Supplemental material

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Supplemental Table 1. Baseline characteristics of patients with nonvalvular atrial fibrillation newly initiating a DOAC, before and after propensity score matching: characteristics not included in propensity score models due to high missingness assessed in the year prior to and including index date

	Patient characteristics before propensity score matching				Patient characteristics after propensity score matching								
	Apixaban	Rivaroxaban	Edoxaban	Dabigatran	Apixaban	Rivaroxaban	ASD	Apixaban	Other DOACs	ASD	Rivaroxaban	Other DOACs	ASD
Number of patients	2,801	2,221	398	261	1,839	1,839		2,276	2,276		1,985	1,985	
Patient characteristics, evaluated as the last value observed in the one year prior to index date													
Marital status							0.222			0.128			0.289
Married; n (%)	32 (1.1%)	21 (0.9%)	8 (2.0%)	1 (0.4%)	21 (1.1%)	18 (1.0%)		28 (1.2%)	28 (1.2%)		19 (1.0%)	26 (1.3%)	
Unmarried; n (%)	13 (0.5%)	11 (0.5%)	3 (0.8%)	0 (0.0%)	8 (0.4%)	11 (0.6%)		9 (0.4%)	12 (0.5%)		11 (0.6%)	8 (0.4%)	
Missing; n (%)	2,756 (98.4%)	2,189 (98.6%)	387 (97.2%)	260 (99.6%)	1,810 (98.4%)	1,810 (98.4%)		2,239 (98.4%)	2,236 (98.2%)		1,955 (98.5%)	1,951 (98.3%)	
Cigarettes per day							0.216			0.150			0.163
mean (sd)	10.50 (5.98)	12.22 (8.33)	12.25 (8.28)	11.15 (5.98)	10.51 (6.01)	12.00 (7.71)		10.34 (6.05)	11.38 (7.72)		12.17 (8.10)	10.99 (6.27)	
median [IQR]	10.00 [5.75, 15.00]	10.00 [5.00, 16.25]	10.00 [6.50, 15.00]	10.00 [6.00, 17.50]	10.00 [5.50, 15.00]	10.00 [5.00, 15.00]		10.00 [5.75, 15.00]	10.00 [5.00, 15.00]		10.00 [5.00, 20.00]	10.00 [6.00, 15.00]	
Missing; n (%)	2,695 (96.2%)	2,127 (95.8%)	382 (96.0%)	248 (95.0%)	1,774 (96.5%)	1,764 (95.9%)		2,190 (96.2%)	2,181 (95.8%)		1,907 (96.1%)	1,913 (96.4%)	
Glasses per day*							0.076			0.043			0.128
mean (sd)	40,314.49 (901,176.02)	14.69 (15.77)	75,469.73 (3,379,675.36)	20.22 (35.00)	58,421.88 (1,084,888.39)	15.00 (16.19)		46,984.77 (972,895.01)	99,476.87 (1,413,606.11)		14.70 (15.95)	62,906.26 (1,806,540.38)	
median [IQR]	10.00 [2.00, 18.00]	10.00 [4.00, 20.00]	12.00 [5.00, 20.25]	10.00 [2.00, 21.50]	10.00 [2.00, 20.00]	10.00 [4.00, 20.00]		10.00 [2.00, 18.00]	10.00 [4.00, 21.00]		10.00 [4.00, 20.00]	10.00 [3.00, 20.00]	
Missing; n (%)	2,301 (82.1%)	1,822 (82.0%)	328 (82.4%)	212 (81.2%)	1,494 (81.2%)	1,504 (81.8%)		1,847 (81.2%)	1,871 (82.2%)		1,626 (81.9%)	1,614 (81.3%)	
BMI (kg/m2)							0.083			0.045			0.074
mean (sd)	29.20 (6.24)	29.86 (6.51)	28.81 (6.28)	29.83 (6.34)	29.23 (6.29)	29.75 (6.42)		29.21 (6.24)	29.49 (6.43)		29.78 (6.48)	29.30 (6.46)	
median [IQR]	28.30 [24.70, 32.60]	28.90 [25.30, 33.40]	27.80 [24.50, 32.23]	29.20 [25.40, 32.90]	28.30 [24.70, 32.40]	28.80 [25.30, 33.40]		28.40 [24.78, 33.00]	28.55 [25.08, 33.00]		28.80 [25.20, 33.40]	28.50 [24.80, 32.60]	
Missing; n (%)	970 (34.6%)	846 (38.1%)	104 (26.1%)	98 (37.5%)	672 (36.5%)	702 (38.2%)		790 (34.7%)	830 (36.5%)		765 (38.5%)	708 (35.7%)	
HbA1c (mmol/mol)							0.066			0.076			0.075
mean (sd)	46.53 (15.17)	48.59 (16.25)	46.69 (14.76)	46.92 (13.99)	46.87 (16.39)	47.94 (16.05)		46.41 (15.13)	47.58 (15.65)		48.34 (16.04)	47.12 (16.24)	
median [IQR]	44.00 [39.00, 52.00]	45.00 [39.00, 54.00]	43.00 [39.00, 52.25]	44.00 [40.00, 52.00]	44.00 [39.00, 53.00]	44.00 [39.00, 53.00]		44.00 [39.00, 52.00]	44.00 [39.00, 53.00]		45.00 [39.00, 54.00]	44.00 [39.00, 53.00]	
Missing; n (%)	1,544 (55.1%)	1,235 (55.6%)	252 (63.3%)	150 (57.5%)	1,025 (55.7%)	1,034 (56.2%)		1,262 (55.4%)	1,299 (57.1%)		1,104 (55.6%)	1,110 (55.9%)	
INR							0.036			0.021			0.044
mean (sd)	4.77 (13.57)	3.77 (8.53)	8.34 (19.23)	2.01 (0.81)	4.33 (12.41)	3.94 (9.40)		4.71 (13.54)	4.44 (11.17)		3.94 (9.07)	4.42 (12.60)	
median [IQR]	2.40 [1.80, 2.80]	2.30 [1.80, 2.90]	2.40 [2.00, 3.20]	2.00 [1.40, 2.38]	2.40 [1.80, 2.80]	2.30 [1.80, 2.90]		2.40 [1.80, 2.80]	2.30 [1.80, 2.90]		2.30 [1.80, 2.90]	2.30 [1.80, 2.75]	
Missing; n (%)	2,464 (88.0%)	1,880 (84.6%)	349 (87.7%)	225 (86.2%)	1,606 (87.3%)	1,575 (85.6%)		1,982 (87.1%)	1,952 (85.8%)		1,685 (84.9%)	1,708 (86.0%)	
GFR (ml/min/1.73 m2)							0.135			0.131			0.145
mean (sd)	61.04 (16.17)	63.66 (15.95)	62.25 (15.62)	64.86 (15.23)	61.49 (16.24)	63.67 (16.01)		61.21 (16.17)	63.30 (15.79)		63.72 (15.97)	61.39 (16.30)	
median [IQR]	61.00 [50.00, 73.00]	64.00 [52.00, 76.00]	60.00 [52.00, 76.00]	65.00 [54.00, 79.00]	61.00 [50.00, 74.00]	64.00 [52.00, 76.00]		61.00 [50.00, 74.00]	64.00 [52.00, 76.00]		64.00 [52.00, 76.00]	60.40 [50.00, 74.00]	
Missing; n (%)	1,052 (37.6%)	870 (39.2%)	190 (47.7%)	94 (36.0%)	736 (40.0%)	714 (38.8%)		879 (38.6%)	909 (39.9%)		781 (39.3%)	786 (39.6%)	
CrCl (ml/min)							0.029			0.017			0.066
mean (sd)	63.93 (22.40)	65.75 (19.46)	56.73 (21.52)	71.84 (4.95)	66.81 (21.09)	66.22 (19.78)		63.89 (21.95)	64.24 (20.10)		65.75 (19.46)	67.14 (22.51)	
median [IQR]	63.00 [48.00, 81.50]	65.00 [52.00, 77.25]	50.00 [40.00, 65.00]	71.00 [68.25, 75.84]	64.50 [49.43, 82.25]	66.35 [51.50, 77.75]		62.50 [48.75, 81.25]	63.50 [47.50, 77.25]		65.00 [52.50, 77.25]	66.50 [46.50, 85.11]	
Missing; n (%)	2,700 (96.4%)	2,175 (97.9%)	383 (96.2%)	256 (98.1%)	1,793 (97.5%)	1,795 (97.6%)		2,194 (96.4%)	2,214 (97.3%)		1,939 (97.7%)	1,943 (97.9%)	
Apixaban and rivaroxaban dosage, evaluated on the index date; n (%)**													
Apixaban 2.5mg	761 (27.2%)	-	-	-	512 (27.8%)	-	-	622 (27.3%)	-		-	499 (25.1%)	
Apixaban 5mg	2,063 (73.7%)	-	-	-	1,342 (73.0%)	-		1,674 (73.6%)	-		-	1,161 (58.5%)	
Rivaroxaban 2.5mg	-	14 (0.6%)	-	-	-	9 (0.5%)		-	9 (0.4%)		12 (0.6%)	-	
Rivaroxaban 10mg	-	18 (0.8%)	-	-	-	15 (0.8%)		-	11 (0.5%)		14 (0.7%)	-	
Rivaroxaban 15mg	-	409 (18.4%)	-	-	-	341 (18.5%)		-	329 (14.5%)		370 (18.6%)	-	
Rivaroxaban 20mg	-	1,793 (80.7%)	-	-	-	1,484 (80.7%)		-	1,368 (60.1%)		1,600 (80.6%)	-	
Edoxaban 15mg	-	-	2 (0.5%)	-	-	-		-	2 (0.1%)		-	1 (0.1%)	
Edoxaban 30mg	-	-	108 (27.1%)	-	-	-		-	103 (4.5%)		-	34 (1.7%)	
Edoxaban 60mg	-	-	295 (74.1%)	-	-	-		-	282 (12.4%)		-	91 (4.6%)	
Dabigatran 75mg	-	-	-	16 (6.1%)	-	-		-	14 (0.6%)		-	16 (0.8%)	
Dabigatran 110mg	-	-	-	123 (47.1%)	-	-		-	91 (4.0%)		-	102 (5.1%)	
Dabigatran 150mg	-	-	-	125 (47.9%)	-	-		-	88 (3.9%)		-	97 (4.9%)	

Characteristics assessed in the year prior to and including index date.

SD = standard deviation; IQR = interquartile range; DOAC = direct oral anticoagulants; ASD = absolute standardized difference.

* Values reported reflect all available data without modification or cleaning.

** Patients with prescriptions for multiple dosages are reported as having all dosages observed

Supplemental Table 2. Per-protocol analysis using a 365d baseline period for all characteristics: Baseline characteristics of patients with nonvalvular atrial fibrillation newly initiating a DOAC, before and after propensity score matching

	Patient characteristics before propensity score matching				Patient characteristics after propensity score matching								
	Apixaban	Rivaroxaban	Edoxaban	Dabigatran	Apixaban	Rivaroxaban	ASD	Apixaban	Other DOACs	ASD	Rivaroxaban	Other DOACs	ASD
Number of patients	2,801	2,221	398	261	1,840	1,840		2,301	2,301		2,023	2,023	
Year of Cohort Entry Date							0.034			0.017			0.038
2014	76 (2.7%)	138 (6.2%)	0 (0.0%)	32 (12.3%)	76 (4.1%)	81 (4.4%)		76 (3.3%)	78 (3.4%)		116 (5.7%)	108 (5.3%)	
2015	365 (13.0%)	548 (24.7%)	0 (0.0%)	81 (31.0%)	357 (19.4%)	359 (19.5%)		362 (15.7%)	372 (16.2%)		441 (21.8%)	436 (21.6%)	
2016	571 (20.4%)	646 (29.1%)	11 (2.8%)	77 (29.5%)	532 (28.9%)	523 (28.4%)		555 (24.1%)	550 (23.9%)		582 (28.8%)	596 (29.5%)	
2017	546 (19.5%)	383 (17.2%)	20 (5.0%)	42 (16.1%)	388 (21.1%)	374 (20.3%)		427 (18.6%)	423 (18.4%)		379 (18.7%)	392 (19.4%)	
2018	530 (18.9%)	257 (11.6%)	115 (28.9%)	21 (8.0%)	242 (13.2%)	256 (13.9%)		393 (17.1%)	385 (16.7%)		257 (12.7%)	250 (12.4%)	
2019	423 (15.1%)	143 (6.4%)	129 (32.4%)	5 (1.9%)	145 (7.9%)	142 (7.7%)		263 (11.4%)	268 (11.6%)		142 (7.0%)	146 (7.2%)	
2020	290 (10.4%)	106 (4.8%)	123 (30.9%)	3 (1.1%)	100 (5.4%)	105 (5.7%)		225 (9.8%)	225 (9.8%)		106 (5.2%)	95 (4.7%)	
Age (years)							0.053			0.038			0.038
mean (sd)	77.35 (8.54)	76.71 (8.62)	77.11 (8.35)	76.23 (8.56)	77.34 (8.60)	76.89 (8.26)		77.14 (8.63)	76.82 (8.39)		76.84 (8.53)	77.17 (8.72)	
median [IQR]	78 [72, 83]	77 [71, 83]	78 [72, 83]	77 [70, 82]	78 [71, 83]	77 [71, 83]		77 [71, 83]	77 [71, 83]		77 [71, 83]	78 [71, 83]	
Age categories (years)							0.021			0.003			0.019
< 55	30 (1.1%)	34 (1.5%)	5 (1.3%)	4 (1.5%)	18 (1.0%)	17 (0.9%)		26 (1.1%)	26 (1.1%)		30 (1.5%)	26 (1.3%)	
55 - 64	131 (4.7%)	120 (5.4%)	18 (4.5%)	13 (5.0%)	96 (5.2%)	92 (5.0%)		116 (5.0%)	117 (5.1%)		99 (4.9%)	100 (4.9%)	
65 - 74	808 (28.8%)	634 (28.5%)	120 (30.2%)	83 (31.8%)	514 (27.9%)	530 (28.8%)		686 (29.8%)	683 (29.7%)		577 (28.5%)	585 (28.9%)	
>= 75	1,832 (65.4%)	1,433 (64.5%)	255 (64.1%)	161 (61.7%)	1,212 (65.9%)	1,201 (65.3%)		1,473 (64.0%)	1,475 (64.1%)		1,317 (65.1%)	1,312 (64.9%)	
Gender							0.003			0.006			0.013
Female	1,070 (38.2%)	785 (35.3%)	158 (39.7%)	81 (31.0%)	661 (35.9%)	664 (36.1%)		864 (37.5%)	857 (37.2%)		730 (36.1%)	717 (35.4%)	
Male	1,731 (61.8%)	1,436 (64.7%)	240 (60.3%)	180 (69.0%)	1,179 (64.1%)	1,176 (63.9%)		1,437 (62.5%)	1,444 (62.8%)		1,293 (63.9%)	1,306 (64.6%)	
Non-Major Bleeding Events	31 (1.1%)	32 (1.4%)	6 (1.5%)	6 (2.3%)	20 (1.1%)	22 (1.2%)	0.010	27 (1.2%)	23 (1.0%)	0.017	29 (1.4%)	23 (1.1%)	0.026
Anemia	79 (2.8%)	63 (2.8%)	5 (1.3%)	9 (3.4%)	52 (2.8%)	50 (2.7%)	0.007	55 (2.4%)	58 (2.5%)	0.008	53 (2.6%)	51 (2.5%)	0.006
Diabetes Mellitus	104 (3.7%)	98 (4.4%)	7 (1.8%)	11 (4.2%)	76 (4.1%)	69 (3.8%)	0.020	85 (3.7%)	89 (3.9%)	0.009	83 (4.1%)	86 (4.3%)	0.007
Hypertension	165 (5.9%)	132 (5.9%)	22 (5.5%)	18 (6.9%)	106 (5.8%)	99 (5.4%)	0.017	138 (6.0%)	131 (5.7%)	0.013	117 (5.8%)	126 (6.2%)	0.019
Heart Failure	208 (7.4%)	161 (7.2%)	19 (4.8%)	13 (5.0%)	126 (6.8%)	119 (6.5%)	0.015	149 (6.5%)	155 (6.7%)	0.010	139 (6.9%)	135 (6.7%)	0.008
Osteoporosis and Hip Fractures	32 (1.1%)	23 (1.0%)	9 (2.3%)	5 (1.9%)	16 (0.9%)	20 (1.1%)	0.022	30 (1.3%)	28 (1.2%)	0.008	23 (1.1%)	18 (0.9%)	0.025
Malignant Neoplasms	111 (4.0%)	77 (3.5%)	17 (4.3%)	12 (4.6%)	73 (4.0%)	63 (3.4%)	0.029	85 (3.7%)	86 (3.7%)	0.002	74 (3.7%)	72 (3.6%)	0.005
Acute Kidney Injury	49 (1.7%)	30 (1.4%)	3 (0.8%)	2 (0.8%)	24 (1.3%)	25 (1.4%)	0.005	31 (1.3%)	33 (1.4%)	0.007	28 (1.4%)	33 (1.6%)	0.020
Chronic Kidney Disease	80 (2.9%)	80 (3.6%)	9 (2.3%)	6 (2.3%)	59 (3.2%)	59 (3.2%)	0.000	73 (3.2%)	70 (3.0%)	0.008	69 (3.4%)	64 (3.2%)	0.014
Asthma and COPD	145 (5.2%)	135 (6.1%)	17 (4.3%)	10 (3.8%)	108 (5.9%)	109 (5.9%)	0.002	125 (5.4%)	123 (5.3%)	0.004	110 (5.4%)	116 (5.7%)	0.013
Dementia	34 (1.2%)	23 (1.0%)	1 (0.3%)	2 (0.8%)	19 (1.0%)	21 (1.1%)	0.005	23 (1.0%)	25 (1.1%)	0.009	22 (1.1%)	21 (1.0%)	0.005
Aspirin	824 (29.4%)	709 (31.9%)	89 (22.4%)	93 (35.6%)	569 (30.9%)	569 (30.9%)	0.000	653 (28.4%)	684 (29.7%)	0.030	643 (31.8%)	628 (31.0%)	0.016
Antiplatelets (other than aspirin)	164 (5.9%)	123 (5.5%)	18 (4.5%)	16 (6.1%)	99 (5.4%)	110 (6.0%)	0.026	130 (5.6%)	127 (5.5%)	0.006	115 (5.7%)	114 (5.6%)	0.002
Warfarin	391 (14.0%)	397 (17.9%)	53 (13.3%)	41 (15.7%)	292 (15.9%)	294 (16.0%)	0.003	350 (15.2%)	344 (15.0%)	0.007	328 (16.2%)	322 (15.9%)	0.008
Antianemic Preparations	519 (18.5%)	334 (15.0%)	49 (12.3%)	33 (12.6%)	276 (15.0%)	294 (16.0%)	0.027	369 (16.0%)	365 (15.9%)	0.005	307 (15.2%)	298 (14.7%)	0.012
NSAIDs	340 (12.1%)	275 (12.4%)	50 (12.6%)	42 (16.1%)	237 (12.9%)	236 (12.8%)	0.002	288 (12.5%)	286 (12.4%)	0.003	261 (12.9%)	250 (12.4%)	0.016
Opioids	862 (30.8%)	640 (28.8%)	113 (28.4%)	73 (28.0%)	532 (28.9%)	534 (29.0%)	0.002	666 (28.9%)	670 (29.1%)	0.004	596 (29.5%)	585 (28.9%)	0.012
SSRIs	240 (8.6%)	181 (8.1%)	36 (9.0%)	17 (6.5%)	147 (8.0%)	157 (8.5%)	0.020	194 (8.4%)	195 (8.5%)	0.002	164 (8.1%)	161 (8.0%)	0.005
Antidepressants (other than SSRIs)	301 (10.7%)	235 (10.6%)	36 (9.0%)	26 (10.0%)	193 (10.5%)	199 (10.8%)	0.011	238 (10.3%)	236 (10.3%)	0.003	214 (10.6%)	207 (10.2%)	0.011
Antiepileptics	210 (7.5%)	150 (6.8%)	25 (6.3%)	19 (7.3%)	124 (6.7%)	127 (6.9%)	0.006	154 (6.7%)	163 (7.1%)	0.015	142 (7.0%)	138 (6.8%)	0.008
Antipsychotics	141 (5.0%)	92 (4.1%)	20 (5.0%)	12 (4.6%)	80 (4.3%)	82 (4.5%)	0.012	109 (4.7%)	103 (4.5%)	0.012	91 (4.5%)	87 (4.3%)	0.010
Benzodiazepines	256 (9.1%)	182 (8.2%)	43 (10.8%)	23 (8.8%)	162 (8.8%)	154 (8.4%)	0.016	196 (8.5%)	201 (8.7%)	0.008	170 (8.4%)	173 (8.6%)	0.005
Lipid Lowering Drugs	1,539 (54.9%)	1,199 (54.0%)	191 (48.0%)	138 (52.9%)	1,012 (55.0%)	998 (54.2%)	0.015	1,216 (52.8%)	1,254 (54.5%)	0.033	1,089 (53.8%)	1,092 (54.0%)	0.003
Insulin	91 (3.2%)	80 (3.6%)	9 (2.3%)	5 (1.9%)	57 (3.1%)	61 (3.3%)	0.012	70 (3.0%)	73 (3.2%)	0.008	61 (3.0%)	67 (3.3%)	0.017
Antihyperglycemics other than Insulins	525 (18.7%)	466 (21.0%)	51 (12.8%)	54 (20.7%)	363 (19.7%)	372 (20.2%)	0.012	421 (18.3%)	446 (19.4%)	0.028	406 (20.1%)	396 (19.6%)	0.012
Antihypertensives	2,611 (93.2%)	2,079 (93.6%)	366 (92.0%)	242 (92.7%)	1,723 (93.6%)	1,718 (93.4%)	0.011	2,141 (93.0%)	2,151 (93.5%)	0.017	1,889 (93.4%)	1,901 (94.0%)	0.024
Antiarrhythmics	94 (3.4%)	91 (4.1%)	10 (2.5%)	10 (3.8%)	67 (3.6%)	70 (3.8%)	0.009	79 (3.4%)	80 (3.5%)	0.002	81 (4.0%)	75 (3.7%)	0.015
Nitrates Cardiac Vasodilators	130 (4.6%)	99 (4.5%)	21 (5.3%)	9 (3.4%)	79 (4.3%)	81 (4.4%)	0.005	105 (4.6%)	105 (4.6%)	0.000	95 (4.7%)	100 (4.9%)	0.012
Cardiac Stimulants	347 (12.4%)	272 (12.2%)	30 (7.5%)	17 (6.5%)	236 (12.8%)	229 (12.4%)	0.011	271 (11.8%)	263 (11.4%)	0.011	237 (11.7%)	235 (11.6%)	0.003
Gastrointestinal Protective Agents	1,214 (43.3%)	893 (40.2%)	173 (43.5%)	106 (40.6%)	752 (40.9%)	761 (41.4%)	0.010	952 (41.4%)	955 (41.5%)	0.003	830 (41.0%)	802 (39.6%)	0.028

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Bisphosphonates and Other Agents Affecting Bone Structure	228 (8.1%)	171 (7.7%)	32 (8.0%)	15 (5.7%)	135 (7.3%)	138 (7.5%)	0.006	192 (8.3%)	188 (8.2%)	0.006	166 (8.2%)	151 (7.5%)	0.028
Systemic Corticosteroids	442 (15.8%)	345 (15.5%)	53 (13.3%)	37 (14.2%)	272 (14.8%)	271 (14.7%)	0.002	353 (15.3%)	358 (15.6%)	0.006	308 (15.2%)	307 (15.2%)	0.001
Antineoplastics	140 (5.0%)	99 (4.5%)	21 (5.3%)	13 (5.0%)	81 (4.4%)	88 (4.8%)	0.018	111 (4.8%)	113 (4.9%)	0.004	93 (4.6%)	90 (4.4%)	0.007
Systemic Antibiotics	1,357 (48.4%)	1,075 (48.4%)	177 (44.5%)	119 (45.6%)	872 (47.4%)	867 (47.1%)	0.005	1,084 (47.1%)	1,097 (47.7%)	0.011	969 (47.9%)	961 (47.5%)	0.008
Systemic Antivirals	31 (1.1%)	32 (1.4%)	3 (0.8%)	3 (1.1%)	22 (1.2%)	22 (1.2%)	0.000	29 (1.3%)	26 (1.1%)	0.012	26 (1.3%)	26 (1.3%)	0.000
Vaccines and Immunoglobulins	137 (4.9%)	204 (9.2%)	11 (2.8%)	24 (9.2%)	119 (6.5%)	131 (7.1%)	0.026	133 (5.8%)	134 (5.8%)	0.002	157 (7.8%)	138 (6.8%)	0.036
CHA2DS2 VASc score							0.013						0.045
0	93 (3.3%)	79 (3.6%)	16 (4.0%)	13 (5.0%)	64 (3.5%)	64 (3.5%)	0.047	83 (3.6%)	80 (3.5%)		74 (3.7%)	73 (3.6%)	
1	518 (18.5%)	442 (19.9%)	79 (19.8%)	57 (21.8%)	347 (18.9%)	354 (19.2%)		452 (19.6%)	459 (19.9%)		392 (19.4%)	379 (18.7%)	
2	1,174 (41.9%)	949 (42.7%)	165 (41.5%)	112 (42.9%)	794 (43.2%)	802 (43.6%)		962 (41.8%)	964 (41.9%)		861 (42.6%)	892 (44.1%)	
3	868 (31.0%)	631 (28.4%)	119 (29.9%)	63 (24.1%)	542 (29.5%)	529 (28.7%)		684 (29.7%)	682 (29.6%)		587 (29.0%)	572 (28.3%)	
4	133 (4.7%)	99 (4.5%)	18 (4.5%)	14 (5.4%)	79 (4.3%)	82 (4.5%)		108 (4.7%)	104 (4.5%)		95 (4.7%)	93 (4.6%)	
5	14 (0.5%)	20 (0.9%)	1 (0.3%)	2 (0.8%)	13 (0.7%)	9 (0.5%)		12 (0.5%)	12 (0.5%)		13 (0.6%)	14 (0.7%)	
6	1 (0.0%)	1 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		1 (0.0%)	0 (0.0%)	
7	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
8	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	

Characteristics reported as N (%) unless otherwise specified.

SD = standard deviation; IQR = interquartile range; DOAC = direct oral anticoagulants; ASD = absolute standardized difference.

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Supplemental Table 3. Per-protocol analysis using a 365d baseline period for all characteristics: Hazard ratio of stroke and secondary outcomes among patients with nonvalvular atrial fibrillation newly initiating DOACs after propensity score matching

	Patients	Events	Rate per 1,000 PY	Patients	Events	Rate per 1,000 PY	Hazard Ratio
Apixaban vs rivaroxaban: primary and secondary outcomes							
Outcome	Apixaban			Rivaroxaban			aHR (95% CI)
Stroke, ITT	1,840	53	11.77	1,840	56	13.00	0.89 (0.61, 1.30)
Stroke, AT	1,840	30	9.26	1,840	32	11.00	0.87 (0.53, 1.43)
All-cause mortality, ITT*	1,846	276	59.46	1,846	264	61.37	0.96 (0.81, 1.14)
Myocardial infarction (MI), ITT	1,840	22	4.84	1,840	25	6.00	0.84 (0.47, 1.48)
Transient ischemic attack	1,840	32	7.08	1,840	29	7.00	1.06 (0.64, 1.76)
Major bleeding event, ITT	1,840	117	26.70	1,840	189	48.00	0.57 (0.46, 0.72)
Composite angina/MI/stroke	1,840	92	20.82	1,840	98	24.00	0.89 (0.67, 1.18)
Apixaban vs rivaroxaban: primary outcome (stroke) among subgroups, ITT							
Subgroup	Apixaban			Rivaroxaban			aHR (95% CI)
Age <75 years	631	12	7.17	631	12	8.00	0.93 (0.42, 2.06)
Age ≥75 years	1,195	37	13.29	1,195	39	15.00	0.89 (0.57, 1.40)
Concomitant aspirin use	400	12	11.54	400	9	9.00	1.24 (0.52, 2.94)
No concomitant aspirin use	1,416	41	12.09	1,416	36	11.00	1.08 (0.69, 1.69)
Prior warfarin use	271	8	12.79	271	10	17.00	0.73 (0.29, 1.86)
No prior warfarin use	1,528	43	11.48	1,528	37	11.00	1.09 (0.70, 1.69)
With diabetes	44	0	0.00	44	2	20.00	<0.001 (<0.001, >999)
Without diabetes	1,771	55	12.70	1,771	50	12.00	1.02 (0.70, 1.50)
With heart failure	83	1	5.72	83	2	11.00	0.49 (0.04, 5.38)
Without heart failure	1,740	47	10.81	1,740	50	13.00	0.87 (0.58, 1.30)
CHA2DS2 VASc 0-1	403	12	11.05	403	7	7.00	1.54 (0.61, 3.93)
CHA2DS2 VASc 2-3	1,334	38	11.74	1,334	36	12.00	0.99 (0.62, 1.56)
CHA2DS2 VASc 4+	61	2	15.19	61	0	0.00	>999 (<0.001, >999)
Analysis of secondary comparisons: primary outcome (stroke), ITT							
Outcome	Apixaban			DOACs other than apixaban			aHR (95% CI)
Stroke	2,301	64	12.41	2,301	65	13.00	0.95 (0.67, 1.34)
Outcome	Rivaroxaban			DOACs other than rivaroxaban			aHR (95% CI)
Stroke	2,023	54	11.47	2,023	58	12.00	0.99 (0.68, 1.43)

PY = person-years; aHR = adjusted hazard ratio; CI = confidence interval; PS = propensity score; ITT = intent-to-treat; AT = as-treated

PS model accounts for age, gender, CHA2DS2 VASc score, year of treatment initiation, and the following diagnoses and treatments in baseline: non-major bleeding events, anemia, diabetes, hypertension, heart failure, osteoporosis/hip fracture, malignant neoplasm, acute kidney injury, chronic kidney disease, asthma/copd, dementia, aspirin, antiplatelets other than aspirin, warfarin, antiameric preparations, NSAIDs, opioids, SSRIs, antidepressants other than SSRIs, antiepileptics, antipsychotics, benzodiazepines, lipid

In analysis of stroke, MI, TIA, major bleeding events, and AMS, patients were followed until occurrence of outcome, death, end of patient registration, or end of study period (12/2020).

* In analysis of all cause mortality, patients were followed until occurrence of outcome (death), end of study period (12/2020), or the later date of end of patient registration and any recorded death within 90 days of end of patient registration. Propensity score matched sample size for analysis of all cause mortality differs from sample size in analysis of other outcomes because of differences in censoring criteria which impact a small number of patients' eligibility for inclusion in analysis at the start of follow-up.
DOACs comprised apixaban, rivaroxaban, edoxaban, dabigatran

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Supplemental Table 4: Length of follow-up and censoring reasons for the primary comparison (stroke, ITT and AT analyses) and secondary comparisons (stroke, ITT analyses) after PS-matching

	Apixaban vs rivaroxaban (ITT)		Apixaban vs rivaroxaban (AT)		Apixaban vs other DOACs (ITT)		Rivaroxaban vs other DOACs (ITT)	
Exposure group	Apixavan	Rivaroxaban	Apixavan	Rivaroxaban	Apixaban	Other DOACs	Rivaroxaban	Other DOACs
Numer of patients	1,839	1,839	1,839	1,839	2,276	2,276	1,985	1,985
Follow-up time, days								
mean (sd)	891.39 (604.23)	839.10 (580.42)	647.66 (535.75)	574.74 (510.77)	829.15 (586.35)	770.05 (553.42)	844.22 (588.55)	894.75 (611.26)
median [IQR]	845 [340, 1,368]	779 [322, 1,284]	506 [197, 1,001]	412 [170, 855]	742 [298, 1,259]	681 [296, 1,170]	784 [318, 1,296]	828 [343, 1,399]
Censor reason								
Death	40 (2.2%)	26 (1.4%)	24 (1.3%)	18 (1.0%)	44 (1.9%)	28 (1.2%)	29 (1.5%)	42 (2.1%)
End of patient registration	943 (51%)	1,074 (58%)	630 (34%)	662 (36%)	1,081 (47%)	1,227 (54%)	1,187 (60%)	1,066 (54%)
End of study period (12/2020)	800 (44%)	682 (37%)	448 (24%)	367 (20%)	1,086 (48%)	953 (42%)	710 (36%)	812 (41%)
Outcome (stroke)	56 (3.0%)	57 (3.1%)	33 (1.8%)	32 (1.7%)	65 (2.9%)	68 (3.0%)	59 (3.0%)	65 (3.3%)
End of index DOAC	-	-	615 (33%)	562 (31%)	-	-	-	-
Start of DOAC from other comparator group	-	-	43 (2.3%)	119 (6.5%)	-	-	-	-
Start of another DOAC (dabigatran, edoxaban)	-	-	46 (2.5%)	79 (4.3%)	-	-	-	-

DOAC = direct oral anticoagulant; ITT = intent-to-treat; AT = as-treated; PS = propensity score.

Apixaban was compared with other DOACs which included rivaroxaban, edoxaban, and dabigatran; rivaroxaban was compared with other DOACs which included apixaban, edoxaban, and dabigatran.