Supplementary Materials

Effectiveness and safety of direct oral anticoagulants for secondary prevention in patients with non-valvular atrial fibrillation

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Table S1. Definition of covariates and study outcomes

Diagnosis	ICD-10-CM code and definition	Diagnostic definition
Inclusion/exclusion criteria		
Atrial fibrillation	I48.0-48.4, I48.9	Admission or outpatient department≥1
Valvular atrial fibrillation	I05.0, I05.2, I05.9, Z95.2-Z95.4	
Pulmonary embolism	I26	Admission≥1
Deep vein thrombosis	I80.2	Admission≥1
Received joint replacement operation	N0711, N1711, N1721, N2070, N3710, N3721, N3717, N3720, N2072, N2077, N3722, N3727	Admission≥1
End stage renal disease	N18.5, Z49	Dialysis≥2
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
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
Dyslipidemia	E78	Admission or outpatient department≥1
Heart failure	I50	Admission or outpatient department≥1
Vascular disease		
Prior MI	I21, I22	Admission or outpatient department≥1
PAD	I70, I73	Admission or outpatient department≥2
Renal disease	I13.1, N03, N05, N10-N19, Z49, Z94.0, Z99.2	Admission or outpatient department≥1
Liver disease	K70, K72-K76, K71.3-K71.7	Admission or outpatient department≥1
COPD	J41-44	Admission≥1
Cancer	C00-97 and RID code (V193)	Admission or outpatient department≥1
Scores		
CHA_2DS_2-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)	
HAS-BLED score*	Hypertension (1 point), liver disease (1 point), renal disease (1 point), stroke history (1 point), bleeding history (1 point), age>65 years (1 point) and drug (concomitant use of NSAID or antiplatelet agent, 1 point)	

Clinical outcome		
Recurrent stroke	I63, I64	Primary diagnosis, admission≥1 (≥3 days) and brain imaging (CT or MRI) ≥1
Intracranial hemorrhage	I60-62	Primary diagnosis, admission≥1 (≥3 days) and brain imaging (CT or MRI) ≥1
Gastrointestinal bleeding		
Major bleeding	Intracranial hemorrhage + gastrointestinal bleeding	
Composite outcome	Recurrent stroke + major bleeding	
Fatal recurrent stroke	In-hospital death from “Recurrent stroke”	
Fatal major bleeding	In-hospital death from “Major bleeding”	
Fatal composite outcome	In-hospital death from “Recurrent stroke + major bleeding”	
All-cause death	In-hospital death from any causes	

Abbreviation: COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; NSAID, non-steroidal anti-inflammatory drug; PAD, peripheral artery disease; RID, Rare Intractable Disease program.

*Labile international normalized ratio (INR) and alcohol use could not be evaluated from claims and were excluded from scoring in this study.

Table S2. Characteristics of study population after IPTW adjustment

	Warfarin	DOAC	ASD	Rivaroxaban	Dabigatran	Apixaban	Edoxaban	ASD
Male	15100 (52.2)	17042 (52.1)	0.003	6399 (52.1)	3284 (52.1)	4583 (52.0)	2776 (52.1)	0.002
Age			0.001					0.003
Mean±SD	74.2±9.1	74.2±9.5		74.3±9.3	74.3±9.6	74.1±9.8	74.4±9.4	
Median (IQR)	75 (69-81)	75 (69-81)		75 (69-81)	75 (69-81)	75 (68-81)	75 (69-81)	
<65 years	3863 (13.4)	4899 (15.0)		1824 (14.9)	929 (14.7)	1361 (15.5)	785 (14.7)	
65-74 years	9784 (33.8)	10096 (30.9)		3795 (30.9)	1960 (31.1)	2687 (30.5)	1654 (31.0)	
75≤ years	15272 (52.8)	17729 (54.2)		6663 (54.3)	3414 (54.2)	4760 (54.0)	2892 (54.2)	
CHA_2DS_2-VASc score			0.002					0.005
Mean±SD	5.9±1.5	5.9±1.4		5.9±1.4	5.9±1.5	5.8±1.4	5.9±1.5	
Median (IQR)	6 (5-7)	6 (5-7)		6 (5-7)	6 (5-7)	6 (5-7)	6 (5-7)	
2	274 (1.0)	346 (1.1)		105 (0.9)	76 (1.2)	111 (1.3)	55 (1.0)	
3≤	28645 (99.0)	32378 (98.9)		12178 (99.1)	6226 (98.8)	8697 (98.7)	5277 (99.0)	
HAS-BLED score			0.002					0.003
Mean±SD	4.23±1.07	4.23±1.1		4.2±1.1	4.2±1.1	4.2±1.1	4.3±1.1	
Median (IQR)	4 (4-5)	4 (4-5)		4 (4-5)	4 (4-5)	4 (4-5)	4 (4-5)	
3≤	27570 (95.3)	31036 (94.8)		11626 (94.7)	5994 (95.1)	8356 (94.9)	5061 (94.9)	
CCI			0.001					0.001
Mean±SD	5.01±2.49	5.0±2.6		5.0±2.6	5.0±2.6	5.0±2.5	5.1±2.6	
Median (IQR)	5 (3-7)	5 (3-7)		5 (3-7)	5 (3-7)	5 (3-7)	5 (3-7)	

3≤	24261 (83.9)	27270 (83.3)		10217 (83.2)	5274 (83.7)	7353 (83.5)	4427 (83.0)	
Hypertension	25961 (89.8)	29429 (89.9)	0.005	11072 (90.1)	5669 (89.0)	7896 (89.6)	4793 (89.9)	0.012
Diabetes mellitus	9577 (33.1)	10867 (33.2)	0.002	4048 (33.0)	2108 (33.5)	2921 (33.2)	1790 (33.6)	0.003
Dyslipidemia	19192 (66.4)	21759 (66.5)	0.003	8172 (66.5)	4154 (65.9)	5865 (66.6)	3567 (66.9)	0.004
Congestive heart failure	12622 (43.7)	14292 (43.7)	0.001	5404 (44.0)	2726 (43.3)	3840 (43.6)	2322 (43.6)	0.007
Myocardial infarction	1703 (5.9)	1928 (5.9)	<0.001	725 (5.9)	374 (5.9)	519 (5.9)	310 (5.8)	0.001
Peripheral arterial disease	7905 (27.3)	8919 (27.3)	0.002	3341 (27.2)	1716 (27.2)	2385 (27.1)	1477 (27.7)	0.003
COPD	3819 (13.2)	4317 (13.2)	<0.001	1636 (13.3)	832 (13.2)	1134 (12.9)	716 (13.4)	0.003
Cancer	2176 (7.5)	2419 (7.4)	0.005	907 (7.4)	463 (7.4)	663 (7.5)	386 (7.2)	0.005
Previous Intracranial hemorrhage	1617 (5.6)	1859 (5.7)	0.004	695 (5.7)	352 (5.6)	499 (5.7)	312 (5.9)	0.003
Previous gastrointestinal bleeding	6061 (21.0)	6780 (20.7)	0.006	2546 (20.7)	1315 (20.9)	1826 (20.7)	1094 (20.5)	0.006
Antiplatelets			0.002					0.001
No antiplatelets	16133 (55.8)	18216 (55.7)		6849 (55.8)	3496 (55.5)	4971 (56.4)	2901 (54.4)	
Aspirin only	6160 (21.3)	7003 (21.4)		2594 (21.1)	1360 (21.6)	1860 (21.1)	1189 (22.3)	
Clopidogrel only	2802 (9.7)	3195 (9.8)		1202 (9.8)	608 (9.6)	853 (9.7)	532 (10.0)	
Dual antiplatelets	3823 (13.2)	4309 (13.2)		1637 (13.3)	838 (13.3)	1124 (12.8)	710 (13.3)	
NSAID	13232 (45.8)	14923 (45.6)	0.003	5607 (45.7)	2886 (45.8)	4016 (45.6)	2413 (45.3)	0.002
Proton pump inhibitors	10022 (34.7)	11275 (34.5)	0.004	4273 (34.8)	2157 (34.2)	3017 (34.3)	1828 (34.3)	0.003

The numbers are presented as mean ± standard deviation, median (IQR), or numbers (percentage) otherwise mentioned.
Abbreviation: ASD, absolute standardized difference; CCI, charlson comorbidity index; COPD, chronic obstructive pulmonary disease; DOAC, direct oral anticoagulant; IPTW, inverse probability treatment weighting; IQR, interquartile range; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation.

Table S3. Subgroup analysis of clinical outcomes according to antithrombotic therapy

Subgroups		Total number	Recurrent stroke	Major bleeding	Composite outcome	All-cause death	Fatal recurrent stroke	Fatal major bleeding	Fatal composite outcome
Sex									
Male	Warfarin	15338	1195 (4.4)	689 (2.4)	1793 (6.7)	1556 (5.4)	201 (0.7)	92 (0.3)	290 (1.0)
	DOAC	16703	533 (3.6)	309 (2.1)	816 (5.6)	1071 (7.2)	124 (0.8)	26 (0.2)	150 (1.0)
Female	Warfarin	13501	1227 (5.6)	606 (2.7)	1747 (8.2)	1493 (6.5)	273 (1.2)	105 (0.5)	375 (1.6)
	DOAC	16026	552 (4.3)	301 (2.3)	833 (6.5)	1059 (8.1)	171 (1.3)	32 (0.2)	201 (1.5)
Age (years)									
≥75	Warfarin	13827	1141 (6.2)	614 (3.2)	1678 (9.4)	2001 (10.4)	313 (1.6)	120 (0.6)	431 (2.2)
	DOAC	18980	622 (4.4)	403 (2.8)	994 (7.1)	1706 (12.0)	227 (1.6)	40 (0.3)	266 (1.8)
<75	Warfarin	15012	1281 (4.1)	681 (2.1)	1862 (6.2)	1048 (3.2)	161 (0.5)	77 (0.2)	234 (0.7)
	DOAC	13749	463 (3.4)	207 (1.5)	655 (4.9)	424 (3.1)	68 (0.5)	18 (0.1)	85 (0.6)
CHA_2DS_2-VASc									
≥3	Warfarin	28506	2397 (4.9)	1288 (2.6)	3509 (7.4)	3042 (5.9)	474 (0.9)	197 (0.4)	665 (1.3)
	DOAC	32436	1082 (4.0)	609 (2.2)	1645 (6.1)	2125 (7.7)	292 (1.0)	58 (0.2)	348 (1.2)
<3	Warfarin	333	25 (3.4)	7 (0.9)	31 (4.2)	7 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
	DOAC	293	3 (1.0)	1 (0.3)	4 (1.3)	5 (1.6)	3 (1.0)	0 (0.0)	3 (1.0)
HAS-BLED									
≥3	Warfarin	27534	2325 (4.9)	1256 (2.6)	3410 (7.4)	2971 (5.9)	454 (0.9)	196 (0.4)	644 (1.3)
	DOAC	30997	1043 (4.0)	597 (2.2)	1594 (6.1)	2064 (7.7)	285 (1.1)	55 (0.2)	338 (1.3)
<3	Warfarin	1305	97 (5.1)	39 (1.9)	130 (6.9)	78 (3.8)	20 (1.0)	1 (0.0)	21 (1.0)
	DOAC	1732	42 (3.3)	13 (1.0)	55 (4.3)	66 (5.1)	10 (0.8)	3 (0.2)	13 (1.0)
Diabetes									
Yes	Warfarin	9869	846 (5.4)	469 (2.9)	1253 (8.2)	1244 (7.5)	172 (1.0)	74 (0.4)	244 (1.5)
	DOAC	10467	408 (4.9)	209 (2.5)	596 (7.2)	805 (9.4)	111 (1.3)	12 (0.1)	123 (1.4)
No	Warfarin	18970	1576 (4.7)	826 (2.4)	2287 (7.0)	1805 (5.1)	302 (0.8)	123 (0.3)	421 (1.2)
	DOAC	22262	677 (3.5)	401 (2.1)	1053 (5.5)	1325 (6.8)	184 (0.9)	46 (0.2)	228 (1.2)

Hypertension									
Yes	Warfarin	26072	2235 (5.0)	1208 (2.6)	3276 (7.5)	2794 (5.9)	433 (0.9)	184 (0.4)	613 (1.3)
	DOAC	29265	1014 (4.1)	573 (2.3)	1542 (6.3)	1923 (7.6)	273 (1.1)	50 (0.2)	321 (1.3)
No	Warfarin	2767	187 (4.0)	87 (1.8)	264 (5.7)	255 (5.1)	41 (0.8)	13 (0.3)	52 (1.0)
	DOAC	3464	71 (2.6)	37 (1.3)	107 (3.9)	207 (7.4)	22 (0.8)	8 (0.3)	30 (1.1)
Heart failure									
Yes	Warfarin	11972	987 (5.3)	532 (2.8)	1444 (8.0)	1474 (7.5)	197 (1.0)	76 (0.4)	271 (1.4)
	DOAC	14780	485 (4.1)	297 (2.5)	759 (6.5)	1094 (9.1)	114 (0.9)	33 (0.3)	146 (1.2)
No	Warfarin	16867	1435 (4.7)	763 (2.4)	2096 (7.0)	1575 (4.8)	277 (0.8)	121 (0.4)	394 (1.2)
	DOAC	17949	600 (3.8)	313 (2.0)	890 (5.7)	1036 (6.5)	181 (1.1)	25 (0.2)	205 (1.3)
CKD									
Yes	Warfarin	5079	356 (5.6)	255 (3.9)	583 (9.4)	854 (12.8)	95 (1.4)	40 (0.6)	132 (2.0)
	DOAC	5438	193 (5.2)	152 (4.0)	334 (9.1)	631 (16.7)	53 (1.4)	15 (0.4)	68 (1.8)
No	Warfarin	23760	2066 (4.8)	1040 (2.3)	2957 (7.1)	2195 (4.8)	379 (0.8)	157 (0.3)	533 (1.2)
	DOAC	27291	892 (3.7)	458 (1.9)	1315 (5.6)	1499 (6.2)	242 (1.0)	43 (0.2)	283 (1.2)
CCI									
≥3	Warfarin	24466	2173 (5.5)	1144 (2.8)	3161 (8.1)	2780 (6.5)	424 (1.0)	172 (0.4)	591 (1.4)
	DOAC	26808	997 (4.5)	555 (2.5)	1508 (7.0)	1979 (8.9)	267 (1.2)	49 (0.2)	314 (1.4)
<3	Warfarin	4373	249 (2.6)	151 (1.6)	379 (4.1)	269 (2.8)	50 (0.5)	25 (0.3)	74 (0.8)
	DOAC	5921	88 (1.6)	55 (1.0)	141 (2.5)	151 (2.6)	28 (0.5)	9 (0.2)	37 (0.6)

Number of events (crude incidence rates, per 100 person-years)

Abbreviation: CCI, charlson comorbidity index; CKD, chronic kidney disease; DOAC, direct oral anticoagulant.

Table S4. Crude and multivariate-adjusted risk of clinical outcomes according to antithrombotic therapy

	Warfarin		DOAC					
Outcome	**Event**	**IR**	**Event**	**IR**	**Crude HR (95% CI)**	**p-value**	**Multivariate adjusted HR (95% CI)**	**p-value**
Recurrent stroke	2422	4.9	1085	3.9	0.61 (0.57-0.66)	<0.001	0.66 (0.61-0.71)	<0.001
Major bleeding	1295	2.5	610	2.2	0.73 (0.66-0.81)	<0.001	0.72 (0.66-0.81)	<0.001
Composite outcome (Recurrent stroke + Major bleeding)	3540	7.4	1649	6.0	0.65 (0.61-0.69)	<0.001	0.68 (0.64-0.72)	<0.001
All-cause death	3049	5.9	2130	7.6	0.95 (0.89-1.00)	0.069	0.84 (0.79-0.89)	<0.001
Fatal recurrent stroke	474	0.9	295	1.0	0.72 (0.62-0.84)	<0.001	0.65 (0.55-0.75)	<0.001
Fatal major bleeding	197	0.4	58	0.2	0.49 (0.36-0.67)	<0.001	0.47 (0.35-0.65)	<0.001
Fatal composite outcome	665	1.3	351	1.2	0.67 (0.58-0.77)	<0.001	0.61 (0.53-0.69)	<0.001

Abbreviation: CI, confidence interval; HR, hazard ratio; IR, incidence rate; DOAC, direct oral anticoagulant.

Table S5. Crude and multivariate-adjusted risk of clinical outcomes according to antithrombotic therapy (Warfarin vs 4 DOACs)

Group	Recurrent stroke	IR	Crude HR (95% CI)	Multivariate adjusted HR (95% CI)
Warfarin	2422	4.9	1(Ref.)	1(Ref.)
Rivaroxaban	388	3.6	0.57 (0.51-0.63)	0.62 (0.55-0.69)
Dabigatran	260	4.1	0.68 (0.60-0.78)	0.76 (0.67-0.86)
Apixaban	322	4.5	0.69 (0.61-0.78)	0.71 (0.63-0.80)
Edoxaban	115	3.5	0.47 (0.39-0.57)	0.49 (0.41-0.60)
Group	**Major bleeding**	**IR**	**Crude HR (95% CI)**	**Multivariate adjusted HR (95% CI)**
Warfarin	1295	2.5	1(Ref.)	1(Ref.)
Rivaroxaban	264	2.4	0.81 (0.71-0.93)	0.82 (0.71-0.94)
Dabigatran	141	2.2	0.77 (0.64-0.91)	0.82 (0.68-0.97)
Apixaban	149	2.1	0.68 (0.57-0.81)	0.64 (0.54-0.76)
Edoxaban	56	1.7	0.51 (0.39-0.67)	0.50 (0.38-0.65)
Group	**Composite outcome**	**IR**	**Crude HR (95% CI)**	**Multivariate adjusted HR (95% CI)**
Warfarin	3540	7.4	1(Ref.)	1(Ref.)
Rivaroxaban	635	5.9	0.65 (0.60-0.71)	0.69 (0.63-0.75)
Dabigatran	385	6.2	0.70 (0.63-0.78)	0.76 (0.69-0.85)
Apixaban	461	6.5	0.69 (0.63-0.76)	0.69 (0.62-0.76)
Edoxaban	168	5.1	0.48 (0.41-0.57)	0.49 (0.42-0.58)
Group	**All-cause death**	**IR**	**Crude HR (95% CI)**	**Multivariate adjusted HR (95% CI)**
Warfarin	3049	5.9	1(Ref.)	1(Ref.)
Rivaroxaban	889	8.0	1.04 (0.96-1.12)	0.92 (0.85-0.99)
Dabigatran	344	5.4	0.72 (0.65-0.81)	0.75 (0.67-0.84)
Apixaban	647	8.9	1.09 (0.99-1.19)	0.86 (0.79-0.94)
Edoxaban	250	7.5	0.78 (0.69-0.89)	0.69 (0.60-0.78)
Group	**Fatal recurrent stroke**	**IR**	**Crude HR (95% CI)**	**Multivariate adjusted HR (95% CI)**
Warfarin	474	0.9	1(Ref.)	1(Ref.)
Rivaroxaban	121	1.1	0.78 (0.63-0.95)	0.71 (0.58-0.87)
Dabigatran	61	1.0	0.73 (0.55-0.95)	0.73 (0.55-0.95)
Apixaban	85	1.2	0.78 (0.62-0.98)	0.64 (0.50-0.81)
Edoxaban	28	0.8	0.46 (0.31-0.67)	0.40 (0.27-0.58)
Group	**Fatal major bleeding**	**IR**	**Crude HR (95% CI)**	**Multivariate adjusted HR (95% CI)**
Warfarin	197	0.4	1(Ref.)	1(Ref.)
Rivaroxaban	30	0.3	0.65 (0.44-0.96)	0.63 (0.42-0.93)
Dabigatran	5	0.1	0.19 (0.08-0.47)	0.20 (0.08-0.49)
Apixaban	15	0.2	0.49 (0.29-0.83)	0.44 (0.26-0.76)
Edoxaban	8	0.2399	0.53 (0.26-1.09)	0.50 (0.24-1.02)
Group	**Fatal composite outcome**	**IR**	**Crude HR (95% CI)**	**Multivariate adjusted HR (95% CI)**
Warfarin	665	1.3	1(Ref.)	1(Ref.)
Rivaroxaban	149	1.3	0.74 (0.62-0.89)	0.69 (0.57-0.82)
Dabigatran	66	1.0	0.60 (0.47-0.78)	0.61 (0.47-0.79)
Apixaban	100	1.4	0.72 (0.58-0.89)	0.60 (0.48-0.75)
Edoxaban	36	1.1	0.47 (0.34-0.67)	0.41 (0.30-0.58)

Abbreviation: CI, confidence interval; HR, hazard ratio; IR, incidence rate; DOAC, direct oral anticoagulant.

Table S6. Characteristics of the study population with warfarin and dosage of DOAC

	(A) Warfarin (n=28839)	(B) Regular dose DOAC (n=12073)	(C) Reduced dose DOAC (n=20656)	A vs. B p value	A vs. C p value	B vs. C p value
Age						
Mean±SD	73.1±9.4	71.7±9.4	77.3±8.3	<0.001	<0.001	<0.001
Median (IQR)	74 (68-79)	73 (66-78)	78 (73-83)	<0.001	<0.001	<0.001
<65 years	4757 (16.5)	2509 (20.8)	1465 (7.1)	<0.001	<0.001	<0.001
65-74 years	10255 (35.6)	4612 (38.2)	5163 (25.0)			
75≤ years	13827 (48.0)	4952 (41.0)	14028 (67.9)			
Male	15338 (53.2)	7269 (60.2)	11222 (54.3)	<0.001	<0.001	<0.001
CHA_2DS_2-VASc score						
Mean±SD	5.8±1.5	5.5±1.5	6.2±8.2	<0.001	<0.001	<0.001
2	333 (1.2)	221 (1.8)	72 (0.4)	<0.001	<0.001	<0.001
3≤	28506 (98.8)	11852 (98.1)	20584 (99.6)			
HAS-BLED score						
Mean±SD	4.2±1.1	4.0±1.1	4.3±1.1	<0.001	<0.001	<0.001
3≤	27534 (95.5)	11103 (92.0)	19894 (96.3)	<0.001	<0.001	<0.001
CCI						
Mean±SD	5.2±2.5	4.7±2.5	5.0±2.5	<0.001	<0.001	<0.001
3≤	24466 (84.8)	9566 (79.2)	17242 (83.5)	<0.001	<0.001	<0.001
Hypertension	26072 (90.4)	10633 (88.1)	18632 (90.2)	<0.001	0.449	<0.001

Diabetes mellitus	9869 (34.2)	3844 (31.8)	6623 (32.1)	<0.001	<0.001	0.676
Dyslipidemia	18774 (65.1)	8412 (69.7)	13487 (65.3)	<0.001	0.655	<0.001
Congestive heart failure	11972 (41.5)	5028 (41.7)	9752 (47.2)	0.803	<0.001	<0.001
Myocardial infarction	1836 (6.4)	546 (4.5)	1283 (6.2)	<0.001	0.484	<0.001
Peripheral arterial disease	7668 (26.6)	3133 (26.0)	5942 (28.8)	0.181	<0.001	<0.001
COPD	4080 (14.2)	1293 (10.7)	2701 (13.1)	<0.001	<0.001	<0.001
Cancer	2000 (6.9)	912 (7.6)	1629 (7.9)	0.026	<0.001	0.278
Previous Intracranial hemorrhage	1530 (5.3)	673 (5.6)	1286 (6.23)	0.271	<0.001	0.017
Previous gastrointestinal bleeding	5039 (17.5)	2684 (22.3)	4994 (24.2)	<0.001	<0.001	<0.001
Antiplatelets						
No antiplatelets	12731 (44.2)	8199 (67.9)	13255 (64.2)	<0.001	<0.001	<0.001
Aspirin only	7990 (27.7)	1793 (14.9)	3390 (16.4)			
Clopidogrel only	2816 (9.8)	1029 (8.5)	2180 (10.6)			
Dual antiplatelets	5302 (18.4)	1052 (8.7)	1831 (8.9)			
NSAID	13940 (48.3)	5440 (45.1)	8881 (43.0)	<0.001	<0.001	<0.001
Proton pump inhibitors	9090 (31.5)	4374 (36.2)	7699 (37.3)	<0.001	<0.001	0.059

The numbers are presented as mean ± standard deviation, median (IQR), or numbers (percentage) otherwise mentioned.

Abbreviation: ASD, absolute standardized difference; CCI, charlson comorbidity index; COPD, chronic obstructive pulmonary disease; DOAC, direct oral anticoagulant; IPTW, inverse probability treatment weighting; IQR, interquartile range; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation.

Table S7. Comparison of clinical outcomes between patients with warfarin and regular dose DOAC

Outcome	Warfarin Event (IR)	Regular dose DOAC Event (IR)	*HR (95% CI)	p-value
Recurrent stroke	2362 (4.8)	477 (4.4)	0.70 (0.63-0.77)	<0.001
Major bleeding	1269 (2.5)	214 (1.9)	0.66 (0.57-0.76)	<0.001
Composite outcome (Recurrent stroke + Major bleeding)	3456 (7.2)	675 (6.2)	0.69 (0.63-0.75)	<0.001
Fatal recurrent stroke	463 (0.9)	99 (0.9)	0.64 (0.51-0.80)	<0.001
Fatal major bleeding	187 (0.4)	15 (0.1)	0.34 (0.19-0.56)	<0.001
Fatal composite outcome	645 (1.2)	114 (1.0)	0.58 (0.47-0.71)	<0.001
All-cause death	2958 (5.7)	651 (5.8)	0.76 (0.70-0.83)	<0.001

* IPTW adjustment

Abbreviation: CI, confidence interval; DOAC, direct oral anticoagulant; HR, hazard ratio; IR, incidence rate.

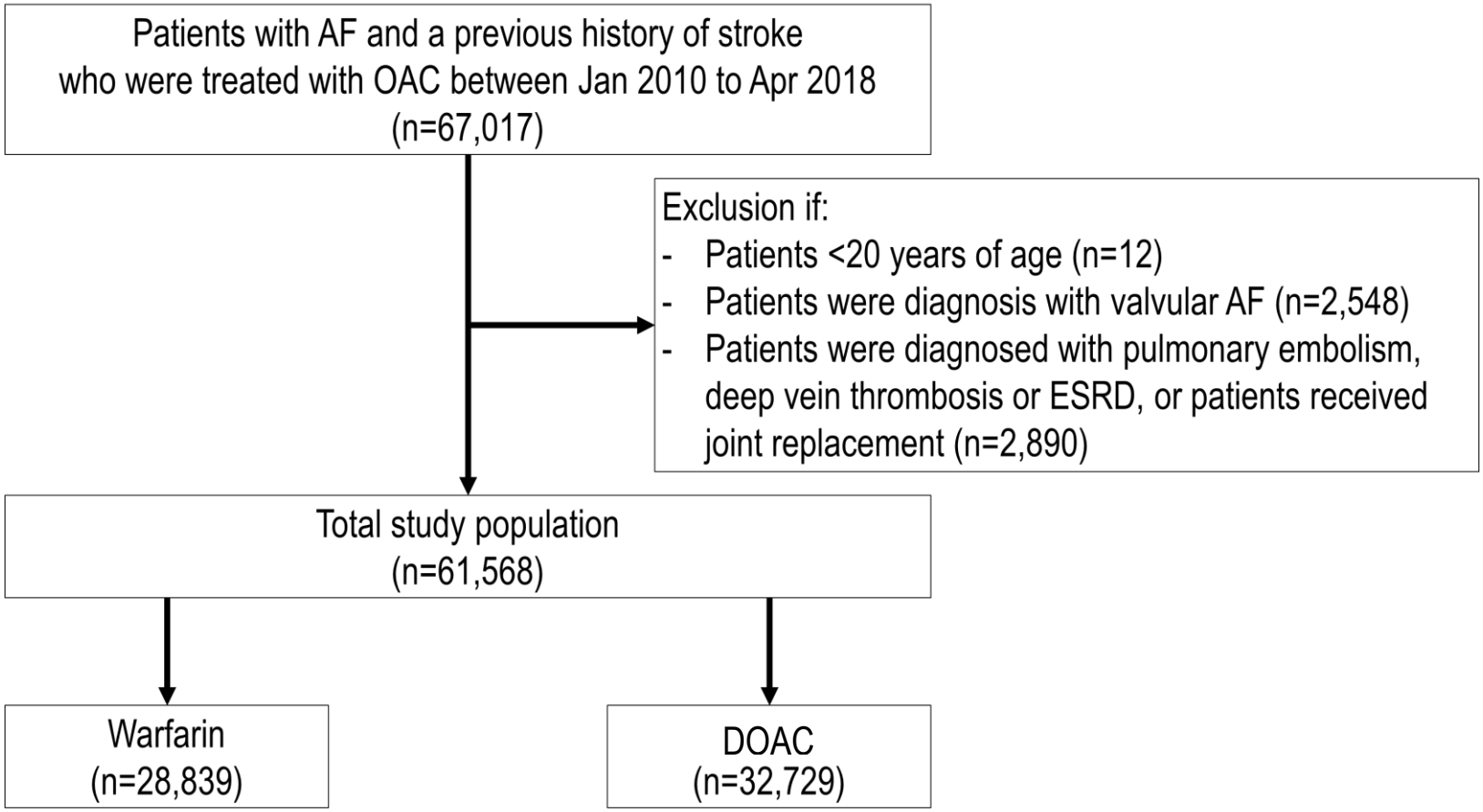

Figure S1. Study flow

AF = atrial fibrillation, DOAC = direct oral anticoagulant, ESRD = end stage renal disease, OAC = oral anticoagulant.

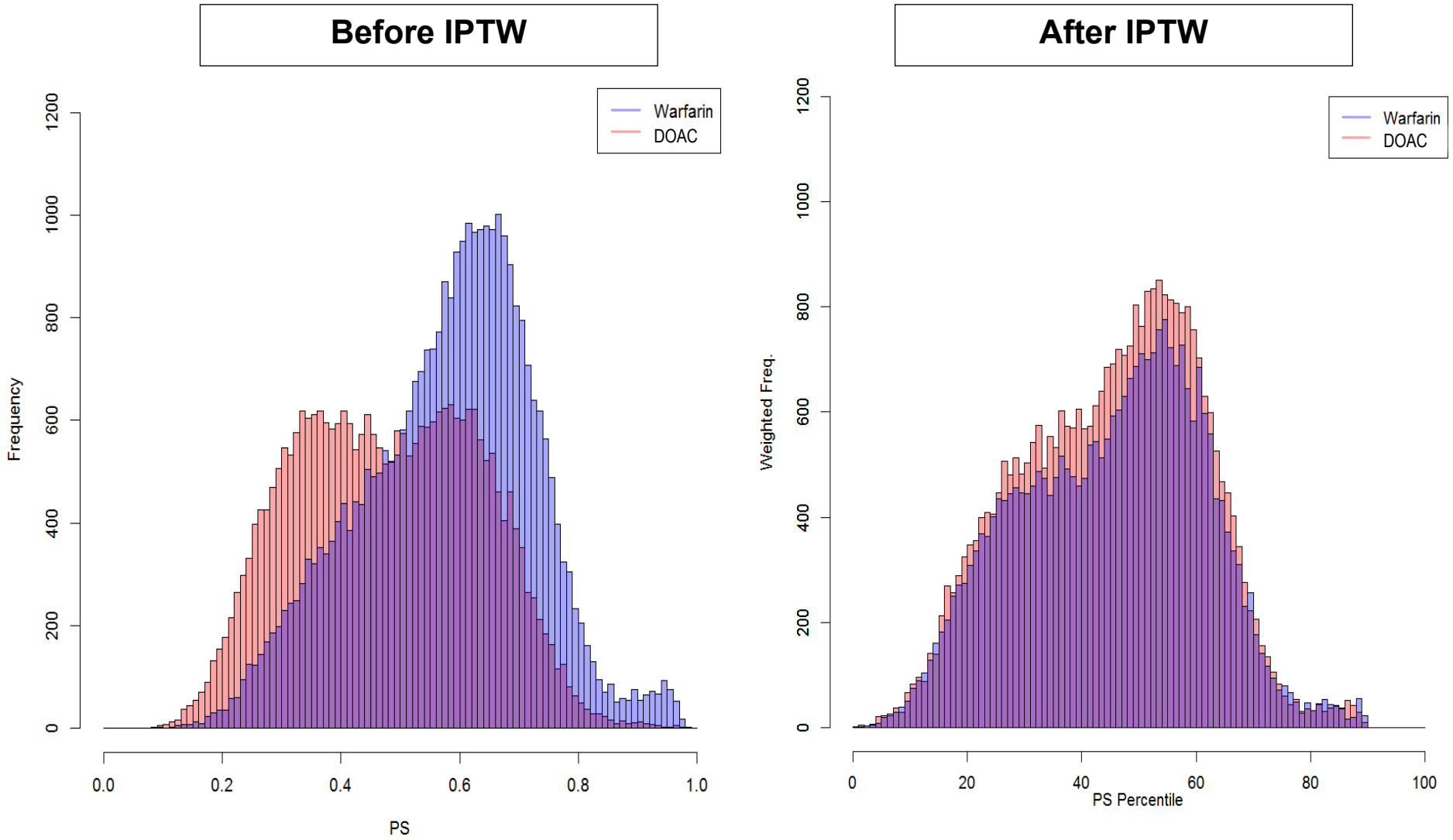

Figure S2. Distribution of propensity scores before and after IPTW

DOAC = direct oral anticoagulant, IPTW = inverse probability of treatment weights, PS = propensity score

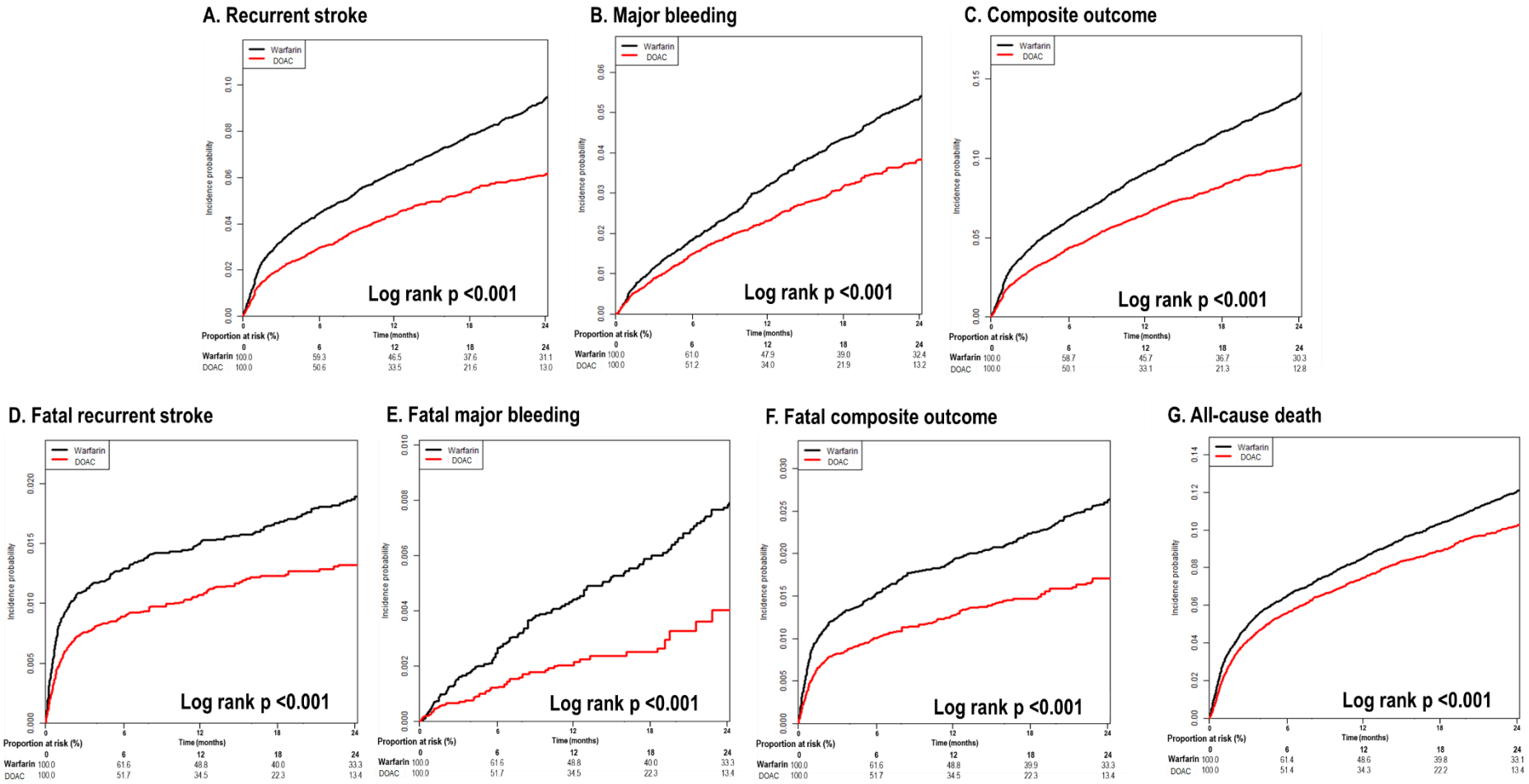

Figure S3. Kaplan-Meier curve of clinical outcomes according to antithrombotic therapy (Warfarin vs. pooled DOACs)

DOAC = direct oral anticoagulant

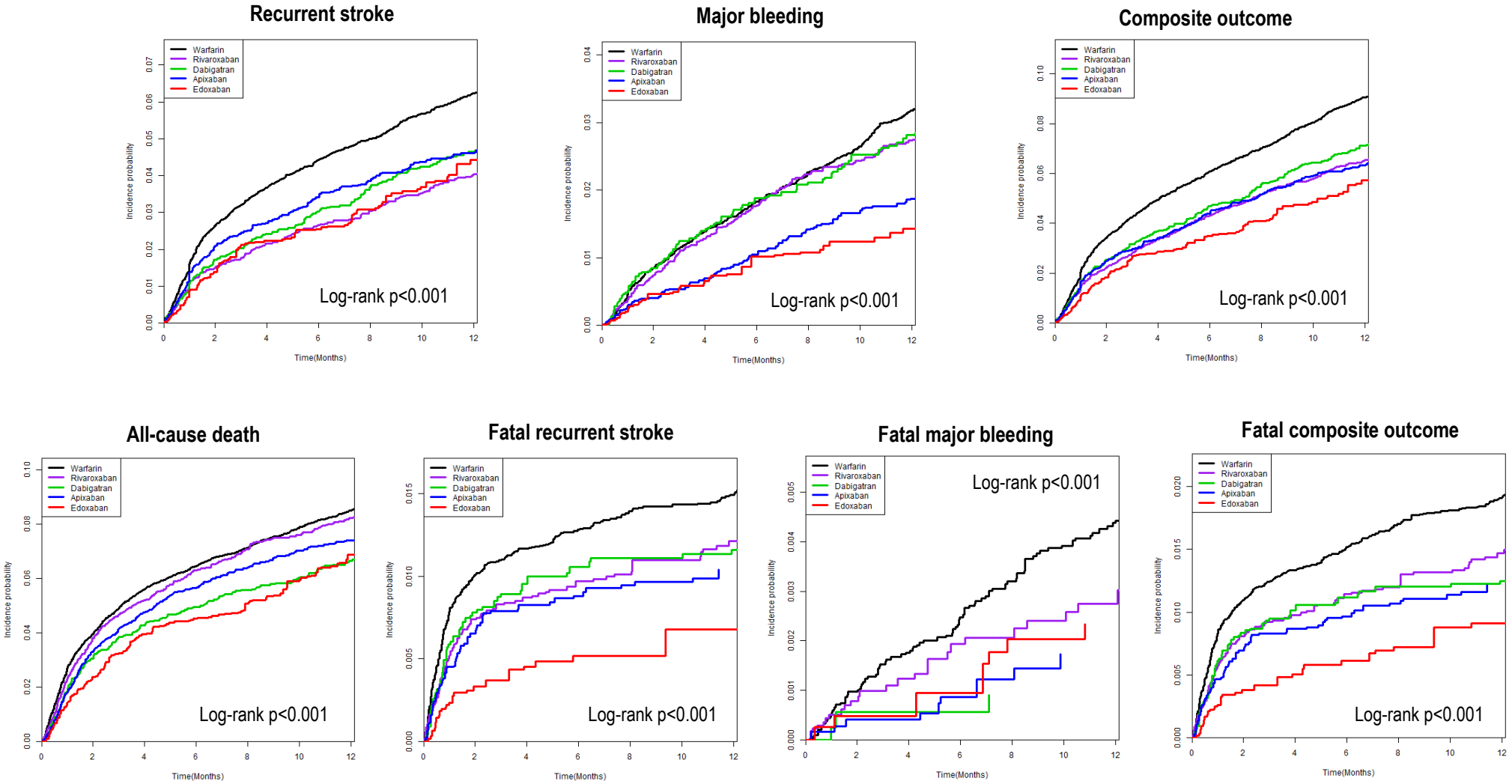

Figure S4. Kaplan-Meier curve of clinical outcomes according to antithrombotic therapy (Warfarin vs. 4 DOACs)

DOAC = direct oral anticoagulant

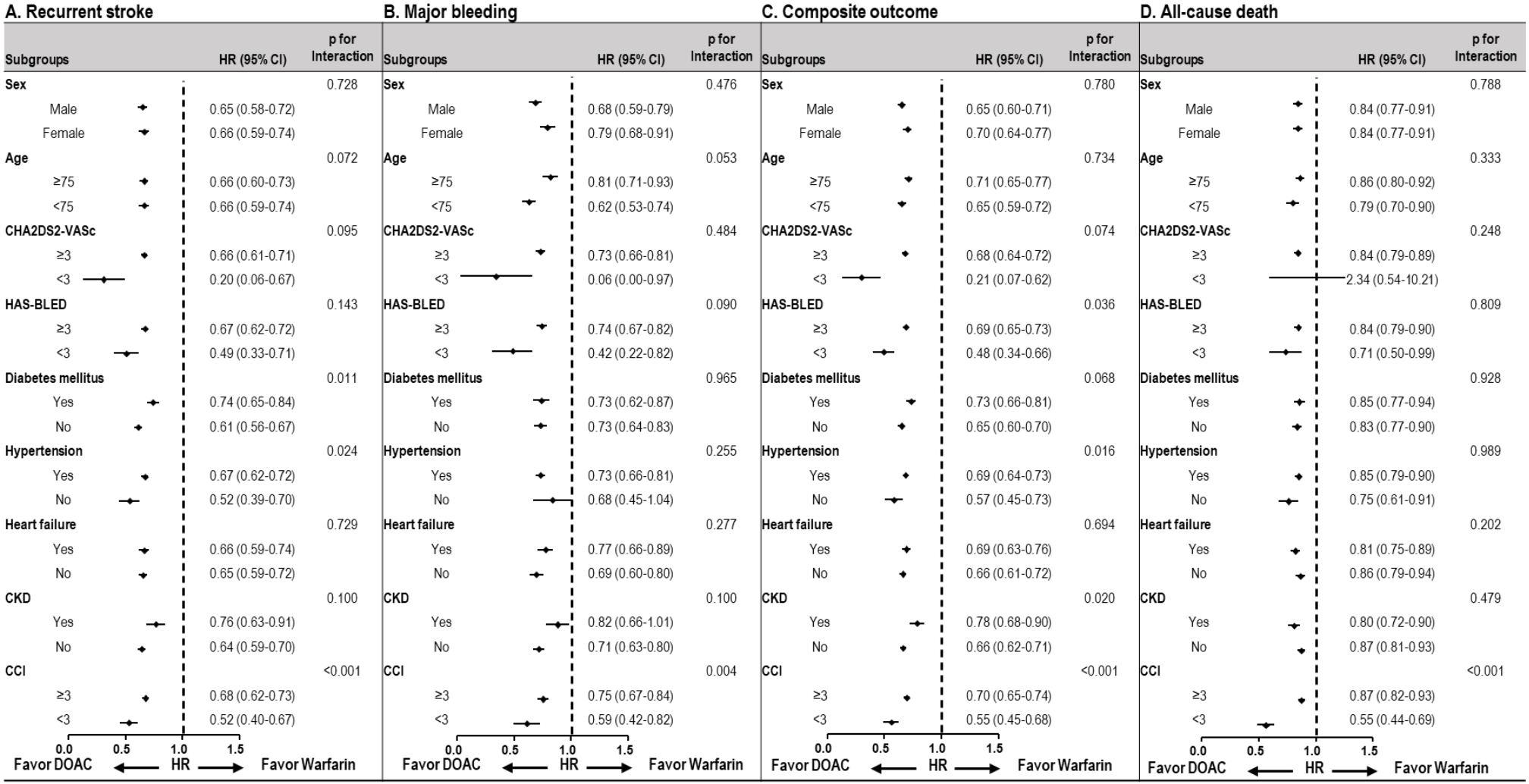

Figure S5. Subgroup analysis of clinical outcomes according to antithrombotic therapy

CCI = charlson comorbidity index, CI = confidence interval, CKD = chronic kidney disease, DOAC = direct oral anticoagulant, HR = hazard ratio

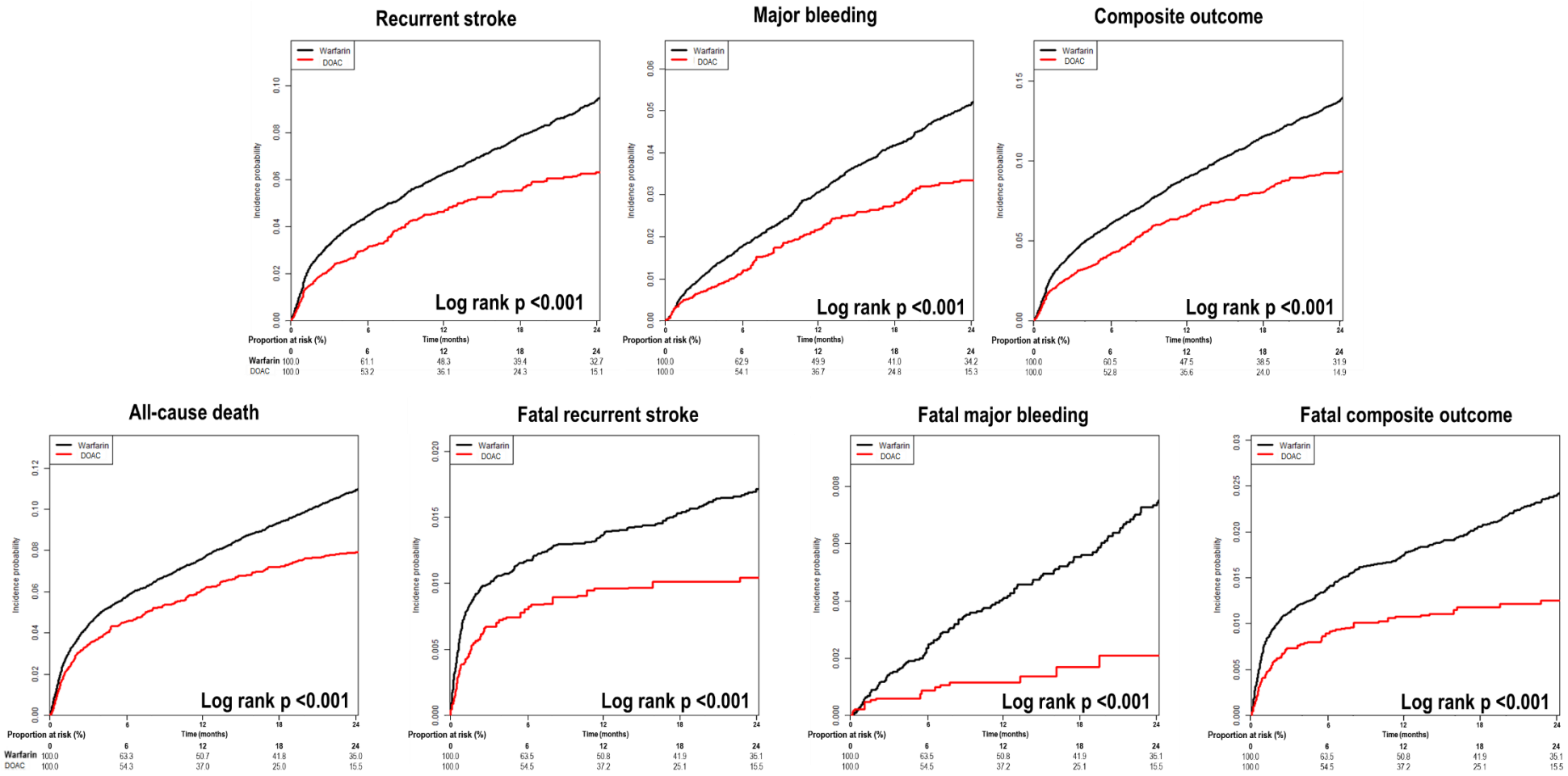

Figure S6. Kaplan-Meier curve of clinical outcomes among patients with warfarin and regular dose DOAC

DOAC = direct oral anticoagulant

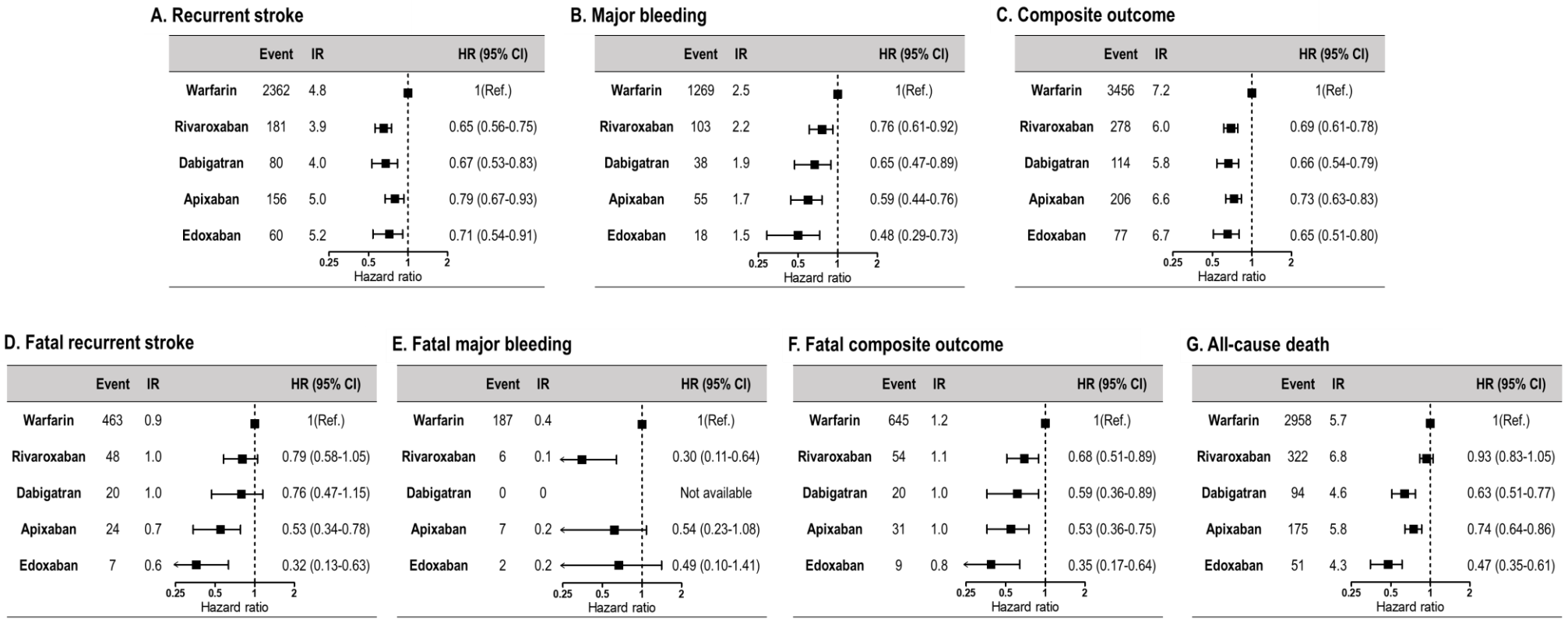

Figure S7. Comparison of clinical outcomes between patients with warfarin and 4 regular dose DOACs

CI = confidence interval, DOAC = direct oral anticoagulant, HR = hazard ratio, IR = incidence rate

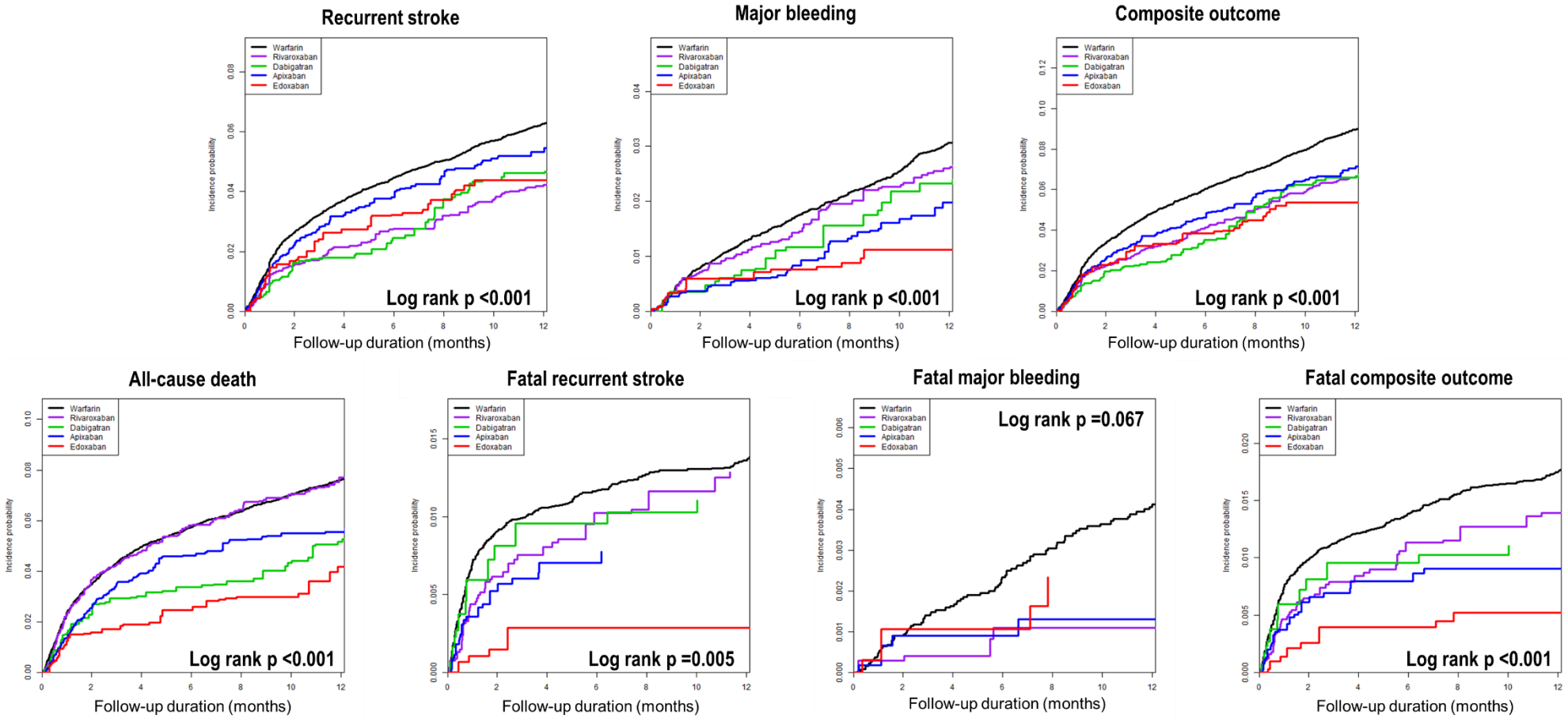

Figure S8. Kaplan-Meier curve of clinical outcomes among patients with warfarin and four different regular dose DOAC

DOAC = direct oral anticoagulant

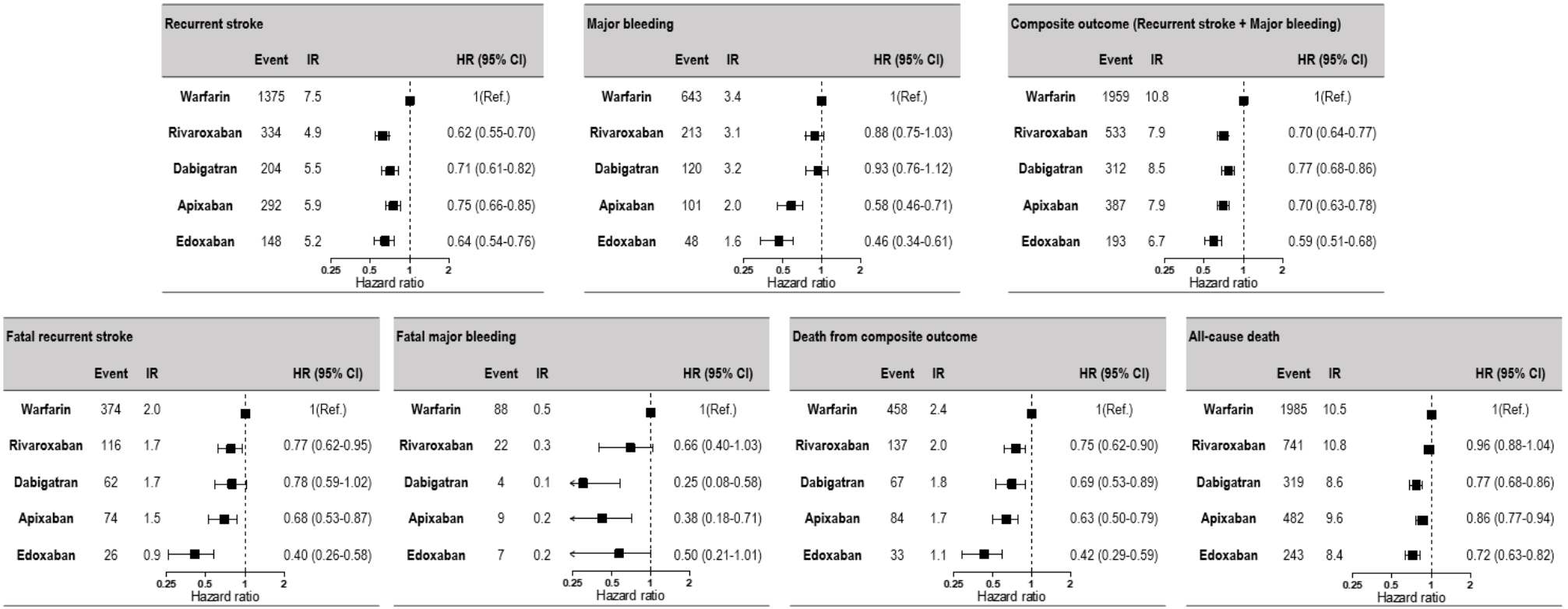

Figure S9. Sensitivity analysis comparing clinical outcomes according to antithrombotic therapy during a 1-year follow-up

CI = confidence interval, HR = hazard ratio, IR = incidence rate