SUPPLEMENTARY MATERIAL

Figure S1. Flowchart for the selection of the study population. Of 52057 cases in the GARFIELD-AF registry, after exclusions and completion of follow-up, 28290 patients had received oral anticoagulation (OAC), 12126 no OAC at baseline.

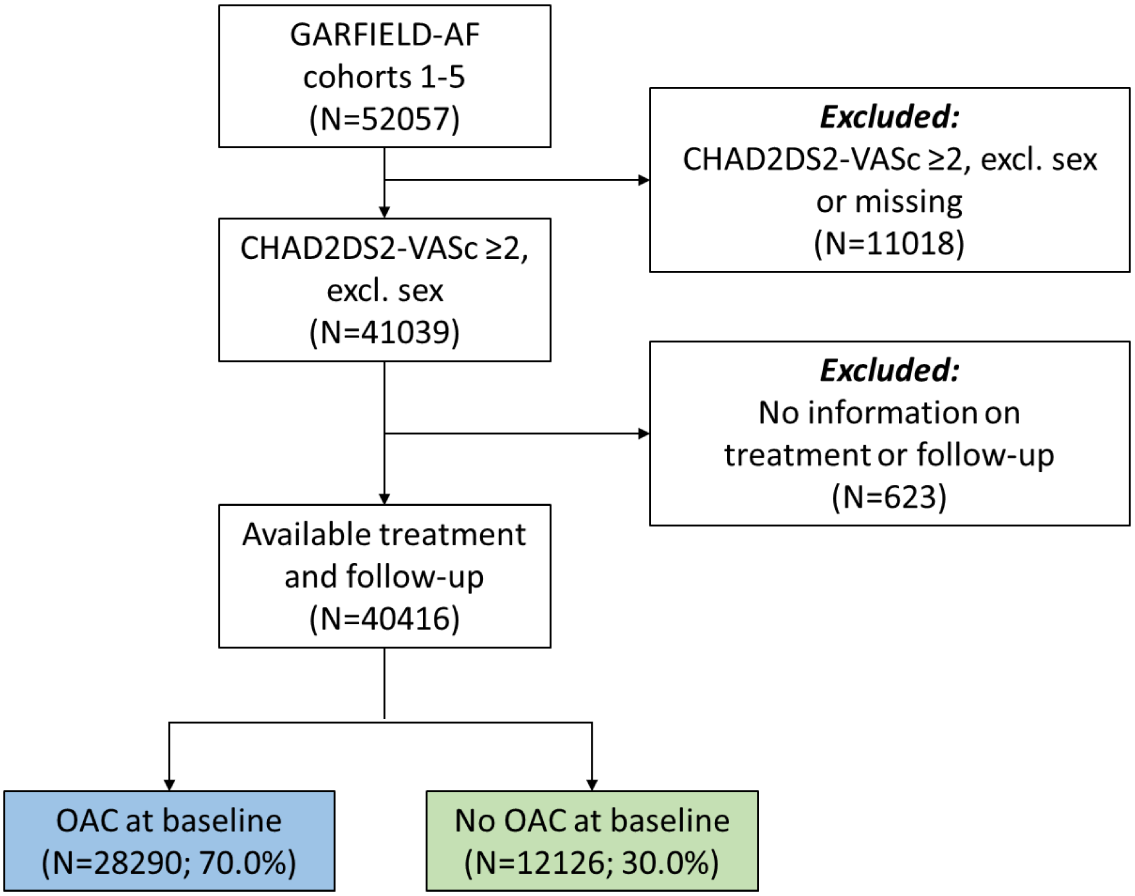

Figure S2. Components of the model predicting withholding of OAC. Associations reported refer to the model with the inclusion of health expenditure per capita information (Model 3)

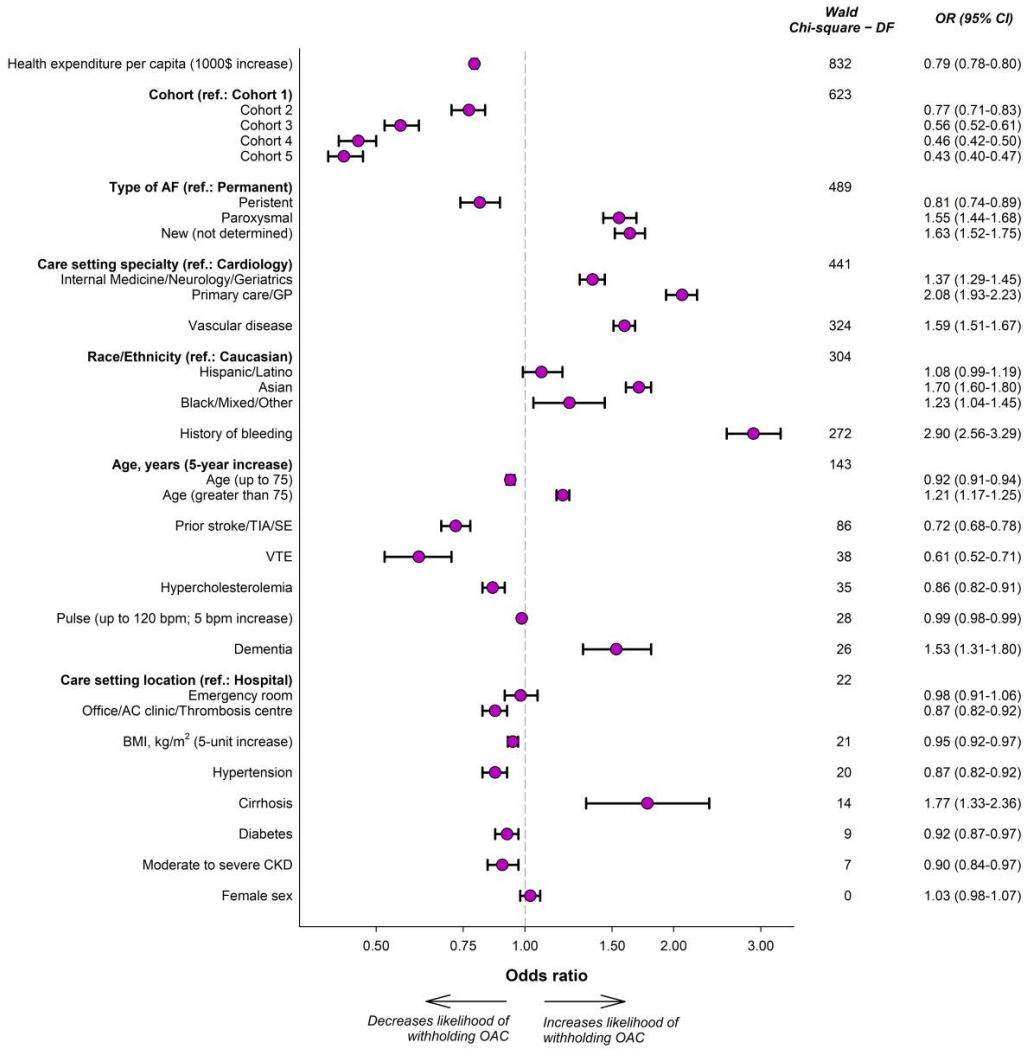

Figure S3. Relationship between country averages of health expenditure per person and OAC use (proportion of OAC-treated high-risk patients). Health expenditure, PPP (current international $) represents the country average between 2010-2016. Axes scales intersect at the averages across all countries and cohorts.

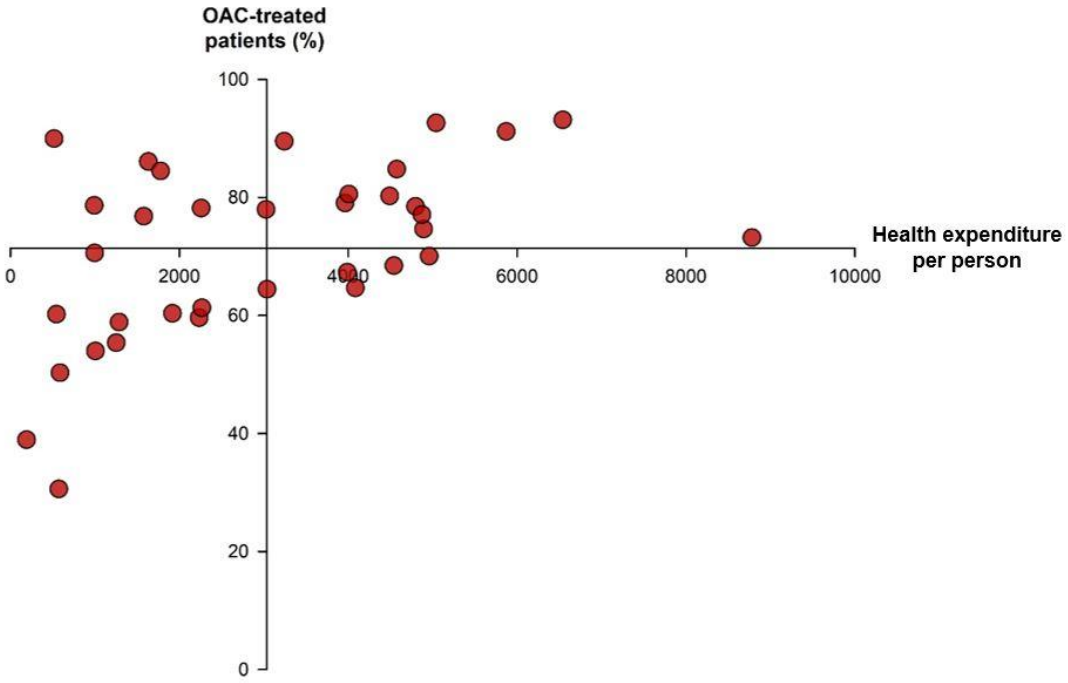

Table S1. List of potential predictors for the OAC withholding models. Variables for which no association with OAC withholding was found are shown in italics.

Demographics

- Sex
- Age
- Ethnicity/Ethnicity
- Country (only for model 2)

Medical and Cardiovascular History

- Hypertension
- Diabetes
- Moderate to severe CKD[1]
- History of bleeding[2]
- Heart failure
- Acute coronary syndromes
- Carotid occlusive disease
- Venous thromboembolism
- Vascular disease[3]
- Prior stroke/TIA/SE
- Hypercholesterolemia

Lifestyle factors

- Current smoking
- Heavy alcohol consumption[4]

Vital signs

- BMI (kg/m^2)
- Pulse (bpm)
- Systolic blood pressure (mmHG)
- Diastolic blood pressure (mmHG)

Atrial fibrillation diagnosis

- Type of atrial fibrillation[5]

Care setting at diagnosis

- Care setting specialty
- Care setting location

Other

- Cohort of enrolment[6]

• Cirrhosis • Hyperthyroidism • Hypothyroidism • Dementia	• Health expenditure per person, PPP, in current international $ (only for model 3)

[1] Defined as CKD stage III to V
[2] Defined as a previous occurrence of bleeding of any severity and type
[3] Defined as peripheral vascular disease and/or coronary artery disease
[4] Investigator-defined
[5] Classified as paroxysmal, persistent, permanent or unclassified
[6] Cohort 1 (period of enrolment 2010-2011), Cohort 2 (2011-2013), Cohort 3 (2013-2014), Cohort 4 (2014-2015), Cohort 5 (2015-2016)

BMI: body mass index, CKD: chronic kidney disease, OAC: oral anticoagulation, SE: systemic embolism, TIA: transient ischemic attack, PPP: purchasing power parity

Table S2. Baseline characteristics among patients treated with OAC at baseline by baseline OAC treatment[1]

Baseline characteristics	OAC treatment		P-value[2]
	VKA (n = 16939)	NOAC (N = 11351)	
Sex, n (col %)			
Male	9024 (53.3)	6057 (53.4)	0.885
Female	7915 (46.7)	5294 (46.6)	
Age, median (Q1; Q3), years	73.0 (67.0;79.0)	74.0 (68.0;80.0)	<0.001
Ethnicity, n (col %)			
White	11748 (70.9)	7348 (66.6)	<0.001
Hispanic/Latino	1283 (7.7)	580 (5.3)	
Asian	3244 (19.6)	2878 (26.1)	
Black/Mixed/Other	296 (1.8)	233 (2.1)	
BMI, median (Q1; Q3), kg/m²	27.5 (24.4;31.2)	26.8 (23.9;30.7)	<0.001
Systolic blood pressure, median (Q1; Q3), mmHg	134.0 (120.0;147.0)	133.0 (120.0;146.0)	0.427
Diastolic blood pressure, median (Q1; Q3), mmHg	80.0 (70.0;90.0)	80.0 (70.0;88.0)	<0.001
Pulse, median (Q1; Q3), bpm	85.0 (72.0;105.0)	84.0 (70.0;108.0)	0.528
Type of atrial fibrillation, n (col %)			
Permanent	2932 (17.3)	1380 (12.2)	<0.001
Persistent	2903 (17.1)	1854 (16.3)	
Paroxysmal	3540 (20.9)	3597 (31.7)	
Unclassified	7564 (44.7)	4520 (39.8)	
Care setting specialty at diagnosis, n (col %)			
Internal medicine/Neurology/Geriatrics	3759 (22.2)	2113 (18.6)	<0.001
Cardiology	10397 (61.4)	8063 (71.0)	

Primary care/general practice	2783 (16.4)	1175 (10.4)	
Care setting location at diagnosis, n (col %)			
Hospital	9829 (58.0)	5764 (50.8)	
Office/Anticoagulation clinic/Thrombosis centre	5082 (30.0)	4519 (39.8)	<0.001
Emergency room	2028 (12.0)	1068 (9.4)	
Medical history, n (col %)			
Heart failure	4544 (26.8)	2835 (25.0)	<0.001
Acute coronary syndrome	2050 (12.1)	1274 (11.3)	0.026
Vascular disease	4770 (28.2)	2928 (25.8)	<0.001
Carotid occlusive disease	611 (3.6)	417 (3.7)	0.741
VTE	636 (3.8)	265 (2.3)	<0.001
Prior stroke/TIA/SE	2587 (15.3)	1592 (14.0)	0.004
History of bleeding	310 (1.8)	243 (2.1)	0.063
Hypertension	14336 (84.7)	9334 (82.3)	<0.001
Hypercholesterolemia	7609 (46.1)	5179 (46.8)	0.0206
Diabetes	4847 (28.6)	2928 (25.8)	<0.001
Cirrhosis	85 (0.5)	40 (0.4)	0.066
Moderate to severe CKD	2242 (13.7)	1304 (11.8)	<0.001
Dementia	196 (1.2)	244 (2.2)	<0.001
Heavy alcohol user, n (col %)	258 (1.8)	167 (1.8)	0.925
Current smoker, n (col %)	1307 (8.4)	907 (8.8)	0.293
Antiplatelet treatment, n (col %)	4345 (25.7)	2235 (19.7)	<0.001
CHA_2DS_2-VASc score, median (Q1; Q3)	4.0 (3.0;5.0)	4.0 (3.0;4.0)	0.003
HAS-BLED score [3], median (Q1; Q3)	1.0 (1.0;2.0)	1.0 (1.0;2.0)	<0.001
GARFIELD-AF death score [4], median (Q1; Q3)	6.0 (3.7; 10.0)	4.8 (2.9; 8.1)	<0.001
GARFIELD-AF stroke score [5], median (Q1; Q3)	1.7 (1.3; 2.4)	1.4 (1.0; 2.0)	<0.001
GARFIELD-AF bleeding score [6], median (Q1; Q3)	2.3 (1.7; 3.2)	1.6 (1.2; 2.3)	<0.001

[1] This study analyzed initial treatment of AF patients, regardless of the AF type which might have been confirmed at later visits;
[2]Calculated using T-test or Wilcoxon-Mann-Whitney for continuous variables, as appropriate, and Chi-squared or Fisher's exact test for categorical variables, as appropriate;
[3] The risk factor 'Labile INRs' is not included in the HAS-BLED score as it is not collected at baseline. As a result, the maximum HAS-BLED score at baseline is 8 points (not 9).
[4] Denotes the expected probability of death within two years from enrolment.
[5] Denotes the expected probability of developing a non-hemorrhagic stroke/SE within two years from enrolment.
[6] Denotes the expected probability of developing a major bleeding within two years from enrolment.
AP: anti-platelet treatment, BMI: body mass index, CKD: chronic kidney disease, NOAC: non-vitamin K oral anticoagulant, OAC: oral anti-coagulant, SE: systemic embolism, TIA: transient ischemic attack, VTE: venous thromboembolism

Table S3. Proportion (%) of patients in each country not on anticoagulant treatment at baseline, by cohort of enrolment

Country	Cohort 1 (2010-2011)	Cohort 2 (2011-2013)	Cohort 3 (2013-2014)	Cohort 4 (2014-2015)	Cohort 5 (2015-2016)
Argentina	-	37.40	43.92	37.28	38.10
Australia	35.63	46.15	40.45	29.13	23.93
Austria	30.25	29.03	25.00	16.67	19.67
Belgium	-	20.25	16.58	12.88	10.22
Brazil	38.75	41.01	40.74	44.12	40.00
Canada	31.75	32.91	29.34	35.59	28.37
Chile	-	25.66	15.07	7.41	9.17
China	76.84	77.58	68.98	64.12	61.68
Czech Republic	-	26.65	21.01	22.60	16.71
Denmark	33.33	27.01	19.51	17.39	10.09
Egypt	-	-	-	6.82	11.00
Finland	29.58	26.36	13.13	12.5	0.00
France	23.48	18.88	22.68	13.97	20.17
Germany	45.72	37.36	19.33	15.62	17.00
Hungary	-	18.82	13.54	14.83	14.92
India	-	57.96	62.45	48.15	69.35
Italy	9.92	11.63	9.16	13.23	7.71
Japan	32.34	23.33	17.37	18.14	18.18
Mexico	60.74	47.58	35.48	38.36	38.75
Netherlands	10.71	10.63	5.64	4.84	2.56
Norway	11.43	1.82	8.33	13.04	21.05
Poland	33.99	32.38	21.69	11.90	10.73
Russia	-	52.52	46.48	41.32	35.75
Singapore	-	43.75	37.04	27.91	33.73
South Africa	-	21.05	27.84	22.86	16.08
South Korea	54.94	42.74	38.50	25.61	27.71
Spain	25.84	21.79	22.53	23.31	15.72
Sweden	36.49	32.81	19.91	11.58	9.59
Switzerland	-	-	-	9.52	5.77
Thailand	-	38.52	38.58	43.29	38.24
Turkey	-	-	-	33.10	27.24
Ukraine	-	62.00	51.34	42.77	42.70
United Arab Emirates	-	-	40.00	43.00	32.18
United Kingdom	40.32	43.49	38.50	24.29	24.07
United States	-	-	17.98	27.13	30.14

Table S4. Components of the model predicting withholding of OAC in cohorts 3 to 5, recruited during the time when NOACs became widely available. Age and BMI are continuous. Their odds ratios illustrate the increased likelihood of withholding OAC for every five units increase (e.g., going from age 45 to 50, or age 80 to 85).

Variable	Wald Chi-square − DF	Odds ratio (95% CI)
Country	1622	
Type of AF (ref.: Permanent/Persistent)	243	
Paroxysmal/New onset (unclassified)		1.76 (1.64-1.89)
History of bleeding	186	3.14 (2.67-3.70)
Care setting specialty (ref.: Cardiology)	120	
Internal Medicine/Neurology/Geriatrics		1.39 (1.28-1.51)
Primary care/GP		1.70 (1.53-1.90)
Age, five-years increase	106	
Age up to 75		0.94 (0.92-0.96)
Age greater than 75		1.22 (1.18-1.27)
Vascular disease	83	1.37 (1.28-1.47)
Cohort (ref.: Cohort 3, 2013-2014)	73	
Cohort 4 (2014- 2015)		0.79 (0.74-0.85)
Cohort 5 (2015 -2016)		0.74 (0.69-0.79)
Prior stroke/TIA/SE	44	0.73 (0.67-0.80)
Care setting location (ref.: Hospital)	33	
Emergency room		1.12 (1.01-1.25)
Office/AC clinic/Thrombosis centre		0.80 (0.74-0.88)
BMI, 5 kg/m^2 increase	23	0.93 (0.90-0.96)
VTE	19	0.62 (0.50-0.76)

Cirrhosis	15	2.13 (1.47-3.08)
Hypertension	14	0.86 (0.79-0.93)
Dementia	13	1.50 (1.21-1.85)
Hypercholesterolemia	6	0.92 (0.86-0.98)
Diabetes	2	0.95 (0.88-1.02)
Race/Ethnicity (ref.: Caucasian)	2	
Hispanic/Latino		1.19 (0.97-1.46)
Asian		1.27 (0.95-1.69)
Black/mixed/other		1.03 (0.82-1.30)

OAC: oral anticoagulation, AF: atrial fibrillation, BMI: body mass index, CKD: chronic kidney disease, GP: general practitioner, SE: systemic embolism, TIA: transient ischemic attack, VTE: venous thromboembolism