

# **Supplementary materials**

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## Online Tables

### Online Table S1. Definitions of covariates

Diagnosis	ICD-10-CM code and definition	Diagnostic definition
<b>Inclusion/exclusion criteria</b>		
<b>Atrial fibrillation</b>	I48.0-48.4, I48.9	Admission $\geq$ 1 or outpatient department $\geq$ 2
<b>Valvular atrial fibrillation</b>	I05.0, I05.2, I05.9, Z95.2-Z95.4	Admission or outpatient department $\geq$ 1
<b>Ischemic stroke</b>	I63, I64	Admission or outpatient department $\geq$ 1
<b>Comorbidities</b>		
<b>Hypertension</b>	I10-I13, I15; and minimum 1 prescription of anti-hypertensive drug (thiazide, loop diuretics, aldosterone antagonist, alpha-/beta-blocker, calcium-channel blocker, angiotensin-converting enzyme inhibitor, angiotensin II receptor blocker).	Admission $\geq$ 1 or outpatient department $\geq$ 2
<b>Diabetes mellitus</b>	or systolic/diastolic blood pressure $\geq$ 140/90 mmHg E11-E14; and minimum 1 prescription of anti-diabetic drugs (sulfonylureas, metformin, meglitinides, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, $\alpha$ -glucosidase inhibitors, and insulin).	Based on the results of 2 <sup>nd</sup> health exam Admission $\geq$ 1 or outpatient department $\geq$ 2
<b>Dyslipidemia</b>	or fasting glucose level $\geq$ 126 mg/dL E78	Based on the results of 2 <sup>nd</sup> health exam Admission or outpatient department $\geq$ 1
<b>Heart failure</b>	or Total cholesterol $\geq$ 240 mg/dL	Based on the results of 2 <sup>nd</sup> health exam
<b>Vascular disease</b>	I50	Admission or outpatient department $\geq$ 1
<b>Prior MI</b>	I21, I22	Admission or outpatient department $\geq$ 1
<b>PAD</b>	I70, I73	Admission or outpatient department $\geq$ 2
<b>CKD</b>	eGFR<60ml/min/1.73m <sup>2</sup>	Based on the results of 2 <sup>nd</sup> health exam
<b>COPD</b>	J41-44	Admission $\geq$ 1
<b>Cancer</b>	C00-97 and RID code (V193)	Admission or outpatient department $\geq$ 1
<b>Health exam questionnaire</b>		
<b>Alcohol consumption</b>	Mild to moderate drinker: alcohol consumption >0g to <30g per day Heavy drinker: alcohol consumption $\geq$ 30g per day	Based on the results of 2 <sup>nd</sup> health exam
<b>Regular exercise</b>	Performing a moderate physical activity more than 30 minutes at least 5 times per week or strenuous	Based on the results of 2 <sup>nd</sup> health exam

	physical activity more than 20 minutes at least 3 times per week.	
Low income	Income lowest 20% and medical aid	
Scores		
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	Heart failure (1 point), hypertension (1 point), age ≥75 years (2 points), diabetes (1 point), previous stroke/systemic embolism/transient ischemic attack (2 points), vascular disease (prior MI or PAD, 1 point) and female sex (1 point)	
Clinical outcome		
Ischemic stroke	I63, I64	Admission≥1 and brain imaging (CT or MRI) ≥1
Fatal ischemic stroke	I63, I64	Ischemic stroke event that led to death within 30-day of its occurrence
Death from cerebrovascular events	I60-69	Any cerebrovascular events that led to death within 30-day of its occurrence

Abbreviation: CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CT, computed tomography; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; MRI, magnetic resonance image; PAD, peripheral artery disease.

**Online Table S2. Hazard ratios of ischemic stroke and all-cause death: unadjusted and model 1**

<b>Smoking status</b>	<b>Unadjusted HR (95% CI)</b>	<b>Model 1 HR (95% CI)</b>
<b>Ischemic stroke</b>	P=0.051	P=<0.001
Never smoker	1 (reference)	1 (reference)
Ex-smoker	0.959 (0.881-1.044)	1.022 (0.917-1.139)
Quitter	0.914 (0.789-1.059)	1.228 (1.046-1.441)
Current smoker	1.102 (0.997-1.218)	1.750 (1.551-1.973)
<b>All-cause death</b>	P=<0.001	P=<0.001
Never smoker	1 (reference)	1 (reference)
Ex-smoker	1.298 (1.215-1.387)	1.138 (1.049-1.236)
Quitter	1.473 (1.330-1.632)	1.831 (1.637-2.048)
Current smoker	1.226 (1.310-1.331)	1.895 (1.723-2.084)

Model 1: age and sex-adjusted

Abbreviation: CI, confidence interval; HR, hazard ratio.

**Online Table S3. The proportion of patients treated with antiarrhythmic drugs and undergoing AF ablation**

	<b>Total (n=97,637)</b>	<b>Never smokers (n=50,036)</b>	<b>Ex- smokers (n=26,621)</b>	<b>Quitters (n=6768)</b>	<b>Current smokers (n=14,212)</b>	<b>p- value</b>
<b>AAD use</b>	23,409 (24.0)	11,273 (22.5)	7328 (27.5)	1760 (26.0)	3048 (21.4)	<0.001
<b>Class Ic</b>	15,587 (16.0)	7613 (15.2)	4861 (18.3)	1033 (15.3)	2080 (14.6)	<0.001
<b>Class III</b>	8045 (8.2)	3763 (7.5)	2533 (9.5)	754 (11.1)	995 (7.0)	<0.001
<b>AF ablation</b>	1145 (1.2)	477 (1.0)	450 (1.7)	110 (1.6)	108 (0.8)	<0.001

AAD was defined as class Ic and III drugs.

Abbreviation: AAD, antiarrhythmic drugs; AF, atrial fibrillation.

**Online Table S4. Hazard ratios of primary and secondary outcomes after additionally adjusting whether performing early rhythm control by antiarrhythmic drugs or AF catheter ablation**

	HR (95% CI)	p-value	HR* (95% CI)	p-value
Ischemic stroke				
Never smoker	1 (reference)	<0.001	0.593 (0.525-0.671)	<0.001
Ex-smoker	1.022 (0.917-1.140)		0.607 (0.541-0.680)	
Quitter	1.191 (1.014-1.399)		0.707 (0.599-0.834)	
Current smoker	1.685 (1.491-1.904)		1 (reference)	
All-cause death				
Never smoker	1 (reference)	<0.001	0.585 (0.532-0.645)	<0.001
Ex-smoker	1.112 (1.024-1.206)		0.651 (0.595-0.711)	
Quitter	1.454 (1.299-1.628)		0.851 (0.756-0.958)	
Current smoker	1.708 (1.551-1.881)		1 (reference)	
Fatal ischemic stroke				
Never smoker	1 (reference)	<0.001	0.452 (0.335-0.612)	<0.001
Ex-smoker	1.063 (0.809-1.396)		0.481 (0.360-0.642)	
Quitter	1.014 (0.651-1.581)		0.459 (0.290-0.726)	
Current smoker	2.211 (1.635-2.989)		1 (reference)	
Death from cerebrovascular events				
Never smoker	1 (reference)	<0.001	0.521 (0.400-0.678)	<0.001
Ex-smoker	1.071 (0.850-1.349)		0.558 (0.434-0.718)	
Quitter	1.290 (0.919-1.809)		0.672 (0.470-0.960)	
Current smoker	1.919 (1.475-2.497)		1 (reference)	

\*HRs are presented the reference group as the current smoker. Abbreviation: AF, atrial fibrillation.

**Online Table S5. The proportion of patients with obstructive sleep apnea**

	Total (n=97,637)	Never smokers (n=50,036)	Ex- smokers (n=26,621)	Quitters (n=6768)	Current smokers (n=14,212)	p- value
OSA	361 (0.4)	133 (0.3)	125 (0.5)	37 (0.5)	66 (0.5)	<0.001

Abbreviation: OSA, obstructive sleep apnea.

**Online Table S6. Hazard ratios of primary and secondary outcomes after additionally adjusting obstructive sleep apnea**

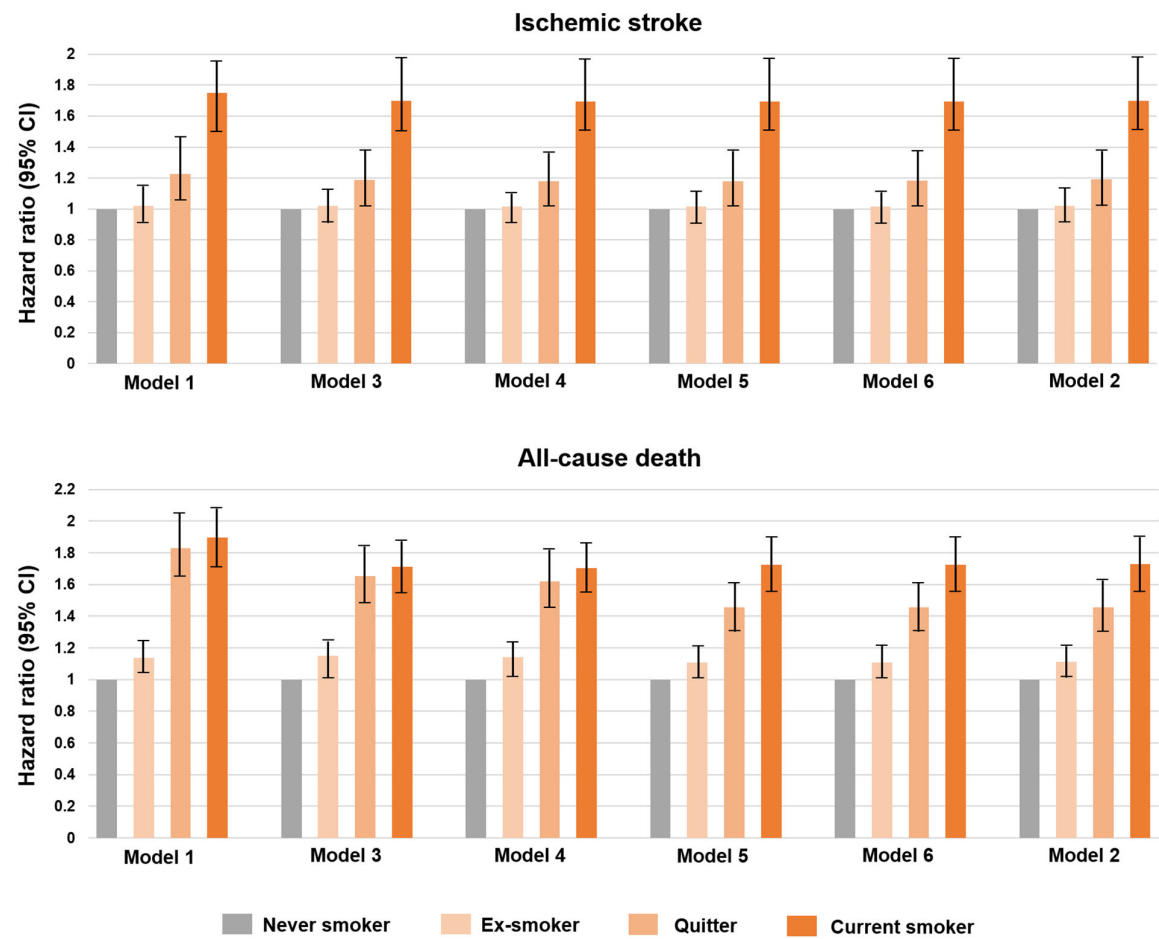
	HR (95% CI)	p-value	HR* (95% CI)	p-value
Ischemic stroke				
Never smoker	1 (reference)	<0.001	0.591 (0.523-0.668)	<0.001
Ex-smoker	1.022 (0.916-1.139)		0.604 (0.539-0.677)	
Quitter	1.194 (1.017-1.403)		0.706 (0.599-0.832)	
Current smoker	1.692 (1.497-1.912)		1 (reference)	
All-cause death				
Never smoker	1 (reference)	<0.001	0.581 (0.528-0.640)	<0.001
Ex-smoker	1.110 (1.023-1.205)		0.645 (0.590-0.705)	
Quitter	1.455 (1.300-1.629)		0.846 (0.752-0.952)	
Current smoker	1.720 (1.562-1.894)		1 (reference)	
Fatal ischemic stroke				
Never smoker	1 (reference)	<0.001	0.449 (0.332-0.606)	<0.001
Ex-smoker	1.061 (0.808-1.394)		0.476 (0.357-0.635)	
Quitter	1.009 (0.647-1.573)		0.453 (0.286-0.717)	
Current smoker	2.229 (1.649-3.013)		1 (reference)	
Death from cerebrovascular events				
Never smoker	1 (reference)	<0.001	0.516 (0.396-0.671)	<0.001
Ex-smoker	1.068 (0.848-1.346)		0.551 (0.428-0.708)	
Quitter	1.285 (0.916-1.804)		0.663 (0.464-0.947)	
Current smoker	1.940 (1.491-2.523)		1 (reference)	

\*HRs are presented the reference group as the current smoker

## Online Figures



Online Figure S1. Hazard ratios for the risk of ischemic stroke and all-cause death in sequentially adjusted multivariable models



Abbreviation: CI, confidence interval.

Model 1: age and sex

Model 3: age, sex, baseline body mass index, heavy drinker, regular exercise, low income, and CHA<sub>2</sub>DS<sub>2</sub>-VASc score

Model 4: age, sex, baseline body mass index, heavy drinker, regular exercise, low income, comorbidities including hypertension, diabetes mellitus, dyslipidemia,

heart failure, prior myocardial infarction, and peripheral artery disease.

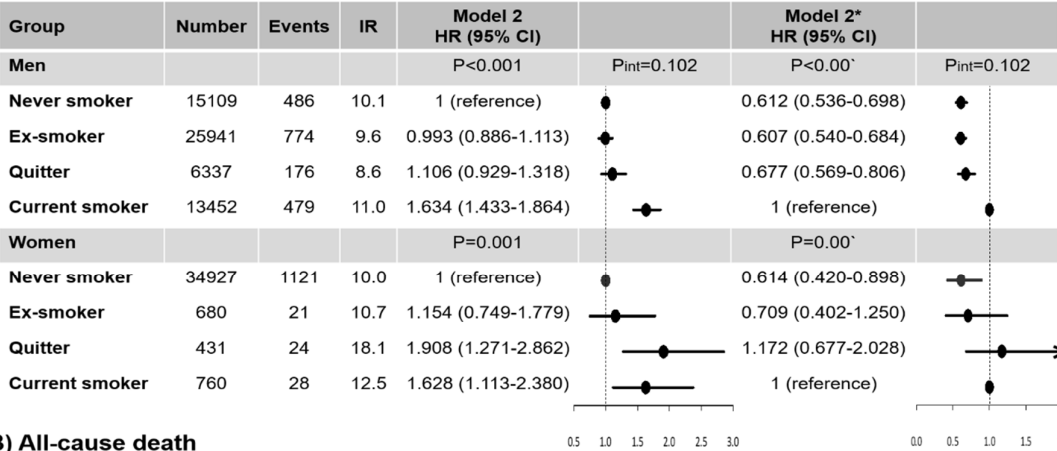
Model 5: model 4 + comorbidities including chronic kidney disease, chronic obstructive pulmonary disease and cancer.

Model 6: model 5 + CHA<sub>2</sub>DS<sub>2</sub>-VASc score

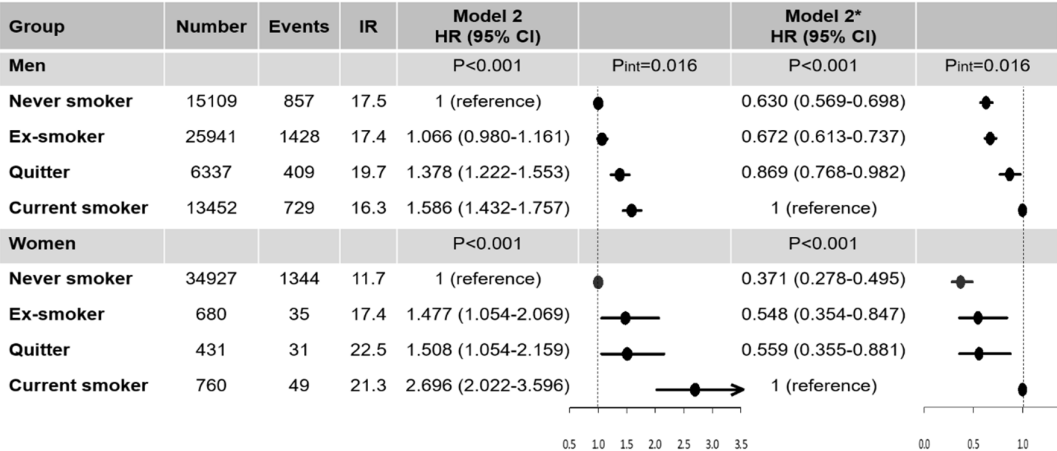
Model 2: model 6 + baseline medications including OACs, aspirin, P2Y<sub>12</sub> inhibitor and statin

Online Figure S2. Hazard ratios of smoking status on the risk of ischemic stroke and all-cause death in men and women

(A) Ischemic stroke



(B) All-cause death



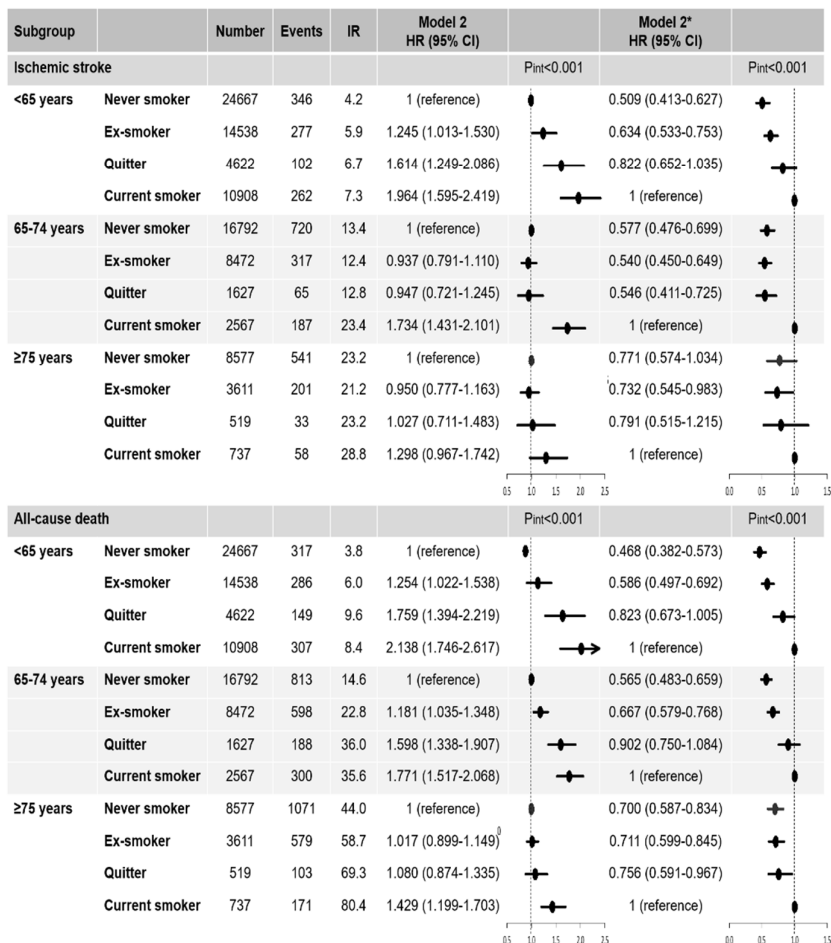
\* With current smokers as the reference group

IR, per 1000 person-years

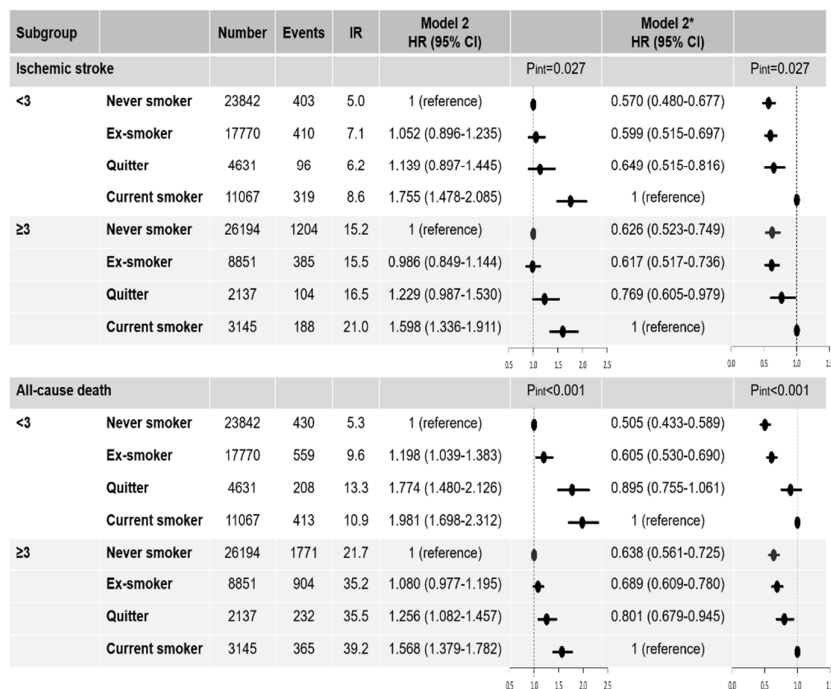
Abbreviation: CI, confidence interval; HR, hazard ratio; IR, incidence rate; P<sub>int</sub>, p for interaction.

**Online Figure S3. Subgroup analyses by age (<65 years, 65 to 74 years, and ≥75 years) and CHA<sub>2</sub>DS<sub>2</sub>-VASc score (<3 and ≥3)**

**(A) Age**



**(B) CHA<sub>2</sub>DS<sub>2</sub>-VASc score**



\* With current smokers as the reference group

IR, per 1000 person-years

Abbreviation: CI, confidence interval; HR, hazard ratio; IR, incidence rate; P<sub>int</sub>, p for interaction.