

**Table 1. Characteristics of patients with high risk of stroke in the evaluation of treatment pattern.**

<b>Characteristics</b>	<b>Overall (%)</b>
Total number of patients	52 178
Age, years - mean (SD)	80.0 (9.9)
Female sex – no. (%)	28 997 (55.6)
<b>Baseline medical conditions - no. (%)</b>	
Congestive heart failure	14 891 (28.5)
Diabetes mellitus	13 586 (26)
Hypertension	30 742 (58.9)
Myocardial infarction	5013 (9.6)
Vascular disease	14 026 (26.9)
Prior ischemic stroke/TIA/SE	12 616 (24.2)
Prior bleeding complications	12 020 (23)
Intracranial bleeding	2251 (4.3)
Gastrointestinal bleeding	6267 (12.0)
Other bleeding complications*	4968 (9.5)
Renal disease	7502 (14.4)
CHA <sub>2</sub> DS <sub>2</sub> -VASc score - mean (SD)	4.1 (1.6)
2	9005 (17.3)
3	12 086 (23.2)
≥4	31 087 (59.6)
CHADS <sub>2</sub> score -mean (SD)	2.4 (1.3)
≤2	30 672 (58.8)
3	11 055 (21.2)
≥4	10 451 (20)
Charlson Comorbidity Index - mean (SD)	1.9 (1.9)
0-3	44 082 (84.5)
4-5	5247 (10.1)
6-7	1533 (2.9)
≥8	1316 (2.5)
<b>Recent use of medication – no. (%)</b>	
Aspirin	29 513 (56.6)
Clopidogrel	3309 (6.3)
Amiodarone	7539 (14.4)
Statin	18 284 (35)
Proton-pump inhibitor	14 340 (27.5)
Histamine type-2 receptor antagonist	23 409 (44.9)
NSAIDs	2887 (5.5)
SSRIs	1524 (2.9)

Values are expressed as frequency (%) unless otherwise specified.

Abbreviations: NSAIDs=nonsteroidal anti-inflammatory drugs; SD=standard deviation; SE=systemic embolism; SSRIs=selective serotonin reuptake inhibitors; TIA=transient ischemic attack.

\*includes epistaxis, hematuria, hemarthrosis, hemorrhage from kidney, throat, and vagina, hemopericardium, and hemoptysis.

**Table 2. Baseline characteristics of patients with atrial fibrillation treated with antiplatelet monotherapy, warfarin, and direct oral anticoagulants.**

Characteristics	Before PS matching				After PS matching			
	Antiplatelet monotherapy (N=18 878)	Warfarin (N=3803)	DOACs (N=4933)	Maximum pair-wise STD*	Antiplatelet monotherapy (N=2588)	Warfarin (N=2588)	DOACs (N=2588)	Maximum pair-wise STD*
Age, years - mean (SD)	80.7 (9.4)	74.2 (9.8)	77.2 (8.6)	0.68	75.5 (10.5)	75.5 (9.1)	76 (9.0)	0.05
Female sex – no. (%)	10 636 (56.3)	2024 (53.2)	2855 (57.9)	0.09	1430 (55.3)	1433 (55.4)	1440 (55.6)	0.01
<b>Baseline medical conditions – no. (%)</b>								
Congestive heart failure	6014 (31.9)	1448 (38.1)	1234 (25)	0.28	816 (31.5)	862 (33.3)	845 (32.7)	0.04
Diabetes mellitus	4557 (24.1)	1064 (28.0)	1196 (24.2)	0.09	670 (25.9)	709 (27.4)	720 (27.8)	0.04
Hypertension	10 600 (56.2)	2035 (53.5)	2638 (53.5)	0.05	1378 (53.2)	1388 (53.6)	1410 (54.5)	0.02
Myocardial infarction	2231 (11.8)	278 (7.3)	285 (5.8)	0.21	189 (7.3)	197 (7.6)	188 (7.3)	0.01
Vascular disease	5777 (30.6)	1016 (26.7)	1077 (21.8)	0.20	660 (25.5)	661 (25.5)	640 (24.7)	0.02
Prior TIA/SE	421 (2.2)	255 (6.7)	281 (5.7)	0.22	129 (5.0)	148 (5.7)	160 (6.2)	0.05
Prior bleeding	1655 (8.8)	341 (9.0)	349 (7.1)	0.07	233 (9.0)	230 (8.9)	215 (8.3)	0.02
Renal disease	2763 (14.6)	425 (11.2)	294 (6.0)	0.29	235 (9.1)	253 (9.8)	242 (9.4)	0.02
CHA <sub>2</sub> DS <sub>2</sub> -VASc score - mean (SD)	3.7 (1.3)	3.5 (1.3)	3.5 (1.3)	0.21	3.4 (1.3)	3.5 (1.3)	3.5 (1.3)	0.07
2	3853 (20.4)	1066 (28)	1262 (25.6)		794 (30.7)	703 (27.2)	653 (25.2)	
3	5160 (27.3)	1091 (28.7)	1557 (31.6)		724 (28)	733 (28.3)	756 (29.2)	
≥4	9865 (52.3)	1646 (43.3)	2114 (42.9)		1070 (41.3)	1152 (44.5)	1179 (45.6)	
CHADS <sub>2</sub> score - mean (SD)	1.9 (1.0)	1.8 (1.0)	1.8 (1.0)	0.17	1.8 (1.1)	1.8 (1.1)	1.8 (1.0)	0.07
0	913 (4.8)	278 (7.3)	393 (8.0)		226 (8.7)	210 (8.1)	186 (7.2)	
1	6267 (33.2)	1306 (34.3)	1820 (36.9)		949 (36.7)	898 (34.7)	848 (32.8)	
≥2	11 698 (62.0)	2219 (58.3)	2720 (55.1)		1413 (54.6)	1480 (57.2)	1554 (60.0)	
Charlson Comorbidity Index - mean (SD)	1.6 (1.8)	1.4 (1.5)	1.1 (1.3)	0.33	1.2 (1.4)	1.3 (1.4)	1.3 (1.4)	0.05
0-3	16 638 (88.1)	3500 (92)	4716 (95.6)		2424 (93.7)	2401 (92.8)	2409 (93.1)	
4-5	1468 (7.8)	227 (6.0)	169 (3.4)		127 (4.9)	144 (5.6)	139 (5.4)	
6-7	434 (2.3)	50 (1.3)	24 (0.5)		22 (0.9)	27 (1.0)	22 (0.9)	
≥8	338 (1.8)	26 (0.7)	24 (0.5)		15 (0.6)	16 (0.6)	18 (0.7)	

**Table 2. Baseline characteristics of patients with atrial fibrillation treated with antiplatelet monotherapy, warfarin, and direct oral anticoagulants (continued).**

Characteristics	Before PS matching				After PS matching			
	Antiplatelet monotherapy (N=18 878)	Warfarin (N=3803)	DOACs (N=4933)	Maximum pair-wise STD*	Antiplatelet monotherapy (N=2588)	Warfarin (N=2588)	DOACs (N=2588)	Maximum pair-wise STD*
<b>Recent use of medication – no. (%)</b>								
Aspirin	11 985 (63.5)	2004 (52.7)	2774 (56.2)	0.22	1361 (52.6)	1423 (55)	1444 (55.8)	0.06
Clopidogrel	1380 (7.3)	209 (5.5)	310 (6.3)	0.07	164 (6.3)	160 (6.2)	147 (5.7)	0.03
Amiodarone	2637 (14.0)	448 (11.8)	615 (12.5)	0.07	297 (11.5)	324 (12.5)	305 (11.8)	0.03
Statin	5334 (28.3)	1408 (37.0)	2004 (40.6)	0.26	1005 (38.8)	1017 (39.3)	1074 (41.5)	0.05
Proton-pump inhibitor	4407 (23.3)	774 (20.4)	1081 (21.9)	0.07	557 (21.5)	568 (21.9)	579 (22.4)	0.02
H2RA	8698 (46.1)	1656 (43.5)	2200 (44.6)	0.05	1076 (41.6)	1156 (44.7)	1134 (43.8)	0.06
NSAIDs	1057 (5.6)	193 (5.1)	269 (5.5)	0.02	140 (5.4)	147 (5.7)	148 (5.7)	0.01
SSRIs	408 (2.2)	68 (1.8)	109 (2.2)	0.03	50 (1.9)	50 (1.9)	44 (1.7)	0.02
<b>Anticoagulation control (for warfarin users only) – no. (%)</b>								
Total number of INR tests		50 596				30 928		
Number of INR tests performed for each patient – median (interquartile range)		9 (5-16)				8 (4-15)		
Time- in- therapeutic range (mean ± SD)		0.47 ± 0.27				0.47 ± 0.28		
<30%		1067 (28.0)				753 (29.1)		
30 to <40%		427 (11.2)				283 (10.9)		
40 to <50%		479 (12.6)				305 (11.8)		
50 to <60%		490 (12.9)				325 (12.6)		
60 to <70%		495 (13.0)				332 (12.8)		
≥70%		845 (22.2)				590 (22.8)		

Abbreviations: DOACs=direct oral anticoagulants; H2RA=histamine type-2 receptor antagonist; INR=international normalized ratio; NSAIDs=nonsteroidal anti-inflammatory drugs; PS=propensity score; SD=standard deviation; SE=systemic embolism; SSRIs=selective serotonin reuptake inhibitors; STD=standardized difference; TIA=transient ischemic attack.

\*The maximum absolute standardized differences among pair-wise comparisons for 1) warfarin vs antiplatelet monotherapy, 2) DOACs vs antiplatelet monotherapy, and 3) DOACs vs warfarin.

**Table 3. Comparisons of outcomes between antiplatelet monotherapy, warfarin, and direct oral anticoagulants after propensity score matching**

	<b>Antiplatelet monotherapy (N=2588)</b>	<b>Warfarin (N=2588)</b>	<b>DOACs (N=2588)</b>	<b>Warfarin vs Antiplatelet monotherapy</b>	<b>DOACs vs Antiplatelet monotherapy</b>	<b>DOACs vs Warfarin</b>
<b>Outcomes</b>	<b>No. of events (Incidence per 100 py)</b>	<b>No. of events (Incidence per 100 py)</b>	<b>No. of events (Incidence per 100 py)</b>	<b>HR (95% CI)</b>	<b>HR (95% CI)</b>	<b>HR (95% CI)</b>
Ischemic stroke	155 (2.7)	103 (1.6)	89 (1.5)	0.51 (0.36-0.71)*	0.69 (0.51-0.94)*	1.18 (0.83-1.67)
Intracranial hemorrhage	41 (0.7)	77 (1.2)	37 (0.6)	1.69 (1.04-2.75)*	0.89 (0.52-1.53)	0.53 (0.34-0.83)*
Gastrointestinal bleeding	117 (2.1)	127 (1.9)	112 (1.9)	0.80 (0.58-1.10)	0.80 (0.56-1.14)	0.95 (0.69-1.30)
All-cause mortality	457 (8.0)	278 (4.3)	229 (3.9)	0.47 (0.39-0.57)*	0.45 (0.37-0.55)*	0.98 (0.78-1.21)

Abbreviations: CI=confidence interval; DOACs=direct oral anticoagulants; HR=hazard ratio; py=person-years. \*p<0.05.

**Table 4. Comparisons of outcomes between antiplatelet monotherapy, warfarin, and direct oral anticoagulants, stratified by the quality of international normalized control of warfarin users after propensity score matching.**

Outcomes	<b>Good INR control (N=922)</b>	<b>APT (N=922)</b>	<b>Good INR control vs APT</b>	<b>Poor INR control (N=1666)</b>	<b>APT (N=1666)</b>	<b>Poor INR control vs APT</b>	p for interaction
	No. of events (Incidence per 100 py)	No. of events (Incidence per 100 py)	HR (95% CI)	No. of events (Incidence per 100 py)	No. of events (Incidence per 100 py)	HR (95% CI)	
Ischemic stroke	35 (1.4)	43 (2.0)	0.58 (0.33-1.04)	68 (1.7)	112 (3.1)	0.47 (0.31-0.71)*	0.57
Intracranial hemorrhage	30 (1.2)	13 (0.6)	2.13 (0.92-4.92)	47 (1.2)	28 (0.8)	1.50 (0.83-2.72)	0.51
Gastrointestinal bleeding	54 (2.1)	36 (1.7)	0.96 (0.56-1.67)	73 (1.8)	81 (2.2)	0.73 (0.50-1.08)	0.43
All-cause mortality	84 (3.3)	155 (7.4)	0.37 (0.26-0.53)*	194 (4.9)	302 (8.4)	0.52 (0.41-0.65)*	0.13

  

Outcomes	<b>Good INR control (N=922)</b>	<b>DOACs (N=922)</b>	<b>DOACs vs Good INR control</b>	<b>Poor INR control (N=1666)</b>	<b>DOACs (N=1666)</b>	<b>DOACs vs Poor INR control</b>	p for interaction
	No. of events (Incidence per 100 py)	No. of events (Incidence per 100 py)	HR (95% CI)	No. of events (Incidence per 100 py)	No. of events (Incidence per 100 py)	HR (95% CI)	
Ischemic stroke	35 (1.4)	31 (1.4)	1.10 (0.61-1.98)	68 (1.7)	58 (1.6)	1.22 (0.79-1.90)	0.77
Intracranial hemorrhage	30 (1.2)	15 (0.7)	0.61 (0.31-1.18)	47 (1.2)	22 (0.6)	0.47 (0.25-0.87)*	0.57
Gastrointestinal bleeding	54 (2.1)	36 (1.7)	0.85 (0.52-1.40)	73 (1.8)	76 (2.1)	1.02 (0.68-1.53)	0.58
All-cause mortality	84 (3.3)	81 (3.8)	1.15 (0.80-1.67)	194 (4.9)	148 (4)	0.89 (0.68-1.17)	0.27

  

Outcomes	<b>Good INR control (N=922)</b>	<b>Poor INR control (N=1666)</b>	<b>Good vs Poor INR control</b>
	No. of events (Incidence per 100 py)	No. of events (Incidence per 100 py)	HR (95% CI)
Ischemic stroke	35 (1.4)	68 (1.7)	0.79 (0.52-1.18)
Intracranial hemorrhage	30 (1.2)	47 (1.2)	1.00 (0.63-1.57)
Gastrointestinal bleeding	54 (2.1)	73 (1.8)	1.15 (0.81-1.64)
All-cause mortality	84 (3.3)	194 (4.9)	0.67 (0.52-0.86)*

Abbreviations: APT= antiplatelet monotherapy; CI= confidence interval; DOACs= direct oral anticoagulants; HR= hazard ratio; INR= international normalized ratio. \*p<0.05.