

One of the aims of GARFIELD-AF is to assist physicians in their understanding of the risk of stroke in patients with atrial fibrillation in everyday practice, by analysing real-world data to reveal acute and long-term outcomes around the world.

Background Information

Atrial Fibrillation (AF) Today

AF is a problem with the rate or rhythm of the heartbeat. When AF occurs, rapid disorganised electrical signals cause the heart's two upper chambers, called the atria, to contract very fast and irregularly. This stops the heart being able pump out enough blood per beat and results in blood pooling. Blood pooling increases the risk of clotting, and blood clots can cause thrombosis, which is the number one cardiovascular killer in the world.¹

Up to 2% of the global population has this type of arrhythmia,² including around 8.8 million people in Europe³ and 5–6.1 million in the United States.⁴ It is estimated that its prevalence will at least double by 2050 as the global population ages.⁴

A blood clot leaving the left atrium could lodge in an artery. If the artery leads to the brain or heart this could cause a stroke or heart attack respectively.⁵

AF is associated with a five-fold increase in stroke risk and 20% of strokes are associated with AF.² Ischaemic strokes related to AF are often fatal, and those patients who do survive are left more frequently and more severely disabled with a greater risk of recurrence than patients with other causes of stroke.² Overall, the risk of mortality from AF-associated stroke is doubled and the cost of care is 50% higher.²

People with AF often have comorbid heart failure and a history of other cardiovascular diseases and risk factors. Consequently, the healthcare costs associated with AF are substantial.

Building a Global Picture on AF Treatment and Outcomes

Enrolment into the GARFIELD-AF Registry closed last year. For the first time, one-year outcomes data are available on all 52,000 prospective patients in the registry, providing a truly global picture of geographic variations in AF treatment practices and outcomes. This backgrounder provides details on the abstracts being presented at the European Society of Cardiology (ESC) Congress 2017.



GARFIELD-AF Registry Status

The largest ongoing prospective registry in patients with AF

- 57,262 patients newly diagnosed with AF; recruitment target of 57,000 exceeded
- Patients have a variety of co-morbidities, including hypertension, type 2 diabetes, hypercholesterolemia and coronary artery disease
- Five cohorts; recruitment began in Dec 2009
- Follow-up duration is 2–8 years to capture the burden of early and late events following the diagnosis of AF

Collecting real-world data on the impact of anticoagulant therapy in AF management

- Informs multiple branches of enquiry
- Records evolving trends in anticoagulant treatment
- Demonstrates wide variations in treatment practice for the prevention of ischaemic stroke
- Measures the economic and societal impact of atrial fibrillation at a regional and global level
- Defines the relative importance of various risk factors in patients with atrial fibrillation who are at risk of stroke

Emerging Registry Insights

New findings from GARFIELD-AF presented at ESC Congress 2017 are as follows:

1. AF generates an overall additional annual cost of 18 billion Euros in 5 of the more populated European countries⁶
2. There is significant geographical variation in the amount and type of health services used by patients with AF⁷
3. Patients with ischaemic cardiomyopathy and AF appear to be under treated – both for stroke prevention and HF perhaps due to the polypharmacy associated with these comorbid conditions⁸
4. Obese patients are younger a time of diagnosis of AF and are more likely to develop persistent or permanent AF⁹
5. Different types of AF are associated with different risks; persistent and permanent AF are associated with higher mortality risk vs paroxysmal AF, but have similar adjusted risks of stroke/systemic embolism and major bleeding in 2 years of follow-up¹⁰
6. Even though some people with AF have no symptoms at diagnosis, their risk of stroke and all-cause mortality is similar to patients with symptomatic AF¹¹
7. Stroke and major bleed event rates increase with the severity of uncontrolled hypertension in patients with AF¹²

Further details are provided below.

Results from the GARFIELD-AF Registry

Impact of body mass index in newly diagnosed AF in the GARFIELD-AF Registry⁹

28,628 patients with newly diagnosed AF were enrolled over a four year period, and just under four-fifths of the patients used in this study had available BMI data. This data was used to stratify the patients, which showed that 71.4% were overweight, obese or morbidly obese. As seen in Table 1, increased BMI correlated with younger age and higher rates of hypertension, hypercholesterolemia, type 2 diabetes, coronary artery disease and congestive heart failure (CHF). Conversely underweight patients, who tended to be older, had the highest prevalence of prior stroke/TIA, bleeding, and moderate to severe chronic kidney disease (CKD). Compared with obese patients, they were less likely to receive oral anticoagulants (53.2% vs 67.2%). The proportion of patients with NYHA class III/IV CHF was similar in both morbidly obese and underweight patients.

As BMI increases, mortality paradoxically decreased in the 2 years after AF diagnosis.

	Underweight <20 n=735	Normal 20 to <25 n=5702	Overweight 25 to <30 n=9074	Obese 30 to <35 n=4520	Morbidly obese 35 to <40 n=1748	≥40 n=762
Age, yrs, median (IQR)	76(68 to 82)	73(64 to 80)	71(62 to 78)	69(62 to 76)	67(61 to 74)	64(57 to 71)
Hist hypertension, %	57.8	69.6	79.0	86.6	89.0	89.6
Raised cholesterol, %	22.8	31.2	42.7	51.0	52.3	51.1
Type 2 diabetes, %	9.0	14.1	19.7	27.5	34.6	41.6
CAD, %	11.9	18.1	21.9	24.2	24.8	19.6
Mod-to-severe CKD, %	12.1	11.5	9.8	10.0	11.3	11.2
Prior stroke, TIA /bleed, %	14.7/4.1	12.7/2.9	12.3/2.6	9.4/2.6	10.2/3.4	9.6/2.0
CHF [NYHA class III/IV]	23.4 [39.9]	19.4 [31.5]	19.4 [29.5]	24.0 [30.0]	29.1 [35.9]	30.2 [39.2]
CHA2DS2-VASc, mean	3.4	3.2	3.1	3.2	3.4	3.2

Table 1. Characteristics by BMI at AF diagnosis.

One-year clinical outcomes and management of patients with ischaemic vs non-ischaemic cardiomyopathy and newly diagnosed AF: results from GARFIELD-AF⁸

39,898 adults with non-valvular atrial fibrillation were assessed to see if they had ischaemic or non-ischaemic cardiomyopathy (34.2% and 65.8% respectively). Patients with ischaemic cardiomyopathy were less likely to receive anticoagulant (anticoagulant treatment alone, and more likely to receive antiplatelet therapy (alone or in combination with anticoagulants) than patients with non-ischaemic cardiomyopathy. Proportionally less patients with ischaemic cardiomyopathy received CHF medication than patients with non-ischaemic cardiomyopathy (86.0% vs 92.6%). Patients with ischaemic cardiomyopathy and AF appear to be under treated – both for stroke prevention and HF.

Overall patients with ischaemic cardiomyopathy had worse outcomes compared to those with non-ischaemic cardiomyopathy. They have a higher rate of stroke, major bleeding, all-cause mortality (including a higher rate of cardiovascular mortality) and new or worsened CHF.

The burden of AF in the more populated European countries: perspectives from the GARFIELD-AF registry⁶

Statistics on the economic burden attributed to AF and related anticoagulant therapy have not been evaluated in detail much, if at all.

Based on AF prevalence estimates, GARFIELD-AF projected the direct and indirect costs attributable to AF in France, Germany, Italy, Spain and the UK. The total annualised direct cost attributable to AF and anticoagulation therapy was calculated as the sum of the annual cost of medical visits (incl. monitoring), drug therapy, hospital admissions, diagnostic procedures and other medical events, quantified in the perspective of the third party payer. Indirect costs suffered by premature mortality were calculated by the years of working life left before retirement age multiplied by county-specific average salary/worker. Estimates indicate that AF generates an overall additional annual cost of 18 billion Euros in the 5 countries – 12 billion Euros attributable to healthcare and 6 billion Euros to premature mortality. The countries with the highest incurred costs were found to be Germany and the UK.

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

Table 2. Country-specific total annualised direct cost.

Global healthcare resource use in 39,670 patients with AF: perspectives from GARFIELD-AF⁷

Global data on healthcare resource use (HCRU) by patients with AF are crucial to optimising patient management and are currently lacking.

39,670 patients enrolled in 35 countries were analysed. By focusing on hospital admissions, outpatient hospital attendance, emergency room admissions, family doctor visits, stroke unit admissions and office-based specialist visits occurring during the first year from enrolment, the GARFIELD-AF registry has found significant geographical variation in the amount and type of health services used by patients. This could be due to the actual availability of services and different models of organisation of care.

Which definition of hypertension best defines thromboembolic risk in patients with atrial fibrillation? Data from the GARFIELD-AF registry¹²

Unadjusted event rates per 100 patient years were calculated according to either the severity at baseline, or history of hypertension. There was variety within the 39,898 patients observed; 7.5% of the group had no other risk factors for stroke as defined by CHAD₂DS₂-VASc and 2.7% had a CHAD₂DS₂-VASc score of 0. Of the 76.7% of 39,398 patients with newly diagnosed AF that had a history of hypertension, 32.6% of these had uncontrolled hypertension (systolic blood pressure (SBP) higher than 140mmHg) at baseline.

Higher event rates of stroke, major bleed and all-cause mortality were identified in patients with a history of hypertension during the year after the diagnosis of AF. In the cases of stroke and major bleed the event rates increased with the severity of uncontrolled hypertension. In contrast to the rates of all-cause mortality was variable, suggesting that uncontrolled hypertension is not a risk factor for all-cause mortality.

	N (%)	Unadjusted event rate per 100 person-years (95% CI)		
		Stroke	Major bleed	All-cause mortality
All Patients	39809 (100)	1.43 (1.32 to 1.56)	0.87 (0.78 to 0.97)	4.25 (4.05 to 4.46)
History	30544 (76.7)	1.52 (1.38 to 1.67)	0.89 (0.79 to 1.01)	4.24 (4.01 to 4.49)
No history	9265 (23.3)	1.15 (0.94, 1.40)	0.79 (0.62, 1.00)	4.27 (3.85, 4.72)
SBP ≤140*	26610 (71.2)	1.42 (1.28 to 1.58)	0.84 (0.73 to 0.96)	4.55 (4.29 to 4.82)
SBP >140*	10771 (28.8)	1.56 (1.34 to 1.82)	0.92 (0.75 to 1.13)	3.63 (3.28 to 4.01)
SBP >150*	5762 (15.4)	1.80 (1.48 to 2.20)	1.10 (0.85 to 1.42)	3.65 (3.17 to 4.19)
SBP >160*	2738 (7.3%)	1.94 (1.47 to 2.56)	1.28 (0.91 to 1.79)	4.23 (3.51 to 5.10)

*Expressed a percent of patients with blood pressure measurements at baseline (i.e. 37381 patients or 93.7%)

Table 3. Event rates for stroke, major bleed and all-cause mortality at 1 year after diagnosis of atrial fibrillation.

Similar clinical outcomes of asymptomatic and symptomatic patients with newly diagnosed AF: results from GARFIELD-AF¹¹

Antithrombotic regimens for AF patients remain similar regardless of their symptom profile. At enrolment 78.0% patients presented with symptoms including palpitations, shortness of breath, chest pain/discomfort, dizziness, tiredness, sweating and fainting, while 22.0% did not. While the symptomatic patients included a higher proportion of men (65.3% vs 52.7%), and had a higher mean age (71.8 years vs 69.0 years), the asymptomatic patients presented with half the symptomatic prevalence of CHF (11.7% vs 23.2%). The measurements of hazard ratios for both groups revealed no significant differences in the rates of stroke and all-cause mortality.

Variations in the location of diagnosis were also observed: asymptomatic patients were more likely to be diagnosed in the physician’s office (42.2% vs 25.0%), whilst symptomatic patients tended to be diagnosed in the hospital or emergency room (60.7% vs 52.6% and 13.6% vs 4.3% respectively).

Difference in two-year outcomes according to type of AF: results from the GARFIELD-AF Registry¹⁰

Type of AF has not been established as a major differential predictor of stroke and death. Data was collected from 28,628 adults with non-valvular AF and one or more stroke risk factor enrolled from 32 countries between March 2010 and October 2014. Patients with paroxysmal (n=10,473, 48.5%), persistent (n=6,020, 27.9%), or permanent AF (n=5,117, 23.7%) by 4 months were included and baseline characteristics, antithrombotic therapy, and 2-year incidence of outcomes were analysed. The key findings were as follows:

- Patients with permanent AF had slightly higher CHA₂DS₂VASc (3.5 vs both 3.1) and HASBLED (1.6 vs both 1.4) vs those with paroxysmal or persistent AF, and they were most likely to be 75 years and above (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 a left ventricular ejection fraction of less than 40% (6.0% vs 12.0% vs 14.4%) or severe HF (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%); and 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 (Table 4).
- Compared to patients with paroxysmal AF, those with persistent or permanent AF had higher risks of all-cause mortality, stroke/systemic embolism (SE) and major bleeding. However, only the difference in mortality persisted after adjustment. Adjusted HRs also showed higher mortality for non-paroxysmal vs paroxysmal AF and for permanent vs paroxysmal/persistent AF. There was no interaction between type of AF and AC therapy.

Investigators concluded that 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 years of follow-up.

%	Paroxysmal AF (n=10,473)	Persistent AF (n=6020)	Permanent AF (n=5117)
VKA +/- AP	38.0	53.9	57.1
FXaI +/- 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

Table 4. Antithrombotic therapy by type of AF.

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

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For more information, visit www.garfieldregistry.org.

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About the TRI

The Thrombosis Research Institute (TRI) is dedicated to bringing new solutions to patients for the detection, prevention and treatment of blood clots. The TRI's goal is to advance the science of real-world enquiry so that the value of real-world data is realised and becomes a critical link in the chain of evidence. Our pioneering research programme, across medical disciplines and across the world, continues to provide breakthrough solutions in thrombosis.

For more information, visit www.tri-london.ac.uk/.

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⁷ Mantovani L, et al. Global healthcare resource use in 39,670 patients with AF: perspectives from GARFIELD AF. Abstract presented at ESC Congress 2017, Barcelona.

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¹⁰ Atar, D, et al. Differences in two-year outcomes according to type of atrial fibrillation: results from the GARFIELD AF registry. Abstract presented at ESC Congress 2017, Barcelona.

¹¹ Gibbs, H, et al. Similar clinical outcomes of asymptomatic and symptomatic patients with newly diagnosed atrial fibrillation: results from GARFIELD AF. Abstract presented at ESC Congress 2017, Barcelona.

¹² Camm, J, et al. Which definition of hypertension best defines thromboembolic risk in patients with atrial fibrillation? Data from the GARFIELD-AF registry. Abstract presented at ESC Congress 2017, Barcelona.