ONLINE SUPPLEMENT

Additional statistical information

In the survival analysis analyzing composite endpoint (CE) for no oral anticoagulation (OAC) patients, patients who started OAC were censored at the time point of the start of OAC. Furthermore, Kaplan-Meier curves were used in patients who received OAC within 3 months after stroke/TIA to analyze the association of OAC timing and the occurrence of the combined endpoint stratified for 'early', 'timely' or 'late' (re-)start of OAC according to the "1–3–6–12 day rule". Group differences were compared using the log-rank test. Bivariate and multivariable Cox regression analyses were used to estimate hazard ratios (HR) for CE within 3 months after the index event. Statistical analysis was performed using SPSS (Version 29, SPSS Inc., Chicago, USA). No adjustment for multiple testing was applied. P-values have to be interpreted cautiously.

Table S1 Baseline characteristics of 650 registry patients with known AF at the time of the index stroke/TIA, hospitalization within 72 hours of symptom onset, and completed 3 months follow-up or pre-defined clinical endpoint (recurrent ischemic stroke, systemic embolism, myocardial infarction, hemorrhagic stroke, major bleed or all-cause death) within three months after stroke/TIA according to (re-)start of oral anticoagulation (OAC) within three months after stroke/TIA.

	OAC (re-)start n = 616	**No OAC (re-)start n = 34**	**p-value**
Age [years]**,** median [IQR]	78 [71-83]	78.5 [72.3-86.8]	0.287
Age groups; n (%)			0.585
18-64 years	66 (10.7)	2 (5.9)	
65-74 years	145 (23.5)	10 (29.4)	
≥75 years	405 (65.7)	22 (64.7)	
Sex (male), n (%)	321 (52.1)	21 (61.8)	0.295
Index stroke: Transient ischemic attack (TIA), n (%)	173 (28.1)	6 (17.6)	0.237
NIHSS score on admission [points], median [IQR]	2 [1-5]	3 [1 - 7.75]	0.094
NIHSS score on admission [points], n (%)			0.052
<8 points	538 (87.3)	25 (73.5)	
8-16 points	60 (9.7)	7 (20.6)	
>16 points	18 (2.9)	2 (5.9)	
Intravenous thrombolysis, n (%)	72 (11.7)	4 (12.1)	1.000
Endovascular treatment, n (%)	46 (7.5)	2 (5.9)	1.000
Carotid endarterectomy, n (%)	6 (1.0)	0 (0.0)	1.000
Cardiovascular risk-factors, n (%)			
Hypertension	549 (89.1)	30 (88.2)	0.780
Heart failure	95 (15.4)	8 (23.5)	0.226
Diabetes mellitus	189 (30.7)	10 (29.4)	1.000
Vascular disease	192 (31.2)	14 (41.2)	0.256
Prior stroke or transient ischemic attack (TIA)	188 (30.5)	8 (23.5)	0.447
Impaired renal function at baseline	267 (44.1)	19 (55.9)	0.215
Oral anticoagulation at baseline, n (%)	396 (64.3)	7 (20.6)	<0.001
Selective serotonin reuptake inhibitor at baseline, n (%)	24 (3.9)	1 (3.0)	1.000
CHA_2DS_2-VASc post-stroke [points], median [IQR]	6 [5-7]	6 [5-7]	0.470
HAS-BLED post-stroke [points], median [IQR]	3 [3-4]	4 [3-5]	<0.001
In-hospital stay [days], median [IQR]	5 [4-7]	6 [4- 9]	0.065

* National Institutes of Health Scale (NIHSS)

Table S2. Baseline characteristics of 521 registry patients with known AF at the time of the index stroke/TIA, hospitalization within 72 hours of symptom onset, and completed 3 months follow-up or pre-defined clinical endpoint (recurrent ischemic stroke, systemic embolism, myocardial infarction, hemorrhagic stroke, major bleed or all-cause death) within three months according to (re-)starting a non-vitamin K dependent oral antagonist (NOAC) or no oral anticoagulant within three months after the index stroke/TIA according to adherence to the to the "1–3–6–12 days rule"[7], setting adherence as reference.

	Non-adherence n=326	Adherence (n=195)	Bivariate analysis OR (95%CI)	p-value	Multivariable analysis OR (95%CI)	p-value
Age, median [IQR]	78 [71-84]	77 [71-82]	1.00 [0.98-1.02]	0.902	1.00 [0.96-1.04]	0.931
Sex (male), n (%)	176 (54.0)	98 (50.3)	1.16 [0.81-1.66]	0.409	1.04 [0.51-2.12]	0.916
Intravenous thrombolysis, n (%)	39 (12.0)	28 (14.4)	0.81 [0.48-1.37]	0.438	0.38 [0.19-0.73]	0.004
Endovascular treatment, n (%)	36 (11.0)	11 (5.6)	2.08 [1.03-4.18]	0.041	2.56 [1.09-6.01]	0.030
Carotid endarterectomy, n (%)	3 (0.9)	1 (0.5)	1.68 [0.19-17.44]	0.611	1.68 [0.16-18.01]	0.666
CHA_2DS_2-VASc post-stroke, median [IQR]	6 [5-7]	6 [5-6]	1.02 [0.89-1.16]	0.798	1.00 [0.56-1.79]	0.992
HAS-BLED post-stroke, median [IQR]	3 [3-4]	3 [3-4]	1.24 [1.01-1.53]	0.041	1.14 [0.82-1.59]	0.422
Infarct size according to imaging, n (%)						
none	132 (45.1)	102 (55.7)	1	0.032	1	0.419
small	134 (45.7)	73 (39.9)	1.42 [0.97-2.08]	0.075	1.18 [0.77-1.79]	0.449
moderate-large	27 (9.2)	8 (4.4)	2.61 [1.14.-5.98]	0.024	1.81 [0.71-4.62]	0.213
Hemorrhagic transformation, n (%)	23 (7.1)	7 (3.6)	2.04 [0.86-4.83]	0.108	0.74 [0.26-2.11]	0.569
In-hospital neurological deterioration , n (%)	26 (8.0)	6 (3.1)	2.73 [1.10-6.76]	0.030	5.25 [1.42-19.37]	0.013
Uncontrolled arterial hypertension, n (%)	15 (4.6)	7 (3.6)	1.30 [0.52-3.24]	0.579	1.08 [0.40-2.92]	0.885
Oral anticoagulation on admission, n (%)	163 (50.0)	133 (68.2)	0.47 [0.32-0.68]	<0.001	0.42 [0.26-0.66]	<0.001

***** Setting adherence to the "1–3–6–12 days rule" as reference. Additionally adjusted for cardiovascular risk-factors: prior stroke or transient ischemic attack (TIA), vascular disease, diabetes mellitus, hypertension, heart failure, impaired renal function at baseline.

Excluding patients (re-)started on a VKA, 195 (40.0%) of 487 patients were (re-)started on a NOAC in adherence with the "1–3–6–12 day rule", including 133 (46.0%) of 298 patients on OAC at the time of stroke, and 62 (31.3%) of 189 patients without OAC at stroke onset. Multivariable analysis, revealed that in-hospital neurological deterioration (OR 5.25, 95%CI 1.42-19.37), and endovascular treatment (OR 2.56, 95%CI 1.09-6.01) were associated with non-adherence to the "1–3–6–12 day rule", while OAC intake at the time of stroke (OR 0.42, 95%CI 0.26-0.66) and intravenous thrombolysis (OR 0.38, 95%CI 0.19-0.73) were associated with adherence .

Table S3 Multivariable multinomial logistic regression model for (non-)adherence to the "1–3–6–12 days rule"[7] in 650 registry patients with known AF at the time of the index stroke/TIA, hospitalization within 72 hours of symptom onset, and completed 3 months follow-up or pre-defined clinical endpoint (recurrent ischemic stroke, systemic embolism, myocardial infarction, hemorrhagic stroke, major bleed or all-cause death) within three months after the index stroke/TIA according to adherence, earlier or later or no (re-)start of OAC (setting adherence as reference).

	Adherence n=255	**"Earlier" n=151**	**Multivariable analysis OR (95%CI)**	**p value**	**"Later" n=210**	**Multivariable analysis OR (95%CI)**	**p value**	**No (re-)start (n=34)**	**Multivariable analysis OR (95%CI)**	**p value**
Age groups; n (%)										
<65 years	22 (8.6)	13 (8.6)	1	-	31 (14.8)	1	-	2 (5.9)	1	-
65-74 years	62 (24.3)	42 (27.8)	1.01 [0.41-2.54]	0.973	41 (19.5)	0.54 [0.24-1.24]	0.148	10 (29.4)	0.68 [0.11-4.35]	0.687
>=75 years	171 (67.1)	96 (63.6)	0.83[0.34- 2.05]	0.692	138 (65.7)	0.72 [0.33-1.58]	0.410	22 (64.7)	0.48 [0.08-2.93]	0.424
Endovascular treatment, n (%)	11 (4.3)	21 (13.9)	3.74 [1.60-8.73]	0.002	14 (6.7)	0.82[0.32-2.12]	0.680	2 (5.9)	0.77 [0.13-4.51]	0.773
HAS-BLED post-stroke, median [IQR]	6 [5-6]	6 [5-7]	1.15 [0.84-1.58]	0.373	6 [5-7]	1.05 [0.79-1.41]	0.722	6 [5-7]	2.11 [1.22-3.66]	0.008
Infarct size according to brain imaging, n (%)										
none	150 (62.5)	61 (42.7)	1	-	89 (47.8)	1	-	13 (46.4)	1	-
small	82 (34.2)	79 (55.2)	2.01 [1.27-3.17]	0.003	70 (37.6)	1.13 [0.73-1.77]	0.587	12 (42.9)	0.72 [0.27-1.91]	0.503
moderate-large	8 (3.3)	3 (2.1)	0.71 [0.17-3.06]	0.650	27 (14.5)	3.87 [1.54-9.74]	0.004	3 (10.7)	1.14 [0.20-6.46]	0.880
Hemorrhagic transformation, n (%)	8 (3.2)	4 (2.6)	0.67 [0.18-2.44]	0.543	19 (9.1)	0.92 [0.33-2.56]	0.878	6 (17.6)	2.49 [0.56-11.19]	0.233
Cardiovascular risk factors										
Vascular disease	74 (29.0)	57 (37.7)	1.43 [0.89-2.29]	0.142	61 (29.0)	1.01 [0.64 -1.61]	0.964	14 (41.2)	0.98 [0.38-2.52]	0.965
Prior stroke or TIA	82 (32.2)	56 (37.1)	1.39 [0.88 -2.20]	0.153	50 (23.8)	0.73 [0.46 -1.15]	0.173	8 (23.5)	0.42 [0.14-1.33]	0.141
In-hospital neurological deterioration , n (%)	9 (3.5)	10 (6.6)	l [0.92-8.89]	0.069	14 (6.7)	3.29 [1.07-10.09]	0.037	7 (20.6)	15.32 [3.33-70.54]	< 0.001
Oral anticoagulation on admission, n (%)	190 (74.5)	107 (70.9)	1.03 [0.61-1.72]	0.919	99 (47.1)	0.37 [0.24-0.58]	< 0.001	7 (20.6)	0.06 [0.02-0.20]	< 0.001

Table S4 Multivariable multinomial logistic regression model for (non-)adherence to the "1–3–6–12 days rule"[7] in 521 registry patients with known AF at the time of the index stroke/TIA, hospitalization within 72 hours of symptom onset, and completed 3 months follow-up or pre-defined clinical endpoint (recurrent ischemic stroke, systemic embolism, myocardial infarction, hemorrhagic stroke, major bleed or all-cause death) within three months after the index stroke/TIA according to adherence, earlier or later or no (re-)start of a NOAC (setting adherence as reference).

	Adherence n=195	**"Earlier" n=112**	**Multivariable analysis OR (95%CI)**	**p value**	**"Later" n=180**	**Multivariable analysis OR (95%CI)**	**p value**	**No (re-)start n=34**	**Multivariable analysis OR (95%CI)**	**p value**
Age groups; n (%)										
<65 years	20 (10.3)	10 (8.9)	1			1			1	
65-74 years	51 (26.2)	28 (25.0)	0.87 [0.31-2.46]	0.789	30 (16.7)	0.40 [0.16-0.95]	0.038	2 (5.9)	0.60 [0.09-3.88]	0.592
>=75 years	124 (63.6)	74 (66.1)	0.87 [0.31-2.42]	0.789	31 (17.2)	0.68 [0.30-1.54]	0.353	10 (29.4)	0.37 [0.06-2.37]	0.297
Endovascular treatment, n (%)	11 (5.6)	20 (17.9)	4.83 [2.00-11.68]	<0.001	119 (66.1)	0.90 [0.35-2.36]	0.833	22 (64.7)	0.71 [0.12-4.20]	0.701
HAS-BLED post-stroke, median [IQR]	3 [3-4]	3 [3-4]	1.30 [0.89-1.88]	0.170	3 [3-4]	1.13 [0.81-1.57]	0.466	4 [3-5]	2.46 [1.38-4.38]	0.002
Infarct size according to imaging, n (%)										
none	102 (55.7)	43 (41.3)	1		76 (47.2)	1		13 (46.4)	1	
small	73 (39.9)	60 (57.7)	1.59 [0.94-2.71]	0.085	62 (38.5)	0.96 [0.59-1.56]	0.879	12 (42.9)	0.57 [0.21-1.56]	0.273
moderate-large	8 (4.4)	1 (1.0)	0.20 [0.02-1.77]	0.147	23 (14.3)	2.96 [1.13-7.76]	0.028	3 (10.7)	0.69 [0.12-4.10]	0.686
Hemorrhagic transformation, n (%)	7 (3.6)	3 (2.7)	0.69 [0.15-3.10]	0.629	14 (7.8)	0.63 [0.20-2.00]	0.436	6 (17.6)	2.13 [0.44-10.30]	0.349
Cardiovascular risk factors										
Vascular disease	59 (30.3)	37 (33.0)	1.02 [0.58-1.78]	0.954	53 (29.4)	0.93 [0.56-1.55]	0.782	14 (41.2)	0.80 [0.30-2.18]	0.666
Prior stroke or TIA	65 (33.3)	44 (39.3)	1.49 [0.88-2.53]	0.141	43 (23.9)	0.72 [0.43-1.18]	0.194	8 (23.5)	0.40 [0.12-1.31]	0.128
In-hospital neurological deterioration, n (%)	6 (3.1)	9 (8.0)	5.09 [1.28-20.26]	0.021	10 (5.6)	3.99 [0.98-16.17]	0.053	7 (20.6)	23.44 [4.10-133.92]	<0.001
Oral anticoagulation on admission, n (%)	133 (68.2)	76 (67.9)	1.07 [0.60-1.91]	0.814	80 (44.4)	0.43 [0.26-0.69]	0.001	7 (20.6)	0.08 [0.02-0.27]	<0.001

Excluding patients (re-)started on a VKA, 112 (23.0%) of 487 patients (re-)started on a NOAC were (re-)started earlier. Multivariable analysis revealed that endovascular treatment (OR 4.83, 95%CI 2.00-11.68), and in-hospital neurological deterioration (OR 5.09, 95%CI 1.28-20.26) were associated with earlier NOAC (re-)start vs. timely (re-)start according to the "1–3–6–12 day rule", while neither infarct size nor OAC intake at the time of stroke had an impact. Overall, 180 (37.0%) of 487 patients were (re)-started later on a NOAC. Multivariable analysis revealed that moderate or large infarct size (OR 2.96, 95%CI 1.13-7.76 vs. no imaging-detected infarction) was associated with late NOAC (re-)start compared to a timely (re-)start according to the "1–3–6–12 day rule", while OAC intake at the time of stroke (OR 0.43, 95%CI 0.26-0.69) and age 65-74 years (OR 0.40, 95%CI 0.16-0.95 vs. age <65 years) was associated with a timely NOAC (re-)start. Comparing patients without OAC (re-)start to patients (re-)started on a NOAC in adherence to the "1–3–6–12 day rule" revealed similar findings (Table S4).

Table S5 Antithrombotic medication at the time of recurrent ischemic stroke, transient ischemic attack (TIA), systemic embolism, myocardial infarction, hemorrhagic stroke, major bleeding or all-cause death within 3 months after index stroke or TIA in 708 registry patients with known AF at the time of the index stroke/TIA, hospitalization within 72 hours of symptom onset, and known starting time of oral anticoagulation after the index stroke/TIA.

	Ischemic stroke n=16	**TIA n=15**	**Systemic embolism n=3**	**Myocardial infarction n=2**	**Hemorrhagic Stroke n=2**	**Major bleeding n=7**	**All-cause death n=12**	**Composite endpoint n=57**
None, n (%)	3(21.4%)	1 (7.1%)	1 (7.1%)	0 (0.0%)	2 (14.3%)	0 (0.0%)	7 (50.0%)	14 (24.6%)
Antiplatelet, n (%)	1 (33.3%)	0 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (33.3%)	3 (5.3%)
Vitamin K antagonist, n (%)	0 (0.0%)	4 (66.7%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	6 (10.5%)
NOAC, n (%)	9 (31.0%)	10 (34.5%)	2 (6.9%)	1 (3.4%)	0 (0.0%)	6 (20.7%)	1 (3.4%)	29 (50.9%)
Therapeutic dose heparin, n (%)	3(60.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (33.3%)	2 (40.0%)	5 (8.8%)

Table S6. Bivariate hazard ratios and multivariable hazard ratios and corresponding 95% confidence intervals on the composite endpoint (recurrent ischemic stroke or TIA, systemic embolism, myocardial infarction, hemorrhagic stroke, major bleeding or all-cause death) according to the adherence to the "1-3-6-12 day rule" for (re-)starting oral anticoagulation in 661 registry patients with known AF at the time of the index stroke/TIA, hospitalization within 72 hours of symptom onset. Patients without (re-)initiation of oral anticoagulation after the index stroke/TIA within 3 months were discarded in this analysis (N=47).

	No endpoint (n=614)	**Composite endpoint (n=47)**	**Bivariate HR (95% CI)**	**Bivariate Cox-model *p value***	**Multivariable Cox-model* HR (95% CI)**	**Multivariable Cox-model *p value***
(Re-)start of oral anticoagulation according to the 1-3-6-12 day rule"						
Timely oral anticoagulation	150 (24.4%)	12 (25.5%)	1	0.745	1	0.681
Early oral anticoagulation	263 (42.8%)	17 (36.2%)	1.19 [0.57-2.50]	0.639	1.17 [0.49-2.78]	0.722
Late oral anticoagulation	201 (32.7%)	18 (38.3%)	1.29 [0.67-2.51]	0.450	1.39 [0.67-2.89]	0.388

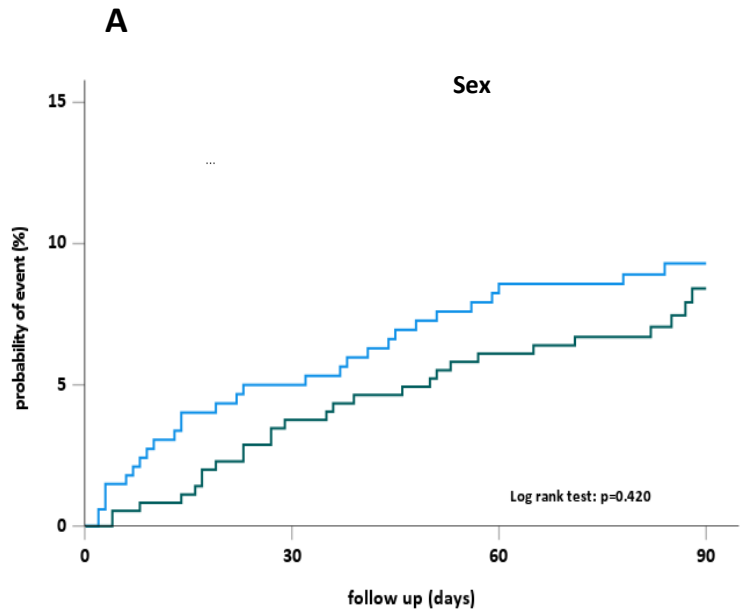
*Additionally adjusted for age, sex, type of index event (stroke vs. transient ischemic attack), National Institutes of Health Scale (NIHSS) score on admission, intravenous thrombolysis, endovascular treatment, carotid endarterectomy, selective serotonin reuptake inhibitor at baseline, CHA2DS2-VASc post-stroke, HAS-BLED post-stroke, oral anticoagulation (OAC) on admission, cardiovascular risk-factors: prior stroke or transient ischemic attack (TIA), vascular disease, diabetes mellitus, hypertension, heart failure, impaired renal function at baseline, duration of in-hospital stay (≤5 vs. >5 days).

Table S7. Multivariable hazard ratios and corresponding 95% confidence intervals on the composite endpoint (recurrent ischemic stroke or TIA, systemic embolism, myocardial infarction, hemorrhagic stroke, major bleeding or all-cause death) according to the adherence to the "1-3-6-12 day rule" for (re-)starting oral anticoagulation, the type of oral anticoagulation (vitamin K antagonist [VKA] vs. non-vitamin K antagonist oral anticoagulants [NOAC]) and their interaction in 661 registry patients with known AF at the time of the index stroke/TIA, hospitalization within 72 hours of symptom onset. Patients without (re-)initiation of oral anticoagulation after the index stroke/TIA within 3 months were discarded in this analysis (N=47).

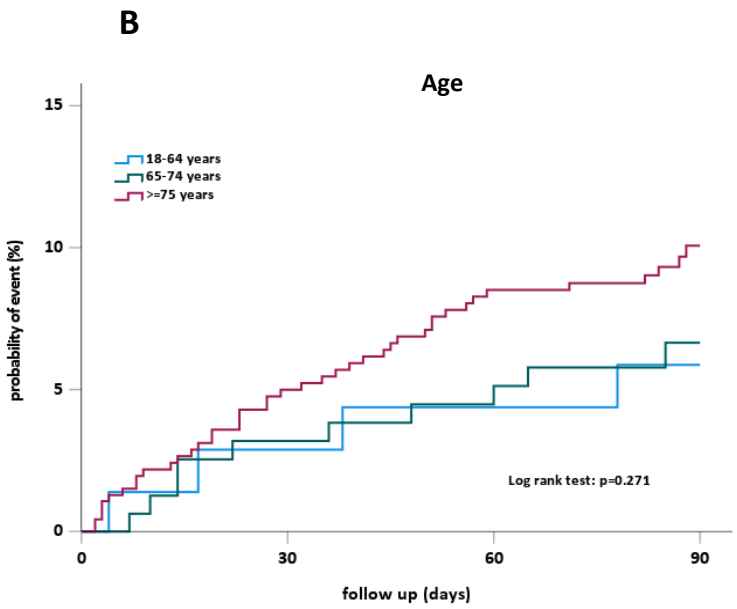
	Multivariable Cox-model* HR (95% CI)	**Multivariable Cox-model *p value***
(Re-)start of oral anticoagulation according to the 1-3-6-12 day rule"		
Timely oral anticoagulation	1	0.584
Early oral anticoagulation	1.08 [0.41-2.83]	0.875
Late oral anticoagulation	1.49 [0.69-3.21]	0.314
Oral anticoagulation		
VKA vs. NOAC	0.62 [0.17-2.26]	0.472
(Re-)start of oral anticoagulation according to the 1-3-6-12 day rule" * oral anticoagulation		
Timely oral anticoagulation * oral anticoagulation	1	0.569
Early oral anticoagulation * oral anticoagulation	1.48 [0.23-9.55]	0.683
Late oral anticoagulation * oral anticoagulation	0.39 [0.03-4.42]	0.446

*Additionally adjusted for age, sex, type of index event (stroke vs. transient ischemic attack), National Institutes of Health Scale (NIHSS) score on admission, intravenous thrombolysis, endovascular treatment, carotid endarterectomy, selective serotonin reuptake inhibitor at baseline, CHA2DS2-VASc post-stroke, HAS-BLED post-stroke, oral anticoagulation (OAC) on admission, cardiovascular risk-factors: prior stroke or transient ischemic attack (TIA), vascular disease, diabetes mellitus, hypertension, heart failure, impaired renal function at baseline, duration of in-hospital stay (≤5 vs. >5 days).

Figure S1 Kaplan Meier curve for the probability of composite endpoint (recurrent ischemic stroke or TIA, systemic embolism, myocardial infarction, hemorrhagic stroke, major bleeding or all-cause death) within three months after the index stroke/TIA according to sex (A) and age (B) in 708 AF patients with known AF at the time of the index stroke/TIA and hospitalization within 72 hours of symptom onset ("complete study cohort"). Log-Rank test was used to test group differences.

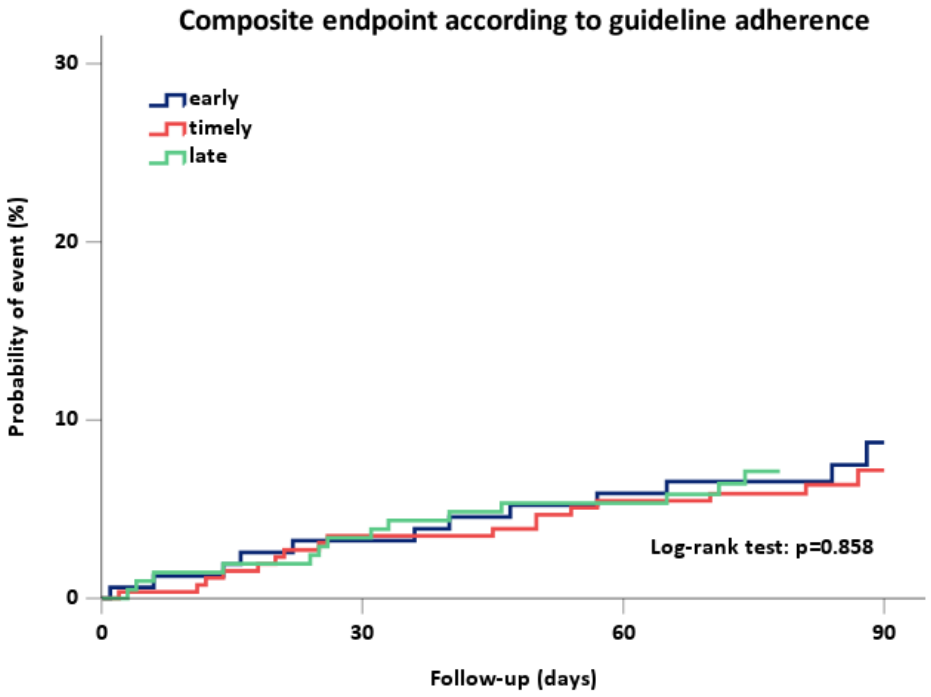


Number at risk				
Female	336	292	280	163
Male	372	328	320	160



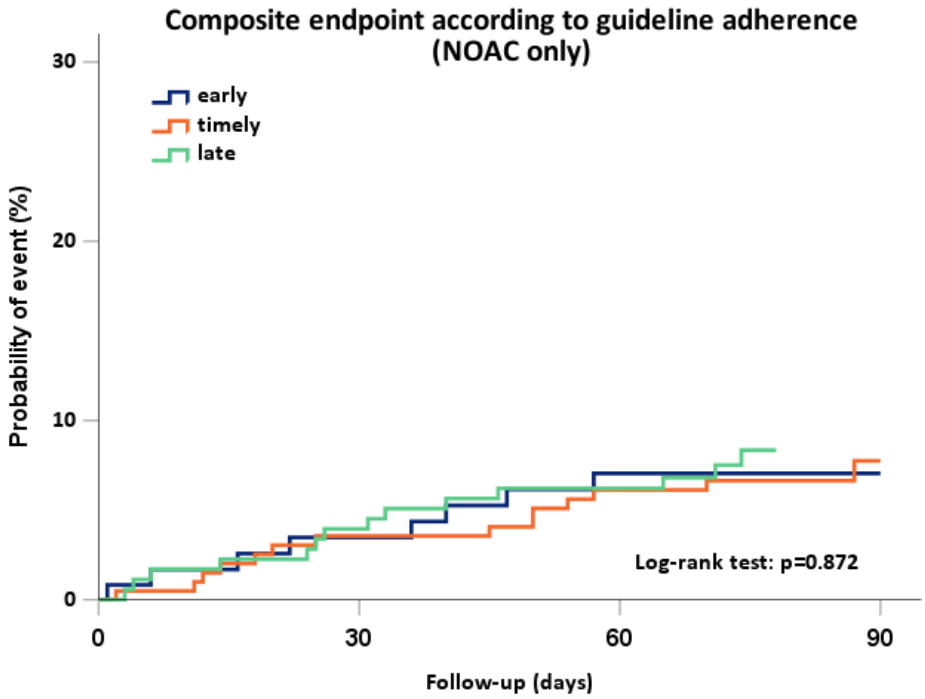
Number at risk				
18-64 years	72	65	64	44
65-74 years	167	150	146	75
>= 75 years	469	405	390	204

Figure S2 Kaplan Meier curve for the probability of composite endpoint (recurrent ischemic stroke or TIA, systemic embolism, myocardial infarction, hemorrhagic stroke, extracranial major bleed or all-cause death) within three months after the index stroke/TIA according to guideline adherence of the "1–3–6–12 days rule" with different timing of (re-)starting of oral anticoagulation ('earlier', 'timely' or 'later' start of oral anticoagulation) in 649 AF patients. Event-time began as soon as the status of guideline adherence was determined for each patient (i.e. for the group 'early' and 'timely' at the day of the OAC start and for the group late at day 13). 12 patients were excluded as the guideline adherence status was undetermined at the time of the event. Log-Rank test was used to test group differences.



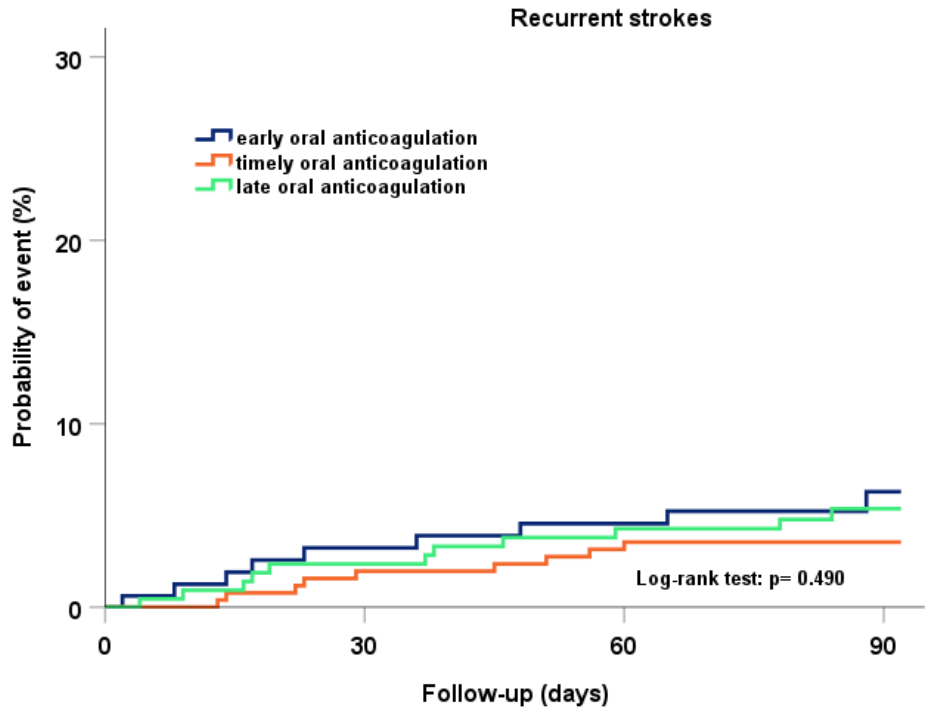
	Number at risk			
Early oral anticoagulation	162	146	142	22
Timely oral anticoagulation	280	245	239	24
Late oral anticoagulation	207	199	193	119

Figure S3 Kaplan Meier curve for the probability of composite endpoint (recurrent ischemic stroke or TIA, systemic embolism, myocardial infarction, hemorrhagic stroke, extracranial major bleed or all-cause death) within three months after the index stroke/TIA according to guideline adherence of the "1–3–6–12 days rule" with different timing of (re-)starting of non-vitamin K antagonist oral anticoagulants (NOAC) ('earlier', 'timely' or 'later' start of oral anticoagulation) in 510 AF patients. Event-time began as soon as the status of guideline adherence was determined for each patient (i.e. for the group 'early' and 'timely' at the day of the OAC start and for the group late at day 13). 11 patients were excluded as the guideline adherence status was undetermined at the time of the event. Log-Rank test was used to test group differences.



	Number at risk			
Early oral anticoagulation	121	108	104	14
Timely oral anticoagulation	212	188	182	14
Late oral anticoagulation	177	170	164	97

Figure S4 Kaplan Meier curve for the probability of recurrent stroke (composite of recurrent ischemic stroke or TIA and hemorrhagic stroke) within three months after the index stroke/TIA in registry patients with (re-)started OAC (early, timely or late) according to the "1-3-6-12 day rule". Log-Rank test was used to test group differences.



	Number at risk			
Early oral anticoagulation	162	146	142	72
Timely oral anticoagulation	280	248	244	122
Late oral anticoagulation	219	205	197	121