

Contemporary stroke prevention strategies in 11 096 European patients with atrial fibrillation: a report from the EURObservational Research Programme on Atrial Fibrillation (EORP-AF) Long-Term General Registry

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Aims

Contemporary data regarding atrial fibrillation (AF) management and current use of oral anticoagulants (OACs) for stroke prevention are needed.

Methods and results

The EURObservational Research Programme on AF (EORP-AF) Long-Term General Registry analysed consecutive AF patients presenting to cardiologists in 250 centres from 27 European countries. From 2013 to 2016, 11 096 patients were enrolled (40.7% female; mean age 69 ± 11 years). At discharge, OACs were used in 9379 patients (84.9%), with non-vitamin K antagonists (NOACs) accounting for 40.9% of OACs. Antiplatelet therapy alone was used by 20% of patients, while no antithrombotic treatment was prescribed in 6.4%. On multivariable analysis, age, hypertension, previous ischaemic stroke, symptomatic AF and planned cardioversion or ablation were independent predictors of OAC use, whereas lone AF, previous haemorrhagic events, chronic kidney disease and admission for acute coronary syndrome (ACS) or non-cardiovascular causes independently predicted OAC non-use. Regarding the OAC type, coronary artery disease, history of heart failure, or valvular heart disease, planned cardioversion and non-AF reasons for admission independently predicted the use of vitamin K antagonists (VKAs). Wide variability among the European regions was observed in the use of NOACs, independently from other clinical factors.

Conclusion

The EORP-AF Long-Term General Registry provides a full picture of contemporary use of OAC in European AF patients. The overall rate of OACs use was generally high (84.9%), and a series of factors were associated with the prescription of OAC. A significant geographical heterogeneity in prescription of NOACs vs. VKAs was evident.

[†] Listed in Supplementary material online, Appendix 1.

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Keywords

Atrial fibrillation • Epidemiology • Thromboembolic risk • Stroke • Mortality • Registry

What's new?

- In recent years, the management of atrial fibrillation (AF) has progressively changed, for example, with the introduction of non-vitamin K antagonist oral anticoagulants (NOACs) instead of vitamin K antagonist (VKA).
- The EURObservational Research Programme on AF Long-Term General Registry provides an overall comprehensive picture of AF management among European countries.
- Treatment with oral anticoagulant was high, mostly due to the progressive uptake of NOACs, and can be associated with various clinical features.
- Geographical variation was found in the prescription of NOACs over VKA, with Northern and Western European countries being those where NOACs were most prescribed.

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia encountered in clinical practice and is particularly frequent in the elderly.^{1,2} AF is associated with adverse outcomes and particularly with a significantly increased risk of stroke, death, and heart failure.¹ Oral anticoagulant (OAC) therapy significantly reduces the risk of AF-related thromboembolic events and mortality and should be recommended in every patient at risk.¹ In recent years, the availability of non-vitamin K antagonist oral anticoagulants (NOACs) as an alternative to vitamin K antagonist (VKA) has offered new opportunities for stroke prevention in AF patients, but there is still the need to assess the actual implementation of these evidence-based therapies in 'real-world' clinical practice.

The European Society of Cardiology (ESC)-sponsored EURObservational Research Programme on AF (EORP-AF) General Long-Term Registry aimed to evaluate contemporary management of AF patients by European cardiologists and physicians, the current use of VKA, NOACs and other treatments in AF, in relation to guideline recommendations. The EORP-AF General Long-Term Registry follows the EORP-AF Pilot Registry, which provided initial information on a smaller cohort from a limited number of countries in the early period following the introduction of NOACs.^{3–5}

The main aim of this article was to report the baseline clinical profile of AF patients enrolled in EORP AF General Long-Term Registry. Secondly, we focused on reporting specifically about OAC therapy use and to explore the main clinical determinants of OAC prescription as well as the factors influencing prescription of either VKA or NOACs.

Methods**Study cohort**

The EORP-AF Long-Term General Registry is a prospective, observational, large-scale multicentre registry sponsored and conducted by the ESC, enrolling AF patients in current cardiology practices in 250 centres from 27 participating ESC countries. Patients were enrolled consecutively

when presenting with AF as primary or secondary diagnosis to inpatients and outpatient cardiology services from October 2013 to September 2016. Main inclusion criteria were the following: (i) the qualifying AF event had to be recorded by a 12-lead ECG, 24 h ECG Holter, or other electrocardiographic documentation within 12 months before enrolment; (ii) age should be 18 years and older; and (iii) written informed consent form. Exclusion criteria were the following: (i) no objective proof of AF; (ii) being previously enrolled in the EORP-AF Pilot Registry; or (iii) being or planned to be enrolled in a pharmacological interventional clinical trial. The study protocol was substantially similar to that of the EORP-AF Pilot Registry reported elsewhere.^{3–5} An institutional review board for every participating institution approved the study protocol. The study was performed according to the European Union Note for Guidance on Good Clinical Practice CPMP/ECH/135/95 and the Declaration of Helsinki.

All data about baseline clinical characteristics and previous clinical history (Table 1), as well as history of previous interventional procedures (see Supplementary material online, Table S1), were collected by any investigator/sub-investigator during the clinical interview and/or using clinical notes and electronic clinical data archives, when available. Specific characteristics about main reasons for admission/consultation and symptomatic status (Table 2), as well as specific diagnostic procedures and interventional procedures performed during the admission/consultation (see Supplementary material online, Table S2), were collected at the moment of enrolment by any investigator and reported in specific study notes. All data collected were then entered into an electronic case report form. Data about the AF qualifying episode were compulsory, and all other data have been provided when available.

Thromboembolic risk was defined according to CHA₂DS₂-VASc [Congestive Heart Failure, Hypertension, Age \geq 75 years, Diabetes Mellitus, Stroke/Transient Ischaemic Attack, Vascular Disease, Age 65–74 years, Sex Category (Female)] score.⁶ Bleeding risk was assessed according to HAS-BLED [Hypertension, Abnormal renal/liver function, Stroke, Bleeding, Labile INR, Elderly (>65 years), Drug/Alcohol consumption].⁷ Symptomatic status was defined according to (European Heart Rhythm Association (EHRA) score.¹

Participating countries were grouped in European regions as follows: (i) Northern Europe—Denmark, Estonia, Latvia, Norway, UK; (ii) Western Europe—Belgium, France, Germany, Netherlands, Switzerland; (iii) Eastern Europe—Bulgaria, Czech Republic, Georgia, Kazakhstan, Kyrgyzstan, Poland, Romania, Russia; and (iv) Southern Europe—Albania, FYR Macedonia, Italy, Malta, Montenegro, Portugal, Serbia, Spain, Turkey.

Statistical analysis

Continuous variables were reported as mean \pm standard deviation or as median and interquartile range (IQR). Among-group comparisons were made using a non-parametric test (Kruskal–Wallis test). Categorical variables were reported as counts and percentages. Among-group comparisons were made using a χ^2 test or the Fisher's exact test (if any expected cell count was less than five). For qualitative variables, with more than two possibilities, the Monte Carlo estimates of the exact *P*-values are used.

A stepwise multiple logistic regression analysis was used to determine the clinical factors associated with OAC prescription, including in the model all the candidate variables (variables with *P* < 0.10 in univariate). A significance level of 0.05 is required to allow a variable into the model (SLENTRY = 0.05) and a significance level of 0.05 is required for a variable to stay in the model (SLSTAY = 0.05). No interaction was tested. A Hosmer and Lemeshow goodness-of-fit test was used to verify that the

Table 1 Baseline characteristics of enrolled patients according to type of AF

	All	First detected	Paroxysmal	Persistent	Long-standing persistent	Permanent	Unknown	P-value
Number of patients	11 096	1733	2850	2124	477	3718	194	
Percentage of all		15.6%	25.7%	19.1%	4.3%	33.5%	1.7%	
Demographics								
Age (years), median (IQR)	71.0 (63.0–77.0)	69.0 (61.0–77.0)	68.0 (60.0–75.0)	68.0 (60.0–75.0)	68.0 (61.0–76.0)	75.0 (67.0–80.0)	72.0 (65.0–79.0)	<0.0001
Age (years), mean ± SD	69.17 ± 11.42	67.77 ± 12.37	66.73 ± 11.93	66.65 ± 11.22	67.71 ± 11.15	73.23 ± 9.43	70.82 ± 10.80	<0.0001
Female gender, n (%)	4512/11 096 (40.7%)	722/1733 (41.7%)	1290/2850 (45.3%)	754/2124 (35.5%)	167/477 (35.0%)	1509/3718 (40.6%)	70/194 (36.1%)	<0.0001
Type of enrolling centre, n (%)								
Specialized	5161/7535 (68.5%)	926/1330 (69.6%)	1436/2122 (67.7%)	1175/1497 (78.5%)	222/340 (65.3%)	1270/2090 (60.8%)	132/156 (84.6%)	<0.0001
No specialized	2374/7535 (31.5%)	404/1330 (30.4%)	686/2122 (32.3%)	322/1497 (21.5%)	118/340 (34.7%)	820/2090 (39.2%)	24/156 (15.4%)	
Site of patient inclusion, n (%)								
Hospitalized	5792/11 095 (52.2%)	1172/1732 (67.7%)	1452/2850 (50.9%)	1186/2124 (55.8%)	237/477 (49.7%)	1657/3718 (44.6%)	88/194 (45.4%)	<0.0001
Outpatient/office based	5303/11 095 (47.8%)	560/1732 (32.3%)	1398/2850 (49.1%)	938/2124 (44.2%)	240/477 (50.3%)	2061/3718 (55.4%)	106/194 (54.6%)	<0.0001
Concomitant disease, n (%)								
Hypertension	6831/10 999 (62.1%)	947/1714 (55.3%)	1703/2836 (60.0%)	1238/2107 (58.8%)	288/472 (61.0%)	2558/3678 (69.5%)	97/192 (50.5%)	<0.0001
Coronary artery disease	3058/10 431 (29.3%)	408/1616 (25.2%)	807/2732 (29.5%)	482/2013 (23.9%)	117/437 (26.8%)	1185/3448 (34.4%)	59/185 (31.9%)	<0.0001
Myocardial infarction	1347/3058 (44.0%)	217/408 (53.2%)	339/807 (42.0%)	209/482 (43.4%)	38/117 (32.5%)	516/1185 (43.5%)	28/59 (47.5%)	0.0007
PCI/PTCA	1234/3058 (40.4%)	177/408 (43.4%)	314/807 (38.9%)	204/482 (42.3%)	42/117 (35.9%)	475/1185 (40.1%)	22/59 (37.3%)	0.5187
CABG	566/3058 (18.5%)	61/408 (15.0%)	114/807 (14.1%)	96/482 (19.9%)	28/117 (23.9%)	255/1185 (21.5%)	12/59 (20.3%)	0.0001
Angina	1004/3058 (32.8%)	105/408 (25.7%)	330/807 (40.9%)	158/482 (32.8%)	39/117 (33.3%)	355/1185 (30.0%)	17/59 (28.8%)	<0.0001
Lone atrial fibrillation	880/11 095 (7.9%)	206/1733 (11.9%)	333/2849 (11.7%)	206/2124 (9.7%)	39/477 (8.2%)	75/3718 (2.0%)	21/194 (10.8%)	<0.0001
Heart failure	4343/11 001 (39.5%)	562/1714 (32.8%)	823/2830 (29.1%)	722/2107 (34.3%)	217/475 (45.7%)	1972/3690 (53.4%)	47/185 (25.4%)	<0.0001
NYHA III/IV	1556/4337 (35.9%)	209/559 (37.4%)	214/822 (26.0%)	229/721 (31.8%)	65/217 (30.0%)	827/1971 (42.0%)	12/47 (25.5%)	<0.0001
Valvular alterations	5527/10 869 (50.9%)	699/1677 (41.7%)	1022/2805 (36.4%)	1009/2078 (48.6%)	279/470 (59.4%)	2434/3654 (66.6%)	84/185 (45.4%)	<0.0001
Dilated cardiomyopathy	987/10 959 (9.0%)	106/1707 (6.2%)	138/2822 (4.9%)	147/2092 (7.0%)	57/472 (12.1%)	524/3678 (14.2%)	15/188 (8.0%)	<0.0001
Hypertrophic cardiomyopathy	339/10 952 (3.1%)	37/1708 (2.2%)	76/2824 (2.7%)	59/2092 (2.8%)	19/470 (4.0%)	148/3670 (4.0%)	<0.0001	
Restrictive cardiomyopathy	21/10 957 (0.2%)	2/1707 (0.1%)		2/2093 (0.1%)	3/472 (0.6%)	11/3675 (0.3%)	3/188 (1.6%)	0.0001
Other cardiomyopathy	432/11 016 (3.9%)	50/1716 (2.9%)	71/2837 (2.5%)	94/2109 (4.5%)	28/473 (5.9%)	185/3690 (5.0%)	4/191 (2.1%)	<0.0001
Congenital heart disease	12/110 978 (1.1%)	19/1710 (1.1%)	24/2827 (0.8%)	33/2102 (1.6%)	7/471 (1.5%)	37/3678 (1.0%)	1/190 (0.5%)	0.2086
Pulmonary arterial hypertension	766/10 898 (7.0%)	82/1699 (4.8%)	102/2812 (3.6%)	114/2080 (5.5%)	32/470 (6.8%)	430/3647 (11.8%)	6/190 (3.2%)	<0.0001
Other cardiac disease	274/10 829 (2.5%)	38/1695 (2.2%)	73/2794 (2.6%)	71/2068 (3.4%)	8/468 (1.7%)	79/3617 (2.2%)	5/187 (2.7%)	0.0771
Chronic obstructive pulmonary disease	979/11 011 (8.9%)	126/1724 (7.3%)	198/2821 (7.0%)	141/2114 (6.7%)	35/472 (7.4%)	458/3689 (12.4%)	21/191 (11.0%)	<0.0001
Hyperthyroidism	497/10 833 (4.6%)	50/1684 (3.0%)	135/2794 (4.8%)	100/2077 (4.8%)	26/460 (5.7%)	184/3627 (5.1%)	2/191 (1.0%)	0.0003
Hypothyroidism	1031/10 850 (9.5%)	136/1688 (8.1%)	295/2795 (10.6%)	192/2078 (9.2%)	35/462 (7.6%)	356/3636 (9.8%)	17/191 (8.9%)	0.0676
Thyroid disease or disorder	1558/10 869 (14.3%)	191/1686 (11.3%)	435/2796 (15.6%)	288/2080 (13.8%)	65/465 (14.0%)	559/3651 (15.3%)	20/191 (10.5%)	0.0004
Cardiovascular risk factors, n (%)								
Diabetes mellitus	2537/11 028 (23.0%)	343/1726 (19.9%)	590/2833 (20.8%)	386/2114 (18.3%)	106/475 (22.3%)	1074/3687 (29.1%)	38/193 (19.7%)	<0.0001
Lipid disorder	4392/10 621 (41.4%)	579/1654 (35.0%)	1211/2752 (44.0%)	817/2027 (40.3%)	192/447 (43.0%)	1539/3559 (43.2%)	54/182 (29.7%)	<0.0001
Current smoker	982/10 269 (9.6%)	219/1657 (13.2%)	309/2686 (11.5%)	202/2009 (10.1%)	49/464 (10.6%)	193/3281 (5.9%)	10/172 (5.8%)	<0.0001
No regular exercise	4094/9525 (43.0%)	596/1522 (39.2%)	935/2465 (37.9%)	685/1762 (38.9%)	182/439 (41.5%)	1625/3186 (51.0%)	71/151 (47.0%)	<0.0001

Continued

Table 1 Continued

	All	First detected	Paroxysmal	Persistent	Long-standing persistent	Permanent	Unknown	P-value
Comorbidities, n (%)								
Previous thromboembolic events	1274/10 992 (11.6%)	149/1720 (8.7%)	309/2831 (10.9%)	225/2109 (10.7%)	52/474 (11.0%)	513/3667 (14.0%)	26/191 (13.6%)	<0.0001
Previous ischaemic stroke	680/10 991 (6.2%)	60/1720 (3.5%)	162/2831 (5.7%)	103/2109 (4.9%)	23/474 (4.9%)	318/3666 (8.7%)	14/191 (7.3%)	<0.0001
Previous TIA	332/10 991 (3.0%)	47/1720 (2.7%)	96/2831 (3.4%)	73/2109 (3.5%)	14/474 (3.0%)	97/3666 (2.6%)	5/191 (2.6%)	0.4243
Haemorrhagic events	572/10 984 (5.2%)	53/1723 (3.1%)	125/2821 (4.4%)	89/2113 (4.2%)	19/473 (4.0%)	281/3665 (7.7%)	5/189 (2.6%)	<0.0001
Malignancy	818/11 021 (7.4%)	141/1721 (8.2%)	208/2840 (7.3%)	155/2111 (7.3%)	35/472 (7.4%)	263/3684 (7.1%)	16/193 (8.3%)	0.8031
Peripheral vascular disease	883/10 853 (8.1%)	109/1692 (6.4%)	199/2793 (7.1%)	133/2077 (6.4%)	43/468 (9.2%)	388/3633 (10.7%)	11/190 (5.8%)	<0.0001
Chronic kidney disease	1379/11 015 (12.5%)	165/1726 (9.6%)	285/2839 (10.0%)	208/2118 (9.8%)	49/472 (10.4%)	656/3668 (17.9%)	16/192 (8.3%)	<0.0001

AF, atrial fibrillation; CABG, coronary artery by-pass graft; IQR, interquartile range; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; SD, standard deviation; TIA, transient ischaemic attack.

Table 2 Patient characteristics on admission/consultation

	All	First detected	Paroxysmal	Persistent	Long-standing persistent	Permanent	Unknown	P-value
Number of patients	11 096	1733	2850	2124	477	3718	194	
Main reason for admission/consultation, n (%)								
Atrial fibrillation	7303/11 095 (65.8%)	1252/1733 (72.2%)	2084/2849 (73.1%)	1781/2124 (83.9%)	341/477 (71.5%)	1730/3718 (46.5%)	115/194 (59.3%)	<0.0001
Acute coronary syndrome	388/11 095 (3.5%)	93/1733 (5.4%)	128/2849 (4.5%)	33/2124 (1.6%)	7/477 (1.5%)	120/3718 (3.2%)	7/194 (3.6%)	
Valvular heart disease	321/11 095 (2.9%)	34/1733 (2.0%)	33/2849 (1.2%)	26/2124 (1.2%)	9/477 (1.9%)	212/3718 (5.7%)	7/194 (3.6%)	
Hypertension	236/11 095 (2.1%)	28/1733 (1.6%)	69/2849 (2.4%)	15/2124 (0.7%)	10/477 (2.1%)	109/3718 (2.9%)	5/194 (2.6%)	
Heart failure	1157/11 095 (10.4%)	128/1733 (7.4%)	132/2849 (4.6%)	112/2124 (5.3%)	45/477 (9.4%)	733/3718 (19.7%)	7/194 (3.6%)	
Other coronary artery disease	321/11 095 (2.9%)	18/1733 (1.0%)	89/2849 (3.1%)	34/2124 (1.6%)	14/477 (2.9%)	158/3718 (4.2%)	8/194 (4.1%)	
Other cardiovascular	820/11 095 (7.4%)	108/1733 (6.2%)	197/2849 (6.9%)	90/2124 (4.2%)	21/477 (4.4%)	372/3718 (10.0%)	32/194 (16.5%)	
Other non-cardiovascular	549/11 095 (4.9%)	72/1733 (4.2%)	117/2849 (4.1%)	33/2124 (1.6%)	30/477 (6.3%)	284/3718 (7.6%)	13/194 (6.7%)	
Symptoms, n (%)								
No	5039/11 096 (45.4%)	566/1733 (32.7%)	1218/2850 (42.7%)	748/2124 (35.2%)	162/477 (34.0%)	2257/3718 (60.7%)	88/194 (45.4%)	<0.0001
Yes	6057/11 096 (54.6%)	1167/1733 (67.3%)	1632/2850 (57.3%)	1376/2124 (64.8%)	315/477 (66.0%)	1461/3718 (39.3%)	106/194 (54.6%)	
If no current—symptoms in the past	2484/5034 (49.3%)	176/566 (31.1%)	771/1216 (63.4%)	345/748 (46.1%)	92/162 (56.8%)	1068/2254 (47.4%)	32/88 (36.4%)	<0.0001

model was optimal. A similar approach was then used to establish the clinical factors associated with either VKA or NOAC prescription. A two-sided P -value <0.05 was considered statistically significant. All analyses were performed using SAS statistical software version 9.3 (SAS Institute, Inc., Cary, NC, USA).

Results

From October 2013 to September 2016, 11 096 patients were enrolled in 250 centres from 27 participating ESC countries, 40.7% female; median (IQR) age 71 (63–77) years. Overall, 5161 (68.5%) patients were enrolled in a specialized centre, whereas 52.2% of patients were enrolled in-hospital and 47.8% were enrolled as outpatients.

Hypertension was the most commonly reported co-morbidity (62.1%), whereas 3058 patients had a concomitant diagnosis of coronary artery disease, with most (44.0%) patients reporting a previous myocardial infarction. A concomitant diagnosis of heart failure was found in 4343 (39.5%) patients with 35.9% reporting New York Heart Association (NYHA) Class III/IV. A previous thromboembolic event (defined as previous stroke, TIA, or systemic embolism) was recorded in 1274 (11.6%) patients. Among non-cardiac risk factors or co-morbidities, chronic kidney disease was the most commonly reported (12.5%). Overall, median (IQR) $\text{CHA}_2\text{DS}_2\text{-VASc}$ was 3 (2–4), whereas median (IQR) HAS-BLED score was 1 (1–2).

AF was the main reason for admission in most of the patients (7303, 65.8%). The most reported AF subtype was permanent AF (33.5%), whereas 25.7% (2850) of patients reported a paroxysmal AF. Baseline and patient characteristics at admission according to AF subtypes are reported in *Tables 1 and 2*.

Baseline clinical characteristics and previous clinical history

Compared to the other subtypes, permanent AF patients were older [median (IQR) age 75 (67–80) years] than those with paroxysmal and persistent AF [median (IQR) age 68 (60–75) years] ($P < 0.0001$). Patients with paroxysmal AF were more likely to be female ($P < 0.0001$). First detected AF patients were more likely to be hospitalized than the other subtypes ($P < 0.0001$).

Both hypertension and coronary artery disease, as well as heart failure, valvular disease and dilated cardiomyopathy, were more commonly reported in patients with permanent AF (all $P < 0.0001$). Conversely, myocardial infarction was more likely have occurred in patients with first detected AF (53.2%; $P = 0.0007$). Lone AF was more prevalent in patients with first detected and paroxysmal AF (11.9% and 11.7%, respectively; $P < 0.0001$).

Among concomitant risk factors, diabetes mellitus and absence of regular exercise were more likely reported in patients with permanent AF (29.1% and 51.0%, respectively; $P < 0.0001$), whereas lipid disorders were more common in patients with paroxysmal AF (44.0%), long-standing AF (43.0%), and permanent AF (43.2%) ($P < 0.0001$). Active smoking was more prevalent in patients with first detected AF. Patients with permanent AF had more prevalent non-cardiac co-morbidities, such as chronic obstructive pulmonary disease (12.4%), previous thromboembolic events (14.0%), previous stroke (8.7%), previous haemorrhagic event (7.7%), peripheral vascular disease (10.7%), and chronic kidney disease (17.9%) (all $P < 0.0001$).

Patient characteristics on admission/consultation

AF was more commonly reported as the main reason for admission/consultation in patients with persistent AF (83.9%), whereas heart failure was the most common reason for admission with permanent AF (19.7%) ($P < 0.0001$). Patients with permanent AF were more likely to be asymptomatic (60.7%), whereas patients with first-detected AF were more commonly symptomatic (67.3%) ($P < 0.0001$). Among the asymptomatic patients, those with paroxysmal AF were more frequently symptomatic in the past (63.4%), compared with other AF subtypes ($P < 0.0001$).

Previous interventions and procedures during admission/consultation

The history of previous interventions is reported in [Supplementary material online, Table S1](#). Approximately a quarter of patients (2347 patients, 23.0%) underwent a pharmacological cardioversion procedure in their recent clinical history, more commonly among inpatients with paroxysmal AF ($P < 0.0001$). Electrical cardioversion was used in 19.2%, especially in those with persistent AF ($P < 0.0001$).

During the admission (or at the moment of consultation), the most common diagnostic investigation procedure was transthoracic echocardiography (86.1%), followed by Holter monitoring (29.0%), coronary angiography (23.7%), and exercise testing (15.9%) (see [Supplementary material online, Table S2](#)). Also, electrical cardioversion was mostly used during admission (or planned during consultation) in patients with persistent AF (45.2%, $P < 0.0001$). Pharmacological cardioversion was mostly used (or planned) in patients with first-detected AF (17.5%) compared to those with paroxysmal AF (12.5%) ($P < 0.0001$).

Thromboembolic and bleeding risks

Thromboembolic and bleeding risks according to AF subtypes have been reported in *Table 3*. Patients with permanent AF reported the highest thromboembolic risk ($\text{CHA}_2\text{DS}_2\text{-VASc}$ mean \pm SD 3.77 \pm 1.65) and bleeding risk (HAS-BLED mean \pm SD 1.83 \pm 1.05) compared to patients with other AF subtypes (both $P < 0.0001$); also, they reported the highest prevalence of most thromboembolic and bleeding risk factors (see [Supplementary material online, Table S3](#)).

Antithrombotic treatments

As shown in *Table 4*, in most of the patients (9379, 84.9%), an OAC drug was used, less likely prescribed in paroxysmal AF and first-detected AF ($P < 0.0001$). Also, 2212 (20.0%) patients were prescribed antiplatelet drugs, with the majority of them treated with aspirin (1987 patients, 17.9%), mostly in patients with first-detected AF and paroxysmal AF (both $P < 0.0001$).

Of those on OAC, half of the patients (50.2%) were treated with a VKA, especially with permanent AF ($P < 0.0001$). Conversely, a NOAC was used in 3835 (34.8%) patients, more likely in those diagnosed with with first-detected and persistent AF ($P < 0.0001$). Among patients treated with OAC, a small proportion was treated with concomitant antiplatelet drugs (1361 patients, 14.5%), more likely in patients with first-detected AF (17.1%) ($P < 0.0001$).

Even in patients with low thromboembolic risk ($\text{CHA}_2\text{DS}_2\text{-VASc}$ 0 in males), 447 (62.8%) patients were treated with OAC (*Figure 1*).

Table 3 Thromboembolic and bleeding risk scores

	All	First detected	Paroxysmal	Persistent	Long-standing persistent	Permanent	Unknown	P-value
CHA ₂ DS ₂ -VASc score								
Median (IQR)	3.0 (2.0–4.0)	3.0 (2.0–4.0)	3.0 (2.0–4.0)	3.0 (1.0–4.0)	3.0 (2.0–4.0)	4.0 (3.0–5.0)	3.0 (2.0–4.0)	<0.0001
Mean ± SD	3.14 ± 1.77	2.84 ± 1.70	2.85 ± 1.79	2.73 ± 1.71	2.97 ± 1.71	3.77 ± 1.65	3.01 ± 1.62	<0.0001
HAS-BLED score								
Median (IQR)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	2.0 (1.0–2.0)	2.0 (1.0–2.0)	<0.0001
Mean ± SD	1.56 ± 1.07	1.42 ± 1.06	1.44 ± 1.08	1.39 ± 1.04	1.42 ± 0.98	1.83 ± 1.05	1.59 ± 0.99	<0.0001

IQR, interquartile range; SD, standard deviation.

Many of these (202 patients, 45.2%) underwent or were planned for a cardioversion procedure (either pharmacological or electrical). In patients with a higher CHA₂DS₂-VASc score, the use of OAC was consistently high (around 80%). On the basis of the HAS-BLED score (Figure 2), 1359 (77.3%) patients with HAS-BLED 0 were treated with OAC as well as a similar, or even higher, proportion of patients in the other score strata.

Overall, patients prescribed with OAC at discharge were older ($P < 0.0001$) and had more prevalent cardiovascular risk factors (diabetes mellitus and lipid disorders), hypertension, and previous thromboembolic events and stroke (see [Supplementary material online, Table S4](#)). Conversely, those patients not prescribed with OAC were more likely to be affected by coronary artery disease, myocardial infarction, peripheral vascular disease, and chronic kidney disease. Comparing patients prescribed with VKA and NOACs (see [Supplementary material online, Table S5](#)), patients prescribed with NOACs were younger and had fewer risk factors and co-morbidities. Patients with less established AF types (first-detected and paroxysmal AF) were less likely prescribed with OAC (see [Supplementary material online, Table S4](#)), but when prescribed they were more likely prescribed with NOACs (see [Supplementary material online, Table S5](#)).

Looking at regional distribution, OAC were more likely prescribed in Western Europe (see [Supplementary material online, Table S4](#)), whereas among OAC prescribed patients, NOACs were more likely prescribed in both Northern and Western Europe (see [Supplementary material online, Table S5](#)), in particular in Northern Europe, as shown by the VKA/NOACs ratio, with Northern Europe being the region that prevalently prescribe NOACs among the others (Figure 3). Considering the year of enrolment, both OAC and NOACs were prevalently more prescribed in the last 2 years of enrolment (both $P < 0.0001$).

After univariate analysis (see [Supplementary material online, Table S6](#)), multivariable logistic analysis recognized several clinical factors as independent predictors of OAC use (Table 5, Panel A). Of these, progressively increasing age ($P < 0.0001$), hypertension ($P < 0.0001$), previous ischaemic stroke ($P = 0.0024$), and worsened symptomatic status ($P < 0.0001$) were directly associated with the use of OAC; conversely, a history of myocardial infarction ($P = 0.0046$), lone AF ($P < 0.0001$), prior haemorrhagic events ($P < 0.0001$), and chronic kidney disease ($P = 0.0152$) were inversely associated with OAC prescription. Compared to first-detected AF, patients with persistent, long-standing persistent and permanent AF were more likely associated with OAC prescription (all $P < 0.0001$). Among reasons for admission/consultation,

those with acute coronary syndrome and hypertension were inversely associated with the use of OACs ($P < 0.0001$ and $P = 0.0031$, respectively). Also, compared to Eastern Europe, all the other European regions were independently associated with OAC prescription (all $P < 0.0001$), in particular those patients coming from Western Europe were those more likely prescribed with OAC (Table 5, Panel A).

With regard to independent predictors of NOAC use vs. VKAs (Table 5, Panel B), after selection of variables through a univariate analysis (see [Supplementary material online, Table S7](#)), multivariable analysis found that history of coronary artery disease ($P < 0.0001$), heart failure ($P = 0.0195$), valvular heart disease ($P < 0.0001$), pulmonary arterial hypertension ($P = 0.0233$), and pharmacological cardioversion ($P = 0.0001$) were inversely associated with NOACs use. Compared to first-diagnosed AF, all other AF subtypes were significantly inversely associated with the use of NOACs. Non-AF related causes of admission were inversely associated with NOACs use. Compared to those in Eastern Europe, patients prescribed with OAC in both Northern and Western Europe were associated with NOACs prescription ($P = 0.0073$ and $P = 0.0018$, respectively), while being in Southern Europe was inversely associated with NOACs prescription ($P = 0.0005$). Looking at the year of enrolment, being enrolled in the EORP-AF Long-Term Registry more recently is directly associated with NOACs prescription (Table 5, Panel B).

Discussion

The EORP-AF Long-Term General Registry provides an updated 'snapshot' of the management of AF in the cardiology setting, including both inpatients and outpatients. The number of patients enrolled (more than 11 000) recruited in 27 countries makes this independent ESC-sponsored registry a relevant reference for depicting current practice for AF patient management in Europe.

A few findings are confirmatory. AF patients are often elderly and very frequently affected by several co-morbidities. Specifically, our registry provides novel data on the current prescription of OACs and on the prescription of NOACs vs. VKAs, with the advantage of being an independent registry. At discharge, OACs were used in 84.9% of patients, with NOACs accounting for around 41% of all OACs prescribed. As compared to EORP-AF Pilot data,³ this implies an increase, even if just moderate, in the overall use of OACs in AF of around 5% and should be viewed as a positive finding, able to counteract the previously reported underuse of oral anticoagulation. As

Table 4 Pharmacological treatments at discharge/after consultation

	All	First detected	Paroxysmal	Persistent	Long-standing persistent	Permanent	Unknown	P-value
Number of patients	11 096	1733	2850	2124	477	3718	194	
Antithrombotic treatment, n (%)								
Any antithrombotic	10 338/11 050 (93.6%)	1550/1717 (90.3%)	2563/2836 (90.4%)	2031/2118 (95.9%)	461/474 (97.3%)	3564/3713 (96.0%)	169/192 (88.0%)	<0.0001
ASA	1987/11 078 (17.9%)	366/1725 (21.2%)	626/2842 (22.0%)	300/2124 (14.1%)	52/477 (10.9%)	598/3716 (16.1%)	45/194 (23.2%)	<0.0001
Clopidogrel	702/11 077 (6.3%)	126/1724 (7.3%)	218/2842 (7.7%)	95/2124 (4.5%)	20/477 (4.2%)	223/3716 (6.0%)	20/194 (10.3%)	<0.0001
Any antiplatelets	2212/11 079 (20.0%)	396/1725 (23.0%)	691/2843 (24.3%)	338/2124 (15.9%)	59/477 (12.4%)	672/3716 (18.1%)	56/194 (28.9%)	<0.0001
VKAs	5544/11 038 (50.2%)	596/1714 (34.8%)	1148/2832 (40.5%)	947/2115 (44.8%)	258/474 (54.4%)	2506/3712 (67.5%)	89/191 (46.6%)	<0.0001
Dabigatran	855/11 033 (7.7%)	102/1711 (6.0%)	249/2831 (8.8%)	250/2115 (11.8%)	50/474 (10.5%)	200/3711 (5.4%)	4/191 (2.1%)	<0.0001
Rivaroxaban	1817/11 030 (16.5%)	379/1710 (22.2%)	489/2829 (17.3%)	451/2115 (21.3%)	89/474 (18.8%)	378/3711 (10.2%)	31/191 (16.2%)	<0.0001
Apixaban	1058/11 029 (9.6%)	242/1709 (14.2%)	268/2829 (9.5%)	262/2115 (12.4%)	39/474 (8.2%)	229/3711 (6.2%)	18/191 (9.4%)	<0.0001
Edoxaban	105/11 031 (1.0%)	35/1711 (2.0%)	32/2829 (1.1%)	9/2115 (0.4%)	1/474 (0.2%)	25/3711 (0.7%)	3/191 (1.6%)	<0.0001
Any NOAC	3835/11 033 (34.8%)	758/1711 (44.3%)	1038/2831 (36.7%)	972/2115 (46.0%)	179/474 (37.8%)	832/3711 (22.4%)	56/191 (29.3%)	<0.0001
Any OAC	9379/11 041 (84.9%)	1354/1715 (79.0%)	2186/2834 (77.1%)	1919/2115 (90.7%)	437/474 (92.2%)	3338/3712 (89.9%)	145/191 (75.9%)	<0.0001
Heparins	376/11 075 (3.4%)	91/1723 (5.3%)	90/2841 (3.2%)	66/2124 (3.1%)	12/477 (2.5%)	106/3716 (2.9%)	11/194 (5.7%)	0.0001
None	712/11 050 (6.4%)	167/1717 (9.7%)	273/2836 (9.6%)	87/2118 (4.1%)	13/474 (2.7%)	149/3713 (4.0%)	23/192 (12.0%)	<0.0001
Antiarrhythmic treatment, n (%)								
Any antiarrhythmic	3064/11 040 (27.8%)	412/1721 (23.9%)	1245/2832 (44.0%)	900/2119 (42.5%)	146/477 (30.6%)	335/3699 (9.1%)	26/192 (13.5%)	<0.0001
Amiodarone	1971/11 042 (17.9%)	304/1721 (17.7%)	645/2834 (22.8%)	588/2119 (27.7%)	107/477 (22.4%)	305/3699 (8.2%)	22/192 (11.5%)	<0.0001
Dronedarone	33/11 046 (0.3%)	3/1723 (0.2%)	16/2832 (0.6%)	10/2121 (0.5%)	1/477 (0.2%)	1/3701 (0.0%)	2/192 (1.0%)	<0.0001
Propafenone	396/11 047 (3.6%)	47/1723 (2.7%)	244/2833 (8.6%)	72/2121 (3.4%)	15/477 (3.1%)	18/3701 (0.5%)		<0.0001
Flecainide	360/11 047 (3.3%)	32/1723 (1.9%)	193/2833 (6.8%)	123/2121 (5.8%)	12/477 (2.5%)			<0.0001
Sotalol	299/11 047 (2.7%)	24/1723 (1.4%)	147/2833 (5.2%)	106/2121 (5.0%)	11/477 (2.3%)	9/3701 (0.2%)	2/192 (1.0%)	<0.0001
None	7976/11 040 (72.2%)	1309/1721 (76.1%)	1587/2832 (56.0%)	1219/2119 (57.5%)	331/477 (69.4%)	3364/3699 (90.9%)	166/192 (86.5%)	<0.0001
Other treatments, n (%)								
Other treatments 'yes'	10 445/11 063 (94.4%)	1609/1728 (93.1%)	2631/2839 (92.7%)	1988/2122 (93.7%)	460/477 (96.4%)	3587/3705 (96.8%)	170/192 (88.5%)	<0.0001
ACE inhibitors	4735/11 042 (42.9%)	715/1723 (41.5%)	1125/2833 (39.7%)	843/2118 (39.8%)	210/477 (44.0%)	1777/3700 (48.0%)	65/191 (34.0%)	<0.0001
ARBs	2096/11 043 (19.0%)	252/1723 (14.6%)	581/2831 (20.5%)	427/2119 (20.2%)	102/477 (21.4%)	709/3702 (19.2%)	25/191 (13.1%)	<0.0001
Beta-blockers	7645/11 048 (69.2%)	1243/1724 (72.1%)	1869/2835 (65.9%)	1457/2121 (68.7%)	349/477 (73.2%)	2604/3700 (70.4%)	123/191 (64.4%)	0.0001
Digoxin	1619/11 042 (14.7%)	196/1722 (11.4%)	147/2831 (5.2%)	228/2120 (10.8%)	78/477 (16.4%)	946/3700 (25.6%)	24/192 (12.5%)	<0.0001
Diuretics	5701/11 042 (51.6%)	757/1723 (43.9%)	1060/2832 (37.4%)	937/2119 (44.2%)	276/476 (58.0%)	2586/3701 (69.9%)	85/191 (44.5%)	<0.0001
Aldosterone blockers	2014/11 040 (18.2%)	247/1722 (14.3%)	281/2831 (9.9%)	282/2119 (13.3%)	104/476 (21.8%)	1076/3701 (29.1%)	24/191 (12.6%)	<0.0001
DHP calcium-channel blockers	1857/11 045 (16.8%)	289/1724 (16.8%)	551/2832 (19.5%)	331/2120 (15.6%)	72/477 (15.1%)	583/3701 (15.8%)	31/191 (16.2%)	0.0014
Statins	4663/11 042 (42.2%)	674/1721 (39.2%)	1274/2832 (45.0%)	845/2120 (39.9%)	206/477 (43.2%)	1595/3702 (43.1%)	69/190 (36.3%)	0.0001
Oral antidiabetics	1689/11 050 (15.3%)	218/1724 (12.6%)	390/2833 (13.8%)	288/2121 (13.6%)	72/477 (15.1%)	704/3704 (19.0%)	17/191 (8.9%)	<0.0001
Insulin	617/11 045 (5.6%)	76/1723 (4.4%)	142/2831 (5.0%)	83/2122 (3.9%)	25/477 (5.2%)	282/3701 (7.6%)	9/191 (4.7%)	<0.0001
Thyroid hormones	944/11 044 (8.5%)	136/1723 (7.9%)	251/2831 (8.9%)	180/2121 (8.5%)	29/477 (6.1%)	337/3700 (9.1%)	11/192 (5.7%)	0.1393
Thyroid-suppressing drugs	218/11 043 (2.0%)	23/1723 (1.3%)	55/2831 (1.9%)	37/2121 (1.7%)	10/477 (2.1%)	93/3700 (2.5%)		0.0131

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid; DHP, dihydropyridine; DRI, direct renin inhibitor; NOAC, non-vitamin K oral anticoagulant; OAC, oral anticoagulant; VKA, vitamin K antagonists.

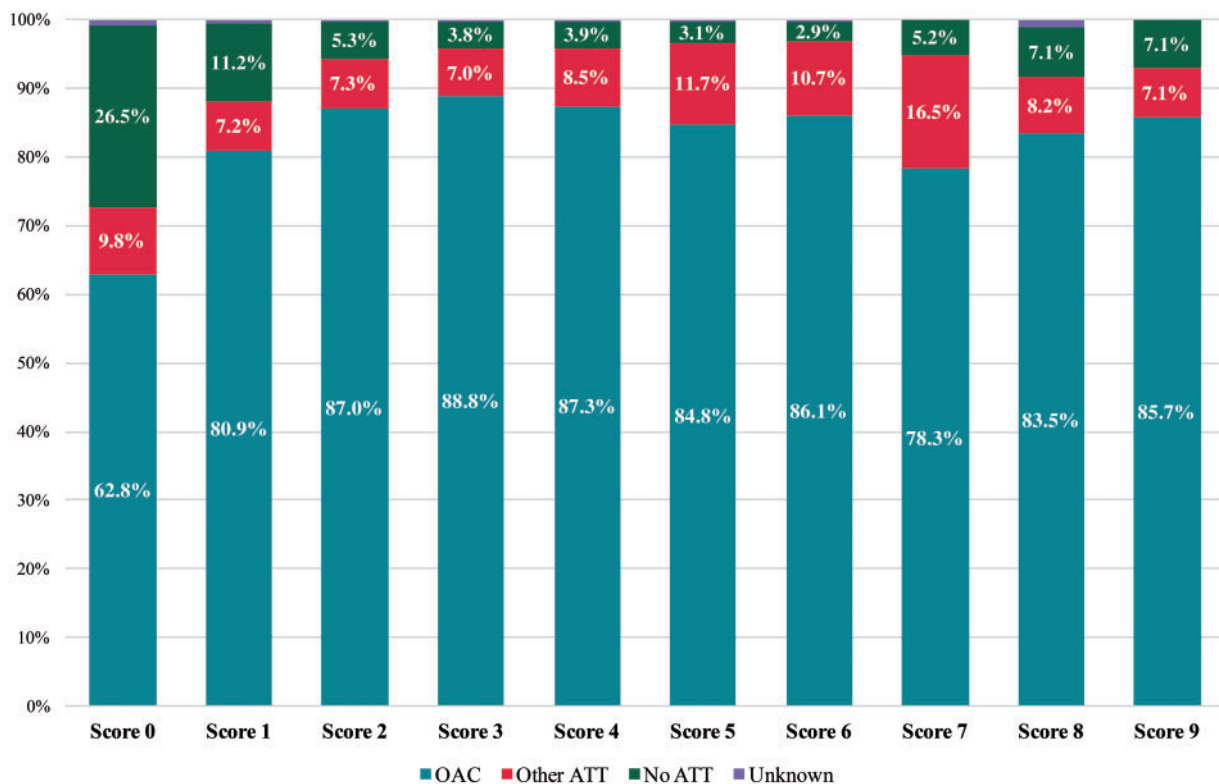


Figure 1 Proportions of patients treated with antithrombotic drugs by CHA₂DS₂-VASc score. ATT, antithrombotic therapy; OAC, oral anticoagulant.

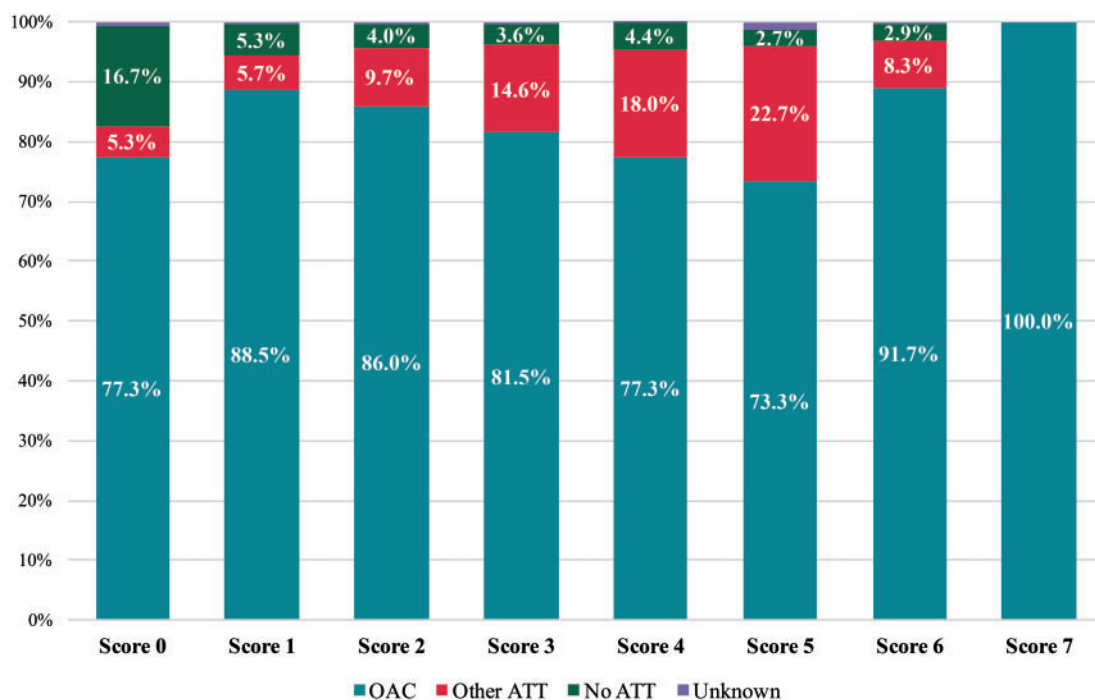
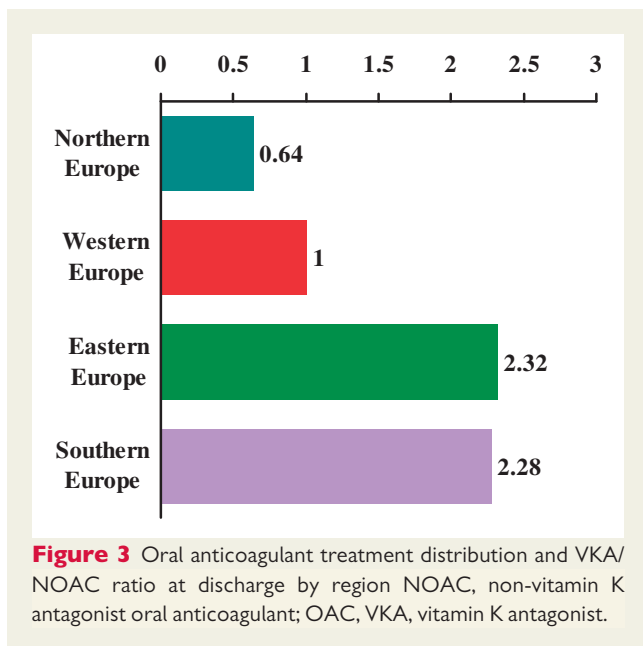


Figure 2 Proportions of patients treated with antithrombotic drugs by HAS-BLED score. ATT, antithrombotic therapy; OAC, oral anticoagulant.



previously reported,³ the rate of prescription according to CHA₂DS₂-VASc and HAS-BLED indicates the tendency to underuse OACs in patients who share both a high risk of bleeding and a high risk of stroke. Conversely, the high proportion of patients treated with OAC among those with low thromboembolic risk (CHA₂DS₂-VASc 0 in males or 1 in females) still depict the need for better implementation of guideline recommendations, notwithstanding that some patients were still undergoing diagnostic workup or were considered for planned cardioversion or ablation procedures, leading to a temporary increase in OAC prescription as per guidelines.¹ Even the lower likelihood of receiving OAC in patients with paroxysmal AF still underlines the lack of adherence to guideline recommendations. Our data show that the progressively increased use of OACs in AF patients is largely due to the progressive increase in NOACs uptake, as evident in several other large observational studies.^{8–10}

In our EORP-AF General Long-Term Registry, we identified independent predictors of OAC use, as well as of NOACs use, and this is a novel finding of specific interest. The use of OACs was related to most clinical characteristics and clinical conditions strongly associated (or perceived as) with an increased thromboembolic risk (i.e. older age, hypertension, previous thromboembolic events, and symptomatic AF), while all those conditions that usually imply an increased risk of bleeding were found associated with OAC non-use (i.e. chronic kidney disease and previous hemorrhagic events). In patients with concomitant cardiovascular disease, OAC therapy was more likely not to be used, despite the current guidelines recommendations.¹

The EORP-AF General Long-Term General Registry clearly outlines a significant implementation of NOACs in thromboembolic prophylaxis of AF, as compared to the picture reported by the EORP-AF Pilot.^{3,11} Over a 4-year period, the rate of prescription of NOACs increased from less than 10% of patients to around 35% of patients, with a significant increase in the latter years independently from all the other clinical factors, much likely reflecting the larger availability of NOACs throughout the European countries. With respect to independent predictors of NOACs, patients less clinically

complex were more likely to be treated with NOACs than compared with VKA.

Comparing our results to data from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation II (ORBIT-AF II) study,¹² different factors were associated with NOAC vs. VKA prescription only partially overlapping with those showed by our results, but a similar pattern was evident, with patients less affected with comorbidities more likely to be prescribed with NOACs. The finding that NOAC prescription is inversely associated with both coronary artery disease and pharmacological cardioversion procedure underlines how, despite some recent studies showing NOACs as safe alternatives in specific procedures such as coronary angiography¹³ and direct cardioversion,¹⁴ there is still a need for more evidence and physician awareness of safety of NOACs in such clinical scenarios. In a recent analysis from the PINNACLE study, an industry-independent US 'real-life' registry, predictors of both OAC and NOACs use were analysed, and patients presenting with cardiovascular and vascular disease were less likely treated both with OACs and NOACs.¹⁰ Our results showed how even in European countries a similar approach is still adopted.

The evidence presented significantly showed that clinical history of heart failure is an important feature in determining the use of NOACs. This evidence, together with those reported by ORBIT-AF II¹² and PINNACLE studies,¹⁰ suggest that despite the data coming from randomized trials showing that NOACs are a valid alternative for AF patients with heart failure,¹⁵ those patients are preferentially treated with VKA.

Our data underline a large variability in the use of NOACs across the European regions, clearly depicting a difference in acknowledgment and application of ESC guidelines, which since 2012 substantially recommend NOACs over VKAs. Despite the large effort to improve the appropriate prescription of OACs and management of AF patients, these differences appear to remain unchanged. Indeed, even in a previous analysis from the EORP AF Pilot, patients coming from Eastern and Southern Europe were less likely to be treated in accordance with the guidelines recommendations,¹⁶ as highlighted also by other data coming from Serbia¹⁷ and Italy.¹⁸ Notwithstanding, given the heterogeneity of health care systems among European countries, differences in affordability, prices, and compensations cannot be excluded as partially influencing the prescription of NOACs.

The specific type of AF (first-detected, paroxysmal, persistent, long-standing persistent, permanent) is associated with different patient profiles in terms of age, co-morbidities and associated diseases, associated symptoms, regular exercise, reason for admission/consultation, and risk factors for stroke and bleeding. Specifically, first-detected AF is usually diagnosed in hospitalized patients and is less frequently asymptomatic.¹⁹ In the EORP-AF Pilot Registry,^{3,20} we found that patients with first-detected AF had characteristics similar to persistent AF patients, but lower use of OAC. In the present analysis of the EORP-AF General Long-Term, we showed some improvement when compared with EORP-AF Pilot.^{3,20}

Strengths and limitations

The main limitation of our analysis is due to the observational nature of the study. Moreover, the EORP-AF General Long-Term Registry is based on cardiologists' practice, so our data would be considered carefully when extended to general practice. Also, since the EORP-

Table 5 Multivariable analysis for Independent predictors of anticoagulant treatments

	Odds ratio	95% CI	P Wald
A. Independent predictors of OAC use^a			
Age	1.018	1.011–1.024	<0.0001
Hypertension	1.362	1.175–1.579	<0.0001
Myocardial infarction	0.747	0.611–0.914	0.0046
Angina	0.508	0.414–0.624	<0.0001
Lone AF	0.320	0.258–0.397	<0.0001
Hyperthyroidism	1.522	1.072–2.191	0.0239
Lipid disorder	1.243	1.083–1.427	0.0020
Previous ischaemic stroke	1.634	1.190–2.243	0.0024
Haemorrhagic events	0.424	0.331–0.543	<0.0001
Malignancy	0.722	0.572–0.912	0.0063
Chronic kidney disease	0.779	0.636–0.953	0.0152
Pharmacological cardioversion for AF	0.814	0.692–0.957	0.0126
Electrical cardioversion for AF	1.819	1.462–2.264	<0.0001
Catheter ablation for AF	1.641	1.141–2.264	0.0075
AF type			
First-detected (reference)			
Paroxysmal	0.921	0.763–1.11	0.3890
Persistent	2.209	1.749–2.788	<0.0001
Long-standing persistent	2.601	1.717–3.940	<0.0001
Permanent	2.214	1.798–2.726	<0.0001
Main reason for admission/consultation			
AF (reference)			
Acute coronary syndrome	0.481	0.357–0.648	<0.0001
Heart failure	1.031	0.797–1.334	0.8145
Hypertension	0.527	0.345–0.806	0.0031
Other cardiovascular	0.810	0.628–1.046	0.1062
Other coronary artery disease	0.807	0.561–1.159	0.2456
Other non-cardiovascular	0.592	0.436–0.804	0.0008
Valvular heart disease	0.802	0.543–1.184	0.2669
EHRA II–IV	1.439	1.259–1.644	<0.0001
Region			
Eastern Europe (reference)			
Northern Europe	1.686	1.330–2.137	<0.0001
Southern Europe	1.443	1.212–1.718	<0.0001
Western Europe	2.840	2.305–3.499	<0.0001
B. Independent predictors of NOACs vs. VKA use^b			
Coronary artery disease	0.761	0.674–0.860	<0.0001
Heart failure	0.869	0.773–0.978	0.0195
Valvular heart disease	0.757	0.678–0.831	<0.0001
Pulmonary arterial hypertension	0.769	0.612–0.965	0.0233
Pharmacological cardioversion for AF	0.781	0.689–0.885	0.0001
AF type			
First detected (reference)			
Paroxysmal	0.755	0.642–0.887	0.0006
Persistent	0.769	0.654–0.905	0.0015
Long-standing persistent	0.612	0.476–0.788	0.0001
Permanent	0.343	0.294–0.402	<0.0001
Main reason for admission/consultation			
AF (reference)			
Acute coronary syndrome	0.613	0.441–0.852	0.0036
Heart failure	0.718	0.583–0.883	0.0017
Hypertension	0.777	0.545–1.107	0.1620
Other cardiovascular	0.496	0.406–0.607	<0.0001
Other coronary artery disease	0.734	0.529–1.017	0.0628
Other non-cardiovascular	0.573	0.455–0.721	<0.0001
Valvular heart disease	0.147	0.087–0.247	<0.0001
Region			
Eastern Europe (reference)			
Northern Europe	1.335	1.081–1.649	0.0073
Southern Europe	0.751	0.639–0.884	0.0005
Western Europe	1.313	1.107–1.559	0.0018

Continued

Table 5 Continued

	Odds ratio	95% CI	P Wald
Year of enrolment			
2013 (reference)			
2014	1.242	0.684–2.257	0.4768
2015	2.399	1.322–4.351	0.0040
2016	3.026	1.668–5.491	0.0003

AF, atrial fibrillation; CI, confidence interval; NOACs, non-vitamin K antagonist oral anticoagulants; OAC, oral anticoagulant; VKA, vitamin K antagonist.

^aHosmer and Lemeshow goodness-of-fit test: $P = 0.0721$, percent concordant = 74.9%.^bHosmer and Lemeshow goodness-of-fit test: $P = 0.1337$, percent concordant = 72.4%.

AF Long-Term Registry followed the Pilot phase and all the enrolling centres were also associated with ESC activities, we could hypothesize some selection bias that led to an overestimation of the overall OAC uptake. A residual selection bias could have been also due to the lack of full monitoring and audit visits that could not certify that enrolment was actually consecutive. Furthermore, several clinical factors could have been either under- or overestimated. Nevertheless, our data provide a comprehensive picture of current European AF patients and cardiologists practice that will provide useful and reliable insights in real-world clinical practice.

Conclusions

The EORP-AF Long-Term General Registry provides a full picture of contemporary use of OACs in AF patients. The overall rate of OAC use was generally high (84.9%), with several clinical factors identified as independently associated with the prescription of OACs and preferential use of NOACs over VKAs. A relevant geographical variability in the prescription of NOACs over VKAs was also highlighted.

Supplementary material

Supplementary material is available at *Europace* online.

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References

- Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B *et al.* 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Europace* 2016;**18**:1609–78.
- Boriani G, Diemberger I, Martignani C, Biffi M, Branzi A. The epidemiological burden of atrial fibrillation: a challenge for clinicians and health care systems. *Eur Heart J* 2006;**27**:893–4.
- Lip GYH, Laroche C, Dan G-A, Santini M, Kalarus Z, Rasmussen LH *et al.* A prospective survey in European Society of Cardiology member countries of atrial fibrillation management: baseline results of EURObservational Research Programme Atrial Fibrillation (EORP-AF) Pilot General Registry. *Europace* 2014; **16**:308–19.
- Lip GYH, Laroche C, Ioachim PM, Rasmussen LH, Vitali-Serdoz L, Petrescu L *et al.* Prognosis and treatment of atrial fibrillation patients by European cardiologists: one year follow-up of the EURObservational Research Programme-Atrial Fibrillation General Registry Pilot Phase (EORP-AF Pilot registry). *Eur Heart J* 2014;**35**:3365–76.
- Proietti M, Laroche C, Opolski G, Maggioni AP, Boriani G, Lip GYH *et al.* 'Real-world' atrial fibrillation management in Europe: observations from the 2-year follow-up of the EURObservational Research Programme-Atrial Fibrillation General Registry Pilot Phase. *Europace* 2017;**19**:722–33.
- Lip GYH, Nieuwlaat R, Pisters R, Lane DA, Crijns HJGM. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* 2010;**137**:263–72.
- Pisters R, Lane DA, Nieuwlaat R, Vos CB, D, Crijns HJGM, Lip GYH. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest* 2010;**138**:1093–100.
- Camm AJ, Accetta G, Ambrosio G, Atar D, Bassand J-P, Berge E *et al.* Evolving antithrombotic treatment patterns for patients with newly diagnosed atrial fibrillation. *Heart* 2017;**103**:307–14.
- Huisman MV, Rothman KJ, Paquette M, Teutsch C, Diener H-C, Dubner SJ *et al.* The changing landscape for stroke prevention in AF: findings from the GLORIA-AF Registry Phase 2. *J Am Coll Cardiol* 2017;**69**:777–85.
- Marzec LN, Wang J, Shah ND, Chan PS, Ting HH, Gosch KL *et al.* Influence of direct oral anticoagulants on rates of oral anticoagulation for atrial fibrillation. *J Am Coll Cardiol* 2017;**69**:2475–84.
- Lip GYH, Laroche C, Dan GA, Santini M, Kalarus Z, Rasmussen LH *et al.* 'Real-World' antithrombotic treatment in atrial fibrillation: the EORP-AF pilot survey. *Am J Med* 2014;**127**:519–29.e1.
- Steinberg BA, Shrader P, Thomas L, Ansell J, Fonarow GC, Gersh BJ *et al.* Factors associated with non-vitamin K antagonist oral anticoagulants for stroke prevention in patients with new-onset atrial fibrillation: Results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation II (ORBIT-AF II). *Am Heart J* 2017;**189**:40–7.
- Gibson CM, Mehran R, Bode C, Halperin J, Verheugt FW, Wildgoose P *et al.* Prevention of bleeding in patients with atrial fibrillation undergoing PCI. *N Engl J Med* 2016;**375**:2423–34.
- Goette A, Merino JL, Ezekowitz MD, Zamoryakhin D, Melino M, Jin J *et al.* Edoxaban versus enoxaparin-warfarin in patients undergoing cardioversion of atrial fibrillation (ENSURE-AF): a randomised, open-label, phase 3b trial. *Lancet* 2016;**388**:1995–2003.
- Xiong Q, Lau YC, Senoo K, Lane DA, Hong K, Lip GYH. Non-vitamin K antagonist oral anticoagulants (NOACs) in patients with concomitant atrial fibrillation and heart failure: a systemic review and meta-analysis of randomized trials. *Eur J Heart Fail* 2015;**17**:1192–200.
- Lip GYH, Laroche C, Popescu MI, Rasmussen LH, Vitali-Serdoz L, Dan GA *et al.* Improved outcomes with European Society of Cardiology guideline-adherent antithrombotic treatment in high-risk patients with atrial fibrillation: a report from the EORP-AF General Pilot Registry. *Europace* 2015;**17**:1777–86.
- Potpara TS, Dan G-A, Trendafilova E, Goda A, Kusljagic Z, Manola S *et al.* Stroke prevention in atrial fibrillation and 'real world' adherence to guidelines in the Balkan Region: the BALKAN-AF Survey. *Sci Rep* 2016;**6**:20432.
- Proietti M, Nobili A, Raparelli V, Napoleone L, Mannucci PM, Lip GYH. Adherence to antithrombotic therapy guidelines improves mortality among elderly patients with atrial fibrillation: insights from the REPOSI study. *Clin Res Cardiol* 2016;**105**:912–20.
- Boriani G, Laroche C, Diemberger I, Fantecchi E, Popescu MI, Rasmussen LH *et al.* Asymptomatic atrial fibrillation: clinical correlates, management, and outcomes in the EORP-AF Pilot General Registry. *Am J Med* 2015;**128**:509–18.
- Boriani G, Laroche C, Diemberger I, Fantecchi E, Popescu MI, Rasmussen LH *et al.* 'Real-world' management and outcomes of patients with paroxysmal vs. non-paroxysmal atrial fibrillation in Europe: the EURObservational Research Programme-Atrial Fibrillation (EORP-AF) General Pilot Registry. *Europace* 2016;**18**:648–57.