightly more than the number of male patients. The proportion of the elderly patients, aged over 65 years and above, was high, accounting for 65.41% and 3,897 patients. The number of inpatients in warm seasons was slightly more than that in cold seasons, accounting for 3,089 (51.85%). The total hospitalization expense per time and the out-of-pocket expense per time were 32,300 million Chinese yuan (CNY) and 15,700 CNY, respectively. During the 2-year study period, PM<sub>2.5</sub> and PM<sub>10</sub> pollutions were the most serious, with 698 and 506 days of average daily concentrations exceeding the WHO standard, respectively, and the average daily concentrations were 42.80 and 66.57 µg/m<sup>3</sup>, respectively. The daily average concentrations of NO<sub>2</sub>, O<sub>3</sub>, CO, and SO<sub>2</sub> were 29.80, 83.42, 0.76, and 10.62 µg/m<sup>3</sup>, respectively. The daily mean values of the temperature and humidity were 17.63 °C and 77.46%, respectively. The analysis of the correlation between various pollutants and meteorological factors is shown in Additional file 1: Table S1. PM<sub>2.5</sub> is positively correlated with other pollutants, except for O<sub>3</sub>, and has the strongest correlation with PM<sub>10</sub> ( $r=0.95$ ,  $P<0.05$ ). There was a moderate correlation between air pollutants and meteorological factors.

### Effect of air pollution exposure on the total population and the subgroups

In the single pollutant model, the association between the air pollutants of different lag days and the number of inpatients with AF is shown in Fig 1.

In general, PM<sub>2.5</sub>, PM<sub>10</sub>, CO, and SO<sub>2</sub> were significantly associated with the number of inpatients with AF. The influence of other air pollutants on the number of inpatients with AF was not observed. In contrast, the impacts of PM<sub>2.5</sub> and PM<sub>10</sub> on the number of AF cases in lag1–lag3 and lag01–lag07 were observed, with the impact of PM<sub>2.5</sub> in lag05 being the largest, where the number of AF cases increased by 2.5% (95% CI=1.006 to 1.044) when the PM<sub>2.5</sub> concentration increased by 10 µg/m<sup>3</sup>. The maximum impact of PM<sub>10</sub> was observed in lag07. When the PM<sub>10</sub> concentration increased by 10 µg/m<sup>3</sup>, the number of AF cases increased by 1.8% (95% CI 1.003, 1.033). The impact of CO on the number of AF cases was observed in lag1–lag4 and lag01–lag07, and the impact was most significant in lag07. The number of inpatients with AF increased by 3.9% (95% CI=1.010–1.070) when the CO concentration increased by 0.1 µg/m<sup>3</sup>. In lag2, SO<sub>2</sub> also

affected the number of AF cases, which increased by 12.7% (95% CI=1.006–1.262) when the SO<sub>2</sub> concentration increased by every 10 µg/m<sup>3</sup>. The specific results of the single pollutant model are shown in Additional file 1: Table S2.

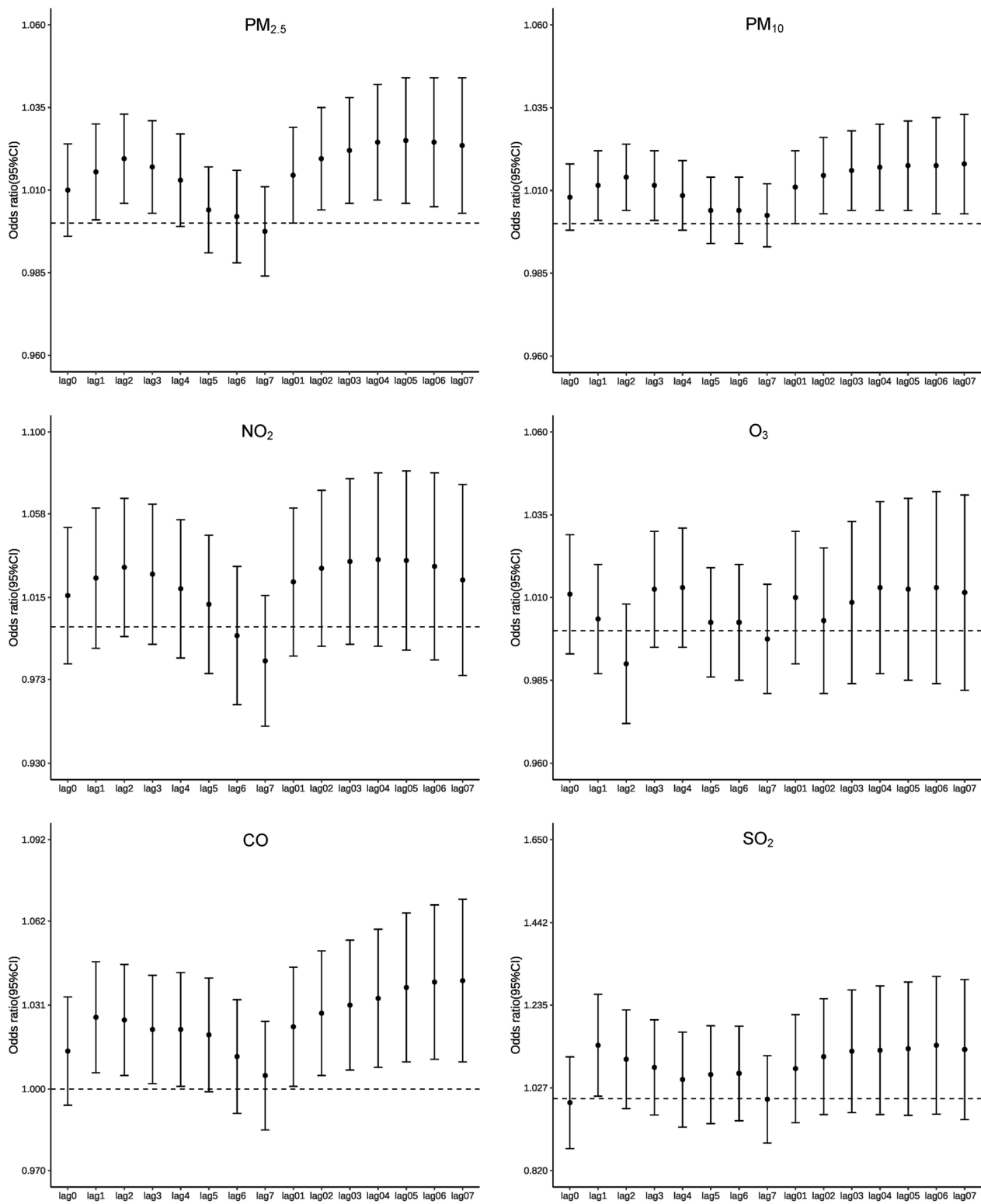
Figure 2 shows the stratified analysis results by age, season, and gender. Compared with the under 65-year-old population, PM<sub>2.5</sub> and PM<sub>10</sub> impacted the elderly patients, aged 65 years and above, more significantly ( $P<0.05$ ). Every 10 µg/m<sup>3</sup> increase in the PM<sub>2.5</sub> or PM<sub>10</sub> concentration, the number of inpatients with AF increased by 2.4% (95% CI=1.004 to 1.044) and 0.4% (95% CI=1.018 to 1.033); The effect of SO<sub>2</sub> on the number of AF cases was more significant in female inpatients, and the difference was statistically significant ( $P<0.05$ ). Every 10 µg/m<sup>3</sup> increase in SO<sub>2</sub> concentration caused the number of inpatients with AF to increase by 20.3% (95% CI=1.033 to 1.401). No statistically significant difference was found in the subgroup comparison of other pollutants.

### Robustness test

Table 2 shows the results of the dual-pollutant model. With the addition of other pollutants, the results of PM<sub>2.5</sub> and PM<sub>10</sub> remained stable. However, with the addition of CO, the correlation between CO and AF was weakened. Similarly, with the addition of PM<sub>2.5</sub> and PM<sub>10</sub> to the CO model, the association between CO and AF was also weakened. With the addition of other pollutants, the association between CO and AF remained stable. Only when NO<sub>2</sub> and O<sub>3</sub> were added to the SO<sub>2</sub> model, the association between SO<sub>2</sub> and AF was stable. When PM<sub>2.5</sub>, PM<sub>10</sub>, and CO were added, the association between SO<sub>2</sub> and AF became weakened. Note that PM<sub>2.5</sub>, PM<sub>10</sub>, and CO had significant correlations with AF in the single pollutant models. After 17 patients' data were eliminated, because they lived more than 50 km away from the air monitoring station, the association between the air pollutants (PM<sub>2.5</sub>, PM<sub>10</sub>, CO, and SO<sub>2</sub>) and the number of inpatients with AF was still significant, compared with the results without the elimination. Moreover, the number of days to reach the maximum effect remained unchanged. The variation ranges of OR and the 95% CI were all less than 0.01%, showing good robustness in the results.

### Attributable risks and economic costs caused by air pollutants

Because PM<sub>2.5</sub> and PM<sub>10</sub> had the highest pollution levels, the longest duration, and the greatest negative health impact during the period of this study, only PM<sub>2.5</sub> and PM<sub>10</sub> were further analyzed for attributable risks from



**Fig. 1** Changes in the risk of hospitalization in AF patients in a single pollutant model

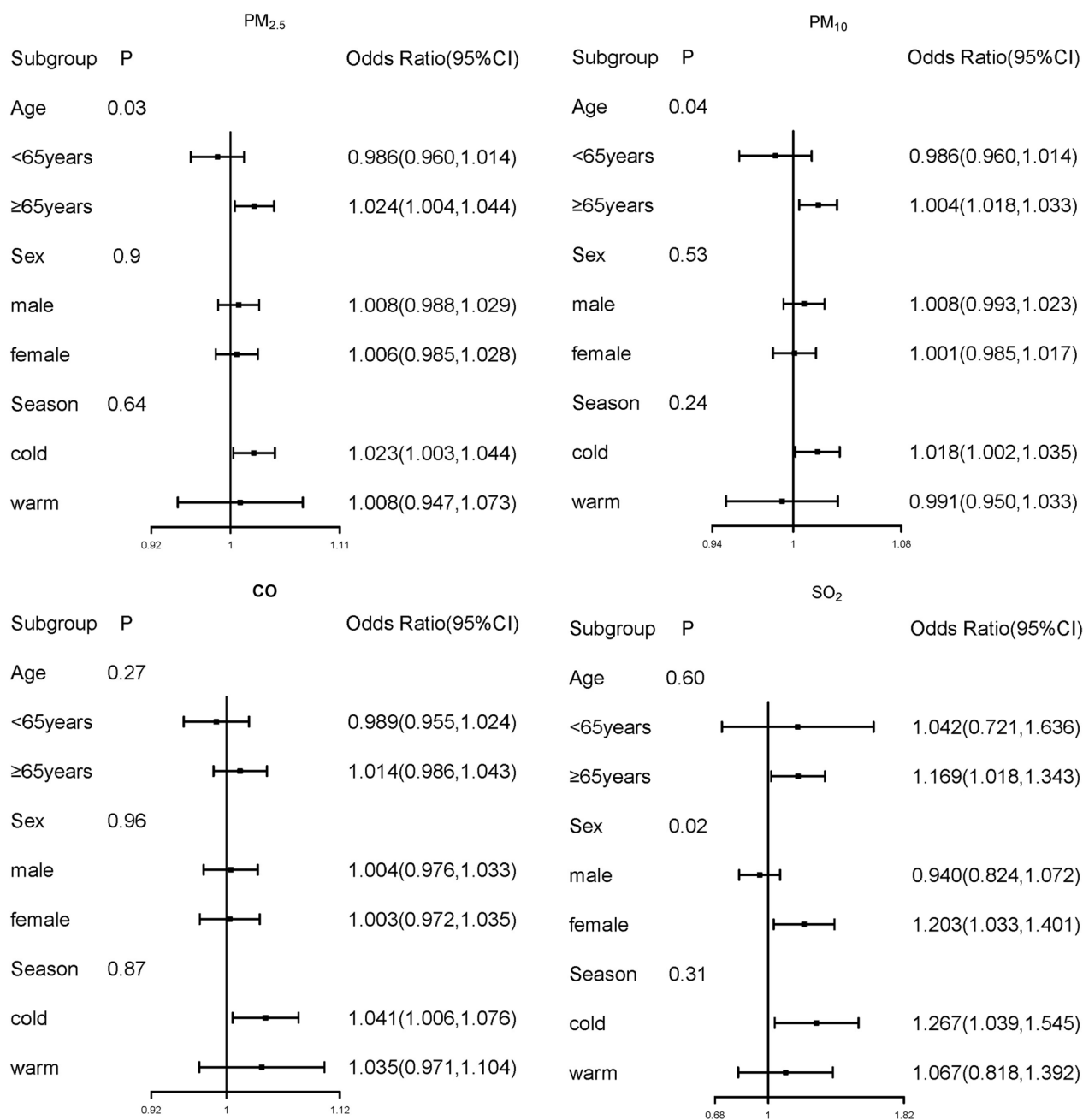


Fig. 2 Changes in hospitalization risks among patients with AF in different subgroups

a conservative point of view. The results are shown in Table 3. Based on the WHO air quality guidelines, 430 patients were admitted to the hospital with AF from 2017 to 2018 due to excessive exposure to PM<sub>2.5</sub>. For PM<sub>10</sub> exposure, the counterpart number of patients was 209. In terms of medical expenses, a total of 1398.31 CNY of total hospitalization expenses and 6.81 million CNY of out-of-pocket expenses were related to excessive exposure to PM<sub>2.5</sub>, while 6.68 million CNY of total

hospitalization expenses and 3.28 million CNY of out-of-pocket expenses were related to excessive exposure to PM<sub>10</sub>.

**Discussion**

Based on the time-series crossover case study, it was found that short-term exposure to air pollutants significantly affects the number of inpatients with AF. As mentioned earlier, PM<sub>2.5</sub>, PM<sub>10</sub>, CO, and SO<sub>2</sub> were

**Table 2** Association of patients with atrial fibrillation with air pollutants in a dual-pollutant model

Pollutant	PM <sub>2.5</sub> lag05	PM <sub>10</sub> lag07	CO lag07	SO <sub>2</sub> lag1
Adjusted PM <sub>2.5</sub>	–	–	1.031 (0.991, 1.073)	1.080 (0.949, 1.229)
Adjusted PM <sub>10</sub>	–	–	1.029 (0.991, 1.067)	1.083 (0.953, 1.230)
Adjusted NO <sub>2</sub>	1.027* (1.003, 1.051)	1.020* (1.001, 1.039)	1.049* (1.012, 1.088)	1.113* (1.001, 1.268)
Adjusted O <sub>3</sub>	1.024* (1.005, 1.043)	1.017* (1.002, 1.032)	1.039* (1.008, 1.070)	1.126* (1.005, 1.262)
Adjusted SO <sub>2</sub>	1.024* (1.003, 1.045)	1.016* (1.001, 1.032)	1.037* (1.006, 1.069)	–
Adjusted CO	1.013 (0.987, 1.039)	1.008 (0.989, 1.028)	–	1.073 (0.946, 1.216)

\**P* < 0.05 means statistically significant

**Table 3** Number of AF inpatients and economic cost attributed to PM exposure in 2017–2018

Years	PM <sub>2.5</sub>			PM <sub>10</sub>		
	AN <sub><i>y</i></sub>	AC <sub>total</sub> <sup>a</sup>	AC <sub>pocket</sub> <sup>a</sup>	AN <sub><i>y</i></sub>	AC <sub>total</sub> <sup>a</sup>	AC <sub>pocket</sub> <sup>a</sup>
2017	184	509.88	267.32	102	282.59	148.16
2018	246	888.42	413.38	107	385.73	179.48
Total	430	1398.31	680.70	209	668.33	327.64

AN<sub>*y*</sub>, AC<sub>total</sub>, and AC<sub>pocket</sub> were calculated based on the largest effect estimates in single pollutant models. AN<sub>*y*</sub>, the number of AF inpatients attributed to exposure to air pollutants on the *i*th day, AC<sub>total</sub> the total hospitalization cost by excessive exposure to air pollutants for *y* years, AC<sub>pocket</sub> the out-of-pocket cost by excessive exposure to air pollutants for *y* years

related to an increase in the number of AF cases once the confounding factors, such as temperature, relative humidity, and holidays, were controlled. However, such a strong relationship was not observed for NO<sub>2</sub> and O<sub>3</sub>. The stratified analysis found that elderly patients were more likely to be affected by PM<sub>2.5</sub> and PM<sub>10</sub>, while women were more likely to be affected by SO<sub>2</sub>. Based on the pollutant concentration in the WHO air quality guidelines, the AF detected in 639 inpatients was attributed to PM<sub>2.5</sub> and PM<sub>10</sub>. The total hospitalization expense due to excessive exposure to particle pollutants was 20.67 million CNY, and the out-of-pocket expense was 10.83 million CNY.

Our results are consistent with existing studies. These results validated the hypothesis that short-term exposures to air pollutants increased the risk of hospitalization due to AF [31–33]. The mechanisms of AF induced by air pollutants are complex and diverse. Although there is no specific theory, there are several possible reasons to explain this relationship. First, previous studies confirmed that air pollutants can cause acute autonomic nervous dysfunction [34, 35], which in turn, can lead to reduced heart rate variability. Therefore, AF may be caused by autonomic nervous dysfunction. Second, air pollutants can also lead to platelet activation, promote thrombosis, and cause myocardial infarction, which damages and destroys the heart, leading to thickness changes in the myocardial fibers or heart muscle. This can cause

abnormal cardiac electrical activities and AF [36]. Finally, air pollution promotes systemic vascular oxidative stress, with subsequent endothelial dysfunction, monocyte activation and some pro-atherogenic changes in lipoproteins [37].

On the day of admission (lag0), there was no detectable air pollutant effect on the number of inpatients with AF inpatients. Instead, a significant lag effect was observed. This is consistent with previous research results. In the single pollutant model, when the concentration of PM<sub>2.5</sub>, PM<sub>10</sub>, or SO<sub>2</sub> increased by 10 µg/m<sup>3</sup> or the concentration of CO increased by 0.1 µg/m<sup>3</sup>, the number of inpatients with AF increased, and the percentage increase reached the greatest for lag05, lag07, lag1, and lag07, respectively. When analyzing the association between weather, air pollution, and the number of ambulance calls caused by AF, Jone et al. found that PM<sub>10</sub> was positively association with the number of ambulance calls on lag4 and lag7 [38]. Marcus et al. found that PM<sub>10</sub> exposure for lag12–24 h during increased the risk of AF in the general population [39]. A study conducted by Liang et al. in Beijing also showed that as time passed, the AF risk of patients visiting the emergency room increased. On lag6, there was a positive correlation between the air pollutants and AF [40]. The results of this study showed evidence that air pollutants are risk factors for the occurrence of AF. As stated by Haley et al. when PM<sub>2.5</sub>-related treatment can be applied to hospitalized patients with cardiovascular



diseases, and that different lag time caused different effects [41]. Our study clarified the timepoints during the course of the impact of air pollutants on AF-related admissions. The findings of this study may contribute to the prevention and treatment of AF.

In the dual-pollutant model, it was observed that adding another pollutant weakened the correlation that was significant in the single-pollutant model, e.g., adding CO to the PM model or adding PM to the SO<sub>2</sub> model. The possible reason for this phenomenon is that the air pollutant is a complex mixture of gas, volatile droplets, and particulate matter. SO<sub>2</sub>, NO<sub>2</sub>, and volatile organic compounds are the main precursors of PM. Therefore, these pollutants do not affect each other independently. Instead, they affect each other due to their common source [42]. Therefore, the individual correlation between each air pollutant and the number of inpatients with AF needs to be considered with caution.

The subgroup analysis found that elderly patients are more susceptible to PM. This is in line with a previous study conducted in Italy [18]. The reason for this observation may be because elderly patients have a high prevalence of cardiopulmonary diseases due to frailty, while the mechanism of AF involves inflammation and atrial pressure. Patients with cardiopulmonary insufficiency have a greater risk of AF [16, 43]. We also found that women were more sensitive to air pollutants, possibly because of their exposure times and biological differences. According to “*the Handbook of Population Exposure Factors in China*” [44], men and women spend different time outdoor (258 min for women and 210 min for men per day). Women may also be weaker in constitution, and thus, air pollutants may deposit in their lungs more easily [45].

To quantify the health benefits of reducing air pollution concentrations, PM was selected in this study to obtain more robust results relating to the economic burden attributable to air pollution, based on the unique characteristics of the air pollutants in Sichuan Province. It was found that the economic burden and the number of hospitalized patients caused by PM<sub>2.5</sub> pollution were 13.98 CNY and 430 people, respectively, both higher than the results given by PM<sub>10</sub>. The reason being PM<sub>2.5</sub> enter bronchioles and alveoli easily due to the small diameters of less than 5 μm [34]. The soluble components of PM<sub>2.5</sub> can directly enter blood circulation through alveolar epithelial cells, stimulate inflammatory cells, and immune cells, to release pro-inflammatory factors, leading to oxidative stress and inflammatory response to cause indirect damage of the body [46, 47]. This is the first assessment of the economic burden of AF hospitalization as attributed to air pollution in the Sichuan Province. This study provided significant evidence supporting the impact of

air pollution on public health, which include economic burdens.

This study has several limitations. First, like most epidemiological studies on acute effects, this study adopted the average concentration of the monitoring stations to calculate the exposure level, which cannot reflect the actual levels of individual exposures. Although the IDW interpolation method was used to estimate individual exposure levels, deviations are possible. Second, patient characteristics were not collected completely, such as BMI, whether they smoked, and whether they wore ICDs. This prevented us from conducting more detailed subgroup analyses to obtain more comprehensive results. Third, the economic burden of air pollution may be underestimated, because the data collected were hospitalization data, which only covered the total hospitalization and the out-of-pocket costs, without including the outpatient costs. Finally, our study of patients hospitalised for symptomatic episodes of atrial fibrillation did not distinguish whether these patients had new-onset or old-onset atrial fibrillation, so we cannot know whether there is a trend toward an increased incidence of new-onset atrial fibrillation due to air pollution. However, this is a major goal for our future research.

## Conclusions

This study revealed that short-term exposure to air pollution increased the risk of AF hospitalization and led to a substantial financial burden. Our results contribute to existing evidence that air pollution can cause AF and damage health. We recommend the need to reduce air pollution to reduce health risks.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12302-022-00709-w>.

**Additional file 1. Detailed results of Pearson correlation analysis and Time series analysis. Table S1.** Pearson correlation coefficient of air pollutants, temperature, and relative humidity in nine cities and prefectures of Sichuan Province, China in 2017–2018. **Table S2.** Changes in the hospitalization risk of AF patients with increasing air pollutant concentrations of 10 μg/m<sup>3</sup> (PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>) or 0.1 μg/m<sup>3</sup> (CO) in the single pollutant model.

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## Author contributions

CL: formal analysis, data curation, writing—original draft preparation, visualization. WJ: conceptualization, methodology, software. XG, YH and JL: data curation. LY: writing—reviewing and editing. All authors read and approved the final manuscript.

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**Availability of data and materials**

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Declarations****Ethics approval and consent to participate**

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

**Consent for publication**

All participants provided written informed consent prior to participation.

**Competing interests**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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