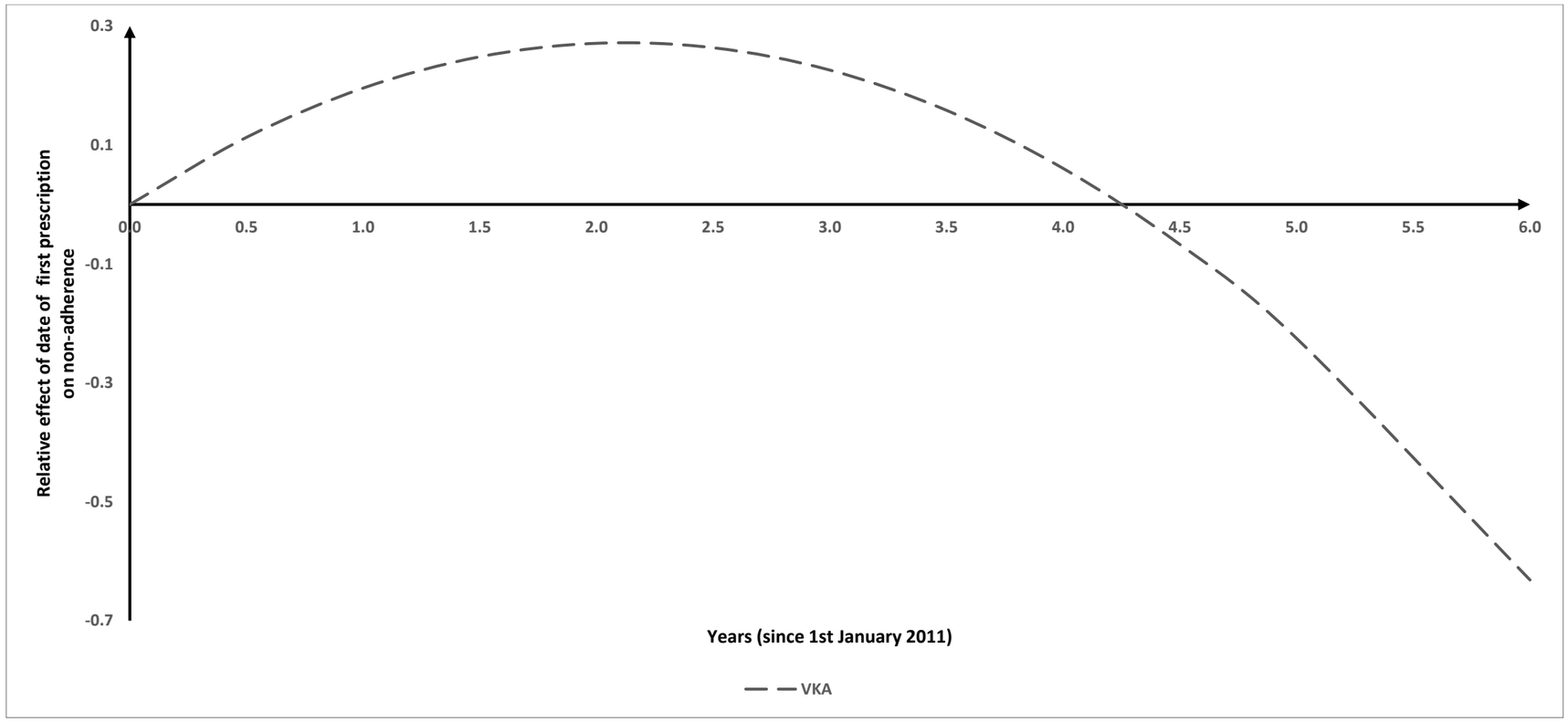
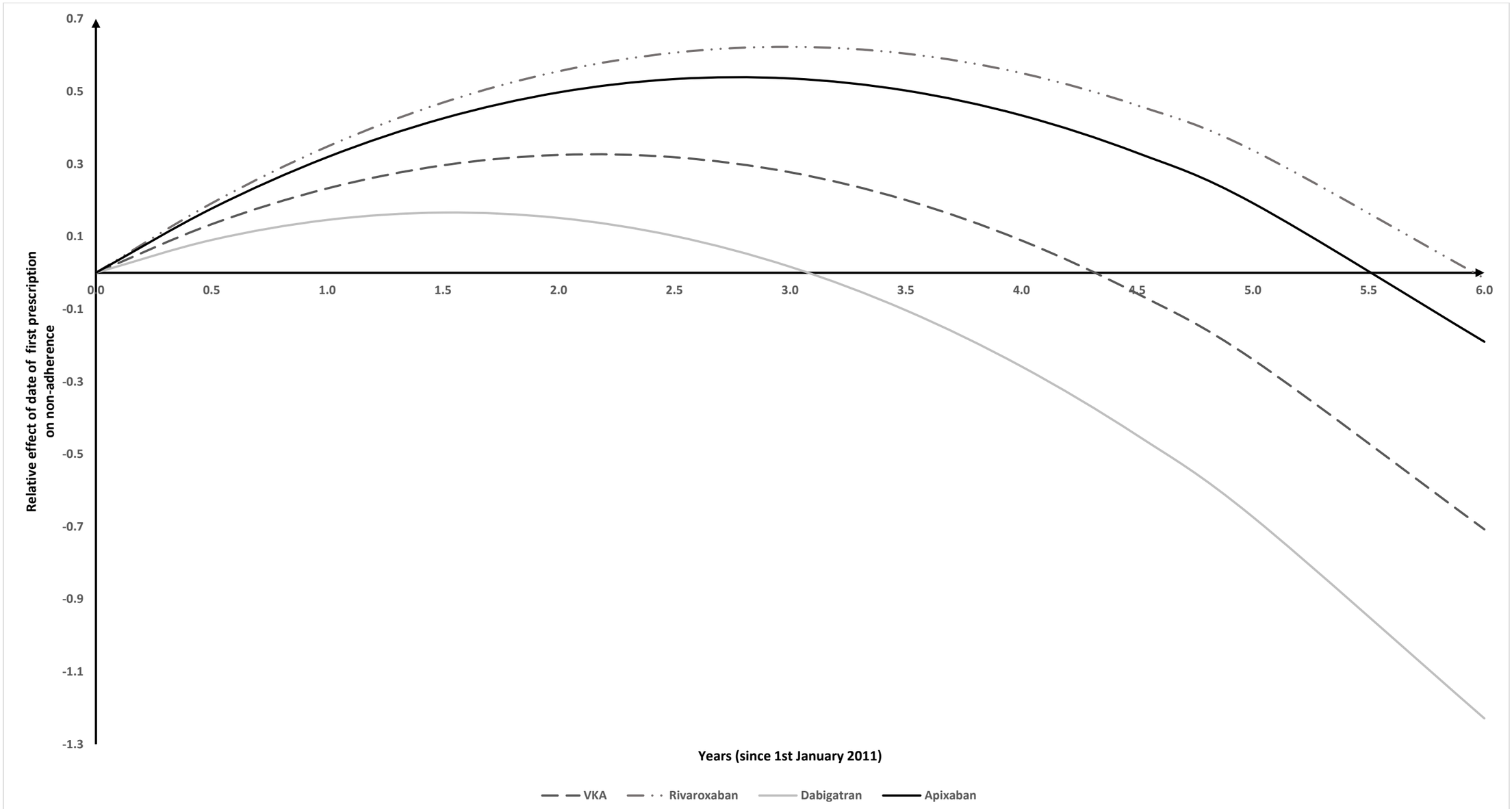
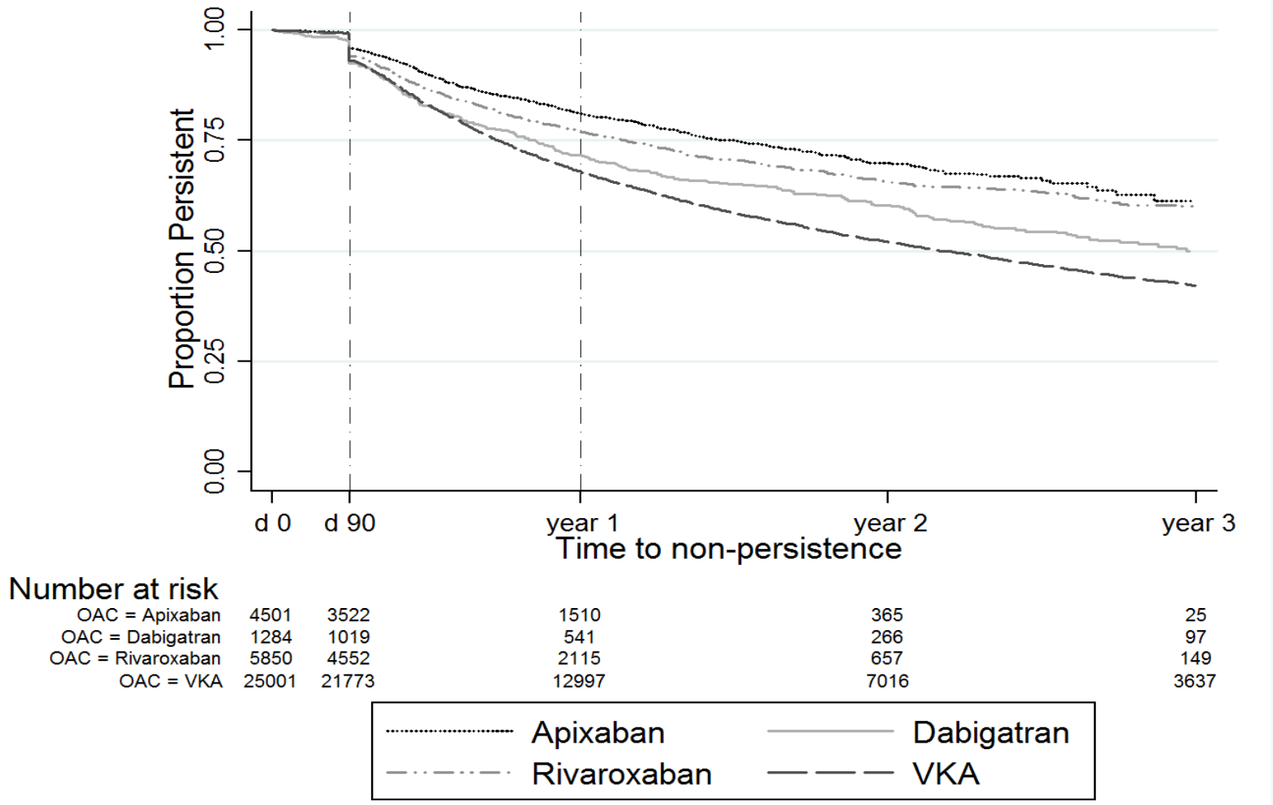
SUPPLEMENTARY WEB MATERIAL



Web Figure 1(a). Relative effect of date of first prescription on non-adherence (as per Table 2)



Web Figure 1. Relative effect of date of first prescription on non-adherence between different OACs (as per Web Table 2(e))



Web Figure 2. Kaplan-Meier analysis of persistence over time, with patients who switch censored at the time they switch

Web Table 1. Clinical trial data for adherence and persistence with direct oral anticoagulants.

Drug	**Dabigatran**	**Rivaroxaban**	**Apixaban**	**Edoxaban**
Clinical trial	RE-LY	ROCKET-AF	ARISTOTLE	ENGAGE AF
Year of publication	2009	2011	2011	2013
Date of NICE approval	15/3/2012	23/5/2012	27/2/2013	23/9/2015
Adherence	-	-	-	-
Persistence with DOAC (%)	78.8 (high dose) 79.3 (low dose)	76.3	74.7	65.6 (high dose) 67.0 (low dose)
Persistence with warfarin (%)	83.4	77.8	72.5	65.5
Time in therapeutic range for warfarin	66%	68%	67%	58%
Median duration of treatment (yrs)	2	1.6	1.8	2.5
Median duration of follow-up (yrs)	2	2.1	1.8	2.8

Web Table 2(a) Likelihood of non-adherence by oral anticoagulant with 6-month restriction on prescription period for patients included in the analysis.

Odds ratios (95% CI)	**Multivariable**	
N	25,058	P-value
VKA	1.00 (-)	
Dabigatran	0.52 (0.44 to 0.60)	<0.001
Rivaroxaban	0.71 (0.66 to 0.78)	
Apixaban	0.70 (0.63 to 0.77)	
CHA_2DS_2Vasc		
[0,1]	1.00 (-)	
[2]	0.97 (0.89 to 1.06)	<0.001
[3,4]	0.90 (0.83 to 0.97)	
[5,9]	0.78 (0.71 to 0.87)	
HASBLED		
[0,2]	1.00 (-)	
[3,9]	1.01 (0.94 to 1.08)	0.85
Number of drugs	0.98 (0.97 to 1.00)	0.008
Townsend Quintile		
[1]	1.00 (-)	
[2]	0.94 (0.88 to 1.01)	<0.001
[3]	0.84 (0.78 to 0.90)	
[4]	0.90 (0.83 to 0.97)	
[5]	0.85 (0.78 to 0.93)	
Date of first prescription (years after 1st January 2011)		
Continuous/ Linear	1.13 (1.06 to 1.21)	<0.001
Continuous/ Quadratic	0.97 (0.96 to 0.98)	
BIC	34443.03	

Web Table 2(b) Likelihood of non-adherence by oral anticoagulant with 12-month restriction on prescription period for patients included in the analysis.

Odds ratios (95% CI)	**Multivariable**	
N	14,127	P-value
VKA	1.00 (-)	
Dabigatran	0.53 (0.43 to 0.66)	<0.001

Odds ratios (95% CI)	Multivariable	
N	14,127	P-value
Rivaroxaban	0.65 (0.57 to 0.73)	
Apixaban	0.65 (0.56 to 0.75)	
CHA_2DS_2Vasc		
[0,1]	1.00 (-)	
[2]	0.95 (0.84 to 1.07)	0.002
[3,4]	0.88 (0.79 to 0.99)	
[5,9]	0.77 (0.66 to 0.88)	
HASBLED		
[0,2]	1.00 (-)	
[3,9]	1.06 (0.96 to 1.16)	0.24
Number of drugs	0.99 (0.97 to 1.00)	0.15
Townsend Quintile		
[1]	1.00 (-)	
[2]	0.89 (0.81 to 0.98)	<0.001
[3]	0.80 (0.73 to 0.89)	
[4]	0.85 (0.76 to 0.94)	
[5]	0.83 (0.73 to 0.94)	
Date of first prescription (years after 1st January 2011)		
Continuous/ Linear	1.14 (1.02 to 1.26)	<0.001
Continuous/ Quadratic	0.97 (0.95 to 0.99)	
BIC	18942.83	

Web Table 2(c) Likelihood of non-adherence by oral anticoagulant with individual CHA_2DS_2Vasc and HASBLED risk factors and other categorical variables.

Odds ratios (95% CI)	Multivariable	
N	31,615	P-value
VKA	1.00 (-)	
Dabigatran	0.54 (0.47 to 0.61)	<0.001
Rivaroxaban	0.77 (0.71 to 0.82)	

Odds ratios (95% CI)	Multivariable	
N	31,615	P-value
Apixaban	0.77 (0.71 to 0.84)	
Congestive cardiac failure	1.03 (0.88 to 1.21)	0.68
Hypertension	1.10 (1.05 to 1.16)	<0.001
Age (years)		
<65	1.00 (-)	
65 to 74	1.00 (0.93 to 1.07)	<0.001
>=75	0.83 (0.77 to 0.88)	
Diabetes	0.92 (0.87 to 0.98)	0.009
Stroke/TIA	0.94 (0.84 to 1.04)	0.22
Vascular disease	1.11 (1.03 to 1.19)	0.006
Female sex	0.90 (0.86 to 0.95)	<0.001
Chronic kidney disease	0.98 (0.93 to 1.04)	0.59
Liver disease	1.02 (0.64 to 1.60)	0.95
Stroke	1.00 (0.88 to 1.14)	0.99
Bleeding	0.96 (0.85 to 1.08)	0.51
Drug use predisposing to bleeding	1.01 (0.68 to 1.51)	0.95
Alcohol misuse	1.05 (0.91 to 1.22)	0.46
Anaemia	0.39 (0.18 to 0.87)	0.022
Number of drugs	0.98 (0.97 to 0.99)	0.002
Townsend Quintile		
[1]	1.00 (-)	
[2]	0.93 (0.87 to 0.99)	<0.001
[3]	0.85 (0.80 to 0.91)	
[4]	0.90 (0.84 to 0.97)	
[5]	0.85 (0.79 to 0.93)	
Date of first prescription (years after 1st January 2011)		
Continuous/ Linear	1.30 (1.22 to 1.37)	<0.001
Continuous/ Quadratic	0.94 (0.93 to 0.95)	
BIC	42896.91	

Web Table 2(d) Likelihood of non-adherence by oral anticoagulant with apixaban as reference category.

Odds ratios (95% CI)	Multivariable	
N	31,615	P-value
Apixaban	1.00 (-)	
Dabigatran	0.70 (0.61 to 0.81)	<0.001
Rivaroxaban	0.99 (0.90 to 1.08)	
VKA	1.29 (1.19 to 1.41)	
CHA_2DS_2Vasc		
[0,1]	1.00 (-)	
[2]	1.00 (0.93 to 1.08)	<0.001
[3,4]	0.94 (0.88 to 1.01)	
[5,9]	0.81 (0.74 to 0.89)	
HASBLED		

Odds ratios (95% CI)	Multivariable	
N	31,615	P-value
[0,2]	1.00 (-)	
[3,9]	0.98 (0.93 to 1.05)	0.62
Number of drugs	0.99 (0.98 to 1.00)	0.067
Townsend Quintile		
[1]	1.00 (-)	
[2]	0.93 (0.87 to 0.99)	<0.001
[3]	0.86 (0.80 to 0.91)	
[4]	0.91 (0.85 to 0.97)	
[5]	0.86 (0.80 to 0.94)	
Date of first prescription (years after 1st January 2011)		
Continuous/ Linear	1.29 (1.22 to 1.37)	<0.001
Continuous/ Quadratic	0.94 (0.93 to 0.95)	
BIC	42880.41	

Web Table 2(e). Likelihood of non-adherence by oral anticoagulant with interactions between time (linear) and OAC.

Odds ratios (95% CI)	Multivariable	
N	31,615	P-value
OAC (effect on first prescribing)		
Apixaban	1.00 (-)	
Dabigatran	1.36 (0.77 to 2.39)	<0.001
Rivaroxaban	0.89 (0.55 to 1.45)	
VKA	1.86 (1.20 to 2.90)	
CHA_2DS_2Vasc		
[0,1]	1.00 (-)	
[2]	1.00 (0.93 to 1.08)	<0.001
[3,4]	0.94 (0.88 to 1.01)	
[5,9]	0.81 (0.74 to 0.89)	
HASBLED		
[0,2]	1.00 (-)	
[3,9]	0.99 (0.93 to 1.05)	0.64
Number of drugs	0.99 (0.98 to 1.00)	0.069
Townsend Quintile		

Odds ratios (95% CI)	Multivariable	
N	31,615	P-value
OAC (effect on first prescribing)		
[1]	1.00 (-)	
[2]	0.93 (0.87 to 0.99)	<0.001
[3]	0.86 (0.80 to 0.91)	
[4]	0.91 (0.85 to 0.97)	
[5]	0.86 (0.80 to 0.94)	
Date of first prescription (years after 1st January 2011)		
Continuous/ Linear	1.48 (1.29 to 1.69)	<0.001
Interacted with Apixaban	1.00 (-)	
Interacted with Dabigatran	0.84 (0.73 to 0.97)	0.002
Interacted with Rivaroxaban	1.03 (0.93 to 1.14)	
Interacted with VKA	0.92 (0.83 to 1.01)	
Continuous/ Quadratic	0.93 (0.92 to 0.94)	<0.001
BIC	42896.51	

Web Table 3. Adherence and persistence with varying definitions status at 1 year for the first OAC ever prescribed after AF.

	Overall	VKA	Dabigatran	Rivaroxaban	Apixaban
	Adherence at 1 year [n (%; 95% CI)]				
Allocated to analysis	N=33,960	N=23,552	N=1,140	N=5,191	N=4,077
PDC threshold					
70%	22,870 (67.3; 66.8-67.8)	15,384 (65.3; 64.7-65.9)	872 (76.5; 73.9-78.9)	3,645 (70.2; 69.0-71.4)	2.969 (72.8; 71.4-74.2)
80%	18,731 (55.2; 54.6-55.7)	12,061 (51.2; 50.6-51.8)	758 (66.5; 63.7-69.2)	3,276 (63.1; 61.8-64.4)	2,636 (64.7; 63.2-66.1)
90%	13,931 (41.0; 40.5-41.5)	8,357 (35.5; 34.9-36.1)	606 (53.2; 50.3-56.0)	2,776 (53.5; 52.1-54.8)	2,192 (53.8; 52.2-55.3)
	Persistence at 1 year [n (%; 95% CI)]				
Allocated to analysis	N=36,636	N=25,001	N=1,284	N=5,850	N=4,501
Prescription gap					
60-day	9,874 (38.6; 38.1-39.2)	7,170 (35.3; 34.7-35.9)	340 (40.8; 37.8-43.7)	1,368 (47.0; 45.5-48.6)	996 (51.5; 49.7-53.3)

90-day	16,879 (65.9; 65.4-66.5)	12,750 (63.4; 62.8-64.0)	521 (61.4; 58.3 64.2)	2,098 (72.3; 70.9-73.7)	1,510 (78.7; 77.1-80.1)
120-day	19,644 (76.8; 76.3-77.2)	15,151 (75.7; 75.2-76.3)	575 (68.1; 65.1-70.8)	2,280 (79.0; 77.7-80.2)	1,638 (85.6; 84.3-86.9)

PDC:Proportion of days covered

Web Table 4. Baseline characteristics according to adherence status at one year after OAC initiation, adopting an 80% threshold for PDC

	Overall		VKA		Dabigatran		Rivaroxaban		Apixaban	
Adherence threshold for PDC: >80%	**1-year Adherent (n=18,731)**	**1-year Non-adherent (n=15,229)**	**1-year Adherent (n=12,061)**	**1-year Non-adherent (n=11,491)**	**1-year Adherent (n=758)**	**1-year Non-adherent (n=382)**	**1-year Adherent (n=3,276)**	**1-year Non-adherent (n=1,915)**	**1-year Adherent (n=2,636)**	**1-year Non-adherent (n=1,441)**
Characteristic										
Age Mean(SD)	74.9(10.5)	73.8(10.1)	74.5(10.2)	74.1(9.9)	73.6(11.2)	72.3(10.9)	75.7(10.9)	73.0(10.9)	76.1(10.4)	72.5(10.9)
Female n(%)	8,695(46.4)	6,542 (43.0)	5,488(45.5)	5,015(43.6)	312 (41.2)	143(37.4)	1,580(48.2)	772(40.3)	1,315(49.9)	612(42.5)
Townsend Quintile (Median; IQR)	(3; 2-4)	(2; 1-4)	(3; 1-4)	(2; 1-4)	(2; 1-3)	(2; 1-3)	(3; 2-4)	(2; 1-3)	(3; 2-4)	(3; 1-4)
Level 1 n(%)	4,261(22.8)	3,915(25.7)	2,803(23.2)	2,951(25.7)	184(24.3)	114(29.8)	667(20.4)	509(26.6)	607(23.0)	341(23.7)
Level 2 n(%)	4,169(22.3)	3,510(23.1)	2,717(22.5)	2,662(23.2)	185(24.4)	107(28.0)	711(21.7)	439(22.9)	556(21.1)	302(21.0)
Level 3 n(%)	3,836(20.5)	2,967(19.5)	2,469(20.5)	2,220(19.3)	175(23.1)	64(16.8)	672(20.5)	415(21.7)	520(19.7)	268(18.6)
Level 4 n(%)	3,013(16.1)	2,444(16.1)	1,955(16.2)	1,882(16.4)	112(14.8)	53(13.9)	545(16.6)	266(13.9)	401(15.2)	243(16.9)
Level 5 n(%)	1,984(10.6)	1,516(10.0)	1,200(10.0)	1,166(10.2)	62(8.2)	27(7.1)	373(11.4)	140(7.3)	349(13.2)	183(12.7)
Missing n(%)	1,468(7.8)	877(5.8)	917(7.6)	610(5.3)	40(5.3)	17(4.5)	308(9.4)	146(7.6)	203(7.7)	104(7.2)
COMORBIDITIES [n(%)]										
Heart failure	1,422(7.6)	1,076(7.1)	921(7.6)	868(7.6)	48(6.3)	19(5.0)	244(7.5)	100(5.2)	209(7.9)	89(6.2)
Hypertension	11,738(62.7)	9,596(63.0)	7,599(63.0)	7,320(63.7)	448(59.1)	215(56.3)	2,015(61.5)	1,196(62.5)	1,676(63.6)	865(60.0)
Diabetes mellitus	3,514 (18.8)	2,673 (17.6)	2,253(18.7)	2,053(17.9)	133(17.6)	62(16.2)	621(19.0)	317(16.6)	507(19.2)	241(16.7)
Stroke/TIA	2,464(13.2)	1,812(11.9)	1,516(12.6)	1,378(12.0)	99(13.1)	48(12.6)	430(13.1)	228(11.9)	419(15.9)	158(11.0)
Vascular disease	2,379(12.7)	2,033(13.4)	1,532(12.7)	1,567(13.6)	88(11.6)	41(10.7)	236(12.3)	392(12.0)	367(13.9)	189(13.1)
Alcohol misuse	476(2.5)	423(2.8)	269(2.2)	282(2.5)	23(3.0)	10(2.6)	92(2.8)	62(3.2)	92(3.5)	69(4.8)
CKD	4,079(21.8)	3,145(20.7)	2,566(21.3)	2,501(21.8)	135(17.8)	61(16.0)	751(22.9)	331(17.3)	627(23.8)	252(17.5)
Liver disease	48(0.3)	41(0.3)	35(0.3)	26(0.2)	2(0.3)	2(0.5)	4(0.1)	7(0.4)	7(0.3)	6(0.4)
Hypercholesterolaemia	13,538(72.3)	10,961(71.2)	8,717(72.3)	8,259(71.9)	542(71.5)	280(73.3)	2,337(71.3)	1,380(72.1)	1,942(73.7)	1,042(72.3)
Smoking Status										
Smoker	1,714(9.2)	1,388(9.1)	1,124(9.3)	991(8.6)	56(7.4)	30(7.9)	313(9.6)	208(10.9)	221(8.4)	159(11.0)

Ex-smoker	7,119(38.0)	5,836(38.3)	4,663(38.7)	4,514(39.3)	291(38.4)	143(37.4)	1,208(36.9)	664(34.7)	957(36.3)	515(35.7)
Never smoked	9,485(50.6)	7,619(50.0)	6,021(49.9)	5,714(49.7)	393(51.9)	198(51.8)	1,685(51.4)	980(51.2)	1,386(52.6)	727(50.5)
Not indicated	413(2.2)	386(2.5)	253(2.1)	272(2.4)	18(2.4)	11(2.9)	70(2.1)	63(3.3)	72(2.7)	40(2.8)
RISK SCORES [n(%)]										
CHA_2DS_2-VASc										
[0,1]	2,893(15.4)	2,517(16.5)	1,866(15.6)	1,774(15.4)	142(18.7)	92(24.1)	516(15.8)	367(19.2)	349(13.2)	284(19.7)
[2]	3,569(19.1)	3,136(20.6)	2,371(19.7)	2,304(20.1)	158(20.8)	92(24.1)	572(17.5)	406(21.2)	468(17.8)	334(23.2)
[3,4]	9,154(48.9)	7,450(48.9)	5,889(48.8)	5,745(50.0)	353(46.6)	154(40.3)	1,615(49.3)	900(47.0)	1,297(49.2)	651(45.2)
[5,9]	3,115(16.6)	2,126(14.0)	1,915(15.9)	1,668(14.5)	105(13.9)	44(11.5)	573(17.5)	242(12.6)	522(19.8)	172(11.9)
HASBLED-1										
[0,2]	14,337(76.5)	11,897(78.1)	9,334(77.4)	8,873(77.2)	614(81.0)	317(83.0)	2,463(75.2)	1,538(80.3)	1,926(73.1)	1,169(81.1)
[3,9]	4,394(23.5)	3,332(21.9)	2,727(22.6)	2,618(22.8)	144(19.0)	65(17.0)	813(24.8)	377(19.7)	710(26.9)	272(18.9)
DRUGS [n(%)]										
Aspirin	10,599(56.6)	8,450(55.5)	6,860(56.9)	6,485(56.4)	428(56.5)	179(46.9)	1,792(54.7)	986(51.5)	1,519(57.6)	800(55.5)
Statin	8,900(47.5)	7,175(47.1)	5,729(47.5)	5,455(47.5)	349(46.0)	151(39.5)	1,493(45.6)	888(46.4)	1,329(50.4)	681(47.3)
BP-lowering drugs	14,882(79.5)	12,145(79.8)	9,610(79.7)	9,234(80.4)	572(75.5)	280(73.3)	2,556(78.0)	1,486(77.6)	2,144(81.3)	1,145(79.5)
Number of Drugs Mean(SD)	5.6(2.2)	5.5(2.2)	5.5(2.2)	5.5(2.2)	5.5(2.2)	5.0(2.2)	5.6(2.2)	5.3(2.2)	5.8(2.2)	5.5(2.2)

Web Table 5(a) Risk of non-persistence by oral anticoagulant with individual CHA_2DS_2Vasc and HASBLED risk factors and other factors.

Hazard ratios (95% CI)	Multivariable
N	34,109
OAC (effect on first prescribing)	
VKA	1.00 (-)
Dabigatran	1.24 (1.09 to 1.42)
Rivaroxaban	0.84 (0.77 to 0.93)
Apixaban	0.52 (0.46 to 0.59)
Time-dependent effect of OAC (per year of prescriptions)	
VKA	1.00 (-)
Dabigatran	0.75 (0.65 to 0.86)
Rivaroxaban	0.69 (0.62 to 0.77)
Apixaban	0.91 (0.79 to 1.06)
Congestive cardiac failure	1.17 (1.05 to 1.31)
Hypertension	0.87 (0.83 to 0.91)
Time-dependent effect of Hypertension (per year of prescriptions)	1.05 (1.01 to 1.09)
Age (years) (effect on first prescribing)	
<65	1.00 (-)
65 to 74	0.68 (0.64 to 0.73)
≥75	0.68 (0.63 to 0.72)
Time-dependent effect of Age (per year of prescriptions)	
<65	1.00 (-)
65 to 74	1.07 (1.01 to 1.13)
≥75	1.13 (1.08 to 1.19)
Diabetes	0.99 (0.94 to 1.03)
Stroke/TIA	0.92 (0.86 to 1.00)
Vascular disease	1.09 (1.03 to 1.14)
Female sex	1.01 (0.97 to 1.04)
Chronic kidney disease	1.07 (1.03 to 1.11)
Liver disease	1.29 (0.95 to 1.76)
Stroke	1.05 (0.96 to 1.16)
Prior bleeding	1.13 (1.04 to 1.23)
Drug use predisposing to bleeding	1.23 (0.94 to 1.63)
Alcohol misuse	1.17 (1.07 to 1.30)
Anaemia	1.15 (0.73 to 1.83)
Number of drugs	1.00 (0.99 to 1.01)
Townsend Quintile	
[1]	1.00 (-)
[2]	0.99 (0.94 to 1.03)
[3]	0.94 (0.90 to 0.99)
[4]	0.95 (0.91 to 1.00)
[5]	0.95 (0.89 to 1.00)
Date of first prescription [a] (years after 1st January 2011)	1.04 (1.02 to 1.05)

[a] Time difference (in years) between the date of the first ever OAC prescription for each patient and the start date of the study (1st January 2011) .
[b] Time-dependent covariates are interacted with survival analysis time (e.g. time on a specific OAC), i.e. (end date of persistence or exit from/end of study - date of first ever OAC prescription)/365.25.

Web Table 5(b) Risk of non-persistence by oral anticoagulant with the same model specification as in Table 3 but with apixaban as reference category.

Hazard ratios (95% CI)	**Multivariable**
N	34,109
OAC (effect on first prescribing)	
Apixaban	1.00 (-)
Dabigatran	2.36 (1.97 to 2.82)
Rivaroxaban	1.61 (1.39 to 1.86)
VKA	1.90 (1.68 to 2.16)
Time-dependent effect of OAC (per year of prescriptions)	
Apixaban	1.00 (-)
Dabigatran	0.82 (0.68 to 1.00)
Rivaroxaban	0.76 (0.64 to 0.91)
VKA	1.10 (0.95 to 1.28)
CHA_2DS_2Vasc (effect on first prescribing)	
[0-1]	1.00 (-)
[2]	0.71 (0.66 to 0.76)
[3,4]	0.66 (0.62 to 0.71)
[5,9]	0.69 (0.63 to 0.76)
Time-dependent effect of CHA_2DS_2Vasc (per year of prescriptions)	
[0,1]	1.00 (-)
[2]	1.05 (0.99 to 1.12)
[3,4]	1.12 (1.07 to 1.18)
[5,9]	1.13 (1.06 to 1.20)
HASBLED	
[0,2]	1.00 (-)
[3,9]	1.04 (0.99 to 1.08)
Number of drugs	1.00 (0.99 to 1.01)
Townsend Quintile	
[1]	1.00 (-)
[2]	0.99 (0.95 to 1.03)
[3]	0.95 (0.91 to 1.00)
[4]	0.97 (0.93 to 1.02)
[5]	0.97 (0.92 to 1.03)
Date of first prescription [a] (years after 1`st January 2011)	1.03 (1.02 to 1.05)

[a] Time difference (in years) between the date of the first ever OAC prescription for each patient and the start date of the study (1st January 2011) .

[b] Time-dependent covariates are interacted with survival analysis time (e.g. time on a specific OAC), i.e. (end date of persistence or exit from/end of study - date of first ever OAC prescription)/365.25.

	Overall			VKA			Dabigatran			Rivaroxaban			Apixaban		
n(%)	**Persistent (n=16862)**	**Non-persistent (n=8401)**	**Censored[a] (n=11373)**	**Persistent (n=12736)**	**Non-persistent (n=6958)**	**Censored[a] (n=5307)**	**Persistent (n=521)**	**Non-persistent (n=322)**	**Censored[a] (n=441)**	**Persistent (n=2098)**	**Non-persistent (n=738)**	**Censored[a] (n=3014)**	**Persistent (n=1507)**	**Non-persistent (n=383)**	**Censored[a] (n=2,611)**
Characteristic															
Age Mean(SD)	74.5(9.6)	72.6(11.4)	75.7(10.7)	74.5(9.4)	72.7(11.2)	76.1(10.2)	73.8(10.0)	71.4(12.9)	74.3(11.0)	74.6(10.1)	72.6(12.1)	75.5(11.1)	74.6(10.4)	71.7(13.1)	75.4(11.0)
Female	7602(45.1)	3634(43.3)	5249(46.2)	5738(45.1)	3006(43.2)	2439(46.0)	204(39.2)	131(40.7)	182(41.3)	949(45.2)	331(44.9)	1387(46.0)	711(47.2)	166(43.3)	1,241(47.5)
Townsend Quintile (Median; IQR)	(3; 1-4)	(2; 1-4)	(2; 1-4)	(2; 1-4)	(2; 1-4)	(2; 2-4)	(2; 1-4)	(2; 1-3)	(2; 1-3)	(3; 2-4)	(2; 1-3)	(2; 1-4)	(3: 2-4)	(3; 1-4)	(3; 1-4)
Level 1	4039(24.0)	2116(25.2)	2702(23.8)	3113(24.4)	1767(25.4)	1242(23.4)	131(25.1)	85(26.4)	129(29.3)	456(21.7)	168(22.8)	722(24.0)	339(22.5)	96(25.1)	609(23.3)
Level 2	3752(22.3)	1907(22.7)	2605(22.9)	2850(22.4)	1577(22.7)	1277(24.1)	123(23.6)	83(25.8)	114(25.9)	460(21.9)	177(24.0)	662(22.0)	319(21.2)	70(18.3)	552(21.1)
Level 3	3445(20.4)	1660(19.8)	2222(19.5)	2582(20.3)	1345(19.3)	1037(19.5)	112(21.5)	74(23.0)	84(19.1)	432(20.6)	165(22.4)	631(20.9)	319(21.2)	76(19.8)	470(18.0)
Level 4	2718(16.1)	1310(15.6)	1833(16.1)	2062(16.2)	1119(16.1)	881(16.6)	86(16.5)	39(12.1)	60(13.6)	343(16.4)	90(12.2)	464(15.4)	227(15.1)	62(16.2)	428(16.4)
Level 5	1725(10.2)	846(10.1)	1229(10.8)	1263(9.9)	707(10.2)	570(10.7)	39(7.5)	28(8.7)	31(7.0)	226(10.8)	63(8.5)	285(9.5)	197(13.1)	48(12.5)	343(13.1)
Missing	1183(7.0)	562(6.7)	782(6.9)	866(6.8)	443(6.4)	300(5.7)	30(5.8)	13(4.0)	23(5.2)	181(8.6)	75(10.2)	250(8.3)	106(7.0)	31(8.1)	209(8.0)
COMORBIDITIES															
Heart failure	1154(6.8)	582(6.9)	963(8.5)	894(7.0)	496(7.1)	518(9.8)	33(6.3)	20(6.2)	26(5.9)	129(6.2)	47(6.4)	210(7.0)	98(6.5)	19(5.0)	209(8.0)
Hypertension	10800(64.1)	4963(59.1)	7182(63.2)	8194(64.3)	4169(59.9)	3457(65.1)	317(60.8)	175(54.4)	258(58.5)	1339(63.8)	403(54.6)	1866(61.9)	950(63.0)	216(56.4)	1,601(61.3)
Diabetes mellitus	3066(18.2)	1443(17.2)	2178(19.2)	2294(18.0)	1210(17.4)	1089(20.5)	96(18.4)	52(16.2)	61(13.8)	384(18.3)	133(18.0)	539(17.9)	292(19.4)	48(12.5)	489(18.7)
Stroke/TIA	2186(13.0)	940(11.2)	1495(13.2)	1611(12.7)	783(11.3)	702(13.2)	66(12.7)	37(11.5)	57(12.9)	295(14.1)	82(11.1)	358(11.9)	214(14.2)	38(9.9)	378(14.5)
Vascular disease	2160(12.8)	1088(13.0)	1543(13.6)	1638(12.9)	924(13.3)	753(14.2)	69(13.2)	31(9.6)	49(11.1)	256(12.2)	87(11.8)	373(12.4)	197(13.1)	46(12.0)	368(14.1)
Alcohol misuse	400(2.4)	242(2.9)	335(3.0)	284(2.2)	182(2.6)	123(2.3)	15(2.9)	14(4.4)	7(1.6)	61(2.9)	26(3.5)	88(2.9)	40(2.7)	20(5.2)	117(4.5)
CKD	3549(21.1)	1697(20.2)	2592(22.8)	2709(21.3)	1417(20.4)	1298(24.5)	94(18.0)	58(18.0)	68(15.4)	426(20.3)	150(20.3)	651(21.6)	320(21.2)	72(18.8)	575(22.0)
Liver disease	33(0.2)	27(0.3)	40(0.4)	24(0.2)	21(0.3)	22(0.4)	1(0.2)	2(0.6)	1(0.2)	3(0.1)	3(0.4)	9(0.3)	5(0.3)	1(0.3)	8(0.3)
Hyper-cholesterolaemia	12391(73.5)	5868(69.9)	8056(70.8)	9323(73.2)	4886(70.2)	3766(71.0)	385(73.9)	227(70.5)	302(68.5)	1546(73.7)	504(68.3)	2117(70.2)	1137(75.5)	251(65.5)	1871(71.7)
Smoking Status															
Smoker	1516(9.0)	798(9.5)	1060(9.3)	1117(8.8)	654(9.4)	501(9.4)	44(8.5)	24(7.5)	35(7.9)	216(10.3)	81(11.0)	288(9.6)	139(9.2)	39(10.2)	236(9.0)
Ex-smoker	6361(37.7)	3179(37.8)	4383(38.5)	4882(38.3)	2674(38.4)	2153(40.6)	191(36.7)	123(38.2)	169(38.3)	741(35.3)	256(34.7)	1127(37.4)	547(36.3)	126(32.9)	934(35.8)
Never smoked	8621(51.1)	4209(50.1)	5643(49.6)	6464(50.8)	3461(49.7)	2542(47.9)	277(53.2)	165(51.2)	224(50.8)	1096(52.2)	377(51.1)	1516(50.3)	784(52.0)	206(53.8)	1361(52.1)
Not indicated	364(2.2)	215(2.6)	287(2.5)	273(2.1)	169(2.4)	111(2.1)	9(1.7)	10(3.1)	13(3.0)	45(2.1)	24(3.3)	83(2.8)	37(2.5)	12(3.1)	80(3.1)
RISK SCORES															
CHA_2DS_2-VASc															
[0-1]	2414(14.3)	1797(21.4)	1644(14.5)	1767(13.9)	1451(20.9)	669(12.6)	88(16.9)	92(28.6)	83(18.8)	336(16.0)	162(22.0)	486(16.1)	223(14.8)	92(24.0)	406(15.6)
[2]	3442(20.4)	1642(19.6)	2104(18.5)	2630(20.7)	1349(19.4)	958(18.1)	115(22.1)	61(18.9)	102(23.1)	413(19.7)	145(19.7)	547(18.2)	284(18.9)	87(22.7)	497(19.0)
[3-4]	8481(50.3)	3767(44.8)	5637(49.6)	6461(50.7)	3150(45.3)	2708(51.0)	256(49.1)	127(39.4)	188(42.6)	1002(47.8)	325(44.0)	1520(50.4)	762(50.6)	165(43.1)	1221(46.8)
[5-9]	2525(15.0)	1195(14.2)	1988(17.5)	1878(14.8)	1008(14.5)	972(18.3)	62(11.9)	42(13.0)	68(15.4)	347(16.5)	106(14.3)	461(15.3)	238(15.8)	39(10.2)	487(18.7)
HASBLED-1															
[0-2]	13084(77.6)	6638(79.0)	8545(75.1)	9872(77.5)	5490(78.9)	3931(74.1)	427(82.0)	255(79.2)	364(82.5)	1618(77.1)	581(78.7)	2306(76.5)	1167(77.4)	312(81.5)	1,944(74.5)
[3-8]	3778(22.4)	1763(21.0)	2828(24.9)	2864(22.5)	1468(21.1)	1376(25.9)	94(18.0)	67(20.8)	77(17.5)	480(22.9)	157(21.3)	708(23.5)	340(22.6)	71(18.5)	667(25.6)
DRUGS															
Aspirin	9647(57.2)	4545(54.1)	6309(55.5)	7305(57.4)	3822(54.9)	3044(57.4)	291(55.9)	162(50.3)	229(51.9)	1167(55.6)	372(50.4)	1574(52.2)	884(58.7)	189(49.4)	1462(56.0)
Statin	8245(48.9)	3639(43.3)	5292(46.5)	6187(48.6)	3100(44.6)	2513(47.4)	240(46.1)	123(38.2)	187(42.4)	1026(48.9)	275(37.3)	1346(44.7)	792(52.6)	141(36.8)	1246(47.7)
BP-lowering drugs	13519(80.2)	6457(76.9)	9147(80.4)	10235(80.4)	5400(77.6)	4367(82.3)	404(77.5)	225(69.9)	331(75.1)	1649(78.6)	553(74.9)	2356(78.2)	1231(81.7)	279(72.9)	2093(80.2)
Number of Drugs Mean(SD)	5.5(2.2)	5.4(2.3)	5.6(2.2)	5.5(2.2)	5.4(2.3)	5.6(2.2)	5.5(2.2)	5.2(2.3)	5.3(2.2)	5.5(2.3)	5.3(2.3)	5.4(2.2)	5.8(2.2)	5.3(2.3)	5.7(2.2)

Web Table 6. Baseline characteristics according to persistence status at one year after OAC initiation, adopting a 90-day prescription gap.

Web Table 7: Non-persistent and primary non-adherent patients with atrial fibrillation who became non-persistent by switching during the whole study period (2011-2016)

	Overall	**VKA**	**Dabigatran**	**Rivaroxaban**	**Apixaban**
Non-persistent					
Total (n)	16,302	13,411	553	1,510	828
Switched; n (%)	3,302 (20.3)	2,518 (18.8)	223 (40.3)	408 (27.0)	153 (18.5)
Primary non-adherence					
Total (n)	1,453	920	97	295	141
Switched; n (%)	657 (45.2)	376 (40.9)	67 (69.1)	151 (51.2)	63 (44.7)

Web Table 8: Risk of non-persistence by oral anticoagulant, with patients who switch censored at the time they switch.

Hazard ratios (95% CI)	**Multivariable**
N	34,109
OAC (effect on first prescribing)	
VKA	1.00 (-)
Dabigatran	0.93 (0.79 to 1.10)
Rivaroxaban	0.81 (0.73 to 0.91)
Apixaban	0.57 (0.50 to 0.66)
Time-dependent effect of OAC (per year of prescriptions)	
VKA	1.00 (-)
Dabigatran	0.90 (0.78 to 1.04)
Rivaroxaban	0.80 (0.71 to 0.90)
Apixaban	1.01 (0.86 to 1.18)
CHA_2DS_2Vasc (effect on first prescribing)	
[0-1]	1.00 (-)
[2]	0.69 (0.63 to 0.75)
[3,4]	0.62 (0.57 to 0.66)
[5,9]	0.63 (0.57 to 0.70)
Time-dependent effect of CHA_2DS_2Vasc (per year of prescriptions)	
[0,1]	1.00 (-)
[2]	1.08 (1.01 to 1.15)
[3,4]	1.19 (1.12 to 1.25)
[5,9]	1.19 (1.11 to 1.28)
HASBLED-1	
[0,2]	1.00 (-)
[3,9]	1.05 (1.00 to 1.10)
Number of drugs	1.00 (0.99 to 1.00)
Townsend Quintile	
[1]	1.00 (-)
[2]	0.99 (0.95 to 1.04)
[3]	0.95 (0.90 to 1.00)
[4]	0.98 (0.93 to 1.04)
[5]	0.97 (0.91 to 1.04)
Date of first prescription [a] (years after 1st January 2011)	0.97 (0.95 to 0.98)

[a] Time difference (in years) between the date of the first ever OAC prescription for each patient and the start date of the study (1st January 2011) .

[b] Time-dependent covariates are interacted with survival analysis time (e.g. time on a specific OAC), i.e. (end date of persistence or exit from/end of study - date of first ever OAC prescription)/365.25.