

SUPPLEMENTAL MATERIAL

Table S1. Diagnosis codes for inclusion, exclusion criteria and study outcomes.

Diagnosis	ICD-9-CM	ICD-10-CM
Inclusion criteria		
Atrial fibrillation	427.31	I48
Ischemic stroke	433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 436	I63, I67.89
Exclusion criteria		
Artificial heart	V42.2, V43.3	Z95.3, Z95.4, Z94.5
valve replacement	National Health Insurance codes : FHV01, FHV02	
Mitral stenosis	394.0, 394.2, 396.0, 396.1, 746.5	I05.0, I05.2, I08.0, Q23.2
Systemic thromboembolism		
Ischemic stroke	433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 436	I63, I67.89
Transient ischemic attack	435.0, 435.1, 435.2, 435.3, 435.8, 435.9	G45.0, G45.1, G45.2, G45.8, G45.9, G46.0, G46.1, G46.2, I67.841, I67.848
Myocardial infarction	410, 412	I21, I22, I25.2
Coronary artery disease	410, 411, 412, 413, 414	I20, I21, I22, I23, I24, I25
Peripheral artery disease	440, 443	I70, I73
Venous thromboembolism	451, 453, 415.1	I80, I82, I26.9, I27.82
Major bleeding		
Intracranial	430, 431, 432	I60, I61, I62

Diagnosis		ICD-9-CM			ICD-10-CM		
hemorrhage							
Gastrointestinal		456.0,	456.20,	531.0,	I85.01,	I85.11,	K25.0,
bleeding		531.2,	531.4,	531.6,	532.0,	K25.2,	K25.4,
		532.2,	532.4,	532.6,	533.0,	K26.0,	K26.2,
		533.2,	533.4,	533.6,	534.0,	K26.6,	K27.0,
		534.2,	534.4,	534.6,	K27.4,	K27.6,	K28.0,
		535.01,	535.11,	535.21,	K28.2,	K28.4,	K28.6,
		535.31,	535.41,	535.51,	K29.01,	K29.21,	K29.31,
		535.61,	562.02,	562.03,	K29.41,	K29.51,	K29.61,
		562.12	562.13,	568.81,	K29.71,	K29.81,	K29.91,
		569.3,	569.85,	578.0,	K57.01,	K57.11,	K57.13,
		578.1, 578.9			K57.21,	K57.31,	K57.33,
					K57.41,	K57.81,	K57.91,
					K57.93,	K66.1,	K62.5,
					K55.21,	K92.0,	K92.1,
					K92.2		
Other	bleeding	287.8,	287.9,	423.0,	459.0,	D69.8,	D69.9,
events		596.7,	599.7,	719.1,	784.7,	N32.8,	R31,
		784.8, 786.3			M25.0,	R04	
Comorbidities							
Congestive	heart	398.91,	402.01,	402.11,	I09.81,	I11.0,	I13.0,
failure		402.91,	404.01,	404.03,	I42.0,	I42.2,	I42.5,
		404.11,	404.13,	404.91,	I42.7,	I42.8,	I42.9,
		404.93,	425.4,	425.5,	I43,	I50	
		425.7, 425.8, 425.9, 428					
Hypertension		401,	402,	403,	404,	405	I10,
Diabetes mellitus		250					I11,
Renal disease		403.01,	403.11,	403.91,	I12.0,	I13.11,	I13.2,
		404.02,	404.03,	404.12,	N19,	Z49,	Z94.0,
		404.13,	404.92,	404.93,	Z99.2		
		585,	586,	V42.0,	V45.1,		
		V56					
Liver disease		570,	571,	572,	573,	V42.7	K70,
					K71,	K72,	K73,
					K74,		

Diagnosis	ICD-9-CM	ICD-10-CM
		K75, K76, K77, Z94.4

ICD-9-CM: The International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM: The International Classification of Diseases, Tenth Revision, Clinical Modification.

Table S2. The anatomical therapeutic chemical codes of the medications

Categories	ATC code	Medication
Oral anticoagulants	B01AA03	Warfarin
	B01AE07	Dabigatran
	B01AF01	Rivaroxaban
	B01AF02	Apixaban
	B01AF03	Edoxaban
Platelet aggregation inhibitors	B01AC04	Clopidogrel
	B01AC05	Ticlopidine
	B01AC06	Aspirin
	B01AC22	Prasugrel
	B01AC23	Cilostazol
	B01AC24	Ticagrelor
Agents acting on the renin-angiotensin system	C09	-
Antiarrhythmics	C01BD01	Amiodarone
	C08DB01	Diltiazem
	C01BD07	Dronedarone
	C01BA01	Quinidine
	C08DA01	Verapamil
Beta blocking agents	C07A	-
Calcium channel blockers	C08C, C08D	-
Digitalis glycosides	C01AA	-
Antiepileptic drugs	N03AB02	Phenytoin
	N03AA02	Phenobarbital
	N03AF01	Carbamazepine
	N03AF02	Oxcarbazepine
	N03AX14	Levetiracetam
	N03AG01	Valproic acid
	N03AX11	Topiramate
HMG-CoA reductase inhibitors	C10AA	-
NSAIDs	M01A	-
Proton pump inhibitors	A02BC	-

ATC: Anatomical therapeutic chemical; NSAIDs: non-steroidal anti-inflammatory drugs.

Table S3. The CHA₂DS₂-VASc scoring items

Condition	ICD-9-CM	ICD-10-CM	Score
Congestive heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4, 425.5, 425.7, 425.8, 425.9, 428	I09.81, I11.0, I13.0, I13.2, I42.0, I42.2, I42.5, I42.6, I42.7, I42.8, I42.9, I43, I50	1
Hypertension	401, 402, 403, 404, 405	I10, I11, I12, I13, I15	1
Age ≥75 years	-	-	2
Diabetes mellitus	250	E08, E09, E10, E11, E13	1
Stroke, transient ischemic attack, or thromboembolism	433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 436 OR 435.0, 435.1, 435.2, 435.3, 435.8, 435.9 OR 415.1, 451, 453	I63, I67.89 OR G45.0, G45.1, G45.2, G45.8, G45.9, G46.0, G46.1, G46.2, I67.841, I67.848 OR I26.9, I27.82, I80, I82	2
Vascular disease (myocardial infarction, peripheral artery disease, or aortic plaque)	410, 412 OR 440, 443	I21, I22, I25.2 OR I70, I73	1
Age 65–74 years	-	-	1
Sex category (female)	-	-	1
Maximum score			9

ICD-9-CM: The International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM: The International Classification of Diseases, Tenth Revision, Clinical Modification.

Table S4. The HAS-BLED scoring items

Condition	Definitions and ICD-CM codes/ ATC codes	Score
Hypertension	ICD-9-CM : 401, 402, 403, 404, 405 ICD-10-CM : I10, I11, I12, I13, I15	1
Abnormal renal and/or hepatic function	Abnormal renal function (Table 7. Renal disease) Abnormal hepatic function (Table 7. Liver disease)	1 point for each
Stroke, transient ischemic attack, or thromboembolism	ICD-9-CM : 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 436 OR 435.0, 435.1, 435.2, 435.3, 435.8, 435.9 OR 415.1, 451, 453 ICD-10-CM : I63, I67.89 OR G45.0, G45.1, G45.2, G45.8, G45.9, G46.0, G46.1, G46.2, I67.841, I67.848 OR I26.9, I27.82, I80, I82	1
Bleeding history	(Table 3. Intracranial hemorrhage, gastrointestinal bleeding, other bleeding events)	1
Labile INR	Not available	-
Elderly	Aged >65 years old	1
Drugs (concomitant use of antiplatelet or NSAIDs) or excessive alcohol drinking	<u>Drugs (concomitant use of antiplatelet or NSAIDs)</u> (Table 2. Platelet aggregation inhibitors, NSAIDs) <u>Excessive alcohol drinking</u> ICD-9-CM : 291, 303, 305.0, 357.5, 425.5, 535.3, 571.0, 571.1, 571.2, 571.3, 980.0, 980.1, 980.9, V11.3, V65.42 ICD-10-CM : F10, G62.1, I42.6, K29.2, K70, T51.0, T51.1, T51.9, Z65.8, Z71.41	1 point for each
Maximum score		8

ICD-9-CM: The International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM: The International Classification of Diseases, Tenth Revision, Clinical Modification; ATC: Anatomical therapeutic chemical; INR: international normalized ratio; NSAIDs: non-steroidal anti-inflammatory drugs.

Table S5. National Health Insurance codes for the stroke severity index

Condition	Coefficient	National Health Insurance procedure codes
Airway suctioning	3.5083	47041C, 47042C
Bacterial sensitivity test	1.3642	13009B, 13010B, 13011B, 13009C, 13010C, 13011C, 13020C, 13021B, 13022B
General ward stay	-5.5761	02006K, 02007A, 02008B, 03001K, 03002A, 03004B, 03005K, 03006A, 03008B, 03026K, 03027A, 03029B
ICU stay	4.1770	02011K, 02012A, 02013B, 03010E, 03011F, 03012G, 03010K, 03011A, 03012B, 03013B, 03013H, 03050H, 03047E, 03048F, 03049G
Nasogastric intubation	4.5809	47017C, 47018C
Osmotherapy (mannitol or glycerol)	2.1448	ATC codes: B05BC01, B05BC92
Urinary catheterization	1.6TT569	47013C, 47014C
Constant	9.6804	

ICU: intensive care unit; ATC: Anatomical therapeutic chemical.

Table S6. Distribution of the inverse probability of treatment weights of the DOAC-change and the DOAC-retain groups.

	DOAC-change group	DOAC-retain group
100% (Max)	2.34	7.66
99%	2.00	5.84
95%	1.88	4.82
90%	1.80	4.60
75%	1.54	4.09
50% (Median)	1.36	3.15
25%	1.29	2.28
10%	1.25	2.13
5%	1.23	2.04
1%	1.19	1.89
0% (Min)	1.15	1.73

Table S7. Number of events and incidence rates of outcomes in patients with change and retain pre-stroke DOAC (≥ 90 and ≥ 180 days of continuous medication use after the last DOAC prescription)

	≥ 90 days of continuous medication use after the last DOAC prescription (N=1,536)				≥ 180 days of continuous medication use after the last DOAC prescription (N=1,315)			
	Number of events (per 100 person-years)		Follow-up time (median, year)		Number of events (per 100 person-years)		Follow-up time (median, year)	
	Change pre-stroke DOAC (N=466)	Retain pre-stroke DOAC (N=1,070)	Change pre-stroke DOAC (N=466)	Retain pre-stroke DOAC (N=1,070)	Change pre-stroke DOAC (N=403)	Retain pre-stroke DOAC (N=912)	Change pre-stroke DOAC (N=403)	Retain pre-stroke DOAC (N=912)
Primary outcome								
Recurrent IS and TIA	41 (5.85)	91 (5.47)	1.24	1.21	29 (4.81)	72 (5.02)	1.16	1.23
Secondary outcome								
Effectiveness								
STE	58 (8.58)	121 (7.29)	1.20	1.19	44 (7.45)	94 (6.57)	1.14	1.20
Safety								
ICH	6 (0.90)	9 (0.58)	1.26	1.28	5 (0.98)	7 (0.53)	1.19	1.28
Major bleeding	21 (2.69)	46 (2.67)	1.25	1.24	14 (2.24)	37 (2.49)	1.18	1.25
All-cause mortality	54 (6.66)	108 (6.33)	1.27	1.28	43 (6.18)	81 (5.56)	1.20	1.29

IS: ischemic stroke; TIA: transient ischemic attack; STE: systemic thromboembolism; ICH: intracranial hemorrhage; IPTW: inverse probability of treatment weighting; DOAC: direct oral anticoagulant

Table S8. Hazard ratios in outcomes of patients with changed and retained pre-stroke direct oral anticoagulant prescription, accounting competing risk.

	aHR	95% CI[†]
Primary outcome		
Recurrent IS and TIA	1.31	0.79-1.47
Secondary outcome		
Effectiveness		
STE	1.26	0.87-1.47
Safety		
ICH	2.94	0.39-4.38
Major bleeding	1.15	0.89-1.53
All-cause mortality	1.08	0.82-1.39

Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval; DOAC, direct oral anticoagulants; ICH, intracranial hemorrhage; IS, ischemic stroke; STE, stroke and systemic thromboembolism; TIA, transient ischemic attack.

[†]Confidence intervals were calculated by bootstrapping.

Figure S1. The distribution of propensity scores of the DOAC-change and DOAC-retain groups (A) before weighting and (B) after weighting.

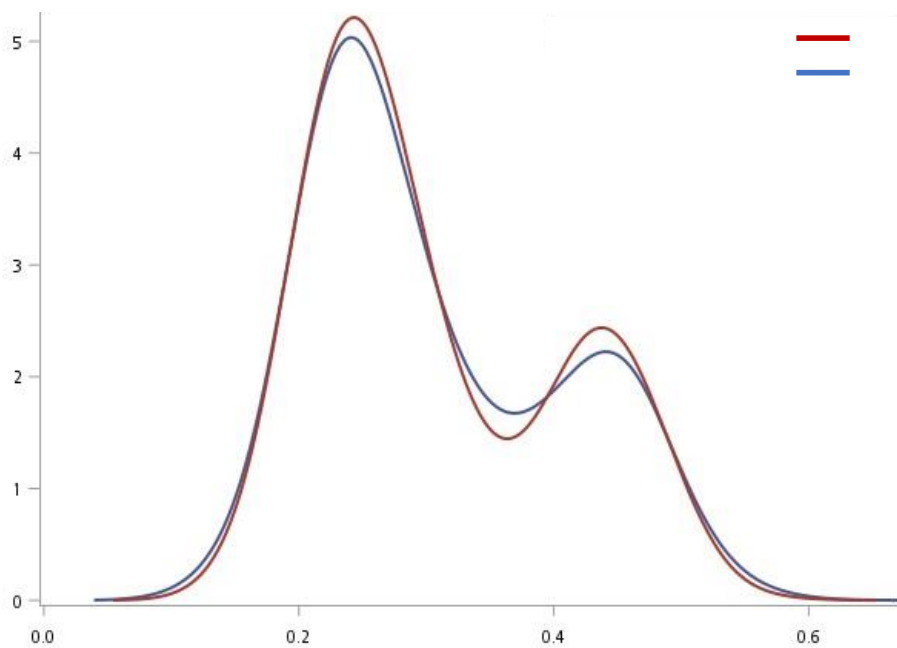
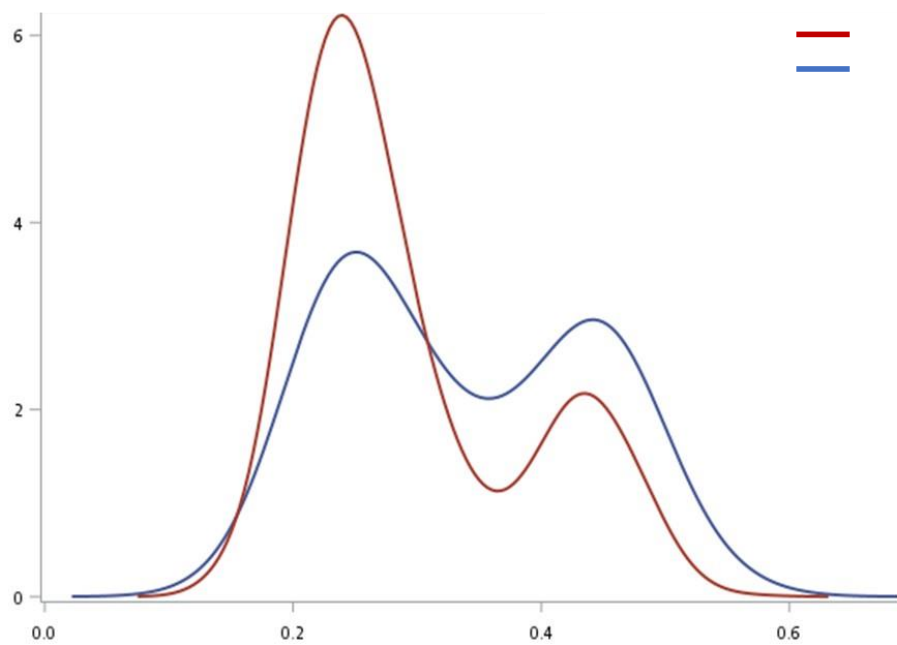


Figure S2. The direct oral anticoagulant (DOAC) prescription before and after ischemic stroke.

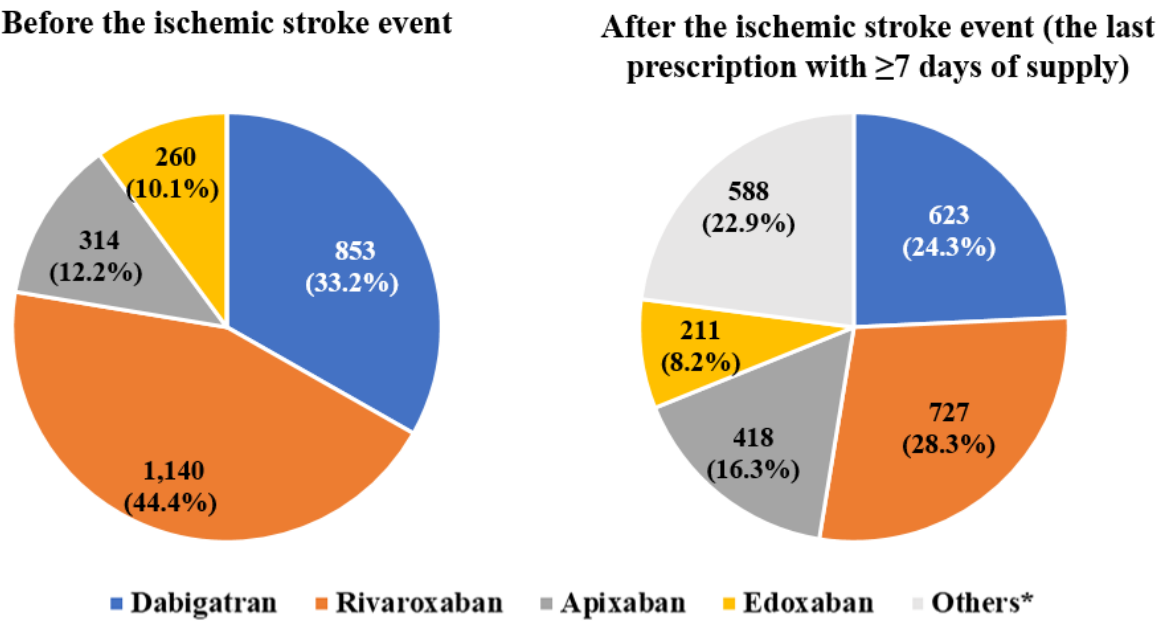


Figure S3. The Kaplan-Meier survival curves for primary outcomes.

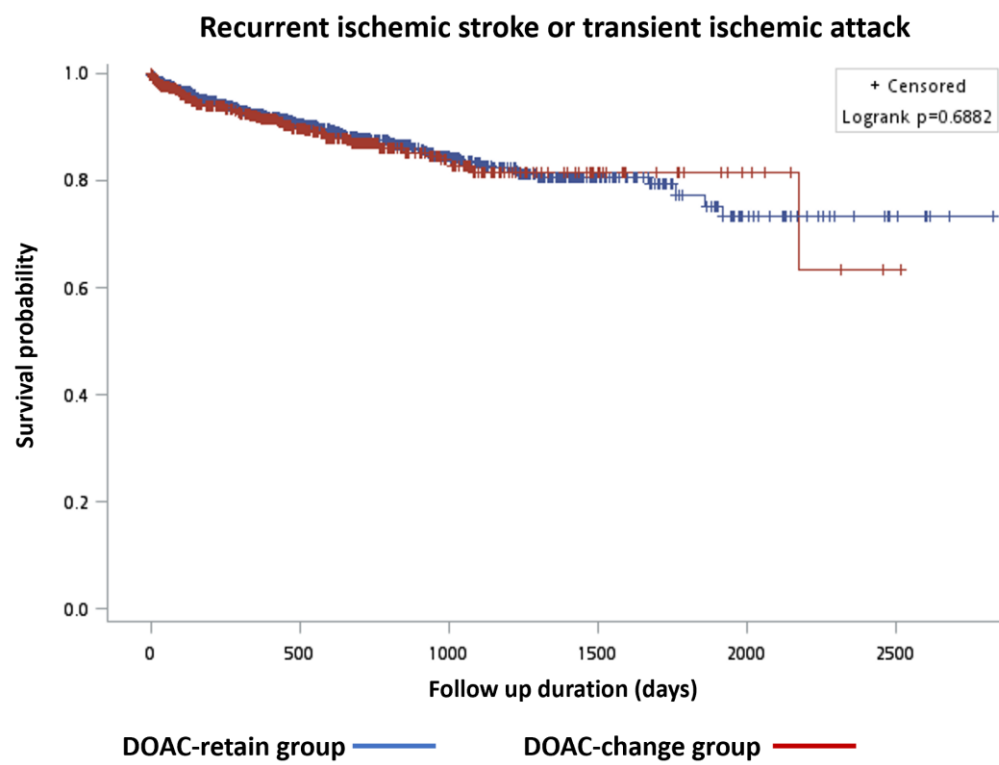


Figure S4. The Kaplan-Meier survival curves for secondary outcomes. (A) intracranial hemorrhage; (B) major bleeding; (C) systemic thromboembolism; and (D) all-cause mortality.

