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## Antithrombotic Treatment Patterns in 10,871 Patients with Newly Diagnosed Nonvalvular Atrial Fibrillation: The GLORIA-AF Registry, Phase II

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Antithrombotic treatment patterns in 10 871 patients with newly diagnosed nonvalvular atrial fibrillation: the GLORIA-AF Registry Program, Phase II

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All authors had access to the data and a role in writing the manuscript **Running head:** Antithrombotic treatment in atrial fibrillation

#### Abstract

*Background:* The Global Registry on Long-Term Oral Antithrombotic Treatment in Patients with Atrial Fibrillation (GLORIA-AF) was designed to provide prospectively collected information on patients with newly diagnosed non-valvular atrial fibrillation at risk of stroke, with the aim of addressing treatment patterns and questions of effectiveness and safety.

*Methods and Results:* In this predefined analysis from GLORIA-AF, the baseline characteristics and initial antithrombotic management of the first 10 000 patients in Phase II of this large Registry Program are presented.

Overall, 32.3% of patients received VKAs and 47.7% received NOACs, whilst 12.3% received antiplatelet treatment and 7.6 % did not receive any antithrombotic treatment. Amongst patients with CHA<sub>2</sub>DS<sub>2</sub>VASc score  $\geq$ 2, 6.7 % received no antithrombotic treatment and 10.0% received aspirin.

In Europe, treatment with dabigatran was as common as treatment with VKAs (38.8% and 37.8%, respectively). More than half of the patients were treated with NOACs (52.4%), whilst antiplatelet treatment was given to 5.7 %, and 4.1% did not receive any antithrombotic treatment. In North America, treatment with dabigatran (25.0%) was as common as with VKAs (26.1%), but overall NOAC use was more common (52.1%) than with VKAs (26.1%); however, 14.1% received antiplatelet treatment, while 7.6 % received no antithrombotic treatment. In Asia, treatment with VKAs (31.9%) was more prevalent than NOACs (25.5 %), but antiplatelet treatment was given to 25.8% and 16.9% did not receive any antithrombotic treatment. In Asia, only 60.7% of patients with

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high stroke risk received oral anticoagulants (OACs). Paroxysmal atrial fibrillation and minimally symptomatic (or asymptomatic) patients were often undertreated with OACs. *Conclusion:* In this analysis, OAC use was high in Europe and North America, with overall NOAC use higher than VKA use. A considerable percentage of high-risk patients in North America still received antiplatelet treatment or were untreated, whilst Asian patients had a high proportion of aspirin use and non-treatment.

Keywords: atrial fibrillation, registry, stroke, anticoagulation

#### Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, which confers a high risk of ischemic stroke and systemic thromboembolism. Adjusted-dose warfarin reduces the risk of stroke or systemic embolism by 64% and all-cause mortality by 26% when compared with placebo(1). In contrast, aspirin reduces stroke occurrence by an estimated 19%, with no reduction in mortality(1).

Although Vitamin K antagonists (VKAs) are very effective in reducing stroke risk, there are many limitations with their use(2). VKAs have many interactions with food and drugs, a narrow therapeutic window, delayed onset and offset of action, and need for frequent coagulation monitoring and drug dose adjustment(2). Also, the efficacy and safety of VKAs is dependent on the quality of anticoagulation control(2), as reflected by the time in therapeutic range (TTR)(3, 4). Guidelines currently recommend a TTR of >70%(5). Unsurprisingly, VKAs were still much underused in patients with atrial fibrillation who were at high risk of stroke, and instead, many patients with atrial fibrillation are prescribed aspirin or no antithrombotic therapy(6, 7).

Now that various non-VKA oral anticoagulants (NOACs), including dabigatran etexilate (dabigatran), rivaroxaban, apixaban, and edoxaban have been approved for stroke prevention in patients with non-valvular atrial fibrillation in many countries, the antithrombotic treatment patterns of practice have changed. It is therefore essential that additional collection of data from routine clinical practice be carried out to understand

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these antithrombotic patterns and to further characterize the broad spectrum of comorbidities and other medication use.

The Global Registry on Long-Term Oral Antithrombotic Treatment in Patients with Atrial Fibrillation (GLORIA-AF) was designed to provide prospectively collected information on patients with newly diagnosed non-valvular atrial fibrillation at risk of stroke, with the aim of addressing treatment patterns and questions of effectiveness and safety. The design and objectives of GLORIA-AF have been previously published(8), and Phase II of this Registry Program was started shortly after the approval of the first NOAC in the respective country. This design allowed the systematic collection of data on antithrombotic treatment of newly diagnosed non-valvular atrial fibrillation patients, especially in the first years after NOAC availability.

In the present predefined analysis from GLORIA-AF, the baseline characteristics and initial antithrombotic management of the first 10 000 patients in Phase II of this large Registry Program are presented.

#### Methods

GLORIA-AF is an ongoing international disease registry program in newly diagnosed non-valvular atrial fibrillation patients, run in three separate phases(8). Phase I, conducted before the approval of dabigatran, used a cross-sectional approach. During Phase II of GLORIA-AF, which has been started per country following the approval of dabigatran, cross-sectional data are collected. In addition, patients initiated on dabigatran will have 2-year follow-up data collected. Phase III will study the effectiveness and safety of dabigatran compared with VKA for stroke prevention in patients with nonvalvular atrial fibrillation, and will commence once baseline patient characteristics are similar enough to conduct comparisons. This will be determined by sufficiently overlapping ranges of the respective propensity score distributions for patients on VKA and dabigatran in the Phase II analysis.

This pre-specified interim analysis of Phase II describes baseline data from the first 10000 patients included in GLORIA-AF Phase II from all five defined geographical regions (*Figure 1*).

#### Patients

Consecutive patients aged  $\geq 18$  years with newly diagnosed non-valvular atrial fibrillation diagnosed at a maximum of 3 months before their baseline visit and a CHA<sub>2</sub>DS<sub>2</sub>VASc (congestive heart failure, hypertension, age  $\geq 75$ , diabetes, stroke, vascular disease, age 65–74, sex category) score  $\geq 1$  were included. Stroke and bleeding risk were assessed based on the CHA<sub>2</sub>DS<sub>2</sub>VASc and HAS-BLED (hypertension, abnormal renal and liver

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function, stroke, bleeding, labile international normalized ratios, elderly, drugs or alcohol) scores, respectively(9, 10). Patients were recruited from a variety of outpatient settings, including university hospitals, specialist offices, and community hospitals.

Patients were excluded for the following reasons: mechanical heart valves or valve disease expected to require valve replacement during the course of the registry, >60 days of VKA treatment in their lifetime for any indication, atrial fibrillation with a generally reversible cause, life expectancy <1 year, or another indication than atrial fibrillation for VKAs. At the baseline visit, in a standard electronic case report form (e-CRF), clinical and demographic characteristics were recorded, as was the type of atrial fibrillation and management approach. The definition of drug treatment groups used for the analysis are shown in Appendix *1*.

#### Study quality assurance

Data were collected in an electronic case report form. Data quality was monitored electronically, as well as through periodic manual medical and data quality reviews, onsite monitoring, and audits. Investigators were asked to consecutively enrol all eligible patients in order to minimize selection bias at the patient level. The design of the registry as well as the scientific oversight of all phases of the program was supported by an academic steering committee.

#### **Statistics**

Baseline data were summarized descriptively, displaying mean and standard deviation and/or median and interquartile ranges for continuous variables. Categorical variables were expressed as absolute frequencies and percentages. All analyses were descriptive in nature. All statistical analyses were performed using SAS software version 9.2.

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#### Results

From November 2011 (date of first patient in) until February 2014 (date of last patient entered in this data cut for the interim analysis), 10 871 patients from 736 centres were enrolled in Phase II of the Registry Program. Of the enrolled patients, 10 675 were eligible for inclusion in the analysis from the following regions: Asia (n = 1957), Europe (n = 4703), North America (n = 3415), Latin America (n = 476), and Africa/Middle East (n = 124). The country participation per defined region is shown in *Figure 1*.

The participating care settings were specialist offices (33.4%), university hospitals (30.8%), community hospitals (12.6%), primary care (11.4%), and other (11.7%). The main prescribing physicians were cardiologists (91.7%). General practitioners, geriatricians, neurologists, and internists enrolled the remaining patients. The median age of the study population was 71 years. Many patients had one or more comorbidities, including hypertension, coronary artery disease, myocardial infarction, and previous stroke. Further patient demographics and medical history are summarized in *Table 1*.

Paroxysmal atrial fibrillation was present in 54.5% of patients, while 34.9% had persistent atrial fibrillation and 10.6% had permanent atrial fibrillation. Atrial fibrillation was symptomatic in 26.8%, minimally symptomatic in 41.7%, and asymptomatic in 31.4% (*Figure 2*).

#### **Stroke and Bleeding Risk Scores**

More than half of the patients enrolled had a CHADS2 score  $\geq 2$  (57%), and 85.5% had CHA<sub>2</sub>DS<sub>2</sub>VASc score  $\geq 2$ . The mean CHADS<sub>2</sub> score was 1.9 (SD 1.1) and the mean CHA<sub>2</sub>DS<sub>2</sub>VASc score was 3.2 (SD 1.5) (*Table 1*). Most (79.3%) patients had HAS-BLED bleeding risk scores of <3. The mean HAS-BLED score was 1.4 (SD 0.9) (*Table 1*).

#### **Selection of Antithrombotic Therapy**

Overall, 32.3% of patients (n = 3449) received VKAs, while 32.2% (n = 3439) received dabigatran. When all NOACs were analysed together, more patients received NOACs (47.7%) than VKAs. Antiplatelet treatment was given to 12.3% of patients overall, while 7.6% of patients did not receive any antithrombotic treatment (*Figure 3*). When assessing treatment pattern per stroke risk scores, in patients with a CHA<sub>2</sub>DS<sub>2</sub>VASc score of 1, 13.2% received no antithrombotic treatment and 20.3% received antiplatelet treatment. Amongst patients with higher stroke risk (CHA<sub>2</sub>DS<sub>2</sub>VASc score  $\geq$ 2), corresponding figures were 6.7% and 10.0%, respectively (*Figure 3*).

#### Selection of Antithrombotic Therapy by Region

For Europe, treatment with dabigatran was as common as treatment with VKAs, with usage by 38.8% and 37.8% of patients, respectively. When all NOACs were considered together, more than half of the patients were treated with NOACs (52.4%). Antiplatelet treatment was given to 5.7% of patients, while 4.1% of patients did not receive any antithrombotic treatment (*Figure 4*).

For North America, treatment with dabigatran (25.0%) was as common as with VKAs (26.1%), but considered altogether, treatment with NOACs was more common (52.1%) than with VKAs (26.1%). A total of 14.1% of patients received antiplatelet treatment, while 7.6 % received no antithrombotic treatment. In Asia, treatment with VKAs (31.9%) was more prevalent than with dabigatran or other NOACs (25.5 %). Antiplatelet treatment was given to 25.8% of patients, while 16.9% of patients did not receive any antithrombotic treatment (*Figure 4*).

When the regional treatment patterns are assessed based on the CHA<sub>2</sub>DS<sub>2</sub>-VASc score in patients with a high stroke risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc Score  $\geq$ 2), the percentage of VKA and NOAC treatments increased (*Figure 5*). For example, in Europe, 91.1% of patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc Score  $\geq$ 2 were treated with VKAs or NOACs. In North America and Latin America, these numbers were 80.7% and 86.1%, respectively. In Asia, only 60.7% of patients with high stroke risk received OACs (*Figure 5*).

## Selection of Antithrombotic Therapy per Type of atrial fibrillation and per Symptoms

*Table 2* presents a summary of atrial fibrillation type and symptom category by antithrombotic treatment choice for stroke. Although patients having paroxysmal atrial fibrillation composed the largest proportion within each of the treatment cohorts (54.5%), aspirin (72.6% of paroxysmal atrial fibrillation patients) and no treatment ("none") groups (62.8% of paroxysmal atrial fibrillation patients) comprised larger percentages

than the VKA (48.3%) and NOAC (dabigatran 51.3%, rivaroxaban 56.2%, apixaban 56.1%) treatment groups.

Although patients with permanent atrial fibrillation composed the smallest proportion of patients within each individual treatment group, VKA and NOAC use were more prevalent. Permanent atrial fibrillation patients were older on average, and included a larger proportion of patients with high CHA<sub>2</sub>DS<sub>2</sub>-VASc stroke risk score compared with the other atrial fibrillation types [full data not shown].

Approximately two-thirds of the patients were symptomatic or minimally symptomatic (28.8% and 41.7%, respectively), while the remaining patients were asymptomatic (31.4%). While VKA and aspirin treatment did not differ per symptom category, some variations in treatment choice by atrial fibrillation symptom category were observed for dabigatran (symptomatic 32.9%, minimally symptomatic 34.7%, and asymptomatic 28.4%). The percentage of patients who did not receive any treatment was higher in asymptomatic and minimally symptomatic patients (8.4% and 8.1%, respectively) as compared with the symptomatic patients (5.9%).

#### Discussion

In this pre-specified interim analysis of the first cohort of more than 10 000 patients entered into Phase II of the GLORIA-AF Registry, our principal findings are as follows: (i) OAC use was high in Europe and North America, with overall NOAC use higher than VKA use; (ii) a considerable percentage of high-risk patients in North America still received antiplatelet treatment or were untreated; (iii) Asian patients had a high proportion of aspirin use and non-treatment despite atrial fibrillation subjects having ≥1 stroke risk factors; (iv) paroxysmal atrial fibrillation and minimally symptomatic (or asymptomatic) patients were often undertreated with OAC; and (iv) aspirin was commonly used in patients at high risk of bleeding patients.

Overall, treatment with VKAs (32.3%) and dabigatran (32.2%) were equally common, followed by rivaroxaban (12%) and antiplatelet treatment (12.3%). When all NOACs were taken together as a group, more patients received NOACs (47.7%) than VKAs (32.3%).

The results of this Phase II analysis reflect the changing field of antithrombotic management in patients with non-valvular atrial fibrillation. First, when compared with earlier registry data(11), many more patients were prescribed antithrombotic treatment. In the present analysis, only 7.6% of patients with an indication for anticoagulation did not receive such. In contrast, the corresponding number was 30% in the EuroHeart survey over the period 2003-2004.<sup>12</sup> Second, NOACs are now more commonly prescribed than VKAs amongst anticoagulated patients, signaling the extent to which clinical practice has

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changed after the introduction of NOACs. Third, antiplatelet treatment was still prescribed in 11.5% of patients, although regional differences are apparent. When subdivided by region, important differences of treatment patterns were observed. In Europe, 52.4% of patients received any NOAC versus 37.8% VKA, only 5.7% received Aspirin or another antiplatelet, and 4.1% received no antithrombotic treatment at all.

In North America twice as many patients received any NOAC (57.5%) compared with VKA (26.1%). When comparing the two regions many more patients in North America received Aspirin or another antiplatelet drug (14.1%) than those in Europe. Finally, in Asia, many patients received antiplatelet treatment (25.7%), while VKAs were more prescribed than any NOAC.

There are important reasons for the higher number of patients being treated with Aspirin in North America and Asia as compared with Europe. In North America, this high number reflects the current guidelines, in which aspirin is still mentioned as an alternative to VKAs or NOACs, irrespective of stroke risky (12). In the latest European guidelines, aspirin is not recommended, although aspirin-clopidogrel (or, less effectively, aspirin) may be considered only after any form of OAC is refused(5).

In Asia, VKAs are less commonly given to patients with non-valvular atrial fibrillation, probably because of the perceived risk of bleeding during treatment(13). VKA-related intracranial bleeding is also higher in Asian patients(13, 14). Second, many Asian patients lack access to good control for VKA therapy and therefore do not receive VKA

treatment(13); and even where VKA is used, the quality of anticoagulation control (as reflected by time in therapeutic range, TTR) may be suboptimal – indeed, TTR is closely related to thromboembolism and bleeding on warfarin(15). Nonetheless, NOACs may be the better option for Asians, given that Asian patients with atrial fibrillation have higher stroke and bleeding rates on warfarin, compared with non-Asians(16). Aspirin use is also common in Asia, but recent studies show that aspirin is neither safe nor effective for stroke prevention in Asians(17). In a recent analysis of Chinese patients with atrial fibrillation, the benefits of warfarin therapy for stroke prevention and intracranial haemorrhage risk were closely dependent on the quality of anticoagulation, as reflected by TTRs(18). Even at the top TTR quartile, warfarin was associated with a higher stroke and intracranial haemorrhage risk than dabigatran(18). Also, NOACs are not reimbursed in many Asian countries.

Among the newly diagnosed non-valvular- atrial fibrillation patients there were predominantly patients with paroxysmal and permanent atrial fibrillation included, while the overall majority of patients (73.1%) were either asymptomatic or had minimal symptoms. This distribution reflects the fact that we included patients early in their disease, but prognosis with respect to the occurrence of ischemic stroke and mortality in asymptomatic patients may be even worse than in symptomatic patients(19, 20).

Other international registries have also reported data on treatment patterns over the recent years. The GARFIELD Registry has reported treatment patterns in patients with newly diagnosed atrial fibrillation over the period 2009-2011(21). The median age, type of atrial fibrillation, and mean CHADS and CHA<sub>2</sub>DS<sub>2</sub>VASc score in that registry were similar to

those patients in the present registry. In GARFIELD, patients with CHADS<sub>2</sub> scores of 0 were included as well, but the registry contained no patients from the United States. Overall, only 4.5% of patients received NOACs, 26.5% received aspirin, and 40.7% of patients with a CHA<sub>2</sub>DS<sub>2</sub>VASc score of  $\geq$ 2 received no antithrombotic treatment(21).

The EORP-AF registry amongst European cardiologists showed that in more than 3000 patients who were enrolled from February 2012 to March 2013, oral anticoagulants were used in 80%, most often VKAs (71.6%), with NOACs being used in 8.4%(22). Other antithrombotics (mostly antiplatelet therapy, especially aspirin) were still used in one-third of the patients. In EORP-AF, the mean CHA<sub>2</sub>DS<sub>2</sub>VASc score was 3.2 and the mean HAS-BLED score was 1.4. The lower use of NOACs in the EORP registry may reflect inclusion of patients up to 2013, while in GLORIA-AF, patients were entered until 2014.

#### Limitations

This study includes patients at enrolling sites and consequently treatment patterns could be influenced by site selection. Two-thirds of study centres were either university hospitals or community hospitals, which may have increased the prevalence of patients treated with either dabigatran or other NOACs. However, we tried to overcome challenges stemming from arbitrary patient selection by asking sites to include consecutive patients from randomly selected representative practices. For operational reasons, at the time point of this interim analysis only a limited number of patients was included in the registry program from certain areas, including Africa, the Middle East, and Latin America. The final analysis of the Phase II baseline data will allow an

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assessment of the included regions in representative manner. In addition, the follow-up of GLORIA-AF Phase II will provide further information on the outcome of the patients as a function of therapies prescribed in daily clinical practice.

#### Conclusion

This interim analysis of the baseline Phase II data of the GLORIA-AF Registry demonstrates that the introduction of the NOACs into clinical practice have significantly influenced treatment patterns, especially in Europe and North America. In these areas of the world, NOACs were proportionally more commonly prescribed than VKAs. Furthermore, high proportions of patients at high risk of stroke still remain untreated or undertreated (e.g. those receiving aspirin); this is most pronounced in Asia but also true in North America and Europe.

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#### **Conflict of interest**

M.V.H.: Has provided consulting for Boehringer Ingelheim. C.S.M.: No conflicts of interest to declare. H.C.D.: Has received honoraria for participation in clinical trials, contribution to advisory boards or oral presentations from Abbott, Allergan, AstraZeneca, Bayer Vital, Bristol-Myers Squibb, Boehringer Ingelheim, CoAxia, Corimmun, Covidien, Daiichi-Sankyo, D-Pharm, Fresenius, GlaxoSmithKline (GSK), Janssen-Cilag, Johnson & Johnson, Knoll, Lilly, Merck Sharp & Dohme, Medtronic, MindFrame, Neurobiological Technologies, Novartis, Novo Nordisk, Paion, Parke-Davis, Pfizer, Sanofi Aventis, Schering-Plough, Servier, Solvay, St. Jude, Syngis, Talecris, Thrombogenics, WebMD Global, Wyeth, and Yamanouchi; received financial support for research projects from AstraZeneca, GSK, Boehringer Ingelheim, Lundbeck, Novartis, Janssen-Cilag, Sanofi Aventis, Syngis, and Talecris; the Department of Neurology at the University Duisburg-Essen received research grants from the German Research Council, German Ministry of Education and Research, European Union, the National Institutes of Health, Bertelsmann Foundation and Heinz-Nixdorf Foundation. H.C.D. has no ownership interest and does not own stocks of any pharmaceutical company. S.J.D.: Currently participating in research sponsored by Boehringer Ingelheim. J.L.H.: Currently conducting research sponsored by Boehringer Ingelheim as a member of the Executive Steering Committee for the GLORIA-AF Registry. K.J.R.: No conflicts of interest to declare. C.T.: Employee of Boehringer Ingelheim. A.E.: Employee of Boehringer Ingelheim. M.P.: Employee of Boehringer Ingelheim. D.B.B.: Employee of Boehringer Ingelheim. G.Y.H.L.: Has served as a consultant for Bayer, Merck, Sanofi, BMS/Pfizer, Daiichi-Sankyo, Biotronik, Medtronic, Portola and Boehringer Ingelheim; has been on the speakers bureau for Bayer, BMS/Pfizer, Boehringer Ingelheim, Daiichi-Sankyo, Medtronic.

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#### **FIGURE LEGENDS**

Figure 1 Definition of Geographical Regions and Country Participation in GLORIA-AF.

- Figure 2 AF Types and Symptom Categories (all Regions).
- Figure 3 Antithrombotic Treatment at Baseline overall and by Stroke Risk (all Regions).
- Figure 4 Antithrombotic Treatment at Baseline by Region.

Figure 5 Antithrombotic Treatment at Baseline by Stroke Risk and Region.

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	Total	
Age, median (IQR), years	71.0 (64.0, 78.0)	
Female, n (%)	4862 (45.5)	
BMI, median (IQR), kg/m <sup>2</sup>	27.80 (24.70, 31.80)	
Creatinine clearance, median (IQR), mL/min	75.2 (56.2, 98.9)*	
Medical history, n (%)		
Previous stroke	999 (9.4)	
Myocardial infarction	1116 (10.5)	
Coronary artery disease	2195 (20.6)	
Congestive heart failure	2530 (23.7)	
Hypertension	7993 (74.9)	
Diabetes mellitus	2454 (23.0)	
Prior bleed	608 (5.7)	
CHADS <sub>2</sub> score class, n (%)		
Low (score = 0)	896 (8.4)	
Moderate (score = 1)	3694 (34.6)	
High (score $\geq 2$ )	6081 (57.0)	
Missing	4 (0.0)	
CHA <sub>2</sub> DS <sub>2</sub> -VASc score class, n (%)		
Score = 1	1551 (14.5)	
Score $\geq 2$	9123 (85.5)	
Missing	1 (0.0)	
HAS-BLED score		
Mean (SD) score	1.4 (0.9	
Missing, n (%)	1299 (12.2	
HAS-BLED score class		
Low (score < 3), n (%)	8469 (79.3	
High (score $\geq$ 3), n (%)	907 (8.5	

### **Table 1: Patient demographics for overall population** (N = 10675)

BMI, body mass index; IQR, interquartile range; \* missing data > 1.5%

CHADS<sub>2</sub>, congestive heart failure, hypertension, age  $\geq$  75, diabetes, stroke (doubled); CHA<sub>2</sub>DS<sub>2</sub>-VASc, congestive heart failure, hypertension, age  $\geq$  75 (doubled), diabetes, stroke (doubled), vascular disease, age 65–74, sex category (female). ASPIRIN, acetylsalicylic acid; HAS-BLED, hypertension, abnormal renal and liver function (1 point each), stroke, bleeding, labile international normalized ratios, elderly (e.g. age > 65 years), drugs or alcohol (1 point each) (where "drugs/alcohol" refers to concomitant use of drugs such as antiplatelet agents, non-steroidal anti-inflammatory drugs drugs, or alcohol abuse etc.); SD, standard deviation; VKA, vitamin K antagonist.

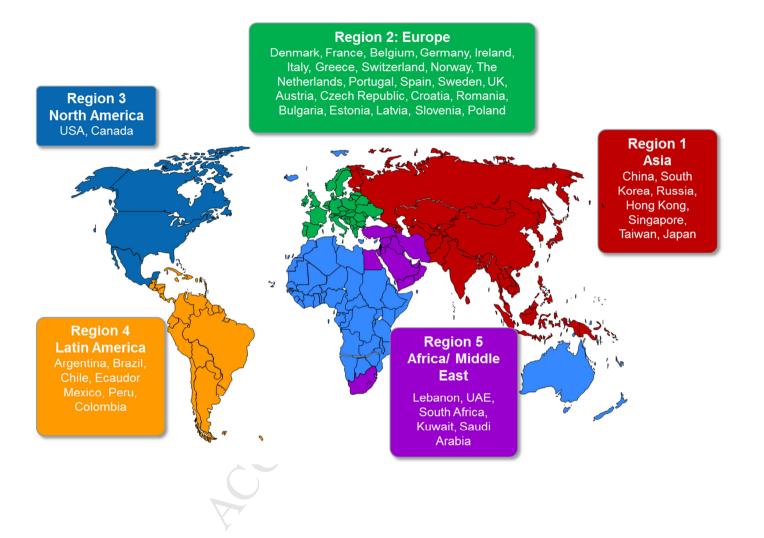
### Table 2: Summary of overall atrial fibrillation type and category by

	DE	VKA	Riva	Apix	ASA	None	Total
All eligible, N	3439	3449	1282	369	1225	814	10 675
AF category, n (%)							
Symptomatic	942	942	349	92	337	168	2866
	(27.4)	(27.3)	(27.2)	(24.9)	(27.5)	(20.6)	(26.8)
Minimally	1544	1407	444	131	530	362	4454
	(44.9)	(40.8)	(34.6)	(35.5)	(43.3)	(44.5)	(41.7)
symptomatic							
Asymptomatic	953	1099	489	146	358	283	3353
	(27.7)	(31.9)	(38.1)	(39.6)	(29.2)	(34.8)	(31.4)
Missing	0	1	0	0	0	1	2
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.1)	(0.0)
Type of AF, n (%)							
Paroxysmal	1764	1667	721	207	889	511	5818
	(51.3)	(48.3)	(56.2)	(56.1)	(72.6)	(62.8)	(54.5)
Persistent	1237	1348	441	123	281	257	3724
	(36.0)	(39.1)	(34.4)	(33.3)	(22.9)	(31.6)	(34.9)
Permanent	438	432	120	39	55	45	1130
	(12.7)	(12.5)	(9.4)	(10.6)	(4.5)	(5.5)	(10.6)
Missing	0	2	0	0	0	1	3
	(0.0)	(0.1)	(0.0)	(0.0)	(0.0)	(0.1)	(0.0)

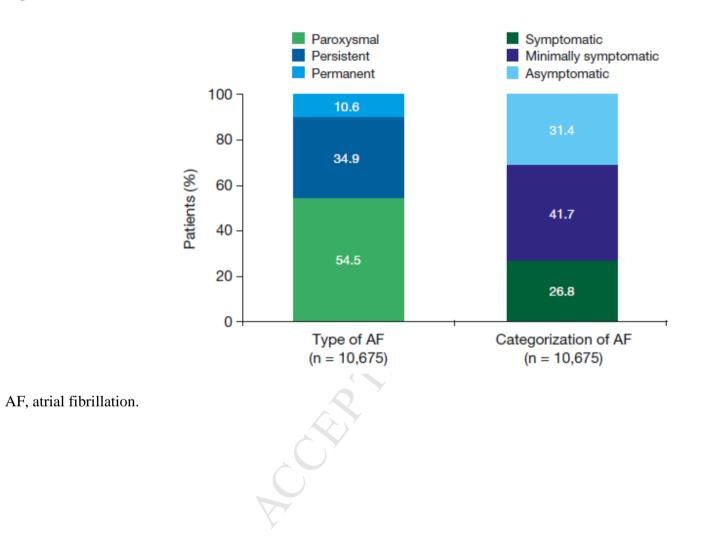
### antithrombotic treatment for stroke prevention

AF, atrial fibrillation; Apix = apixaban; ASA, acetylsalicyclic acid; DE, dabigatran etexilate; Riva, rivaroxaban; SD, standard deviation; VKA, vitamin K antagonist.

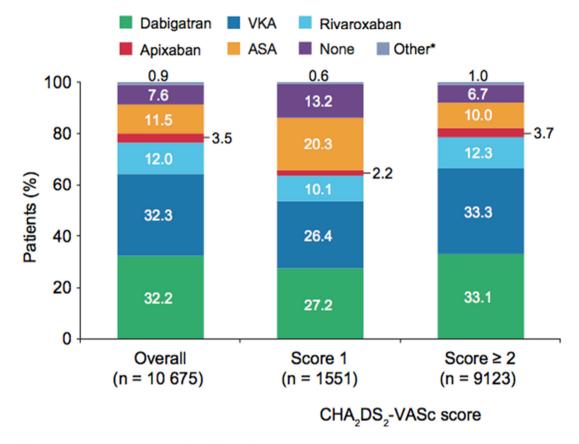
#### Figure 1







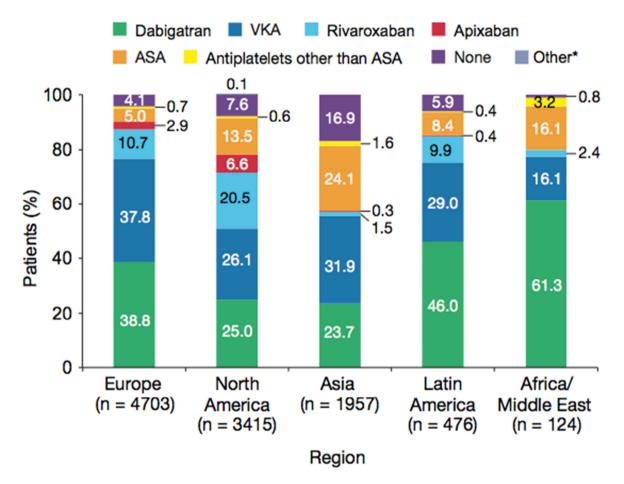




\*Other includes antiplatelets other than ASA. CHA<sub>2</sub>DS<sub>2</sub>-VASc score missing for one patient.

\*Other includes antiplatelets other than Aspirin. Scores refer to CHA<sub>2</sub>DS<sub>2</sub>-VASc score, which was missing for one patient.

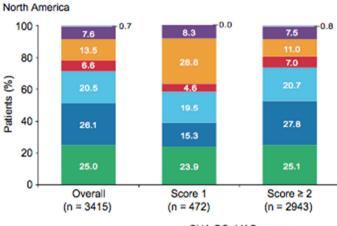




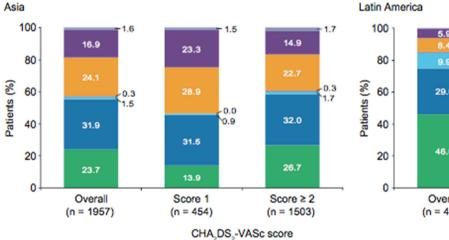
\*Other includes combination of oral anticoagulants.

#### Figure 5

Dabigatran VKA Rivaroxaban Apixaban ASA None Other Europe 4.1 0.7 100 0.8 3.4 -2.9 0.4 9.5 6.8 4.7 2.9 2.6 80 Patients (%) 60 38.6 37.8 31.7 40 20 38.8 0 Overall Score 1 Score ≥ 2 (n = 4703) (n = 546) (n = 4156) CHA,DS,-VASc score missing CHA, DS,-VASc score for one patient.







Latin America

-0.4 0.0 0.5 5.1 5.9 10.4 -0.5 -0.4 -0.0 28.6 29.0 31.3 46.0 Overall Score 1 Score ≥ 2 (n = 476) (n = 67) (n = 409) CHA, DS,-VASc score

'Other includes antiplatelets other than ASA and combination of oral anticoagulants.

### Appendix 1:

Definition of Treatment Groups

Name	Definition
Dabigatran	Patients with DE +/- other antithrombotics,
	excluding patients with DE + (other NOAC, VKA)
VKA	Patients with VKA +/- other antithrombotics,
	excluding patients with VKA + {(NOAC})
Rivaroxaban	Patients with Rivaroxaban +/- other
	antithrombotics, excluding patients with
	Rivaroxaban + {(other NOAC, VKA})
Apixaban	Patients with Apixaban +/- other antithrombotics,
	excluding patients with Apixaban + {(other
	NOAC, VKA})
Aspirin	Patients with Aspirin +/- other antithrombotics,
	excluding patients with Aspirin +/- {(NOAC,
	VKA})
None	Patients without any antithrombotic treatment
Total	All patients, irrespective of treatment

Dabigatran, dabigatran etexilate; Aspirin, acetylsalicylic acid; VKA, vitamin K

antagonist

#### **Clinical significance**

- In this global registry of patients with atrial fibrillation, oral anticoagulation use was high in Europe, whilst antiplatelet treatment was given to 5.7 %, and no antithrombotic therapy in 4.1%.
- In North America, overall NOAC use was more common than with warfarin; however, 14.1% received antiplatelet treatment, and 7.6% received no antithrombotic treatment.
- In Asia, there was a high proportion of aspirin use and non-treatment amongst AF patients.