Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Data Source and Covariates

Data Source

In brief, the government provides mandatory health insurance coverage to the entire Korean population, approximately 50 million people. The Korean NHIS database contains demographic data as well as information about enrollees' medical expenses, such as diagnoses, examinations, prescription dispensing records, and inpatient and outpatient procedure records.^{1,2} The International Classification of Diseases, Tenth Revision, Clinical Modification codes were used to classify diagnoses. Additionally, enrollees aged 40 years or older are recommended to undergo a biannual health screening conducted by the Korean National Health Insurance Corporation. The health examination consists of anthropometric measurements, blood pressure, a laboratory examination, and a chest X-ray, as well as a self-reported questionnaire on health behaviors such as smoking, alcohol consumption, and physical activity. In 2014, 75% of participants participated.² These data are linked with the Korean NHIS database as a National Health Screening database.

Covariates

Comorbidities included hypertension, diabetes mellitus, dyslipidemia, heart failure, prior myocardial infarction (MI), peripheral artery disease (PAD), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), and cancer.³-6 The CHA2DS2-VASc score for assessing stroke risk was calculated combining covariate information (**Online Table 1**).¹ Baseline medications, including OACs (i.e. warfarin or direct oral anticoagulants, DOACs), aspirin, P2Y₁₂ inhibitors, and statin, were identified between the date of AF diagnosis and the date of the second health examination. As patients' baseline variables, body mass index, waist circumference, systolic and diastolic blood pressure, fasting glucose, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and estimated glomerular filtration rate at the second health examination were collected. Alcohol consumption was categorized into non-drinker, mild to moderate drinker (>0g/day to <30 g/day), and heavy drinker (≥30 g/day). Regular exercise was defined as performing >30 minutes of moderate physical activity ≥5 times a week or >20 minutes of strenuous physical activity ≥5 times per week. Low income was defined as having income in lower 20% among the entire Korean population of subjects supported by the Medical Aid program.

eTable 1. Definitions of Covariates

Diagnosis	ICD-10-CM code and definition	Diagnostic definition
Inclusion/exclusion criteria		
Atrial fibrillation	I48.0-48.4, I48.9	Admission≥1 or outpatient department≥2
Valvular atrial fibrillation	I05.0, I05.2, I05.9, Z95.2-Z95.4	Admission or outpatient department≥1
Dementia	F00-03, F107, G30, G231, G310, G311, G318 and prescription of medication for dementia, including galantamine, rivastigmine, donepezil, or memantine	Admission or outpatient department ≥1
Comorbidities		
Hypertension	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≥1 or outpatient department≥2
	or systolic/diastolic blood pressure ≥ 140/90 mmHg	Based on the results of 2 nd health exam
Diabetes mellitus	E11-E14; and minimum 1 prescription of anti-diabetic drugs (sulfonylureas, metformin, meglitinides, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, α -glucosidase inhibitors, and insulin).	Admission≥1 or outpatient department≥2

	or fasting glucose level ≥ 126 mg/dL	Based on the results of 2 nd health exam
Dyslipidemia	E78	Admission or outpatient department≥1
	or Total cholesterol ≥ 240 mg/dL	Based on the results of 2 nd health exam
Heart failure	I50	Admission or outpatient department≥1
Vascular disease		
Prior MI	I21, I22	Admission or outpatient department≥1
PAD	170, 173	Admission or outpatient department≥2
СКО	eGFR<60ml/min/1.73m ²	Based on the results of 2 nd health exam
COPD	J41-44	Admission≥1
Cancer	C00-97 and RID code (V193)	Admission or outpatient department≥1
Health exam questionnaire		
Alashal cangumntion	Mild to moderate drinker: alcohol consumption >0g to <30g per day	Deced on the receits of 2nd health avers
Aiconoi consumption	cular disease r MI 121,122 Admission or outpatient department≥1 170,173 Admission or outpatient department≥2 D eGFR<60ml/min/1.73m² Based on the results of 2nd health exam PD J41-44 Admission≥1 Admission or outpatient department≥1 the exam questionnaire	Based on the results of Z nd health exam

Regular exercise	Performing a moderate physical activity more than 30 minutes at least 5 times per week or strenuous physical activity more than 20 minutes at least 3 times per week.	Based on the results of 2 nd health exam
Low income	Income lowest 20% and medical aid	
Scores		
CHA ₂ DS ₂ -VASc score	Heart failure (1 point), hypertension (1 point), age ≥75 years (2 point embolism/transient ischemic attack (2 points), vascular disease (prior MI or PA	
Clinical outcome		
Dementia	F00-03, F107, G30, G231, G310, G311, G318 and prescription of medication for dementia, including galantamine, rivastigmine, donepezil, or memantine	Admission or outpatient department ≥1
Alzheimer Disease	F00, G30 and prescription of medication for dementia, including galantamine, rivastigmine, donepezil, or memantine	Admission or outpatient department ≥1
Vascular Dementia	F01 and prescription of medication for dementia, including galantamine, rivastigmine, donepezil, or memantine	Admission or outpatient department ≥1

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.

eTable 2. Hazard Ratios of Dementia: Unadjusted and Models 1 and 2

Smoking status	Number	Events	IR	Unadjusted HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)
Dementia				P=<0.001	P=<0.001	P=<0.001
Never smoker	65579	3773	18.4	1.898 (1.734,2.078)	0.673 (0.607,0.746)	1 (reference)
Ex-smoker	34670	1308	12.3	1.277 (1.155,1.412)	0.689 (0.622,0.762)	1.019 (0.940,1.106)
Quitter	8919	310	10.9	1.128 (0.980,1.297)	0.866 (0.753,0.996)	1.163 (1.026,1.317)
Current smoker	17084	534	9.7	1 (reference)	1 (reference)	1.406 (1.267,1.560)
A-Dementia				P=<0.001	P=<0.001	P=<0.001
Never smoker	65579	2871	14	2.097 (1.881,2.337)	0.707 (0.626,0.799)	1 (reference)
Ex-smoker	34670	942	8.9	1.336 (1.184,1.507)	0.700 (0.620,0.790)	0.986 (0.896,1.084)
Quitter	8919	214	7.5	1.130 (0.955,1.338)	0.855 (0.722,1.012)	1.089 (0.939,1.263)
Current smoker	17084	368	6.7	1 (reference)	1 (reference)	1.336 (1.181,1.512)
V-Dementia				P=<0.001	P=<0.001	P=<0.001
Never smoker	65579	553	2.7	1.258 (1.032,1.535)	0.512 (0.405,0.649)	1 (reference)
Ex-smoker	34670	229	2.2	1.011 (0.809,1.262)	0.603 (0.482,0.755)	1.177 (0.961,1.442)
Quitter	8919	51	1.8	0.840 (0.605,1.166)	0.674 (0.485,0.936)	1.193 (0.874,1.629)
Current smoker	17084	118	2.1	1 (reference)	1 (reference)	1.908 (1.503,2.423)

Model 1: age and sex-adjusted

Model 2: age, sex, body mass index, heavy drinker, regular physical activity, low income, diabetes, hypertension, dyslipidemia, previous myocardial infarction, previous stroke, previous congestive heart failure, peripheral artery disease, chronic obstructive pulmonary disease, cancer, chronic kidney disease, CHA2DS2-VASc score, warfarin, non–vitamin K antagonist oral anticoagulants, aspirin, clopidogrel, statin.

Abbreviation: CI, confidence interval; HR, hazard ratio; IR, incidence rate.

eTable 3. Hazard Ratios of Dementia in Each Group Stratifying by the Smoking Amount

Smalring status	Smoking amount	Number	Events	IR	Unadjusted	Model 1	Model 2
Smoking status	(pack-years)	Number	Events	IK	HR (95% CI)	HR (95% CI)	HR (95% CI)
Dementia					< 0.001	< 0.001	< 0.001
Never smoker	0	65579	3773	18.4	1 (reference)	1 (reference)	1 (reference)
Ex-smoker	>0 to <10	10178	307	9.8	0.532 (0.474,0.598)	0.958 (0.845,1.087)	0.978 (0.862,1.109)
	≥10 to <20	8870	293	10.7	0.586 (0.520,0.660)	1.026 (0.901,1.169)	1.032 (0.907,1.175)
	≥20 to <30	6404	250	12.7	0.694 (0.611,0.789)	1.06 (0.923,1.218)	1.064 (0.927,1.223)
	≥30	9218	458	16.5	0.904 (0.820,0.996)	1.061 (0.949,1.185)	1.024 (0.916,1.145)
Quitter	>0 to <10	1795	55	9.4	0.509 (0.39,0.664)	1.252 (0.958,1.636)	1.165 (0.891,1.522)
	≥10 to <20	2038	56	8.6	0.469 (0.361,0.611)	1.288 (0.986,1.683)	1.148 (0.879,1.501)
	≥20 to <30	1689	47	8.7	0.476 (0.357,0.634)	1.083 (0.810,1.450)	0.988 (0.738,1.322)
	≥30	3397	152	14.2	0.777 (0.661,0.914)	1.389 (1.171,1.648)	1.242 (1.046,1.474)
Current smoker	>0 to <10	3577	94	8.1	0.439 (0.357,0.538)	1.434 (1.164,1.766)	1.338 (1.086,1.648)
	≥10 to <20	4647	116	7.8	0.425 (0.353,0.511)	1.365 (1.128,1.652)	1.307 (1.079,1.583)
	≥20 to <30	3645	135	11.5	0.628 (0.529,0.745)	1.736 (1.451,2.077)	1.633 (1.364,1.954)
	≥30	5215	189	11.2	0.607 (0.524,0.702)	1.454 (1.244,1.699)	1.379 (1.178,1.614)

IR, per 1000 person-years

Model 1: age and sex-adjusted

Model 2: age, sex, hypertension, diabetes mellitus, dyslipidemia, heart failure, prior MI, PAD, CKD, COPD, cancer, BMI, heavy drinker, regular exercise, low income, use of OAC, use of antiplatelet agent, use of statin, and CHA₂DS₂-VASc score.

Abbreviation: CI, confidence interval; HR, hazard ratio; IR, incidence rate.

Table 4. Sensitivity Analysis With 1-Year Landmark Analysis: Hazard Ratios of Dementia at Landmark Time: Unadjusted and Models 1 and 2

Smoking status	Unadjusted HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)		
Dementia					
Never smoker	1.872 (1.687,2.078)	0.666 (0.591,0.750)	0.697 (0.618,0.785)		
Ex-smoker	1.297 (1.156,1.456)	0.700 (0.623,0.787)	0.733 (0.652,0.824)		
Quit-smokers	1.105 (0.940,1.299)	0.843 (0.717,0.991)	0.805 (0.684,0.947)		
Current smoker	1 (reference)	1 (reference)	1 (reference)		
Alzheimer disease					
Never smoker	2.082 (1.837,2.359)	0.715 (0.621,0.824)	0.752 (0.652,0.866)		
Ex-smoker	1.388 (1.209,1.594)	0.728 (0.634,0.837)	0.765 (0.665,0.880)		
Quit-smokers	1.140 (0.939,1.383)	0.857 (0.706,1.040)	0.814 (0.670,0.988)		
Current smoker	1 (reference)	1 (reference)	1 (reference)		
Vascular dementia					
Never smoker	1.274 (1.014,1.602)	0.492 (0.374,0.647)	0.492 (0.373,0.648)		
Ex-smoker	1.033 (0.800,1.334)	0.614 (0.475,0.795)	0.618 (0.476,0.802)		
Quit-smokers	0.746 (0.502,1.108)	0.593 (0.399,0.881)	0.552 (0.371,0.821)		
Current smoker	1 (reference)	1 (reference)	1 (reference)		

Model 1: age and sex-adjusted

Model 2: age, sex, hypertension, diabetes mellitus, dyslipidemia, heart failure, prior MI, PAD, CKD, COPD, cancer, BMI, heavy drinker, regular exercise, low income, use of OAC, use of antiplatelet agent, use of statin, and CHA₂DS₂-VASc score.

Abbreviation: CI, confidence interval; HR, hazard ratio

All, p for trends < 0.001

eTable 5. Baseline Characteristics of Quit and Current Smoker Groups Before and After Propensity Score Matching

		Before PS matching	.		After PS matching	
	Quit-smoker	Current smoker	ASD	Quit-smoker	Current smoker	ASD
Number	8918	17084		8573	8573	
Age (years)	59.1 (11.9)	56.2 (12.5)	0.234	58.8 (11.9)	58.9 (12.1)	0.009
<65 years	5753 (64.5)	12,411 (72.7)		5606 (65.4)	5560 (64.9)	
65 to <75 years	2371 (26.6)	3553 (20.8)		2226 (26.0)	2215 (25.8)	
≥75 years	795 (8.9)	1120 (6.6)		741 (8.6)	798 (9.3)	
Sex (Male)	8354 (93.7)	16,134 (94.4)	0.032	8029 (93.7)	8031 (93.7)	0.001
CHA ₂ DS ₂ -VASc	2.4 (1.6)	1.7 (1.5)	0.284	2.4 (1.6)	2.4 (1.6)	0.003
0	846 (9.5)	2405 (14.1)		834 (9.7)	851 (9.9)	
1	2084 (23.4)	5339 (31.3)		2050 (23.9)	2150 (25.1)	
≥2	5989 (67.2)	9340 (54.7)		5689 (66.4)	5572 (65.0)	
Hypertension	6106 (68.5)	10,939 (64.0)	0.093	5834 (68.1)	5843 (68.2)	0.002
Diabetes mellitus	2266 (25.4)	4096 (24.0)	0.033	2165 (25.3)	2111 (24.6)	0.014
Dyslipidemia	984 (11.0)	2060 (12.1)	0.032	958 (11.2)	959 (11.2)	< 0.001
Heart failure	2456 (27.5)	3679 (21.5)	0.139	2320 (27.1)	2367 (27.6)	0.012
Prior MI	766 (8.6)	850 (5.0)	0.144	686 (8.0)	698 (8.1)	0.005
PAD	1761 (19.7)	3195 (18.7)	0.026	1695 (19.8)	1681 (19.6)	0.004

CKD	1186 (13.3)	1543 (9.0)	0.135	1092 (12.7)	1111 (13.0)	0.006
COPD	2059 (23.1)	2990 (17.5)	0.139	1902 (22.2)	1857 (21.7)	0.012
Cancer	729 (8.2)	513 (3.0)	0.226	587 (6.9)	505 (5.9)	0.039
OAC	3000 (33.6)	3771 (22.1)	0.260	2791 (32.6)	2823 (32.9)	0.008
Warfarin	2422 (27.2)	2988 (17.5)	0.233	2251 (26.3)	2295 (26.8)	0.011
DOAC	822 (9.2)	1027 (6.0)	0.121	753 (8.8)	753 (8.8)	<0.001
Aspirin	1889 (21.2)	3513 (20.6)	0.015	1823 (21.3)	1838 (21.4)	0.004
P2Y ₁₂ inhibitor	838 (9.4)	1079 (6.3)	0.114	780 (9.1)	800 (9.3)	0.008
Statin	1789 (20.1)	2690 (15.8)	0.112	1686 (19.7)	1684 (19.6)	< 0.001
BMI (kg/m2)	24.6 (3.4)	24.4 (3.4)	0.067	24.6 (3.4)	24.6 (3.5)	0.001
Heavy drinker	722 (8.1)	2665 (15.6)	0.233	720 (8.4)	674 (7.9)	0.019
Regular exercise	2056 (23.1)	3376 (19.8)	0.080	1941 (22.6)	1979 (23.1)	0.010
Low income	1500 (16.8)	3057 (17.9)	0.028	1452 (16.9)	1420 (16.6)	0.0100

Continuous variables are presented as mean \pm standard deviation and categorical variables are presented as numbers (percentage).

Abbreviation: ASD, absolute standardized difference; BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DOAC, direct oral anticoagulant; MI, myocardial infarction; OAC, oral anticoagulant; PAD, peripheral artery disease; PS, propensity score.

eTable 6. Event Number, Incidence Rate, and Hazard Ratio of Dementia After Propensity Score Matching

	Number	Events	IR	HR (95% CI)	p-value
Total dementia					0.037
Current smoker	8573	344	12.8	1 (reference)	
Quit-smoker	8573	298	10.9	0.848 (0.726-0.991)	
Alzheimer disease					0.059
Current smoker	8573	240	8.9	1 (reference)	
Quit-smoker	8573	205	7.5	0.836 (0.694-1.007)	
Vascular dementia					0.012
Current smoker	8573	77	2.9	1 (reference)	
Quit-smoker	8573	50	1.8	0.636 (0.446-0.908)	

IR, per 1000 person-years

Abbreviation: CI, confidence interval; HR, hazard ratio; IR, incidence rate.

eTable 7. Competing Risk Analysis

	Model 2 HR (95% CI)	p-value	Model 2a HR (95% CI)	p-value
Total dementia		< 0.001		< 0.001
Never smoker	0.736 (0.663-0.819)		1 (reference)	
Ex-smoker	0.746 (0.673-0.827)		1.013 (0.933-1.100)	
Quit-smoker	0.839 (0.727-0.968)		1.139 (1.003-1.294)	
Current smoker	1 (reference)		1.358 (1.222-1.509)	
Alzheimer disease		< 0.001		< 0.001
Never smoker	0.777 (0.685-0.881)		1 (reference)	
Ex-smoker	0.761 (0.673-0.861)		0.980 (0.890-1.078)	
Quit-smoker	0.829 (0.698-0.984)		1.067 (0.916-1.242)	
Current smoker	1 (reference)		1.287 (1.135-1.459)	
Vascular dementia		< 0.001		< 0.001
Never smoker	0.539 (0.425-0.682)		1 (reference)	
Ex-smoker	0.631 (0.504-0.791)		1.171 (0.955-1.436)	
Quit-smoker	0.631 (0.452-0.88)		1.171 (0.862-1.59)	
Current smoker	1 (reference)		1.856 (1.466-2.351)	

Model 2a showed hazard ratio of each group compared to never smoker as a reference group. Abbreviation: CI, confidence interval; HR, hazard ratio.

eFigure 1. Sensitivity Analysis With 1-Year Landmark Analysis: Hazard Ratios of Smoking Status on the Risk of Total Dementia, Alzheimer Disease, and Vascular Dementia

Group	Number	Events	IR	Model 2 HR (95% CI)		Model 2a HR (95% CI)	
Total dementia				P<0.001	į	P<0.001	
Never smoker	55299	2799	19.4	0.697 (0.618-0.785)	•	1 (Reference)	•
Ex-smoker	29139	992	13.4	0.733 (0.652-0.824)	•	1.052 (0.958-1.156)	•
Quit-smoker	7783	229	11.4	0.805 (0.684-0.947)	•	1.156 (1.000-1.336)	•
Current smoker	14740	405	10.3	1 (Reference)	•	1.436 (1.273-1.619)	•
Alzheimer's dementia				P<0.001		P<0.001	
Never smoker	55299	2135	14.8	0.752 (0.652-0.866)	•	1 (Reference)	•
Ex-smoker	29139	728	9.8	0.765 (0.665-0.880)	•	1.017 (0.913-1.134)	•
Quit-smoker	7783	162	8.1	0.814 (0.670-0.988)	•	1.083 (0.913-1.284)	•
Current smoker	14740	278	7.1	1 (Reference)	•	1.331 (1.154-1.534)	•
Vascular dementia				P<0.001		P<0.001	
Never smoker	55299	419	2.9	0.492 (0.373-0.648)	•	1 (Reference)	•
Ex-smoker	29139	174	2.3	0.618 (0.476-0.802)	-	1.257 (0.993-1.592)	•
Quit-smoker	7783	34	1.7	0.552 (0.371-0.821)		1.122 (0.770-1.636)	•
Current smoker	14740	89	2.3	1 (Reference)	•	2.034 (1.543-2.681)	-
					0.1 1	10 0.1	1

For model 2a, never smokers acted as the reference group. IR, per 1000 person-years. Abbreviation: CI, confidence interval; HR, hazard ratio; IR, incidence rate.

eFigure 2. Subgroup Analyses by Sex, Age, CHA₂DS₂-VASc Score, and Previous Stroke (Total Dementia)

(A) Sex									Subgroup		Number	Events	IR	Model 2 HR (95% CI)		Model 2a HR (95% CI)	
Subgroup		Number	Events	IR	Model 2 HR (95% CI)		Model 2a HR (95% CI)		Total Dementia					111(307001)		111(3070 01)	
Total dementia								P _{int} =0.691	<65 years	Never smoker	29023	284	2.9	0.501 (0.376-0.668)	+	1 (Reference)	
Men	Never smoker	19901	845	13.6	0.720 (0.641-0.808)	•	1 (Reference)	÷		Ex-smoker	17133	128	2.3	0.639 (0.495-0.825)	•	1.275 (0.958-1.698)	
	Ex-smoker	33802	1250	12.1	0.728 (0.654-0.811)	•	1.011 (0.927-1.104)	÷		Quit-smoker	5753	61	3.2	0.863 (0.630-1.180)		1.721 (1.234-2.400)	
	Quit-smoker	8354	269	10.1	0.841 (0.724-0.978)	•	1.169 (1.017-1.343)	•		Current smoker	12411	115	2.8	1 (Reference)	Ļ	1.995 (1.497-2.658)	
	Current smoker	16134	478	9.1	1 (Reference)	÷	1.389 (1.237-1.560)	•	65-74 years	Never smoker	23508	1562	21.0	0.704 (0.602-0.822)	•	1 (Reference)	
Women	Never smoker	45678	2928	20.4	0.683 (0.523-0.891)	•	1 (Reference)	•	·	Ex-smoker	11827	519	14.7	0.687 (0.590-0.800)	•	0.976 (0.857-1.112)	
	Ex-smoker	868	58	23.4	0.785 (0.543-1.135)	-+	1.150 (0.886-1.492)	+		Quit-smoker	2371	138	18.9	0.797 (0.647-0.982)	•	1.133 (0.936-1.371)	
	Quit-smoker	565	41	23.2	0.726 (0.485-1.089)		1.063 (0.781-1.449)	+		Current smoker	3553	252	22.5	1 (Reference)	Ļ	1.421 (1.216-1.661)	
	Current smoker	950	56	20.1	1 (Reference)	•	1.464 (1.122-1.911)	-	≥ 75 years	Never smoker	13048	1927	57.3			1 (Reference)	
					0.1	1	10 0.1	i	10	Ex-smoker	5710	661	45.2	0.810 (0.682-0.961)	•	1.030 (0.920-1.153)	
										Quit-smoker	795	111	52.5	anno anno e processo de l'escalación de	•	1.062 (0.869-1.298)	
										Current smoker	1120	167	57.4	1 (Reference)	Ļ	1.272 (1.071-1.510)	

(C) CHA ₂ DS	S ₂ -VASc								(D) Prior hi	istory of stro	ke						
Subgroup		Number	Events	IR	Model 2 HR (95% CI)		Model 2a HR (95% CI)		Subgroup		Number	Events	IR	Model 2 HR (95% CI)		Model 2a HR (95% CI)	
Total Dementia								P _{int} =0.603	Total Dementia								P _{int} =0.058
<3	Never smoker	25862	379	4.3	0.661 (0.535-0.817)	•	1 (Reference)	•	(-)	Never smoker	17044	591	11.0	0.702 (0.622-0.793)	•	1 (Reference)	÷
	Ex-smoker	19450	268	4.2	0.611 (0.501-0.745)	•	0.924 (0.767-1.113)	į.		Ex-smoker	29065	876	9.7	0.721 (0.640-0.812)	•	1.026 (0.931-1.131)	
	Quit-smoker	5070	72	4.2	0.853 (0.645-1.127)	4	1.289 (0.982-1.693)	-		Quit-smoker	6856	170	7.7	0.823 (0.695-0.975)	•	1.172 (1.006-1.364)	•
	Current smoker	11828	165	4.1	1 (Reference)	•	1.512 (1.224-1.868)	-		Current smoker	14504	354	7.4	1 (Reference)	i	1.424 (1.261-1.607)	•
≥3	Never smoker	39717	3394	28.9	0.720 (0.638-0.812)	•	1 (Reference)	•	(+)	Never smoker	2857	254	31.0	0.759 (0.619-0.930)	•	1 (Reference)	•
	Ex-smoker	15220	1040	24.3	0.755 (0.670-0.852)	•	1.049 (0.958-1.149)	÷		Ex-smoker	4737	374	28.0	0.742 (0.608-0.905)	•	0.978 (0.842-1.136)	+
	Quit-smoker	3849	238	21.0	0.810 (0.687-0.953)	•	1.125 (0.977-1.295)	+		Quit-smoker	1498	99	22.1	0.786 (0.609-1.014)	•	1.036 (0.832-1.290)	+
	Current smoker	5256	369	24.5	1 (Reference)	•	1.389 (1.231-1.568)	•		Current smoker	1630	124	26.2	1 (Reference)	•	1.318 (1.076-1.616)	•
						0.1 1	10 0.1	1 10							0.1 1	10 0.1	1

For model 2a, never smokers acted as the reference group.

IR, per 1000 person-years Abbreviation: CI, confidence interval; HR, hazard ratio; IR, incidence rate; Pint, p for interaction.

eFigure 3. Subgroup Analyses by Sex, Age, CHA2DS2-VASc Score, and Previous Stroke (Alzheimer Disease)

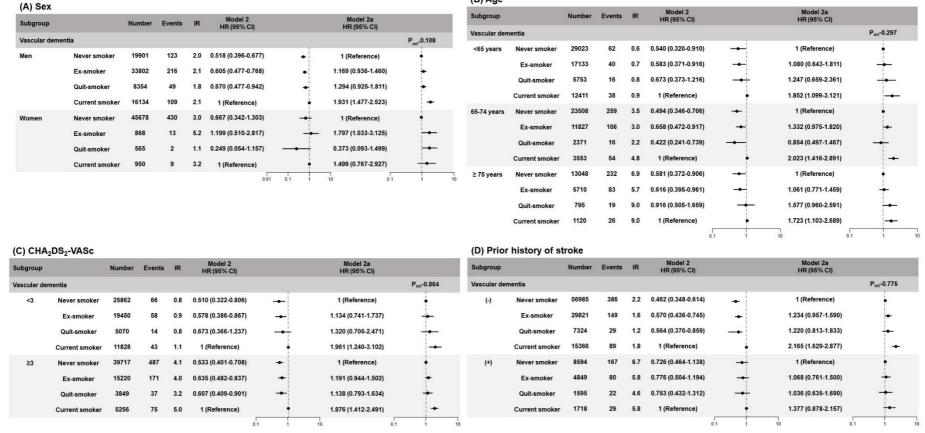
									(B) Age								
(A) Sex					Model 2	_	Model 2a		Subgroup		Number	Events	IR	Model 2 HR (95% CI)		Model 2a HR (95% CI)	
Subgroup		Number	Events	IR	HR (95% CI)		HR (95% CI)		Alzheimer's	lementia							P _{int} =0.519
Alzheimer's	s dementia							P _{int} =0.749	<65 years	Never smoker	29023	192	2.0	0.512 (0.353-0.742)	-	1 (Reference)	+
Men	Never smoke	r 19901	634	10.2	0.763 (0.665-0.876)	•	1 (Reference)	÷		Ex-smoker	17133	72	1.3	0.646 (0.459-0.908)	-	1.262 (0.869-1.832)	•
	Ex-smoker	33802	907	8.8	0.753 (0.662-0.858)	•	0.987 (0.891-1.093)	•		Quit-smoker	5753	33	1.7	0.827 (0.542-1.263)	+	1.616 (1.041-2.510)	-
	Quit-smoker	8354	178	6.7	0.812 (0.676-0.976)	•	1.064 (0.899-1.259)	•		Current smoker	12411	64	1.6	1 (Reference)	÷	1.954 (1.347-2.833)	-
	Current smo	ker 16134	325	6.2	1 (Reference)		1.310 (1.141-1.504)	•	65-74 years	Never smoker	23508	1147	15.4	0.748 (0.621-0.901)	•	1 (Reference)	
Women	Never smoke	r 45678	2237	15.6	0.661 (0.488-0.896)	•	1 (Reference)	· ·		Ex-smoker	11827	357	10.1	0.688 (0.572-0.827)	•	0.919 (0.788-1.073)	.
	Ex-smoker	868	35	14.1	0.599 (0.383-0.937)	-	0.906 (0.648-1.266)	†		Quit-smoker	2371	99	13.6	0.838 (0.654-1.075)	-	1.121 (0.895-1.402)	4
	Quit-smoker	565	36	20.3	0.793 (0.508-1.237)	-	1.199 (0.861-1.668)	+		Current smoker	3553	172	15.4	1 (Reference)	•	1.337 (1.110-1.610)	•
	Current smo	ker 950	43	15.4	1 (Reference)	•	1.512 (1.116-2.048)	•	≥ 75 years	Never smoker	13048	1532	45.5	0.787 (0.649-0.954)	•	1 (Reference)	
					0.1		1 10 0.1	1 10		Ex-smoker	5710	513	35.1	0.800 (0.660-0.971)	•	1.017 (0.895-1.155)	÷
										Quit-smoker	795	82	38.8	0.773 (0.586-1.019)	•	0.982 (0.778-1.238)	
																	1
										Current smoker	1120	132	45.4	1 (Reference)	·	1.271 (1.048-1.541)	•
											1120	132	45.4		1 1	1.271 (1.048-1.541)	•
C) CHA ₂	DS ₂ -VASc								(D) Prior			132	45.4		1 1		•
		Number Ev	ents IR	+	Model 2 IR (95% CI)		Model 2a HR (95% CI)		(D) Prior	Current smoker		132 Events	45.4 IR		1		<u></u>
(C) CHA ₂ Subgroup Alzheimer's c		Number Ev	ents IR		Model 2 IR (95% CI)			P _{int} -0.446		Current smoker	roke			Model 2		10 0.1 Model 2a	P _{int} -0.0849
Subgroup			ents IR 71 3.1		Model 2 IR (95% CI) 1 (0.550-0.919)	•		P _{int} -0.446	Subgroup	Current smoker	roke		IR	Model 2		10 0.1 Model 2a	_
Subgroup Alzheimer's c	dementia	25862 2		0.71	IR (95% CI)	•	HR (95% CI)	P _{int} -0.446	Subgroup Alzheimer's o	Current smoker history of st	roke Number	Events	IR 12.2	Model 2 HR (95% CI)		Model 2a HR (95% CI)	_
Subgroup Alzheimer's c	dementia Never smoker	25862 2 19450 1	71 3.1	0.71	1R (95% CI)		HR (95% CI) 1 (Reference)	P _{int} -0.446	Subgroup Alzheimer's o	Current smoker history of st	roke Number	Events	IR 12.2	Model 2 HR (95% CI) 0.746 (0.646-0.862)	•	Model 2a HR (95% CI)	_
Subgroup Alzheimer's c	dementia Never smoker Ex-smoker	25862 2 19450 1 5070	71 3.1 74 2.7	0.71 0.58 0.86	1 (0.550-0.919) 3 (0.456-0.746)	•	HR (95% CI) 1 (Reference) 0.820 (0.656-1.026)	P _{int} -0.446	Subgroup Alzheimer's o	Current smoker history of st ementia Never smoker Ex-smoker	roke Number 56985 29821	2197 669	IR 12.2 7.2	Model 2 HR (95% CI) 0.746 (0.646-0.862) 0.739 (0.641-0.852)	•	Model 2a HR (95% CI) 1 (Reference) 0.990 (0.884-1.108)	_
Subgroup Alzheimer's c	Never smoker Ex-smoker Quit-smoker Current smoker	25862 2 19450 1 5070 4	71 3.1 74 2.7 18 2.8	0.71 0.58 0.86	1 (0.550-0.919) 3 (0.456-0.746) 5 (0.613-1.220)	•	HR (95% CI) 1 (Reference) 0.820 (0.656-1.026) 1.217 (0.875-1.692)	P _{int} -0.446	Subgroup Alzheimer's o	Current smoker history of st ementia Never smoker Ex-smoker Quit-smoker	roke Number 56985 29821 7324	2197 669 148	IR 12.2 7.2 6.3 5.5	Model 2 HR (95% CI) 0.746 (0.646-0.862) 0.739 (0.641-0.852) 0.846 (0.692-1.034)	•	Model 2a HR (95% CI) 1 (Reference) 0.990 (0.884-1.108) 1.133 (0.948-1.353)	_
Subgroup Alzheimer's c	dementia Never smoker Ex-smoker Quit-smoker Current smoker	25862 2 19450 1 5070 4 11828 1 39717 2	71 3.1 74 2.7 18 2.8 06 2.6	0.71 0.58 0.86 1	1 (0.550-0.919) 3 (0.456-0.746) 5 (0.613-1.220) (Reference)	-	HR (95% CI) 1 (Reference) 0.820 (0.656-1.026) 1.217 (0.875-1.692) 1.407 (1.089-1.818)	P _{int} -0.446	Subgroup Alzheimer's c	Current smoker history of st ementia Never smoker Ex-smoker Quit-smoker Current smoker	roke Number 56985 29821 7324 15366	2197 669 148 275	12.2 7.2 6.3 5.5 27.2	Model 2 HR (95% CI) 0.746 (0.646-0.862) 0.739 (0.641-0.852) 0.846 (0.692-1.034) 1 (Reference)	•	Model 2a HR (95% CI) 1 (Reference) 0.990 (0.884-1.108) 1.133 (0.948-1.353) 1.340 (1.160-1.547)	_
subgroup Izheimer's c	dementia Never smoker Ex-smoker Quit-smoker Current smoker Never smoker	25862 2 19450 1 5070 4 11828 1 39717 20 15220 7	71 3.1 74 2.7 18 2.8 06 2.6 500 22.1	0.71 0.58 0.86 1 0.75	1 (0.550-0.919) 3 (0.456-0.746) 5 (0.613-1.220) (Reference) 0 (0.651-0.864)	-	1 (Reference) 0.820 (0.656-1.026) 1.217 (0.875-1.692) 1.407 (1.089-1.818) 1 (Reference)	P _{int} -0.446	Subgroup Alzheimer's c	current smoker history of st ementia Never smoker Ex-smoker Quit-smoker Current smoker Never smoker	FOR Number 56985 29821 7324 15366 8594	2197 669 148 275	12.2 7.2 6.3 5.5 27.2	Model 2 HR (95% CI) 0.746 (0.646-0.862) 0.739 (0.641-0.852) 0.846 (0.692-1.034) 1 (Reference) 0.772 (0.606-0.985)	•	Model 2a HR (95% CI) 1 (Reference) 0.990 (0.884-1.108) 1.133 (0.948-1.353) 1.340 (1.160-1.547) 1 (Reference)	_

For model 2a, never smokers acted as the reference group.

IR, per 1000 person-years

Abbreviation: CI, confidence interval; HR, hazard ratio; IR, incidence rate; Pint, p for interaction.

eFigure 4. Subgroup Analyses by Sex, Age, CHA2DS2-VASc Score, and Previous Stroke (Vascular Dementia)



(B) Age

For model 2a, never smokers acted as the reference group.

IR, per 1000 person-years

Abbreviation: CI, confidence interval; HR, hazard ratio; IR, incidence rate; Pint, p for interaction.

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