

AF has been identified. Published reports suggest that prolonged cardiac rhythm monitoring in patients with cryptogenic stroke leads to identification of AF in approximately 5–35%. The detection rate is proportionate to the duration of monitoring with the highest rates reported with use of implantable loop recorder (ILR). It remains unclear what burden of AF is required to increase stroke risk and whether short bursts of AF are truly pathologic or simply normal phenomena, detected in the general population.

**Purpose:** The purpose of this study was to examine the time to detection and burden of AF as detected by ILR among patients with and without previous stroke.

**Methods:** This was a case-control study of all patients who received an ILR implant at our institution between March 2009 and October 2016. Patients' paper and electronic medical records were reviewed. Time from implant to AF detection was noted and the longest AF episode was recorded and classified as <30s, >30s or >6 minutes. Patients with previous stroke (cases) were compared with those without previous stroke (control).

**Results:** Of 495 subjects studied, ILR was implanted following stroke in 222 and for assessment of syncope or palpitation in 273. AF was detected in 95 subjects (43%) versus 33 control subjects (12%) ( $p < 0.0001$ ). Time to AF detection and burden of arrhythmia are described in Table 1.

Table 1. Time to detection and duration of AF in subjects with (Case) and without (Control) prior stroke

	Case	Control
Time to detection (days), median	131	169
Longest episode <30 sec, n (%)	26 (28)	7 (21.2)
Longest episode 30 sec – 6 mins, n (%)	39 (41)	9 (27.2)
Longest episode >6 min, n (%)	27 (29.3)	17 (51.5)

**Conclusion:** In patients with cryptogenic stroke, median time to diagnosis of AF (when present) was 131 days, shorter than the control group. Where AF was detected in Cases, the majority had arrhythmia lasting more than 30s. This study reinforces the importance of considering prolonged cardiac monitoring in the optimal management of patients with unexplained stroke. It also highlights the fact that it is still not clear how much AF is required to increase the risk of stroke.

## P4600 | BEDSIDE

### Prescribing of dabigatran etexilate in accordance with the European label for stroke prevention in atrial fibrillation: Findings from the GLORIA-AF Registry

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**Background:** With the introduction of the non-VKA oral anticoagulants (NOACs) stroke prevention in non-valvular AF (NVAf) has rapidly changed; European guidelines now incorporate NOACs, such as dabigatran etexilate (DE) as an alternative to VKAs.

**Purpose:** To assess the utilization of DE in patients with newly diagnosed NVAf at risk for stroke in GLORIA-AF in Europe (EU) and describe compliance with EU DE label recommendations.

**Methods:** Prescribing in accordance with pre-specified EU label definitions for stroke prevention in AF was assessed at baseline. As the DE indication in the EU label was updated in Dec 2013, regarding stroke risk factors, label compliance was assessed before and after Dec 2013. Dosing was considered non-compliant with the EU label in patients prescribed DE 110 mg bid (DE110) who met all of the following criteria: <75 years of age, no verapamil, no gastritis, no high bleeding risk and CrCl  $\geq 50$  mL/min. Dosing in those prescribed DE 150 mg bid (DE150) was considered non-compliant with the EU-label if they were  $\geq 80$  years of age or on verapamil.

**Results:** Of 7504 patients enrolled in GLORIA-AF Phase II in the EU, DE was prescribed to 2538 eligible patients in 22 European countries with the EU label. Dosing regimen and characteristics of DE110 and DE150 patients are summarized (table). Overall, most DE patients (86.3%) were treated in accordance with the EU DE indication. Before 1 Dec 2013, 80.4% of patients were treated according to the indication included in the EU label this increased to 93.2% after the

Table 1

	DE 150 mg bid (n=1336)	DE 110 mg bid (n=1178)
Mean age, years (SD)	66.8 (8.5)	75.6 (9.3)
Female, %	40.0	51.8
Mean CrCl, mL/min (SD)*	92.7 (32.6)	69.1 (29.6)
Mean CHA <sub>2</sub> DS <sub>2</sub> -VAsC (SD)*	2.8 (1.3)	3.8 (1.4)
Mean HAS-BLED score (SD)†	1.1 (0.8)	1.4 (0.8)

\*Data from 1063 (DE150) and 949 (DE110) patients. †Data from 1122 (DE150) and 1056 (DE110) patients.

label update on 1 Dec 2013. Among patients treated with DE150, 4.4% should have received DE110 according to EU label recommendations and 22.7% of patients treated with DE110 should rather have received DE150. In some instances, however, physicians could have appropriately prescribed either dose as dose selection should be based on an individual assessment of the thromboembolic and bleeding risk of the respective patient.

**Conclusion:** The majority of DE patients in GLORIA-AF in Europe were prescribed DE in accordance with the DE EU label recommendations.

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## P4601 | BEDSIDE

### Differences in two-year outcomes according to type of atrial fibrillation: results from the GARFIELD-AF registry

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**Purpose:** Atrial fibrillation (AF) burden and type of AF have not been established as major differential predictors of stroke and death. The aim of this work was to analyse outcomes by type of AF and by antithrombotic therapy.

**Methods:** 28,628 adults ( $\geq 18$  yrs) with nonvalvular AF and  $\geq 1$  investigator-defined stroke risk factor were enrolled in the ongoing, prospective GARFIELD-AF registry from 32 countries in Mar 2010–Oct 2014. Patients classified as having paroxysmal (n=10,473, 48.5%), persistent (n=6020, 27.9%), or permanent AF (n=5117, 23.7%) by 4 mos were included in the analysis of baseline characteristics, antithrombotic therapy, and 2yr incidence of outcomes.

**Results:** Patients with permanent AF had slightly higher CHA<sub>2</sub>DS<sub>2</sub>-VAsC (3.5 vs both 3.1) and HAS-BLED (1.6 vs both 1.4) vs those with paroxysmal or persistent AF, and they were most likely to be  $\geq 75$  yrs (48.3% vs 33.6% vs 34.3%). Compared to patients with other AF types, those with paroxysmal AF were less likely to be obese (26.7% vs 30.9% vs 33.2%) or to have LVEF <40% (6.0% vs 12.0% vs 14.4%) or severe HF (NYHA Class III/IV; 25.3% vs 33.0% vs 38.8%), but they were as likely to have history of vascular disease: stroke/transient ischaemic attack 12.2% vs 10.7% vs 13.5%; carotid occlusive disease 2.9% vs 2.8% vs 4.1%; ACS 9.4% vs 8.3% vs 9.6%. Patients with paroxysmal AF were less likely to receive anticoagulant (AC) therapy ( $\pm$ antiplatelets, AP) vs those with persistent or permanent AF and more likely to receive AP only or no antithrombotics (Tab). Compared to patients with paroxysmal AF, those with persistent or permanent AF had higher risks of all-cause mortality, stroke/systemic embolism (SE) and ma-

#### Antithrombotic therapy by type of AF

%	Paroxysmal AF (n=10,473)	Persistent AF (n=6,020)	Permanent AF (n=5,117)
VKA +/- AP	38.0	53.9	57.1
FXa +/- AP	13.1	9.8	9.0
DTI +/- AP	7.0	7.7	5.8
AP only	26.8	19.7	19.7
None	15.1	9.0	8.3

AF, atrial fibrillation; AP, antiplatelet; DTI, direct thrombin inhibitor; FXa, factor Xa inhibitor; VKA, vitamin K antagonist.

#### Stroke/Systemic Embolism

	Adjusted HR (95% CI)
Permanent v Paroxysmal	0.96 (0.71 to 1.31)
Permanent v Persistent	0.96 (0.69 to 1.34)
Persistent v Paroxysmal	1.07 (0.80 to 1.44)
Persistent & Permanent vs Paroxysmal	1.06 (0.83 to 1.35)
Permanent vs Paroxysmal & Persistent	0.99 (0.75 to 1.31)

#### Major Bleed

	Adjusted HR (95% CI)
Permanent v Paroxysmal	1.17 (0.78 to 1.75)
Permanent v Persistent	1.31 (0.85 to 2.03)
Persistent v Paroxysmal	1.09 (0.72 to 1.65)
Persistent & Permanent vs Paroxysmal	1.15 (0.81 to 1.62)
Permanent vs Paroxysmal & Persistent	1.22 (0.85 to 1.75)

#### All Cause Mortality

	Adjusted HR (95% CI)
Permanent v Paroxysmal	1.67 (1.37 to 2.02)
Permanent v Persistent	1.14 (0.94 to 1.38)
Persistent v Paroxysmal	1.42 (1.16 to 1.73)
Persistent & Permanent vs Paroxysmal	1.53 (1.29 to 1.81)
Permanent vs Paroxysmal & Persistent	1.40 (1.19 to 1.65)

Hazard ratios were adjusted for age, gender, race, smoking, diabetes, hypertension, stroke/transient ischaemic attack/systemic embolism, history of bleeding, cardiac failure, vascular disease, moderate-to-severe chronic kidney disease, anticoagulant treatment and heavy alcohol consumption (only for major bleeding).

Adjusted HRs for 2yr outcomes by AF type

for bleeding. However, only the difference in mortality persisted after adjustment (Fig). Adjusted HRs also showed higher mortality for non-paroxysmal vs paroxysmal AF and for permanent vs paroxysmal/persistent AF (Fig). We found no interaction between type of AF and AC therapy.

**Conclusion:** Persistent and permanent AF were associated with higher mortality risk vs paroxysmal AF but had similar adjusted risks of stroke/SE and major bleeding in 2 yrs of follow-up.

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**P4602 | BEDSIDE**

**Similar clinical outcomes of asymptomatic and symptomatic patients with newly diagnosed atrial fibrillation: results from GARFIELD-AF**

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**Purpose:** To compare the characteristics, treatment and outcomes of asymptomatic vs symptomatic patients with newly diagnosed nonvalvular atrial fibrillation (NVAF).

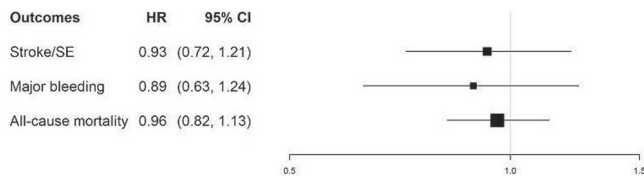
**Methods:** 39,898 adults (≥18 yrs) with NVAF diagnosed in the past 6 wks and ≥1 investigator-defined stroke risk factor were enrolled in the prospective GARFIELD-AF registry from 35 countries from Mar 2010–Sep 2015. At enrolment 28,843/78.0% patients presented with symptoms (palpitations, shortness of breath, chest pain/discomfort, dizziness, tiredness, sweating, fainting, other), 8125/22.0% did not (data missing in 2930). We analysed baseline characteristics, antithrombotic therapy and 1-yr incidence of outcomes.

**Results:** The asymptomatic group included more men (65.3% vs 52.7%), and had a higher mean age (71.8 vs 69.0 yrs) and lower prevalence of congestive heart failure (CHF, 11.7% vs 23.2%), including NYHA Class III–IV CHF (17.1% vs 34.9%) vs the symptomatic group. The two groups had similar mean CHA<sub>2</sub>DS<sub>2</sub>-VASc (both 3.2 [SD 1.6]) and HAS-BLED (1.5 [0.9], 1.4 [0.9]). Fewer asymptomatic patients were diagnosed in a hospital (52.6% vs 60.7%) or emergency room (4.3% vs 13.6%) and more in an office (42.2% vs 25.0%). Use of antithrombotic therapies was similar in both groups (Tab). Unadjusted and adjusted HRs showed no difference in the rate of stroke/systemic embolism (SE) or of major bleeding in the two groups. Unadjusted HRs showed slightly lower all-cause mortality (0.87 [95% CI 0.77; 0.99]) in asymptomatic patients, although this difference was not present after adjustment for baseline characteristics. The annual incidence rates of stroke/SE and all-cause mortality were 1.40 and 3.81 per 100 person-yrs in asymptomatic patients, despite anticoagulation in 68.3%.

**Antithrombotic therapy at diagnosis**

%	Asymptomatic patients (n=8061)	Symptomatic patients (n=28,420)
VKA +/- AP	43.2	42.6
FXa +/- AP	18.5	15.1
DTI +/- AP	6.6	6.9
AP only	18.9	23.3
None	12.8	12.2

AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist.



Hazard ratios were adjusted for age group, gender, race, smoking, diabetes, hypertension, previous stroke/transient ischaemic attack/systemic embolism, history of bleeding, cardiac failure, vascular disease, moderate-to-severe renal disease, anticoagulant treatment, type of atrial fibrillation and alcohol consumption. Reference group: Patients with symptomatic NVAF.

Adjusted hazard ratios of 1-yr outcomes

**Abstract P4603 – Table 1. Country-specific TADC**

Country	UK (N=2,347)		Spain (N=1,949)		France (N=1,221)		Italy (N=1,518)		Germany (N=2,823)	
Cost	Mean (SEM) (£)	%	Mean (SEM) (£)	%	Mean (SEM) (£)	%	Mean (SEM) (£)	%	Mean (SEM) (£)	%
Drug	113 (4.9)	4.0	136.7 (5.5)	11.0	369.2 (13.6)	21.7	106.2 (5.3)	6.9	277.9 (6.6)	11.1
Inpatient	2,118.3 (186.0)	74.1	793.5 (127.6)	63.9	1,109.9 (180.1)	65.2	1,294.7 (362.4)	83.7	1,968.5 (166.1)	78.6
Outpatient	625.5 (16.6)	21.9	311.0 (26.1)	25.1	222.9 (18.8)	13.1	145.9 (25.7)	9.4	257.6 (76.0)	10.3
Total	2,857.3 (187.8)	100	1,241.2 (131.7)	100	1,702.0 (181.2)	100	1,546.8 (363.4)	100	2,504.1 (183.4)	100

**Conclusion:** One-fifth of patients newly diagnosed with NVAF had no symptoms. Prescription of antithrombotic therapies was similar in asymptomatic and symptomatic patients. Adjusted 1-yr mortality, stroke/SE and major bleeding were the same in each group, indicating that asymptomatic newly diagnosed AF is not benign. This supports systematic approaches to detect and treat asymptomatic NVAF.

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**P4603 | BEDSIDE**

**The burden of atrial fibrillation in the more populated European countries: perspectives from the GARFIELD-AF registry**

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**Purpose:** We evaluated the economic burden attributable to atrial fibrillation (AF) and related anticoagulant (AC) therapy in patients with incident AF during the first yr from diagnosis in the 5 more populated European countries.

**Methods:** GARFIELD-AF is an ongoing, prospective, non-interventional study of adults (≥18 yrs) with newly diagnosed nonvalvular AF and ≥1 stroke risk factor. We analysed GARFIELD-AF patients enrolled in France, Germany, Italy, Spain, UK during 2010–5. Total annualised direct cost (TADC) attributable to AF was calculated as the sum of the annual cost of medical visits (incl. monitoring), drug therapy, hospital admissions, diagnostic procedures and other medical events attributable to AF, quantified in the perspective of the third-party payer. We focused on the incremental cost specifically attributable to events related to AF and to AC therapy.

For indirect costs, we identified patients who died during follow-up whose death happened during working age (ie before local age of retirement). We calculated yrs of working life lost as the difference between the age of retirement and the age at death. We used the human capital approach and county-specific average salary/worker to calculate the cost of production losses attributable to premature mortality.

Based on AF prevalence estimates, we projected the direct and indirect costs attributable to AF in the 5 countries.

**Results:** Enrolled patients generated a total of 8,574 person-yrs of observation. TADCs are shown in Table 1. Twenty-seven deaths occurred during working age. Mean loss of working yrs/patient was 6.4 (SD 6.8) and 7.6 (7.2) yrs for females and males, with a total of 198.4 working yrs lost, corresponding to €263,696/patient who died during working age. Estimates indicate that AF generates in the 5 countries an overall additional annual cost of 18 billion Euro, 12 billion Euro attributable to healthcare and 6 billion Euro to premature mortality.

**Conclusions:** AF imposes a high financial, economic and human burden to societies. Based on population dynamics, the burden is likely to grow in the future. Premature mortality substantially adds to the already considerable direct cost of the disease.

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**P4604 | BEDSIDE**

**Residual stroke risk of anticoagulated patients with atrial fibrillation: PREFER in AF European registry**

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**Background:** Stroke prevention is a major goal in the treatment of AF. The resid-