Original research

Associations between air pollution and the risk of first admission and multiple readmissions for cardiovascular diseases

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ABSTRACT

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Objectives We aimed to investigate the associations between air pollutants and the risk of admission and multiple readmission events for cardiovascular disease (CVD).

Methods A total of 285009 participants free of CVD at baseline from the UK Biobank were included in this analysis. Four major cardiovascular admission events were identified during the follow-up: chronic ischaemic heart disease (CIHD), cerebrovascular disease. atrial fibrillation and heart failure. We used Prentice, Williams and Peterson-Total Time model to examine the association between ambient air pollution and first admission, as well as multiple readmissions for these CVDs.

Results During a median follow-up of 12 years. 17 176 (6.03%) participants were hospitalised with CVDs, and 6203 (36.11%) patients with CVD had subsequent readmission events for CVDs. We observed significant associations between air pollution and both first admission and readmission for CVDs, with generally stronger associations on readmission for cardiovascular events. For example, the adjusted HRs for the first admission and subsequent readmission for cerebrovascular disease were 1.130 (95% CI 1.070 to 1.194) and 1.270 (95% CI 1.137 to 1.418) for each IQR increase of particulate matter with a diameter $\leq 2.5 \, \mu m$. The corresponding HRs for CIHD were 1.060 (95% CI 1.008 to 1.114) and 1.120 (95% CI 1.070 to 1.171).

Sex stratified analyses showed that the associations were generally more pronounced among females than males. **Conclusion** This study provides evidence that ambient air pollutants might play an important role in both first admission and readmission for cardiovascular events. In addition, patients with pre-existing CVDs may be more vulnerable to air pollution compared with healthy population.

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INTRODUCTION

Cardiovascular disease (CVD) is a leading cause of disability and mortality globally, accounting for 40% of all deaths among the elderly population,¹ and its prevalence is expected to rise in the future. With the progress made in the diagnosis and treatment of CVDs, the survival rate has improved, but individuals who have been affected by CVDs are at an increased risk of experiencing recurrent

WHAT IS ALREADY KNOWN ON THIS TOPIC

- \Rightarrow Ambient air pollution has been regarded as an important preventable risk factor of cardiovascular diseases (CVDs).
- \Rightarrow Although the majority of previous studies have focused on the incidence risk of CVD. there have been few investigations on the association between air pollution and the risk of readmission for CVD.

WHAT THIS STUDY ADDS

- \Rightarrow During a median follow-up of 12 years, we found ambient air pollutants might play an important role in both first admission and readmission for cardiovascular events.
- \Rightarrow In addition, patients with pre-existing CVDs may be more susceptible to air pollution as compared with individuals who are healthy.

HOW THIS STUDY MIGHT AFFECT RESEARCH, **PRACTICE OR POLICY**

 \Rightarrow Considering the significant burden from CVD globally, further compounded by decreased rate of CVD due to advancements in medical care, the findings of this study may have important implications for implementing effective prevention measures for CVD and for guiding environmental regulatory decisions.

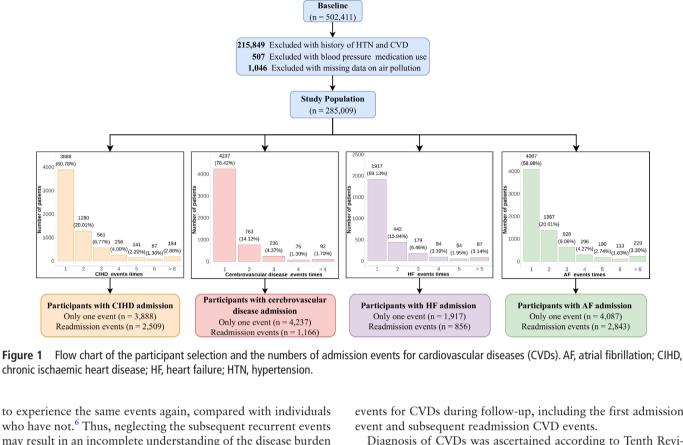
CVD events. Therefore, it is crucial to examine the modifiable risk factors of the recurrent CVD events among the patients with CVD.

Ambient air pollution has been regarded as an important preventable risk factor of CVDs.² The health effect of air pollution could be explained by the inflammation and oxidative stress, which can result in cardiac automatic dysfunction.³ Furthermore, studies have reported that air pollution is relevant for incident CVD events and for CVD events that occur in subsequent years.⁴

Although most previous studies have focused on the association between air pollution and the incidence risk of CVDs, there has been little research into the association between air pollution and the risk of recurrence for CVDs.⁵ From both clinical and preventive perspectives, individuals who have suffered from a non-fatal CVD might be more likely



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who have not.⁶ Thus, neglecting the subsequent recurrent events may result in an incomplete understanding of the disease burden experienced by an individual over time.⁷ To address this research gap, we conducted this study to

4000

2000

nor

000

0

Cardiac risk factors and prevention

141

Participants with CIHD admission

Only one event (n = 3,888)

Readmission events (n = 2,509)

(2 20%)/1

> 6

6

explore the potential relationship between air pollution and both initial and subsequent readmission for cardiovascular events. This study will contribute important evidence to guide future research on the cardiovascular risk posed by air pollution, and help to shed light on the long-term impact of exposure to air pollution on cardiovascular health.

METHODS

Study population

4000 (60.78%)

2000

The UK Biobank is a national prospective cohort study in the UK. Between 2006 and 2010, over half a million participants aged 40-70 years were recruited at 22 assessment centres. Participants completed questionnaires on their lifestyle, environment and medical history at the beginning of recruitment. Among the 502411 initially recruited participants, 215849 and 507 were excluded due to a history of CVDs and blood pressure medication. A total of 286055 participants were finally included in this analysis (figure 1).

Follow-up and outcome ascertainment

Non-elective hospital admissions of the participants were obtained from England's Hospital Episode Statistics database, the Scottish Morbidity Record and the Patient Episode Database for Wales. Data on disease ascertainment during the follow-up were available up to 14 years. Mortality data for England and Wales were obtained from the National Health Service (NHS) Digital, and for Scotland from the NHS Central Register. All the participants were followed-up for the hospital admissions started at the recruitment date and ended at the date of death, loss to follow-up or the last date with available data, whichever came first. Total admission events were defined as admission

events for CVDs during follow-up, including the first admission event and subsequent readmission CVD events.

113

6 > 6

(2.74%)/*

Diagnosis of CVDs was ascertained according to Tenth Revision of the International Classification of Diseases (ICD-10). We focused on four major cardiovascular events: chronic ischaemic heart disease (CIHD), cerebrovascular disease, heart failure (HF) and atrial fibrillation (AF). CIHD was defined as ICD-10 codes I25; cerebrovascular disease was coded as ICD-10 codes I60-I69; HF was defined as ICD-10 codes I50 and AF was defined as ICD-10 codes I48.

Air pollution exposure assessment

The annual mean concentrations of air pollutants were obtained from the UK's Department for Environment, Food & Rural Affairs, which provides high-resolution (1 km×1 km grid cells) near-surface air pollution data. The air pollutants included particulate matter with a diameter $\leq 2.5 \,\mu m$ (PM_{2,5}), PM₁₀, nitrogen oxides (NO₂) and nitrogen dioxide (NO₂). Exposure assessments were based on geocoded residential address history of the participants. We then matched the annual air pollution concentrations to each participant's residential locations using bilinear interpolation. The average estimate of air pollutant exposure in the first 3 years of recruitment was calculated by weighting the time spent at each location.

Covariates

A directed acyclic graph (online supplemental figure 1) was developed to identify potential covariates.8 We selected the following covariates in the multivariate models: age, sex, relative humidity, ambient temperature, ethnicity, physical activity, income, and education. Individual exposure of relative humidity and ambient temperature was assessed based on the Met Offices' HadUK-Grid dataset using a bilinear interpolation method. Multiple imputation with the method of chained equations was performed to impute missing covariate values to make full use

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	No CVDs admission event	Single admission for CVDs	Readmissions for CVDs	
	(n=267 833)	(n=10973)	(n=6203)	P value
Age of recruit (years, mean±SD)	54.26±8.07	59.21±7.28	60.19±7.13	< 0.001
Vale (n, %)	110768 (41.36)	6266 (57.10)	3800 (61.26)	< 0.001
thnicity (n, %)				< 0.001
White	252 001 (94.09)	10 491 (95.61)	5924 (95.50)	
Missing	1491 (0.56)	68 (0.62)	58 (0.94)	
Air pollution (µg/m³, mean±SD)				
PM _{2.5}	10.48±2.13	10.37±2.04	10.47±2.07	< 0.001
PM ₁₀	16.63±2.89	16.48±2.75	16.61±2.80	< 0.001
NO ₂	20.74±6.93	20.49±6.54	20.91±6.76	< 0.001
NO _x	31.53±13.42	31.06±12.67	31.84±13.20	< 0.001
Meteorological factors (mean±SD)				
Relative humidity (%)	80.65±2.34	80.70±2.57	80.68±2.13	0.124
Ambient temperature (°C)	10.56±0.74	10.52±0.73	10.54±0.71	< 0.001
ducational attainment (n, %)				< 0.001
High	97800 (36.52)	3221 (29.35)	1558 (25.12)	
Intermediate	15 485 (5.78)	826 (7.53)	475 (7.66)	
Low	104706 (39.09)	3832 (34.92)	2097 (33.81)	
Other	44842 (16.74)	2819 (25.69)	1883 (30.36)	
Missing	5000 (1.87)	275 (2.51)	190 (3.06)	
ncome (£) (n, %)				< 0.001
>100 000	15 382 (5.74)	400 (3.65)	162 (2.61)	
52 000-100 000	55 580 (20.75)	1573 (14.34)	724 (11.67)	
31 000–51 999	64849 (24.21)	2222 (20.25)	1185 (19.10)	
18000–30 999	54 512 (20.35)	2524 (23.00)	1413 (22.78)	
<18 000	40285 (15.04)	2449 (22.32)	1566 (25.25)	
Missing	37 225 (13.90)	1805 (16.45)	1153 (18.59)	
Physical activity (n, %)				<0.001
Low	38526 (14.38)	1564 (14.25)	950 (15.32)	
Moderate	89049 (33.25)	3381 (30.81)	1888 (30.44)	
High	90747 (33.88)	3773 (34.38)	2030 (32.73)	
Missing	49511 (18.49)	2255 (20.55)	1335 (21.52)	
3MI (n, %)				< 0.001
Normal	106 520 (39.77)	3512 (32.01)	1835 (29.58)	
Obese	46 419 (17.33)	2452 (22.35)	1465 (23.62)	
Overweight	111 731 (41.72)	4864 (44.33)	2787 (44.93)	
Underweight	1790 (0.67)	64 (0.58)	42 (0.68)	
Missing	1373 (0.51)	81 (0.74)	74 (1.19)	
Drinking frequency (n, %)				< 0.001
Never	18 641 (6.96)	910 (8.29)	579 (9.33)	
Occasional	58 894 (21.99)	2403 (21.90)	1329 (21.43)	
Moderate	136583 (51.00)	5184 (47.24)	2841 (45.80)	
Heavy	52 912 (19.76)	2434 (22.18)	1419 (22.88)	
Missing	803 (0.30)	42 (0.38)	35 (0.56)	
moking status (n, %)		· · · · · · · · · · · · · · · · · · ·		<0.001
Never	155 778 (58.16)	5356 (48.81)	2789 (44.96)	
Previous	82 723 (30.89)	3904 (35.58)	2229 (35.93)	
Current	27911 (10.42)	1647 (15.01)	1116 (17.99)	
Missing	1421 (0.53)	66 (0.60)	69 (1.11)	

 $\mathsf{BMI}, \mathsf{body} \ \mathsf{mass} \ \mathsf{index}; \ \mathsf{CVD}, \mathsf{cardiovascular} \ \mathsf{disease}; \ \mathsf{NO}_2, \ \mathsf{nitrogen} \ \mathsf{dioxide}; \ \mathsf{NO}_{x'} \ \mathsf{nitrogen} \ \mathsf{oxides}; \ \mathsf{PM}, \ \mathsf{particulate} \ \mathsf{matter}.$

of the data. Five datasets including imputed data were generated and combined using Rubin's rules.⁹

Statistical analysis

Continuous variables were presented as mean±SD. Frequencies of categorical variables were computed. Comparisons among

groups were conducted using t-test, Pearson's χ^2 test or Fisher's exact test, as appropriate. The time intervals between sequential readmission events for CVDs after first admission were graphically displayed using Kaplan-Meier survival curves.

We used the Prentice, Williams and Peterson total time (PWP-TT) model to estimate the associations between air pollution

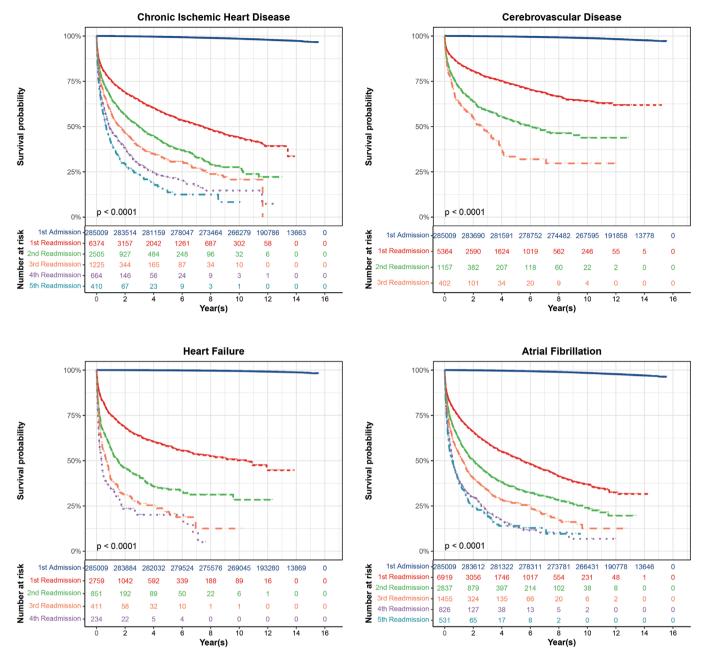


Figure 2 Kaplan-Meier survival curve for the time to each admission for four major cardiovascular diseases during follow-up.

and cardiovascular readmission events. The PWP-TT model is an extension of Cox proportional hazard model that allows investigating the first, and the subsequent multiple recurrent events. It is based on the assumption that recurrent events within the individual are related and an individual is at risk for the successive event only if he/she experienced a previous event.¹⁰ Since the small number of events in a stratum might cause unreliable estimate, the readmission analysis was restricted to the stratum with the number of patients >1% of all the patients.¹¹ We conducted an additional analysis stratified by each time of readmission to explore the association between air pollution and cardiovascular events in different sequential risk sets. We modelled the associations between air pollutants and the risk of cardiovascular admission events in two steps with increasing adjustment for confounders: model 1 adjusting for age and sex, and model 2 additionally adjusting for relative humidity, ambient temperature, ethnicity, physical activity, income and education.

We used natural cubic spline function with df of 3 to graphically analyse the dose-response relationship between air pollution and the risk admission events for CVDs. We conducted stratified analyses by sex, ethnicity, education level, income, physical activity, body mass index (BMI), smoking status and drinking frequency to estimate the effect modification, and further examined the difference across each stratification by the two-sample z-test.¹²

Sensitivity analyses

To account for potential exposure misclassification resulting from residential mobility, we further conducted the analyses among participants who maintained a consistent residential

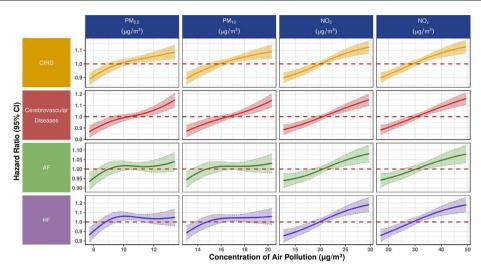


Figure 3 Dose-response curve of the association between air pollutants and the total admission events for cardiovascular diseases during followup. AF, atrial fibrillation; CIHD, chronic ischaemic heart disease; HF, heart failure; NO₂, nitrogen oxides; NO₂, nitrogen dioxide; PM, particulate matter.

address during the follow-up. The overlapped participants of four CVDs might lead to statistical selection bias,¹³ we thus performed a sensitivity analysis for participants with only one of the four CVDs.

The results were presented as hazard ratios (HRs) per interquartile range (IQR) increase of air pollution with 95% Confidence interval CIs. Data management and analyses were performed using R V.4.0.1.

RESULTS

Among the 285009 participants, 6397 (2.24%) developed CIHD, 6930 (2.43%) developed AF, 5403 (1.90%) developed cerebrovascular disease and 2773 (0.97%) developed HF during a median follow-up time of 12 years (figure 1). In summary, 39.22% of the patients with CIHD, 41.02% of the patients with AF, 21.58% of the patients with cerebrovascular disease and 30.87% of the patients with HF had subsequent recurrent events after the first admission.

Mean age of the participants without CVDs admission, with single CVDs admission and CVDs readmissions was 54.26 years, 59.21 years and 60.19 years, respectively. For participants with single CVDs admission, the mean concentrations of $PM_{2.5}$, PM_{10} , NO_2 and NO_x were 10.37 (SD 2.04) µg/m³, 16.48 (SD 2.75) µg/m³, 20.49 (SD 6.54) µg/m³ and 31.06 (SD 12.67) µg/m³, respectively. For participants with CVDs readmissions, corresponding concentrations were 10.47 (SD 2.07) µg/m³, 16.61 (SD 2.80) µg/m³, 20.91 (SD 6.76) µg/m³ and 31.84 (SD 13.20) µg/m³, respectively. In summary, compared with those without CVDs admission events during follow-up, patients with CVD were relatively older, more likely to be men and tended to have higher exposure levels of air pollution (table 1).

Kaplan-Meier survival curves displayed that patients who were readmitted more frequently had a significantly higher probability of subsequent readmissions compared with those who had fewer admissions (figure 2). A log-rank test showed statistically significant differences among the times of readmission for the

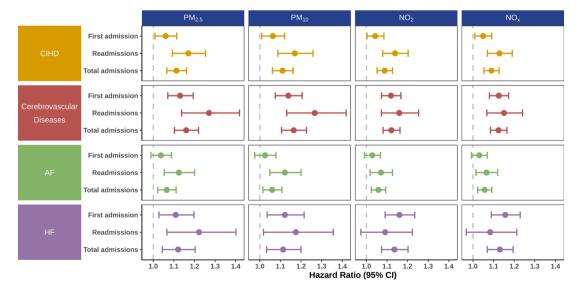


Figure 4 The associations of each IQR increase in air pollution with first admission, readmissions and total admissions for CVDs (HR and 95% CI). IQR increments are 2.79 μ g/m³ for PM_{2.5}, 3.81 μ g/m³ for PM₁₀, 8.15 μ g/m³ for NO₂ and 15.92 μ g/m³ for NO_x. AF, atrial fibrillation; CIHD, chronic ischaemic heart disease; HF, heart failure; NO_x, nitrogen oxides; NO₂, nitrogen dioxide; PM, particulate matter.

Table 2	Table 2 HR with 95% CI for each IQR increase of air pollution on the total cardiovascular admissions during follow-up by using PWP-TT model	h IQR increase of air poll	ution on the total cardiov	ascular admissions durin	g follow-up by using PW	P-TT model		
	CIHD		Cerebrovascular disease		AF		HF	
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
$PM_{2.5}$	1.047 (1.017 to 1.077)	1.113 (1.066 to 1.162)	1.099 (1.064 to 1.135)	1.160 (1.103 to 1.219)	1.063 (1.034 to 1.093)	1.065 (1.022 to 1.111)	1.090 (1.043 to 1.140)	1.121 (1.044 to 1.203)
PM ₁₀	1.046 (1.017 to 1.077)	1.110 (1.061 to 1.162)	1.102 (1.067 to 1.138)	1.164 (1.105 to 1.227)	1.062 (1.032 to 1.092)	1.060 (1.015 to 1.107)	1.088 (1.040 to 1.138)	1.113 (1.033 to 1.200)
NO2	1.069 (1.042 to 1.097)	1.089 (1.052 to 1.126)	1.117 (1.087 to 1.147)	1.121 (1.081 to 1.163)	1.062 (1.035 to 1.088)	1.058 (1.024 to 1.093)	1.109 (1.067 to 1.153)	1.136 (1.074 to 1.202)
NO	1.072 (1.045 to 1.100)	1.090 (1.053 to 1.127)	1.119 (1.090 to 1.149)	1.124 (1.085 to 1.165)	1.061 (1.035 to 1.088)	1.057 (1.023 to 1.091)	1.107 (1.065 to 1.150)	1.130 (1.070 to 1.195)
Model 1 a 15.92 µg/n	Model 1 adjusted for age and sex; model 2 further adjusted for relative humidity, ambient 15.92 $\mu g^{\rm m^3}$ for NO $_{\rm o}$.	2 further adjusted for relative	e humidity, ambient temperatu	re, ethnicity, physical activity,	income and education. IQR ir	temperature, ethnicity, physical activity, income and education. IQR increments are 2.79 µg/m ³ for PM _{2.9} , 3.81 µg/m ³ for PM ₁₀ , 8.15 µg/m ³ for NO ₂ and	M _{2.5} , 3.81 μg/m³ for PM ₁₀ , 8.15	i µg/m ³ for NO ₂ and
AF, atrial fi	AF, atrial fibrillation; CIHD, chronic ischaemic heart disease; HF, heart failure; NO ₂ , nitrogen dioxide; NO ₂ , nitrogen oxides; PM, particulate matter; PWP-TT, Prentice, Williams and Peterson-Total Time.	mic heart disease; HF, heart fa	ilure; NO2, nitrogen dioxide; N	0 _x , nitrogen oxides; PM, parti	culate matter; PWP-TT, Prentio	e, Williams and Peterson-Total	Time.	

CVDs (p<0.0001). Compared with cerebrovascular disease and CIHD, HF and AF had higher likelihood of readmission (online supplemental table 1). For example, the cumulative probability without readmission after the first readmission at 3 years was 77.23%, 64.40%, 63.68% and 59.74% for cerebrovascular disease, CIHD, HF and AF, respectively.

The dose-response curves between air pollutants and first admission events (online supplemental figure 2), readmission events (online supplemental figure 3) and total cardiovascular events (figure 3) during follow-up were found to be monotonic and approximately linear. Exposure to air pollutants was positively associated with the increase of risk of total admission events for CVDs during follow-up. Consistently positive associations were observed on the first admission, readmission and total admission events for four major CVDs (figure 4, table 2, online supplemental tables 2.3 for specific HRs). The associations on the first admission for CVDs were generally smaller than the associations on multiple readmissions events and total admission events during follow-up in CIHD, cerebrovascular diseases, HF and AF; this was opposite for the associations between oxides of nitrogen (NO₂ and NO₂) and HF. Specifically, the adjusted HR of the first admission, readmission and total admission events for CIHD were 1.060 (95% CI 1.008 to 1.114), 1.120 (95% CI 1.070 to 1.171) and 1.113 (95% CI 1.066 to 1.162) for each IQR increase of PM, , respectively. For cerebrovascular disease, these HRs were 1.130 (95% CI 1.070 to 1.194), 1.270 (95% CI 1.137 to 1.418) and 1.160 (95% CI 1.103 to 1.219), respectively. The associations between oxides of nitrogen and the first admission for HF were stronger than those in readmission for HF and total admissions for HF events during follow-up, with adjusted HR of 1.160 (95% CI 1.091 to 1.234), 1.091 (95% CI 0.973 to 1.223) and 1.136 (95% CI 1.074 to 1.202) for each IQR increase of NO₂, respectively.

Sex stratified analysis showed that the associations on total admission events for CIHD, AF and HF were generally stronger in females than males (table 3). For example, HRs for each IQR increase of NO₂ on total admissions for CIHD during follow-up were 1.109 (95% CI 1.051 to 1.171) and 1.071 (95% CI 1.026 to 1.117) in females and males, respectively. These HRs on total admissions for AF were 1.087 (95% CI 1.033 to 1.144) and 1.045 (95% CI 1.003 to 1.088) in females and males, respectively. In addition, the associations between PM2 5, PM10, NO2 and NO, and total admission for cerebrovascular disease in males were generally stronger than those in female. However, there were no significant disparity in the risk of total admission between sexes (p for difference >0.05). In addition, no significant effect modifications of ethnicity, education level, income or physical activity, BMI, drinking frequenct and smoking status were observed for any of the pollutants for the first admission and readmissions (online supplemental figures 4-7).

Additional analyses further examined the associations between air pollutants and specific stratum of each readmission event in four CVDs based on the PWP-TT stratified model (online supplemental tables 4-7). We observed that ambient air pollutants were associated with the first admission of each of the CVD, and subsequent readmission risk. For example, HRs for per IQR increase of PM₂, on the first, second, third, fourth and fifth readmission for CIHD were 1.084 (95% CI 1.005 to 1.168), 1.157 (95% CI 1.031 to 1.299), 1.125 (95% CI 0.966 to 1.310), 1.018 (95% CI 0.836 to 1.240) and 1.015 (95% CI 0.787 to 1.309), respectively.

The overlapped participants of four CVDs were shown in a Venn Diagram (online supplemental figure 8). The results of the analysis conducted for those participants with only one of

Table :	3 Sex stratified HR	with 95% CI for each	IQR inc	Table 3 Sex stratified HR with 95% CI for each IQR increase of the air pollution on the total cardiovascular events during follow-up by using PWP-TT model	tion on the total card	liovascu	ular events during foll	ow-up by using PWP	-TT mod	6		
	CIHD		٩	Cerebrovascular disease	e	٩	AF		۵.	HF		۵.
	Female	Male	value*	value* Female	Male	value*	value* Female	Male	value*	value* Female	Male	value*
PM _{2.5}	1.069 (0.993 to 1.150)	1.069 (0.993 to 1.150) 1.128 (1.072 to 1.188) 0.23 1.145 (1.063 to 1.234)	0.23	1.145 (1.063 to 1.234)	1.170 (1.094 to 1.253)	0.67	1.170 (1.094 to 1.253) 0.67 1.055 (0.988 to 1.125) 1.085 (1.029 to 1.144) 0.66 1.149 (1.024 to 1.289) 1.112 (1.019 to 1.213) 0.51	1.085 (1.029 to 1.144)	0.66	1.149 (1.024 to 1.289)	1.112 (1.019 to 1.213)	0.51
PM ₁₀	1.079 (1.000 to 1.166)	1.079 (1.000 to 1.166) 1.119 (1.060 to 1.182) 0.45	0.45	1.139 (1.054 to 1.231)	1.183 (1.103 to 1.269) 0.47	0.47	1.058 (0.989 to 1.132)	1.058 (0.989 to 1.132) 1.073 (1.016 to 1.134) 0.43	0.43	1.159 (1.028 to 1.307) 1.090 (0.994 to 1.196)	1.090 (0.994 to 1.196)	0.75
NO2	1.109 (1.051 to 1.171)	1.109 (1.051 to 1.171) 1.071 (1.026 to 1.117) 0.32	0.32	1.086 (1.030 to 1.144)	1.150 (1.093 to 1.209)	0.12	1.150 (1.093 to 1.209) 0.12 1.087 (1.033 to 1.144) 1.045 (1.003 to 1.088) 0.54 1.160 (1.064 to 1.264) 1.120 (1.041 to 1.205)	1.045 (1.003 to 1.088)	0.54	1.160 (1.064 to 1.264)	1.120 (1.041 to 1.205)	0.23
Ň	1.106 (1.050 to 1.166)	1.106 (1.050 to 1.166) 1.074 (1.029 to 1.120) 0.38 1.092 (1.037 to 1.150)	0.38		1.150 (1.095 to 1.207)	0.16	1.150 (1.095 to 1.207) 0.16 1.086 (1.033 to 1.142) 1.044 (1.002 to 1.086) 0.60 1.151 (1.057 to 1.254) 1.117 (1.041 to 1.199)	1.044 (1.002 to 1.086)	0.60	1.151 (1.057 to 1.254)	1.117 (1.041 to 1.199)	0.22
Model ad *Estimate AF, atrial	lodel adjusted for relative humidity, aml Estimated using the two-samplie z-test. F, atrial fibrillation; CIHD, chronic ischaei	Model adjusted for relative humidity, ambient temperature, age, ethnicity, physical activity, income and *Estimated using the two-samplie z-test. AF, atrial fibrillation; CIHD, chronic ischaemic heart disease; HF, heart failure; NO ₂ , nitrogen dioxide; NO,	ethnicity, eart failure	Model adjusted for relative humidity, ambient temperature, age, ethnicity, physical activity, income and education. IQR increments are 2.79 µg/m ³ for PM ₁₂ , 3.81 µg/m ³ for PM ₁₂ , 3.81 µg/m ³ for PM ₁₂ , 8.15 µg/m ³ for NO ₂ i *Estimated using the two-samplie z-test. Af, atrial fibrillation; CIHD, chronic ischaemic heart disease; HF, heart failure; NO ₂ , nitrogen dioxide; NO ₂ , nitrogen oxides; PM, particulate matter; PWP-TT, Prentice, Williams and Peterson-Total Time.	l education. IQR increments , nitrogen oxides; PM, partic	s are 2.79 culate ma	d education. IQR increments are 2.79μ g/m ³ for PM ₁₂ , 3.81 μ g/m ³ for PM ₁₀ , 8.15 μ g/m ³ for NO ₂ and 15.92 μ g/m ³ for NO ₂ , nitrogen oxides; PM, particulate matter, PWP-TT, Prentice, Williams and Peterson-Total Time.	ior PM ₁₀ , 8.15 µg/m ³ for NO _. ims and Peterson-Total Time	and 15.92	µg/m³ for NO _x .		

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the four CVDs were consistent with the main analysis (online supplemental table 8). In addition, out of the 285009 participants, >70% of them did not change their residential address during the follow-up (online supplemental table 9). The associations between air pollution and admission events for the CVDs during follow-up in participants who did not change their residential addresses remain stable (online supplemental table 10).

DISCUSSION

In this study, the relationship between air pollutants exposure and total cardiovascular events during follow-up was investigated. CIHD, cerebrovascular disease, AF and HF were the most common recurrent cardiovascular events in the study population of 286055 middle-aged and older participants. Ambient air pollutants exposure was significantly associated with the first admission and readmission risk of these four CVDs. Sex did not appear to significantly modify the associations between exposure to air pollution and the recurrent CVD events, except for the associations of HF.

Proper assessment of the disease burden and implementation of effective preventive measures require comprehensive consideration of all subsequent events following the first occourance.¹⁴ However, numerous studies have mainly reported the associations between air pollutants and incidence of CVDs,¹⁵ only a few studies have examined their role in recurrent cardiovascular events.⁶ These studies have only considered the effects of air pollution exposure on the first recurrent event among patients with a history of CVDs, rather than the multiple cardiovascular events since the first occurrence of CVDs.¹⁶¹⁷ This may be largely due to traditional statistical methods, which are only capable of focusing on single events. Therefore, we employed the PWP-TT model, a well-developed statistical tool for analysing recurrent event data, to accurately and comprehensively assess the relationship between the air pollution exposure and the total cardiovascular events that occur during the follow-up.¹⁸ In addition, PWP-TT model is capable of estimating the association between air pollution and the risk of multiple sequential events simultaneously by taking accounts for the order of events.¹⁹

This study explored the associations between air pollutants and the dynamic progression of CVDs, suggesting that four air pollutants (PM₂, PM₁₀, NO₂ and NO₂) were associated with the increased risk of total admission events for CVDs. This result is consistent with previous studies that reported a significant effect of air pollution on the risk of CVDs in Europe.²⁰ Additionally, previous studies also proposed that individuals with existing CVDs might be more susceptible to the air pollution exposure.²¹ Similarly, we observed a tendency towards an increase in the risk of readmission for CVDs in response to exposure to air pollutant, which is significantly higher than the risk associated with the first hospitalisation event. Previous studies had also found that the exposure to air pollution was associated with recurrent event of acute myocardial infarction,²² and cerebrovascular disease.²¹ However, few studies have focused on the role of air pollution on the multiple readmission events. This is the first study to investigate the association between air pollution and total admission events for CVDs during follow-up in middleaged and elderly participants. More research is needed to further disentangle the relationship between air pollution and recurrent cardiovascular events.

Several biological mechanisms have been proposed to explain the observed associations. Among these mechanisms, oxidative stress and inflammation are considered the leading pathways by which air pollutants increase risk of CVDs.²³ Exposure to

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air pollution can trigger the upregulation of pathways that generate reactive oxygen species and ultimately lead to endothelial dysfunction, atherosclerosis and thrombosis.²⁴ Moreover, individuals with poor physiological conditions are more likely to be exacerbated by exposure to air pollution, especially for the patients with pre-existing CVDs, air pollution exposure may accelerate thrombosis and thus increase the risk of the recurrence of CVDs.²⁵ Thus, early identification of these preventable risk factors in patients with pre-existing CVDs is of critical significance in the primary prevention efforts and public health policy.

There were generally stronger associations between air pollutants and total CVD events in females compared with males. However, sex differences were not statistically significant. Consistent results in previous studies regarding the sex-related cardiovascular effects of air pollution,²⁶ the following physiological differences may be the primary reason for the sexual differences in the susceptibility of CVDs. Elderly women have a higher incidence and severity of CVDs compared with men due to the decreased levels of sex hormones.²⁷ In addition, the key systems involved in the development of CVDs, such as immune system and sympathetic nervous system, are activated differently in males and females.²⁸ Furthermore, participants with abnormal BMI, smoking and drinking were associated with an increased risk of both first admission and readmission for CVDs triggered by air pollution,²⁹ although the degree of risk may vary among these factors.

Strengths and limitations

The main strength of this study is the large and well-characterised sample in UK Biobank, as well as the extensive linkages to health records derived from the national healthcare system with universal coverage and rigorous follow-up protocols. In addition, the health data collected by the UK Biobank spans over 14 years, providing extensive follow-up, which enabled the reliable identification of multiple CVD events of the participants.

There are limitations that warrant noting. First, indoor air pollution was not considered due to limited measurements of indoor air pollution exposure. Second, information on potential time-varying confounders were not available, therefore, residual confounding is another issue. However, air pollution emissions have been shown to be stable over decades remained relatively stable according to the UK official statistics.³⁰ Therefore, it is reasonable to believe that the exposure estimates of air pollutants at baseline could represent the long-term exposure. In addition, we did not consider the blood pressure medication during the follow-up due to the lack of the information, which might lead to bias in the estimated associations between air pollution and recurrent CVDs.

CONCLUSION

Our study provides evidence that ambient air pollutants might be an important risk factor for the first admission, and the subsequent multiple readmissions for CVD. Given the heavy CVD burden, compounded by decreased mortality of CVD due to medical advances, this study may have important implications for the carrying out prevention measures for CVD and for guiding environmental regulatory decisions.

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 ZMQ and HLin drafted the manuscript. DL, CW and ZZ contributed to the discussion. MV, AK and HLi revised the manuscript. HLin is the guarantor of the work. All authors critically reviewed and edited the manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The study was approved by the North West Multicenter Research Ethical Committee (11/NW/03820). Every participant provided informed written consent.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. This research was conducted using the UK Biobank resource under access application 69550. UK Biobank will make the data available to all bona fide researchers for all types of health-related research that is in the public interest, without preferential or exclusive access for any persons. All researchers will be subject to the same application process and approval criteria as specified by UK Biobank. For more details on the access procedure, see the UK Biobank website: http://www.ukbiobank.ac.uk/register-apply.

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Supplementary Materials

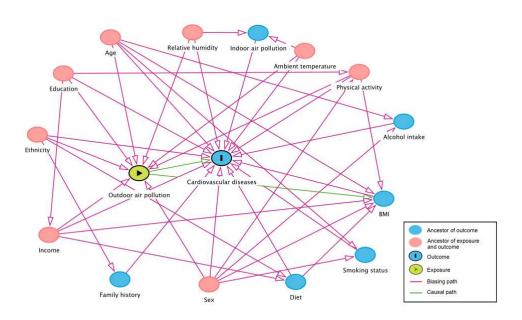


Figure S1. Directed acyclic graph for the associations between air pollution exposure and cardiovascular diseases, created with the help of dagitty.net.

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	1 Year	3 Years	5 Years	7 Years	9 Years	11 Years	13 Years
1 st Readmission							
CIHD	75.65%	64.40%	56.39%	50.94%	45.60%	41.66%	39.15%
Cerebrovascular disease	84.90%	77.23%	72.75%	68.56%	64.70%	62.81%	61.87%
HF	75.14%	63.68%	58.06%	53.44%	51.48%	47.47%	44.68%
AF	74.04%	59.74%	51.53%	44.74%	38.34%	34.45%	31.61%
2 nd Readmission							
CIHD	66.16%	49.80%	39.67%	32.87%	27.53%	23.76%	-
Cerebrovascular disease	71.58%	58.63%	52.83%	47.99%	45.22%	43.81%	-
HF	56.75%	41.63%	34.52%	31.23%	31.23%	28.39%	-
AF	61.89%	42.96%	34.76%	30.29%	26.07%	21.41%	19.63%
3 rd Readmission							
CIHD	58.13%	38.84%	31.37%	27.25%	22.10%	20.72%	
Cerebrovascular disease	62.96%	46.97%	33.39%	31.93%	29.65%	29.65%	-
HF	39.64%	26.80%	21.72%	12.54%	12.54%	-	-
AF	53.55%	33.90%	26.64%	20.48%	16.13%	12.57%	-
4 th Readmission							
CIHD	48.35%	28.75%	21.60%	17.27%	14.66%	14.66%	
HF	34.58%	20.07%	20.07%	10.03%	-	-	-
AF	39.21%	21.64%	12.97%	10.28%	6.86%	6.86%	-
5 th Readmission							
CIHD	41.42%	23.39%	13.70%	12.45%	8.30%	-	-
AF	37.82%	19.70%	13.99%	12.82%	9.62%	-	-

Table S1. The cumulative probability without readmission after an admission event for cardiovascular diseases during the follow-up.

-: Not available.

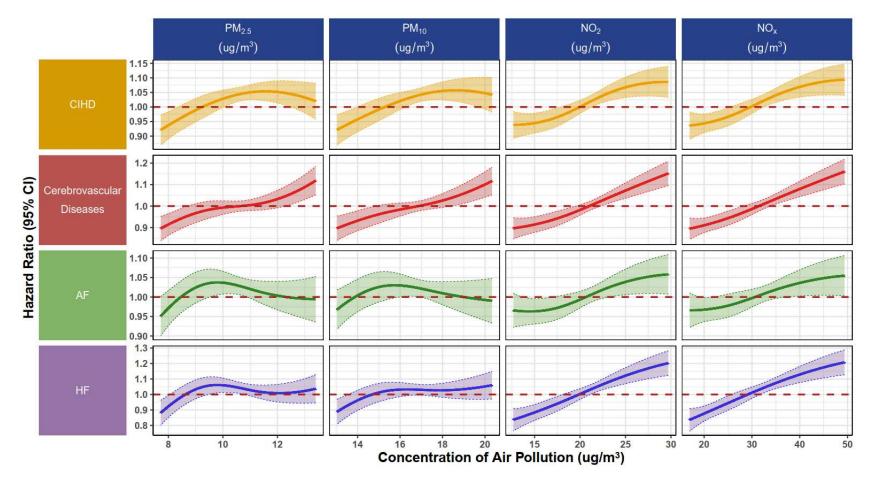


Figure S2. Dose-response curve of the association between air pollutants and the first admission events for CVDs during follow-up.



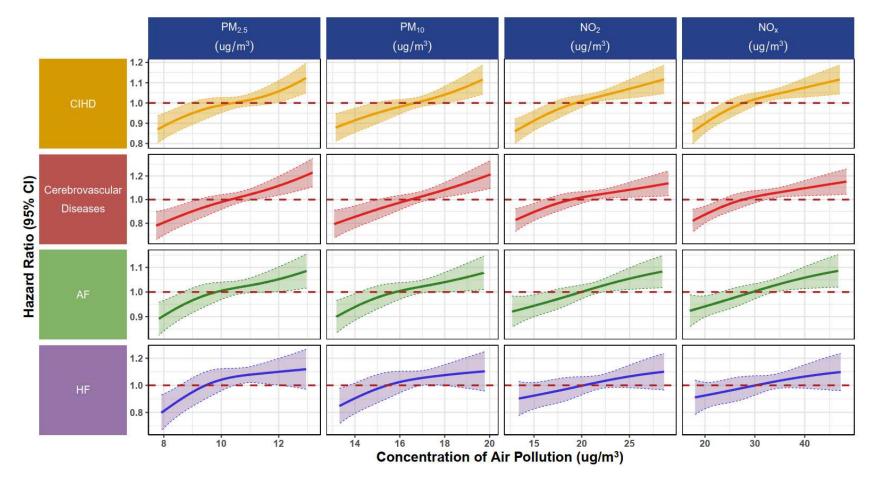


Figure S3. Dose-response curve of the association between air pollutants and the readmission events for CVDs during follow-up.

	CI	HD	Cerebrovaso	cular Disease	A	лF	H	IF
	Model 1	Model 2						
PM _{2.5}	1.014 (0.981,	1.060 (1.008,	1.078 (1.040,	1.130 (1.070,	1.037 (1.005,	1.037 (0.988,	1.076 (1.024,	1.109 (1.027,
	1.047)	1.114)	1.117)	1.194)	1.070)	1.088)	1.131)	1.197)
PM_{10}	1.017 (0.984,	1.063 (1.009,	1.083 (1.045,	1.138 (1.075,	1.033 (1.001,	1.025 (0.975,	1.086 (1.033,	1.122 (1.035,
	1.051)	1.120)	1.123)	1.205)	1.066)	1.078)	1.141)	1.215)
NO_2	1.039 (1.009,	1.043 (1.003,	1.112 (1.078,	1.119 (1.073,	1.033 (1.004,	1.029 (0.991,	1.129 (1.081,	1.160 (1.091,
	1.070)	1.085)	1.147)	1.168)	1.063)	1.068)	1.178)	1.234)
NO _x	1.044 (1.014,	1.049 (1.009,	1.116 (1.082,	1.125 (1.080,	1.033 (1.004,	1.030 (0.993,	1.127 (1.080,	1.157 (1.089,
	1.075)	1.091)	1.151)	1.173)	1.063)	1.070)	1.176)	1.229)

Table S2. Hazard ratio (95% CIs) for each IQR increase of air pollution on the first cardiovascular admission during follow-up by using PWP-TT model.

	CI	HD	Cerebrovaso	cular Disease	A	٨F	H	IF
	Model 1	Model 2						
PM _{2.5}	1.099 (1.048,	1.120 (1.070,	1.172 (1.097,	1.270 (1.137,	1.120 (1.070,	1.124 (1.053,	1.183 (1.084,	1.222 (1.066,
	1.152)	1.171)	1.251)	1.418)	1.171)	1.200)	1.291)	1.401)
PM_{10}	1.098 (1.045,	1.119 (1.069,	1.165 (1.092,	1.266 (1.130,	1.119 (1.069,	1.122 (1.048,	1.159 (1.061,	1.175 (1.017,
	1.152)	1.171)	1.242)	1.419)	1.171)	1.200)	1.266)	1.356)
NO_2	1.109 (1.063,	1.093 (1.051,	1.150 (1.089,	1.159 (1.073,	1.093 (1.051,	1.071 (1.018,	1.106 (1.020,	1.091 (0.973,
	1.158)	1.137)	1.213)	1.253)	1.137)	1.126)	1.199)	1.223)
NO _x	1.106 (1.060,	1.091 (1.049,	1.146 (1.087,	1.151 (1.067,	1.091 (1.049,	1.066 (1.014,	1.105 (1.020,	1.083 (0.968,
	1.154)	1.134)	1.208)	1.241)	1.134)	1.120)	1.197)	1.213)

Table S3. Hazard ratio (95% CIs) for each IQR increase of air pollution on the multiple cardiovascular readmissions during follow-up by using PWP-TT model.

Air Poluti	on Subgroup	First admission	HR (95% CI)	P Value	Reau	missions HR (95% CI)	P Valu
PM2.5	Non-white White		0.990 (0.789, 1.242) 1.065 (1.011, 1.121)	0.539		1.081 (0.763, 1.531) 1.171 (1.092, 1.256)	0.658
	High education level Low education level	+=-1	1.079 (0.973, 1.197) 1.061 (1.001, 1.124)	0.772		1.225 (1.063, 1.413) 1.161 (1.073, 1.256)	0.516
	High income Low income		1.005 (0.930, 1.086) 1.105 (1.034, 1.181)	0.069		1.162 (1.034, 1.306) 1.185 (1.089, 1.289)	0.793
	Enough physical activity Lack of physical activity		1.056 (0.998, 1.116) 1.081 (0.961, 1.215)	0.725		1.148 (1.063, 1.239) 1.263 (1.088, 1.467)	0.265
	Normal BMI Abnormal BMI		1.055 (0.958, 1.162) 1.064 (1.003, 1.129)	0.887		1.174 (1.016, 1.357) 1.167 (1.080, 1.260)	0.938
	No Drinking Drink		1.084 (0.919, 1.280) 1.057 (1.003, 1.114)	0.772		1.240 (0.973, 1.578) 1.164 (1.084, 1.250)	0.626
	No smoking Smoke	+	1.036 (0.960, 1.118) 1.070 (1.001, 1.144)			1.138 (1.021, 1.270) 1.177 (1.076, 1.288)	0.645
PM10	Non-white White		1.003 (0.791, 1.272) 1.069 (1.012, 1.128)	0.609 -		1.113 (0.763, 1.623) 1.169 (1.085, 1.259)	0.804
	High education level Low education level		1.070 (0.958, 1.197) 1.074 (1.011, 1.141)	0.956		1.234 (1.064, 1.433) 1.158 (1.065, 1.260)	0.466
	High income Low income	├- ₽ - - ₽ -	1.000 (0.921, 1.086) 1.118 (1.043, 1.198)	0.042		1.159 (1.024, 1.311) 1.184 (1.082, 1.295)	0.782
	Enough physical activity Lack of physical activity		1.055 (0.995, 1.119) 1.104 (0.975, 1.250)	0.518		1.149 (1.059, 1.246) 1.245 (1.062, 1.461)	0.378
	Normal BMI Abnormal BMI	+++++++++++++++++++++++++++++++++++++++	1.061 (0.958, 1.175) 1.065 (1.001, 1.133)	0.953		1.205 (1.032, 1.407) 1.157 (1.067, 1.255)	0.649
	No Drinking Drink	++++	1.088 (0.915, 1.294) 1.060 (1.003, 1.120)	0.778		1.250 (0.979, 1.596) 1.161 (1.076, 1.253)	0.574
	No smoking Smoke		1.028 (0.949, 1.114) 1.079 (1.005, 1.158)	0.377		1.152 (1.025, 1.295) 1.165 (1.059, 1.281)	0.885
NO2	Non-white White		1.066 (0.884, 1.285) 1.045 (1.004, 1.088)	0.84		1.018 (0.762, 1.360) 1.141 (1.079, 1.206)	0.45
	High education level Low education level	8 -■-	1.024 (0.947, 1.109) 1.070 (1.022, 1.120)	0.352	Hand I	1.200 (1.073, 1.342) 1.130 (1.060, 1.205)	0.363
	High income Low income	⊢∎-I ⊢∎-I	0.994 (0.935, 1.056) 1.095 (1.040, 1.154)	0.017		1.176 (1.080, 1.280) 1.124 (1.047, 1.207)	0.425
	Enough physical activity Lack of physical activity	 =- =	1.036 (0.992, 1.083) 1.076 (0.981, 1.180)	0.475		1.145 (1.078, 1.217) 1.110 (0.982, 1.255)	0.653
	Normal BMI Abnormal BMI		1.061 (0.984, 1.144) 1.037 (0.989, 1.086)	0.611	}-= }=-	1.283 (1.149, 1.432) 1.107 (1.040, 1.178)	0.022
	No Drinking Drink		1.042 (0.914, 1.187) 1.042 (0.999, 1.086)	0.998	H=+	1.089 (0.921, 1.286) 1.146 (1.082, 1.213)	0.57
	No smoking Smoke		1.004 (0.946, 1.065) 1.058 (1.003, 1.116)	0.195		1.165 (1.057, 1.284) 1.118 (1.046, 1.195)	0.497
NOX	Non-white White	H H	1.075 (0.911, 1.268) 1.051 (1.010, 1.094)	0.801 -		0.993 (0.759, 1.299) 1.132 (1.072, 1.196)	0.348
	High education level Low education level	H-B-I H-H-I	1.034 (0.957, 1.117) 1.075 (1.027, 1.124)	0.395	Hand I	1.194 (1.070, 1.331) 1.119 (1.051, 1.192)	0.316
	High income Low income		0.997 (0.938, 1.059) 1.102 (1.048, 1.159)	0.012		1.167 (1.073, 1.269) 1.113 (1.038, 1.193)	0.397
	Enough physical activity Lack of physical activity		1.041 (0.997, 1.087) 1.089 (0.995, 1.192)		Heri	1.133 (1.067, 1.203) 1.111 (0.985, 1.253)	0.78
	Normal BMI Abnormal BMI		1.067 (0.991, 1.149) 1.044 (0.997, 1.092)	0.616	<u>}-</u> ∎ -=-	1.268 (1.139, 1.411) 1.099 (1.033, 1.169)	0.023
	No Drinking Drink		1.038 (0.915, 1.178) 1.049 (1.007, 1.093)	0.88	H=1	1.086 (0.930, 1.269) 1.136 (1.074, 1.203)	0.591
	No smoking Smoke	<u>⊢∎-1</u>	1.008 (0.950, 1.069) 1.065 (1.011, 1.122)	0.167		1.162 (1.054, 1.280) 1.105 (1.036, 1.180)	0.405

Figure S4. Hazard ratio (HR with 95% CI) for each IQR increase of air pollution on the first and readmission events for CIHD during follow-up, stratified by ethnicity, education level, income, and physical activity.

(Note: High educational level is defined as: high educational attainment, Low educational level is defined as intermediate, low, and other educational attainment, High income is defined as income higher $31,000 \pm$, Low income is defined as income lower than $30,999 \pm$, Enough physical activity is defined as moderate or high physical activity, Lack of physical activity is defined as low physical activity.)

Air Polution		irst admission	HR (95% CI)	P Value		leadmissions HR (95% CI)	P Valu
PM2.5	Non-white White	He-I	1.015 (0.742, 1.389) 1.134 (1.073, 1.199)	0.494	-	1.959 (0.861, 4.457) 1.257 (1.123, 1.407)	0.295
	High education level Low education level	1 + 8 −1 18 −1	1.080 (0.969, 1.205) 1.150 (1.079, 1.226)	0.329		1.333 (1.048, 1.696) 1.251 (1.103, 1.418)	0.643
	High income Low income	┝╼┥	1.035 (0.947, 1.131) 1.194 (1.114, 1.281)	0.013		1.085 (0.895, 1.314) 1.339 (1.170, 1.532)	0.078
	Enough physical activity Lack of physical activity		1.144 (1.076, 1.216) 1.080 (0.953, 1.224)	0.418		1.235 (1.094, 1.395) 1.563 (1.167, 2.093)	0.145
	Normal BMI Abnormal BMI		1.235 (1.123, 1.360) 1.078 (1.008, 1.152)	0.022		1.274 (1.047, 1.551) 1.284 (1.120, 1.472)	0.951
	No Drinking Drink		1.253 (1.051, 1.493) 1.116 (1.054, 1.183)	0.222	Ha-I H	1.212 (0.873, 1.683) 1.283 (1.138, 1.445)	0.751
	No smoking Smoke		1.158 (1.071, 1.251) 1.103 (1.020, 1.191)	0.385		1.355 (1.148, 1.600) 1.231 (1.058, 1.431)	0.402
PM10	Non-white White		1.062 (0.761, 1.482) 1.139 (1.075, 1.207)	0.685	-	1.892 (0.718, 4.981) 1.255 (1.118, 1.408)	0.41
	High education level Low education level	⊢ (⊢(1.089 (0.969, 1.223) 1.160 (1.085, 1.239)	0.357		1.349 (1.047, 1.736) 1.243 (1.093, 1.413)	0.572
	High income Low income	┝┿╋╾┥ ┝┿╋╾┥	1.043 (0.950, 1.144) 1.205 (1.120, 1.297)	0.016		1.072 (0.876, 1.312) 1.351 (1.177, 1.550)	0.064
	Enough physical activity Lack of physical activity	H=-1	1.151 (1.080, 1.227) 1.093 (0.958, 1.246)	0.485		1.242 (1.095, 1.409) 1.510 (1.132, 2.014)	0.223
	Normal BMI Abnormal BMI	<u>⊢</u> ∎	1.251 (1.131, 1.383) 1.081 (1.008, 1.159)	0.019		1.249 (1.025, 1.521) 1.294 (1.122, 1.492)	0.775
	No Drinking Drink	He-I	1.314 (1.092, 1.582) 1.119 (1.054, 1.188)	0.106	H	1.161 (0.835, 1.614) 1.281 (1.133, 1.448)	0.582
	No smoking Smoke	<u>⊢∎- </u> ⊢∎-	1.153 (1.063, 1.251) 1.120 (1.033, 1.214)	0.614		1.331 (1.118, 1.585) 1.236 (1.062, 1.439)	0.531
NO2	Non-white White	H=1	1.121 (0.897, 1.401) 1.117 (1.070, 1.165)	0.974		1.135 (0.632, 2.038) 1.160 (1.072, 1.256)	0.941
	High education level Low education level	H=-1 H=-1	1.059 (0.979, 1.147) 1.151 (1.096, 1.209)	0.082	H=-1	1.280 (1.091, 1.501) 1.120 (1.021, 1.227)	0.154
	High income Low income		1.062 (0.994, 1.135) 1.172 (1.110, 1.236)	0.024	법	1.166 (0.991, 1.372) 1.145 (1.043, 1.258)	0.85
	Enough physical activity Lack of physical activity	H=-1	1.130 (1.079, 1.184) 1.087 (0.987, 1.197)	0.469	H.	1.199 (1.090, 1.318) 1.100 (0.895, 1.354)	0.461
	Normal BMI Abnormal BMI	H=H	1.176 (1.096, 1.261) 1.085 (1.030, 1.143)	0.072	H I	1.170 (1.030, 1.329) 1.156 (1.045, 1.280)	0.887
	No Drinking Drink	}∎ }=-	1.110 (0.970, 1.271) 1.118 (1.071, 1.168)	0.922	Hall I	0.953 (0.761, 1.195) 1.199 (1.098, 1.310)	0.063
	No smoking Smoke	1	1.121 (1.055, 1.190) 1.125 (1.061, 1.192)	0.933	Ħ	1.152 (1.007, 1.319) 1.176 (1.066, 1.298)	0.809
NOX	Non-white White		1.108 (0.907, 1.353) 1.124 (1.078, 1.172)	0.89	Hand I	1.145 (0.686, 1.911) 1.152 (1.067, 1.243)	0.983
	High education level Low education level	┝╼╾┥ ┝╼╾┥	1.072 (0.992, 1.158) 1.154 (1.100, 1.212)	0,109		1.286 (1.104, 1.499) 1.107 (1.013, 1.211)	0.098
	High income Low income	H=- H=-	1.071 (1.003, 1.144) 1.174 (1.114, 1.237)	0.032		1.161 (0.993, 1.358) 1.133 (1.034, 1.241)	0.791
	Enough physical activity Lack of physical activity		1.137 (1.087, 1.190) 1.088 (0.991, 1.195)	0.406	H.	1.186 (1.081, 1.301) 1.103 (0.905, 1.345)	0.518
	Normal BMI Abnormal BMI	H=H H=H	1.184 (1.107, 1.268) 1.090 (1.036, 1.147)	0.055	Ħ	1.159 (1.030, 1.304) 1.150 (1.040, 1.273)	0.929
	No Drinking Drink	H=+	1.101 (0.966, 1.254) 1.126 (1.079, 1.175)	0.744		0.937 (0.755, 1.162) 1.192 (1.094, 1.299)	0.042
	No smoking Smoke		1.129 (1.065, 1.197) 1.129 (1.067, 1.196)	0.995	H	1.149 (1.007, 1.312) 1.161 (1.056, 1.276)	0.904
		0.9 1 1.1 1.2 1.3 1.4 1.5 Hazard Ratio		c	0.7 1.3 1.9 2.5 3.1 Hazard Ratio		

Figure S5. Hazard ratio (HR with 95% CI) for each IQR increase of air pollution on the first and readmission events for cerebrovascular disease during follow-up, stratified by ethnicity, education level, income, and physical activity. (Note: High educational level is defined as: high educational attainment, Low educational level is defined as intermediate, low, and other educational attainment, High income is defined as income higher 31,000 £, Low income is defined as income lower than 30,999 £, Enough physical activity is defined as moderate or high physical activity, Lack of physical activity is defined as low physical activity.)

Air Poluti	on Subgroup	First admission	HR (95% CI)	P Value		missions HR (95% CI)	P Valu
PM2.5	Non-white White		1.001 (0.686, 1.461) 1.038 (0.989, 1.090)	0.852		0.910 (0.591, 1.400) 1.128 (1.056, 1.205)	0.334
	High education level Low education level	H=-1 H=-1	1.060 (0.968, 1.159) 1.037 (0.979, 1.099)	0.695	H = I	1.091 (0.959, 1.242) 1.140 (1.056, 1.231)	0.569
	High income Low income		1.060 (0.984, 1.143) 1.032 (0.968, 1.099)	0.586		1.039 (0.935, 1.154) 1.165 (1.072, 1.266)	0.093
	Enough physical activity Lack of physical activity	/ ₩₩	1.031 (0.977, 1.087) 1.071 (0.956, 1.199)	0.55	H#H 	1.099 (1.022, 1.180) 1.298 (1.112, 1.515)	0.056
	Normal BMI Abnormal BMI	Heri	1.000 (0.918, 1.091) 1.053 (0.994, 1.116)	0.335	Heri	1.056 (0.936, 1.192) 1.142 (1.057, 1.235)	0.284
	No Drinking Drink		0.933 (0.782, 1.115) 1.046 (0.995, 1.100)	0.226		0.960 (0.790, 1.167) 1.149 (1.073, 1.231)	0.089
	No smoking Smoke		0.991 (0.924, 1.062) 1.078 (1.008, 1.152)	0.088		1.129 (1.028, 1.239) 1.099 (1.004, 1.203)	0.689
PM10	Non-white White		0.999 (0.667, 1.498) 1.026 (0.975, 1.080)	0.899	Heri I	0.895 (0.577, 1.389) 1.127 (1.052, 1.206)	0.31
	High education level Low education level	I-m-I Hm-I	1.034 (0.941, 1.138) 1.033 (0.973, 1.098)	0.988	F-∎-1 F=-1	1.072 (0.935, 1.229) 1.145 (1.058, 1.238)	0.417
	High income Low income	Ha-I Ha-I	1.051 (0.971, 1.137) 1.022 (0.956, 1.092)	0.594	⊢∎- ⊢∎-	1.024 (0.917, 1.143) 1.174 (1.078, 1.279)	0.054
	Enough physical activity Lack of physical activity		1.013 (0.959, 1.072) 1.086 (0.963, 1.224)	0.309	}=+ -=	1.091 (1.013, 1.174) 1.327 (1.131, 1.558)	0.029
	Normal BMI Abnormal BMI		0.981 (0.896, 1.074) 1.043 (0.981, 1.108)	0.275	H	1.039 (0.917, 1.177) 1.146 (1.058, 1.243)	0.194
	No Drinking Drink		0.925 (0.765, 1.118) 1.034 (0.981, 1.090)	0.266		0.990 (0.815, 1.202) 1.144 (1.065, 1.228)	0.17
	No smoking Smoke		0.978 (0.910, 1.052) 1.064 (0.991, 1.141)	0.106		1.129 (1.026, 1.242) 1.094 (0.996, 1.202)	0.645
NO2	Non-white White		1.295 (0.969, 1.731) 1.024 (0.986, 1.064)	0.115		1.040 (0.753, 1.436) 1.076 (1.022, 1.133)	0.839
	High education level Low education level	He-I Jeel	0.998 (0.933, 1.068) 1.056 (1.008, 1.105)	0.178	H-m-I H=I	1.077 (0.965, 1.201) 1.079 (1.017, 1.145)	0.976
	High income Low income		1.053 (0.993, 1.115) 1.029 (0.978, 1.082)	0.561		1.019 (0.936, 1.108) 1.113 (1.043, 1.188)	0.101
	Enough physical activity Lack of physical activity		1.025 (0.983, 1.068) 1.045 (0.954, 1.145)	0.695		1.062 (1.005, 1.122) 1.141 (1.005, 1.295)	0.309
	Normal BMI Abnormal BMI		1.014 (0.949, 1.083) 1.029 (0.983, 1.078)	0.714	Hard Hard	0.978 (0.881, 1.085) 1.101 (1.038, 1.168)	0.052
	No Drinking Drink	H	0.906 (0.784, 1.048) 1.039 (1.000, 1.081)	0.073		1.029 (0.893, 1.185) 1.083 (1.026, 1.143)	0.505
	No smoking Smoke		1.001 (0.948, 1.058) 1.047 (0.995, 1.103)	0.244	He-I He-I	1.082 (1.004, 1.165) 1.043 (0.974, 1.116)	0.474
NOX	Non-white White		1.260 (0.986, 1.611) 1.026 (0.988, 1.065)	0.104		0.992 (0.736, 1.337) 1.071 (1.019, 1.127)	0.617
	High education level Low education level	He-1 Jeel	1.000 (0.936, 1.070) 1.056 (1.010, 1.105)	0.186	H-m-I H-m-I	1.070 (0.961, 1.192) 1.073 (1.013, 1.137)	0.967
	High income Low income		1.045 (0.986, 1.106) 1.038 (0.988, 1.090)	0.863	⊢∎-1 ⊨≡-1	1.020 (0.940, 1.108) 1.102 (1.035, 1.174)	0.145
	Enough physical activity Lack of physical activity		1.024 (0.983, 1.067) 1.059 (0.969, 1.158)	0.496		1.058 (1.003, 1.116) 1.131 (1.001, 1.278)	0.326
	Normal BMI Abnormal BMI		1.015 (0.951, 1.084) 1.032 (0.986, 1.080)	0.689	H=H H=H	0.981 (0.887, 1.084) 1.094 (1.032, 1.159)	0.065
	No Drinking Drink		0.918 (0.795, 1.059) 1.041 (1.001, 1.081)	0.097		1.018 (0.892, 1.161) 1.079 (1.024, 1.138)	0.416
	No smoking Smoke		1.005 (0.951, 1.062) 1.047 (0.996, 1.102)	0.275		1.074 (0.999, 1.155) 1.039 (0.972, 1.110)	0.502
		0.9 1 1.1 1.3 1.5 Hazard Ratio			0.75 0.95 1.15 1.35 Hazard Ratio		

Figure S6. Hazard ratio (HR with 95% CI) for each IQR increase of air pollution on the first and readmission events for AF during follow-up, stratified by ethnicity, education level, income, and physical activity.

(Note: High educational level is defined as: high educational attainment, Low educational level is defined as intermediate, low, and other educational attainment, High income is defined as income higher $31,000 \pm$, Low income is defined as income lower than $30,999 \pm$, Enough physical activity is defined as moderate or high physical activity, Lack of physical activity is defined as low physical activity.)

White 1.121 (1034, 1.215) 1.193 (1030, 1.382) High education level we docation level wincome 1.116 (0.944, 1.319) 0.869 1.050 (0.778, 1.369) 1.0150 (1078, 1.369) High income Lack of physical activity 1.111 (1.014, 1.319) 0.050 1.111 (1.036, 1.322) Enough physical activity Lack of physical activity 1.111 (1.018, 1.214) 0.677 1.120 (0.996, 1.366) Normal BMI Abnormal BMI 1.152 (0.970, 1.230) 0.672 0.951 (0.734, 1.268) 1.229 (1.026, 1.342) No smoking Drink 1.127 (1.037, 1.225) 0.672 0.901 (0.558, 1.348) 1.229 (1.018, 1.510) 0.672 0.901 (0.558, 1.348) 1.229 (1.018, 1.510) 0.672 NO2 Non-white 1.558 (0.865, 1.788) 0.632 1.280 (0.373, 1.526) 1.090 (0.958, 1.245) NO2 Non-white 1.558 (0.865, 1.788) 0.632 1.096 (0.958, 1.277, 1.559) 1.090 (0.958, 1.228) High income Low income 1.115 (1.102, 1.274) 1.091 (0.956, 1.362) 1.096 (0.958, 1.228) NO2 Non-white 1.156 (1.093, 1.228) 0.632 1.096 (0.958, 1.228) 1.096 (0.958, 1.228) High education level Low income 1.166 (1.093, 1.289) 0.632 1.096 (0.958, 1.228) 1.097 (0.958, 1.228) Non-white 1.155 (1.073, 1.222) 0.538 1.100 (0.968, 1.223) 1.097 (0.9550, 1.245) Normal BMI A	P Value
High income	0.743
Low income I H 1.190 (1084, 1307) I 1.209 (1030, 1497) Lack of physical activity I 1.114 (0.937, 1324) 0.51 Normal BMI 1.114 (0.937, 1324) 0.51 Normal BMI 1.114 (0.937, 1324) 0.51 No Drinking 1.129 (1031, 1210) 1.239 (1034, 1213) 0.394 Normal BMI 1.129 (1032, 1210) 0.394 Normal BMI 1.138 (1034, 1231) 0.466 No amoking 1.139 (1034, 1215) 0.477 High education level 1.119 (0.947, 1220) 0.477 High education level 1.119 (0.947, 1230) 0.474 High education level 1.119 (0.947, 1230) 0.474 High education level 1.119 (0.947, 1230) 0.487 High education level 1.119 (0.947, 1230) 0.487 High education level 1.119 (0.947, 1329) 0.487 High education level 1.119 (0.947, 1329) 0.487 High education level 1.119 (0.947, 1329) 0.487 High education level 1.119 (0.944, 1329) 0.499 High education level 1.119 (0.944, 1329) 0.499 High education level 1.119 (0.944, 1329) 0.499 High education level 1.119 (0.947, 1329) 0.487 High education level 1.119 (0.947, 1329) 0.497 High education level 1.119 (0.947, 1329) 0.48 High education level 1.119 (0.947, 1239) 0.497 High education level 1.119 (0.947, 1239) 0.48 High education lev	0.398
Lack of physical activity Lack of physical activity No Drinking No Drinking Hith No arnoking Hith No Drinking No Drinking Hith No arnoking Hith No arnoking Hith No arnoking Hith No arnoking Hith No arnoking Hith No arnoking Hith No Drinking Hith No arnoking Hith No Drinking Hith No Arnoking Hith No Drinking Hith No Arnoking Hith No	0.895
Abnorma BMI Image: 1.129 (1034, 1233) Image: 1.129 (1034, 1233) Image: 1.117 (1032, 1230) Image: 1.117 (10	0.62
Drink Int 11/17 (1032, 1210) Imit 11/18 (108) (10, 975, 1221) Imit 11/18 (108) (128) (108) (0.148
Smoke 1.13 (1005, 1.233) 1.139 (1005, 1.233) PM10 Non-write 1.069 (0.661, 1.727) 0.847 High education level 1.114 (1005, 1.233) 1.050 (0.789, 1.366) High education level 1.114 (1005, 1.232) 1.119 (1001, 1.413) High education level 1.114 (1005, 1.234) 1.119 (1001, 1.413) High education level 1.114 (1005, 1.234) 1.116 (0.986, 1.525) Lack of physical activity 1.112 (1001, 1.230) 1.116 (0.986, 1.525) No Drinking 1.112 (1001, 1.230) 0.846 No Drinking 1.129 (1017, 1.524) 0.911 No morthie 1.229 (10.285, 1.389) 1.209 (10.285, 1.389) NO2 Non-wrhite 1.228 (1017, 1.321) 0.627 High education level 1.116 (1009, 1.220) 1.233 (1004, 1.344) NO2 Non-wrhite 1.258 (1086, 1.788) 0.632 High education level 1.116 (1048, 1.285), 0.744 1.096 (0.973, 1.372) High education level 1.156 (1009, 1.228) 0.632 1.096 (0.973, 1.372) High education level 1.156 (1077, 1.229) 0.632	0.315
White 1.121 (1034, 1.215) 1.193 (1030, 1.382) High education level we discation level bit income 1.116 (0.944, 1.318) 0.869 1.050 (0.778, 1.369) High income 0.994 (0.867, 1.139) 0.026 1.151 (0.086, 1.525) Enough physical activity Lack of physical activity 1.111 (1.018, 1.214) 0.671 1.156 (0.097, 1.559) Normal BMI Anormal BMI 1.112 (1.038, 1.225) 0.671 1.128 (1.018, 1.226) No smoking Mink 1.127 (1.039, 1.225) 0.901 (0.555, 1.388) 0.2091 (0.555, 1.388) No smoking 1.127 (1.037, 1.225) 0.901 (0.555, 1.388) 1.213 (1.018, 1.610) No smoking 1.127 (1.037, 1.225) 1.280 (0.877, 1.579) 1.280 (0.877, 1.579) No 1.056 (0.079, 1.230) 0.672 1.280 (0.835, 1.480) 1.280 (0.836, 1.490) No 1.191 (0.502, 1.348) 0.672 1.280 (0.837, 1.579) 1.091 (0.995, 1.342) No 1.191 (0.502, 1.348) 0.672 1.280 (0.837, 1.672) 1.091 (0.995, 1.342) No 1.191 (0.521, 3.480) 0.672 1.096 (0.872, 1.572) 1.096 (0.872, 1.572) No 1.191 (0.521, 3.480) 0.672 1.096 (0.858, 1.290) 1.096 (0.858, 1.290) <	0.227
Low education level 1.134 (10.5, 1.242) 1.139 (1.016, 1.413) High income 0.94 (0.857, 1.329) 1.151 (0.663, 1.525) Low income 1.152 (0.956, 1.399) 1.151 (0.663, 1.525) Enough physical activity 1.114 (0.05, 1.245) 1.120 (0.957, 1.854) Normal BMI 1.162 (0.956, 1.399) 1.120 (0.957, 1.254) Normal BMI 1.135 (10.36, 1.245) 0.965 (0.734, 1.268) Normal BMI 1.132 (0.970, 1.231) 0.672 0.901 (0.855, 1.388) Drink 1.129 (1.057, 1.257) 0.901 (0.855, 1.388) NO2 Non-white 1.290 (0.970, 1.230) 0.68 1.280 (1.918, 1.419) High education level 1.191 (1.052, 1.244) 0.907 (0.786, 1.900) Low education level 1.191 (1.052, 1.244) 0.907 (0.786, 1.900) High education level 1.191 (1.052, 1.244) 0.907 (0.786, 1.190) Low education level 1.191 (1.052, 1.244) 0.907 (0.786, 1.900) Enough physical activity 1.120 (1.015, 1.388) 1.025 (0.841, 1.249) Normal BMI 1.160 (1.037, 1.299) 0.888 1.025 (0.841, 1.249) Normal BMI 1.160 (0.901, 1.358) 0.628 0	0.785
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Low education level Image: Mark 1 1.165 (1.091, 1.243) 1.086 (0.955, 1.236) High income Low income 1.146 (1.038, 1.266, 0.593) 0.968 (0.787, 1.190) Low income 1.145 (1.041, 1.271) 1.124 (0.982, 1.286) Lack of physical activity Image: Mark 1 1.147 (1.076, 1.223) 0.475 Lack of physical activity Image: Mark 1 1.146 (1.045, 1.301) 1.096 (0.962, 1.248) Normal BMI Image: Mark 1 1.166 (1.045, 1.301) 0.761 1.004 (0.829, 1.217) No Drinking Image: Mark 1 1.166 (1.045, 1.301) 0.611 (0.577, 1.139) 1.110 (0.965, 1.223) No smoking Image: Mark 1 1.161 (1.094, 1.223) Image: Mark 1 1.160 (0.974, 1.381) No smoking Image: Mark 1 1.109 (1.017, 1.208, 0.311 Image: Mark 1 1.160 (0.974, 1.381) No smoking Image: Mark 1 1.177 (1.089, 1.271) 1.090 (0.867, 1.175) 1.090 (0.867, 1.175) 0.9111, 1, 1, 1, 5 0.7 1, 1, 19, 25, 3, 1 1.090 (0.867, 1.175) 1.091 (0.877, 1.139) 1.091 (0.877, 1.175)	0.284
Low income Image: 1185 (1.104, 1.271) Image: 1185 (1.104, 1.271) Image: 1185 (1.104, 1.271) Image: 1184 (0.982, 1.288) Enough physical activity Lack of physical activity Image: 1186 (1.104, 1.271) Image: 1180 (0.848, 1.352) 1.096 (0.962, 1.248) Normal BMI Image: 1186 (1.045, 1.301) (0.761) Image: 1180 (0.848, 1.352) 1.004 (0.829, 1.271) No Drinking Drink Image: 1116 (0.915, 1.359) (0.703) Image: 1116 (0.955, 1.251) 0.811 (0.577, 1.139) No smoking Smoke Image: 1109 (1.017, 1.208) (0.311) Image: 1116 (0.974, 1.381) 1.160 (0.974, 1.381) 0.9111 1.1 3 1.5 0.7 1.3 1.9 2.5 3.1 Image: 1116 (0.974, 1.375) Image: 1116 (0.974, 1.375)	0.93
Lack of physical activity 1.210 (1.060, 1.380) 1.1070 (0.848, 1.352) Normal BMI Abnormal BMI I 1.166 (1.045, 1.301) 0.761 1.108 (0.949, 1.217) No Drinking Drink 1.116 (0.915, 1.359) 0.703 1.10 (0.984, 1.359) 1.100 (0.9849, 1.242) No smoking Smoke 1.116 (0.916, 1.329) 0.713 1.9 25 3.1	0.234
Abnormal BMI Image: 1143 (1.069, 1.222) Image: 1.085 (0.949, 1.242) No Drinking Drink Image: 1.116 (0.915, 1.359) 0.703 0.811 (0.577, 1.139) 1.110 (0.985, 1.251) No smoking Smoke Image: 1.109 (1.017, 1.208) 0.311 Image: 1.160 (0.974, 1.381) 1.177 (1.089, 1.271) 0.911.1 1.3 1.5 0.7 1.3 1.9 2.5 3.1	0.863
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0.911.1 1.3 1.5 0.7 1.3 1.9 2.5 3.1	0.087
0.9 1 1.1 1.3 1.5 0.7 1.3 1.9 2.5 3.1	0.239
Hazard Ratio Hazard Ratio	

Figure S7. Hazard ratio (HR with 95% CI) for each IQR increase of air pollution on the first and readmission events for HF during follow-up, stratified by ethnicity, education level, income, and physical activity.

(Note: High educational level is defined as: high educational attainment, Low educational level is defined as intermediate, low, and other educational attainment, High income is defined as income higher $31,000 \pm$, Low income is defined as income lower than $30,999 \pm$, Enough physical activity is defined as moderate or high physical activity, Lack of physical activity is defined as low physical activity.)

Table S4. Hazard ratio (95% CIs) for each IQR increase of air pollution on CIHD during follow-up by strata-specific P	PWP-TT model.

			Model 1					Model 2		
	1^{st}	2^{nd}	3 rd	4^{th}	5 th	1^{st}	2^{nd}	3 rd	4^{th}	5 th
	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission
PM _{2.5}	1.089 (1.011,	1.158 (1.035,	1.140 (0.978,	1.069 (0.879,	1.051 (0.824,	1.084 (1.005,	1.157 (1.031,	1.125 (0.966,	1.018 (0.836,	1.015 (0.787,
	1.173)	1.295)	1.329)	1.301)	1.342)	1.168)	1.299)	1.310)	1.240)	1.309)
PM_{10}	1.082 (1.004,	1.152 (1.028,	1.162 (0.995,	1.042 (0.856,	1.072 (0.838,	1.073 (0.995,	1.151 (1.021,	1.140 (0.978,	0.992 (0.812,	1.039 (0.803,
	1.166)	1.292)	1.356)	1.268)	1.372)	1.158)	1.297)	1.330)	1.212)	1.345)
NO_2	1.098 (1.028,	1.120 (1.009,	1.258 (1.091,	0.995 (0.828,	0.977 (0.775,	1.083 (1.013,	1.114 (0.998,	1.231 (1.072,	0.961 (0.794,	0.962 (0.760,
	1.173)	1.242)	1.450)	1.196)	1.232)	1.157)	1.243)	1.413)	1.164)	1.218)
NO _x	1.095 (1.026,	1.113 (1.002,	1.246 (1.082,	0.991 (0.826,	0.954 (0.762,	1.080 (1.010,	1.106 (0.990,	1.219 (1.065,	0.953 (0.788,	0.937 (0.745,
	1.170)	1.236)	1.436)	1.190)	1.194)	1.154)	1.236)	1.397)	1.154)	1.177)

Table S5. Hazard ratio (95% CIs) for each IQR increase of air pollution on cerebrovascular disease during follow-up by strata-specific PWP-TT model.

		Model 1		Model 2			
	1 st Readmission	2 nd Readmission	3 rd Readmission	1 st Readmission	2 nd Readmission	3 rd Readmission	
PM _{2.5}	1.162 (1.057, 1.276)	1.071 (0.908, 1.264)	0.865 (0.676, 1.105)	1.161 (1.056, 1.277)	1.074 (0.909, 1.268)	0.871 (0.680, 1.114)	
PM_{10}	1.149 (1.047, 1.261)	1.061 (0.901, 1.250)	0.889 (0.699, 1.132)	1.149 (1.046, 1.263)	1.063 (0.902, 1.253)	0.902 (0.709, 1.148)	
NO_2	1.077 (0.994, 1.167)	1.016 (0.879, 1.175)	0.947 (0.774, 1.159)	1.071 (0.986, 1.163)	1.010 (0.872, 1.171)	0.976 (0.799, 1.191)	
NO _x	1.070 (0.988, 1.159)	1.008 (0.872, 1.166)	0.932 (0.765, 1.137)	1.065 (0.981, 1.155)	1.004 (0.866, 1.163)	0.959 (0.789, 1.166)	

		Mod	lel 1		Model 2			
	1^{st}	2^{nd}	3 rd	4^{th}	1^{st}	2^{nd}	3 rd	4 th
	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission
PM _{2.5}	1.118 (0.989,	1.019 (0.817,	0.934 (0.702,	1.105 (0.758,	1.126 (0.991,	1.008 (0.803,	0.929 (0.699,	1.113 (0.761,
	1.264)	1.271)	1.241)	1.611)	1.280)	1.265)	1.233)	1.627)
PM_{10}	1.082 (0.957,	1.028 (0.830,	0.890 (0.678,	1.082 (0.743,	1.091 (0.959,	1.019 (0.815,	0.891 (0.678,	1.110 (0.763,
	1.225)	1.273)	1.170)	1.577)	1.242)	1.272)	1.172)	1.614)
NO_2	1.001 (0.899,	1.114 (0.935,	0.785 (0.616,	0.924 (0.633,	1.003 (0.896,	1.102 (0.921,	0.815 (0.640,	0.974 (0.669,
	1.115)	1.327)	1.000)	1.350)	1.122)	1.320)	1.038)	1.420)
NO _x	0.994 (0.894,	1.103 (0.929,	0.794 (0.626,	0.955 (0.653,	0.995 (0.890,	1.090 (0.913,	0.823 (0.649,	1.006 (0.692,
	1.106)	1.310)	1.009)	1.397)	1.112)	1.301)	1.044)	1.462)

Table S6. Hazard ratio (95% CIs) for each IQR increase of air pollution on HF during follow-up by strata-specific PWP-TT model.

Table S7. Hazard ratio (95% CIs) for each IQR increase of air pollution on AF during follow-up by strata-specific PWP-TT model.

	Model 1					Model 2				
	1^{st}	2^{nd}	3 rd	4^{th}	5 th	1^{st}	2^{nd}	3 rd	4^{th}	5 th
_	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission	Readmission
PM _{2.5}	1.084 (1.010,	1.159 (1.046,	1.008 (0.880,	0.987 (0.826,	1.246 (0.980,	1.076 (1.002,	1.145 (1.032,	1.004 (0.876,	0.968 (0.807,	1.194 (0.932,
	1.164)	1.284)	1.155)	1.181)	1.583)	1.156)	1.270)	1.150)	1.161)	1.530)
PM_{10}	1.107 (1.031,	1.151 (1.040,	1.009 (0.882,	1.009 (0.842,	1.279 (1.006,	1.098 (1.022,	1.138 (1.027,	1.005 (0.878,	0.987 (0.821,	1.224 (0.954,
	1.188)	1.275)	1.155)	1.208)	1.626)	1.180)	1.262)	1.151)	1.186)	1.571)
NO_2	1.144 (1.075,	1.122 (1.027,	0.980 (0.874,	1.009 (0.861,	1.209 (1.002,	1.135 (1.067,	1.119 (1.023,	0.979 (0.873,	0.994 (0.847,	1.163 (0.956,
	1.217)	1.226)	1.099)	1.182)	1.459)	1.209)	1.223)	1.098)	1.167)	1.415)
NO _x	1.136 (1.068,	1.127 (1.032,	0.975 (0.870,	1.007 (0.860,	1.205 (1.006,	1.128 (1.059,	1.122 (1.027,	0.974 (0.869,	0.993 (0.846,	1.159 (0.960,
	1.209)	1.230)	1.093)	1.181)	1.444)	1.201)	1.226)	1.092)	1.166)	1.400)

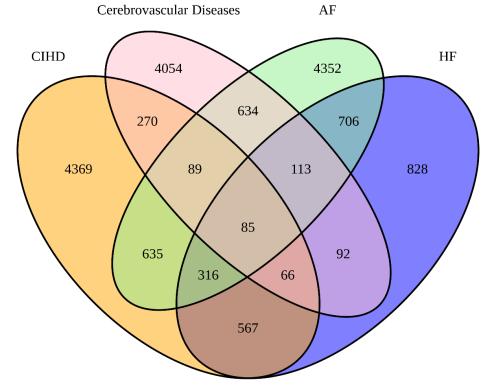


Figure S8. Overlapped participants of four cardiovascular diseases in Venn Diagram.

	CIHD (n = 4,369)		Cerebrovascular Disease $(n = 4,054)$		\mathbf{AF} (n = 4,352)		HF (n = 828)	
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
PM _{2.5}	1.041 (1.007,	1.092 (1.044,	1.066 (1.030,	1.126 (1.068,	1.050 (1.017,	1.039 (0.991,	1.042 (0.953,	1.128 (1.004,
	1.076)	1.143)	1.103)	1.187)	1.085)	1.090)	1.140)	1.267)
PM_{10}	1.035 (1.002,	1.079 (1.029,	1.060 (1.025,	1.112 (1.053,	1.048 (1.015,	1.029 (0.980,	1.023 (0.933,	1.080 (0.957,
	1.070)	1.131)	1.096)	1.173)	1.082)	1.080)	1.121)	1.218)
NO_2	1.034 (1.003,	1.039 (1.000,	1.047 (1.016,	1.060 (1.015,	1.022 (0.992,	1.007 (0.969,	1.048 (0.965,	1.124 (1.018,
	1.065)	1.078)	1.079)	1.107)	1.052)	1.046)	1.138)	1.241)
NO _x	1.041 (1.010,	1.048 (1.009,	1.056 (1.024,	1.073 (1.028,	1.027 (0.997,	1.015 (0.977,	1.054 (0.970,	1.133 (1.027,
	1.073)	1.087)	1.088)	1.120)	1.057)	1.054)	1.145)	1.250)

Table S8. Hazard ratio (95% CIs) for each IQR increase of air pollution on total admission events during follow-up among the participants with only one of the four cardiovascular diseases.

Frequency	Number of participants	Proportion
Did not change	201775	70.54%
Changed once	48408	16.92%
Changed twice	14792	5.17%
Changed three times	12101	4.23%
Changed four times	4756	1.66%
Changed five times	1886	0.66%
Changed six times	828	0.29%
Changed seven times	276	0.10%
Changed more than 7 times	187	0.07%

Table S9. The frequency of changing residential address of the participants during follow-up.

Table S10. Hazard ratio (HR with 95% CI) for each IQR increase of air pollution on the admission events for cardiovascular disease during
follow-up in participants who did not change their residential addresses.

	Air Pollution	CIHD	Cerebrovascular Disease	AF	HF
First Admission	PM _{2.5}	1.060 (1.008, 1.114)	1.130 (1.070, 1.194)	1.037 (0.988, 1.088)	1.109 (1.027, 1.197)
	PM_{10}	1.063 (1.009, 1.120)	1.138 (1.075, 1.205)	1.025 (0.975, 1.078)	1.122 (1.035, 1.215)
	NO_2	1.043 (1.003, 1.085)	1.119 (1.073, 1.168)	1.029 (0.991, 1.068)	1.160 (1.091, 1.234)
	NO _x	1.049 (1.009, 1.091)	1.125 (1.080, 1.173)	1.030 (0.993, 1.070)	1.157 (1.089, 1.229)
Readmissions	PM _{2.5}	1.170 (1.093, 1.254)	1.270 (1.137, 1.418)	1.124 (1.053, 1.200)	1.222 (1.066, 1.401)
	PM_{10}	1.170 (1.088, 1.258)	1.266 (1.130, 1.419)	1.122 (1.048, 1.200)	1.175 (1.017, 1.356)
	NO_2	1.139 (1.079, 1.203)	1.159 (1.073, 1.253)	1.071 (1.018, 1.126)	1.091 (0.973, 1.223)
	NO _x	1.129 (1.070, 1.191)	1.151 (1.067, 1.241)	1.066 (1.014, 1.120)	1.083 (0.968, 1.213)
Total Admissions	PM _{2.5}	1.047 (1.017, 1.077)	1.099 (1.064, 1.135)	1.063 (1.034, 1.093)	1.090 (1.043, 1.140)
	PM_{10}	1.046 (1.017, 1.077)	1.102 (1.067, 1.138)	1.062 (1.032, 1.092)	1.088 (1.040, 1.138)
	NO_2	1.069 (1.042, 1.097)	1.117 (1.087, 1.147)	1.062 (1.035, 1.088)	1.109 (1.067, 1.153)
	NO _x	1.072 (1.045, 1.100)	1.119 (1.090, 1.149)	1.061 (1.035, 1.088)	1.107 (1.065, 1.150)