British Journal of General Practice

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DOI: <https://doi.org/10.3399/BJGP.2021.0548>

To access the most recent version of this article, please click the DOI URL in the line above.

Received 21 September 2021

Revised 17 January 2022

Accepted 19 January 2022

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Author Accepted Manuscript

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Two-year outcomes of UK patients newly diagnosed with atrial fibrillation: findings from the prospective observational cohort study GARFIELD-AF

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Keywords: atrial fibrillation, stroke, anticoagulation, all-cause mortality, bleeding

Word count: 2,437

Abstract

Background

Outcomes of patients newly diagnosed with atrial fibrillation (AF) in the post-vitamin K antagonist only era are not well known

Aim

To determine the two-year outcomes of patients newly diagnosed with AF, and the effectiveness of oral anticoagulants in everyday practice.

Design & Setting

Observational prospective cohort study in UK primary care.

Method

3574 patients aged ≥ 18 years with a new AF diagnosis were enrolled. We applied a propensity score using an overlap weighting scheme to obtain unbiased estimates of the treatment effect of anticoagulation vs no anticoagulation on the occurrence of death, non-haemorrhagic stroke/systemic embolism(SE) and major bleeding within 2 years of diagnosis.

Results

Overall, 65.8% received anticoagulant therapy, 20.8% received an antiplatelet only; 13.4% received neither. During the study period, the overall incidence rates (95% CI) of all-cause mortality, non-haemorrhagic stroke/SE, and major bleeding were 4.15 (3.69 to 4.66), 1.45 (1.19 to 1.77), and 1.21 (0.97 to 1.50) per 100 person-years respectively. Anticoagulation treatment compared with no anticoagulation treatment was associated with significantly lower all-cause mortality aHR 0.70 (95% CI 0.53 to 0.93), significantly lower risk of non-haemorrhagic

stroke/SE (aHR 0.39 [95% CI 0.24 to 0.62]) and a non-significant higher risk of major bleeding (aHR 1.31 [(95% CI 0.77 to 2.24]).

Conclusions

Our data support a benefit of anticoagulation in reducing stroke and death, without an increased risk of a major bleed among patients with new onset AF. Anticoagulation of the group of patients at high risk of stroke not receiving anticoagulation may further improve outcomes.

What is already known on this topic

- AF increases the risk of stroke and death; anticoagulation reduces these risks at the cost of an increased risk of bleeding
- There has been an increase in the proportion of patients with AF receiving anticoagulants, with patients receiving either vitamin K antagonists (VKA) or direct acting oral anticoagulants (DOACs)
- Evidence on outcomes following the change in treatment patterns in the UK is limited

What this study adds

- The benefit of anticoagulation in this real-world cohort of patients with AF affirms recommendations in AF management guidelines
- Addressing gaps in anticoagulation of patients with AF may reduce AF-related stroke and death

Introduction

Atrial fibrillation (AF) increases the risk of ischaemic stroke fivefold and the risk of death twofold (1). AF-related strokes are more severe than strokes in people without AF and are more likely to be fatal, lead to long term disability, extended hospital stay and increased healthcare costs (2). Anticoagulation therapy reduces the risk of AF-related stroke (and systemic embolism, SE) and death, with a 68% relative risk reduction for ischaemic stroke and a 25% reduction in the relative mortality (3). Anticoagulation however increases the risk of bleeding with the most serious complication being intracranial haemorrhage which can be fatal (4). Anticoagulant drugs recommended by AF guidelines have included vitamin K antagonists (VKAs) usually warfarin, and direct acting oral anticoagulants (DOACs) namely dabigatran, rivaroxaban, apixaban, and edoxaban (4-6). The latest NICE AF guideline (2021) recommends anticoagulation for patients with a CHADS-VASc ≥ 2 with a DOAC as a first-choice anticoagulant and VKA as an alternative if DOACs are contraindicated or not tolerated (7).

Since the introduction of DOACs in clinical practice several UK studies have reported the clinical management of AF and changes in prescribing patterns, indicating increases in anticoagulant use overall and good uptake of DOACs (8-12). However, evidence on outcomes of UK patients newly diagnosed with atrial fibrillation at risk of stroke in the post-VKA only era is limited.

This paper investigates the 2-year event rates for non-haemorrhagic stroke/SE, all-cause mortality and major bleeding in the UK patients enrolled in the Global Anticoagulant in the FIELD – Atrial Fibrillation registry (GARFIELD-AF).

Methods

Study design

GARFIELD-AF is a prospective, observational, international registry of adults (≥ 18 years) newly diagnosed with AF (13). GARFIELD-AF was conducted in 35 countries worldwide, including the Americas, Europe, Africa, Asia-Pacific and the Middle East between 2010 and 2018. The UK study was conducted in accordance to the published study protocols (13, 14). Participants were enrolled into five prospective sequential cohorts between 2011 and 2016. Inclusion criteria comprised men and women aged ≥ 18 years with new diagnosis of non-valvular AF of up to 6 weeks prior to entry into the registry and an investigator-determined risk factor for stroke, meaning the risk factors for stroke were not pre-specified in the protocol and left to the clinical judgement of the site investigator. Eligible patients were recruited consecutively at participating sites to prevent selection bias. All participants provided informed consent. Patients were followed up for a minimum of 2 years (study end) or the occurrence of the event of interest or loss to follow-up, whichever came first. Patients with transient AF, secondary to a reversible cause, and patients for whom follow-up was not possible were excluded.

Setting

The UK specific study recruited from primary care with 185 sites (GP practices) across the country. Participants were enrolled between June 2011 and August 2016. Ethical approval was obtained from a National Health Service Research Ethics Committee and relevant local Research and Development approvals were obtained. Data were collected from participants' primary care records at baseline and at four-month intervals up to 24 months post-diagnosis using an electronic case report file by trained local site staff.

Variables

Data collected at baseline included patient characteristics, medical history, and antithrombotic therapy initiated at diagnosis. The main outcomes were non-haemorrhagic stroke and systemic embolism (SE), major bleeding and death. Major bleeding was defined as clinically overt bleeding associated with: a fall in haemoglobin of ≥ 2 g/dl OR a transfusion of ≥ 2 units of packed red blood cells or whole blood, or a critical site (intracranial, intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, retroperitoneal), or a fatal outcome. The full classification of bleeding events is in Supplementary Box 1. Anticoagulant use was measured as anticoagulation prescribed at diagnosis. Anticoagulant use includes patients receiving anticoagulants with an antiplatelet (i.e with or without an antiplatelet).

Statistical analysis

Continuous variables are expressed as mean (SD) and categorical variables as frequency and percentage. Use of antithrombotic therapy as baseline was analysed by CHA₂DS₂VASc and HAS-BLED scores; HAS-BLED was modified to exclude fluctuations in the INR as these data were not available. Females with no other risk factors were assigned a CHA₂DS₂VASc score of 0. The occurrence of major outcomes non-haemorrhagic stroke/SE, major bleeding and mortality is presented using number of events and person time event rate per 100 person years and 95% CI. Only the first occurrence of each event was taken into account.

We applied a propensity score using an overlap weighting scheme to reduce biased estimates of the treatment effect. Weights were applied to Cox proportional hazards models to estimate the effects of anticoagulants (OAC) vs no OAC comparison on the occurrence of death, non-haemorrhagic stroke/SE and major bleeding within 2 years of enrolment. This newly developed method of overlap propensity weighting avoids excluding patients (as with matching) and gives the most weight to propensities where there is equipoise. This applied method overlaps weights

and optimizes the efficiency of comparisons by defining the population with the most overlap in the covariates between treatment groups. This scheme eliminates the potential for outlier weights by avoiding a weight based on a ratio calculation using values bounded by 0 and 1. Thus, when using overlap weights, many of the concerns regarding the assessment and the trimming of the weights are eliminated(15). Covariates evaluated in the weighting scheme included demographic characteristics (sex, age, ethnicity), lifestyle factors (current smoking, alcohol consumption), clinical measurements at diagnosis (BMI, heart rate, blood pressure), medical history (congestive heart failure, acute coronary syndromes, vascular disease, carotid occlusive disease, prior stroke/TIA/SE, prior bleeding, VTE, hypertension, hypercholesterolemia, diabetes, cirrhosis, moderate to severe CKD, dementia, hyperthyroidism, hypothyroidism) and baseline antiplatelet use.

Treatment was defined as the first treatment received at the time of enrolment, approximating ‘intention-to-treat’. Patients with missing values were not removed from the study; multiple imputation combining estimates from five imputed datasets was applied for the comparative effectiveness analysis.

Data analysis was performed centrally by study statisticians using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Participants

3574 patients were prospectively enrolled to the UK study, comprising 6.9% (3574/52057) of the global cohort. 2.5% (89/3574) were lost to follow up and had incomplete 2-year data.

At baseline, the mean age (SD) was 74.5 (9.5) years, and 42.6% (1522/3574) of participants were females, 98.8% (3441/3483) Caucasian. The median (Q1;Q3) CHA₂DS₂-VASc and HAS-BLED scores were 3.0 (2.0;4.0) and 2.0 (1.0; 2.0), respectively (Table 1). 89.3% (3150/3528) had a CHA₂DS₂-VASc score ≥ 2 and 18.9% (479/2530) had a HAS-BLED score ≥ 3 .

Antithrombotic treatment

65.8% (2344/3564) of participants received anticoagulant therapy at diagnosis; of these 70.6% (1656/2344) received VKA and 29.4% (688/2344) received a DOAC. 12.5% (447/3564) received anticoagulant therapy and an antiplatelet (AP), 20.8% (742/3564) received an antiplatelet only, and 13.4% (478/3564) received neither anticoagulant nor antiplatelet therapy. Anticoagulant therapy was prescribed in 67.1% (2108/3142) of patients with CHA₂DS₂-VASc ≥ 2 , 56.1% (161/287) of patients with CHA₂DS₂-VASc =1 (i.e. men with a score of 1) and 47.2% (42/89) of patients with CHA₂DS₂-VASc =0 (i.e. women with a score of 1 and men with a score of 0). 51.6% (247/479) of patients with HAS-BLED ≥ 3 received anticoagulation.

The proportion of patients receiving anticoagulant therapy increased progressively with CHA₂DS₂-VASc score (Figure 1A.) The proportion of patients receiving anticoagulant therapy peaked in patients with HAS-BLED score of 1, then decreased with increasing HAS-BLED score. (Figure 1B). The proportion of patients receiving AP only according to CHA₂DS₂-VASc score ranged from 17.1% to 21.7%. The proportion of patients receiving AP only increased progressively with HAS-BLED score from 0 in patients with a HAS-BLED score of 0 to 47.7% in patients with a HAS-BLED score from 4 to 9.

Most baseline characteristics were similar in patients who received anticoagulant therapy and patients who did not receive anticoagulant therapy; however, a higher proportion of patients receiving anticoagulation had hypertension, diabetes, prior stroke and venous

thromboembolism whilst a higher proportion of patients with heavy alcohol consumption and history of bleeding did not receive anticoagulants (Table 2).

Clinical outcomes

At two-year follow up, the incidence rates (95% CI) of all-cause mortality, non-haemorrhagic stroke/SE, and major bleeding were 4.15 (3.69-4.66), 1.45 (1.19-1.77), and 1.21 (0.97-1.50) per 100 person-years (PY), respectively.

The rates of all-cause mortality, non-haemorrhagic stroke/SE and major bleeding increased with increasing CHA₂DS₂-VASc and HAS-BLED scores (Figure 2).

Event rates by treatment at baseline

The incidence rates (95% CI) per 100PY of all-cause mortality, non-haemorrhagic stroke/SE were and major bleeding in patients who received anticoagulation were 3.89 (3.35-4.52), 1.05 (0.79-1.40) and 1.26 (0.97-1.64) respectively (Table 3). Comparatively, patients who did not receive anticoagulation had a higher rate of all-cause mortality and non-haemorrhagic stroke (4.68 (3.87-5.66); 2.21 (1.67-2.920), and a lower rate of major bleeding 1.11 (0.75-1.65). Patients receiving DOAC had similar rates of all-cause mortality and stroke to patients receiving VKA (3.98 [3.03-5.23] and 1.00 [0.58-1.73] vs (3.85 [3.22-4.61]) and 1.07 [0.75-1.51]) but lower rates of major bleeding (0.77 [0.41-1.43] vs 1.46 [1.09-1.96]). The rates (95% CI) of all-cause mortality, non-haemorrhagic stroke/SE, and major bleeding in patients who received AP only were 4.35 (3.37-5.60), 2.61 (1.87-3.63) and 1.17 (0.72-1.91) (Table 3).

Effectiveness of anticoagulant use

After adjustment for demographic and lifestyle factors, clinical measures at diagnosis and medical history, anticoagulant use was associated with significantly lower all-cause mortality

(aHR 0.70 (0.53-0.93; $p = 0.013$) and non-haemorrhagic stroke (aHR 0.39 (0.24-0.62; $p < 0.0001$) and non-significant higher major bleeding (aHR 1.31 (0.77-2.24; $p = 0.326$) (Figure 3).

Treatment changes are described in Supplementary Box 2.

Discussion

Statement of principal findings

In this recent cohort of UK patients newly diagnosed with AF, death was the most frequent clinical outcome at two years occurring at 2.9 times the rate of non-haemorrhagic stroke and 3.4 times the rate of major bleeding. Death remained the most frequent outcome regardless of whether patients were receiving anticoagulation or not.

Our findings regarding the benefit of anticoagulation fits with previous meta-analyses of randomised controlled trials in the VKA era as well as the DOAC trials (16) (17-20). The estimated lower risk of 30% and 61% for all-cause mortality and non-haemorrhagic stroke/SE in anticoagulated UK patients are similar to the results from these studies. The estimated 31% higher risk of major bleeding did not reach statistical significance, which might be due to the relatively small number of these events in this cohort of patients.

Comparison of main clinical outcomes in the UK and global cohort

As in the UK cohort, death was the most frequent outcome in the global cohort (21), occurring at over three times the rate of stroke/SE and almost 5 times the rate of major bleeding. Nevertheless, the two-year event rates per 100 person-years (95% CI) were numerically higher in the UK cohort compared to the global cohort excluding the UK: all-cause mortality 4.15 (3.69-4.65) vs 3.80 (3.68-3.93), stroke 1.45 (1.19-1.77) vs 0.97 (0.91-1.04) and major bleeding

1.21 (0.97-1.50) vs 0.96 (0.90-1.03). Overall, a similar proportion received anticoagulation at baseline (65.8 vs 66.9%); the median (Q1,Q3) CHA₂DS₂-VASc score was similar for the UK and global cohort (median CHA₂DS₂-VASc 3.0 [2.0;4.0] vs 3.0 [2.0 to 4.0] but the median HAS-BLED scores were higher in the UK cohort (median HAS-BLED 2.0 [1.0; 2.0] vs 1.0 [1.0 to 2.0]).

The reduction in the risk of all-cause mortality and stroke/SE was more marked in the UK cohort compared to the global cohort (30% vs 18% and 61% vs 29% respectively), and the increment in the risk of bleeding was not statistically significant in the UK but statistically significant in the global cohort (aHR 1.31 [0.77 - 2.24] vs 1.46 [1.1 – 1.86], respectively) (22).

Overall though, the findings on the relative effects of anticoagulation in the global study are reproduced in this UK only cohort. Marginal differences might be due to the wider uncertainty around the obtained estimates in the UK data. In addition, the global analysis on effectiveness of anticoagulants was based on a different group of patients comprising patients enrolled to Cohort 3 to 5 and patients with a CHA₂DS₂-VASc $\geq$ 2.

Strengths and weaknesses of the study

GARFIELD-AF was conducted to high quality standards and data for 20% of the UK cohort was monitored against source documentation. Enrolling patients within 6 weeks of diagnosis ensured the sample included patients who may not survive long after AF diagnosis by capturing disease burden early on.

The main limitation of the study is that the analysis is intention to treat based on therapy initiated at diagnosis and does not account for treatment changes during the two-year follow up. Also, the study did not collect data on deprivation and therefore unable to adjust for

deprivation in the analysis. Despite having applied appropriate propensity score methodology to balance confounding factors across treatment groups, we cannot exclude the presence of unobserved confounding.

Implications for clinicians and policymakers

Findings regarding the benefit of anticoagulation for reduction of all-cause mortality and stroke/SE without a significant increase in the risk of bleeding suggests that for most patients the benefits of anticoagulation outweigh the risks, and affirms recommendations relating to anticoagulation in AF management guidelines.

The findings regarding non-significant increase in the risk of bleeding are reassuring, particularly as 46% of patients with HAS-BLED score of 4-6 received anticoagulation. Nevertheless, this finding should be interpreted with caution, and it must be emphasised that despite the benefit, anticoagulation is recommended for patients at increased risk of stroke with CHA₂D₂-VASc score ≥ 2 and should be considered for those patients with a CHA₂D₂VASc score of 1.

There is scope for improvement in the management of patients newly diagnosed with AF to align with NICE guidelines(7). Overall, 67.1% of participants at high risk of stroke received anticoagulation at diagnosis. We have previously reported progressive increase in the proportion of patients in the UK cohort receiving anticoagulation, with 75.6% of the final cohort of patients (diagnosed June 2015 to July 2016) receiving anticoagulation (23). Further increment in the proportion of patients at high risk of stroke receiving anticoagulation will optimise anticoagulation in patients with AF and improve outcomes. On the other hand, 47.2% of patients defined as very low risk in the NICE guidelines (CHA₂D₂-VASc score of 0 for men or 1 for women) received anticoagulation which is contrary to the guidelines. In addition, the practice of prescribing AP alone (20.8%) is contrary to AF guidelines; the guidelines indicate

patients at risk of stroke must receive anticoagulants or no antithrombotic therapy. The practice of prescribing anticoagulant with AP (12.5%) is also not recommended in the guidelines.

The elderly profile of the patient population and the prevalence of comorbidities are likely to be contributory factors to the all-cause mortality. The prominence of all-cause mortality as an outcome indicates more attention should be given to mortality risk in the management of patients newly diagnosed with AF.

Acknowledgment: We thank physicians, nurses and patients contributing to the GARFIELD-AF registry. Editorial support was provided by Dr Surekha Damineni (TRI, London, UK). Programming support was provided by Madhusudana Rao (TRI, London, UK). FDRH acknowledges part support from the NIHR Applied Research Collaboration (ARC) Oxford Thames Valley and the NIHR Oxford OUH BRC.

Data sharing: Requests for patient level data can be made to the head of statistics at TRI (kpieper@tri-london.ac.uk). These requests should include a protocol summary and a summary of the statistical analysis plan. The request will be reviewed by the data sharing committee for approval and next steps will be discussed with the requestor.

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Competing interests: FDRH has received occasional consult or speaker fees from Pfizer/BMS, BI and Bayer outside the submitted work. AJC has received institutional grants and personal fees from Bayer, Boehringer Ingelheim, Pfizer/BMS and Daiichi Sankyo. K.A.A. Fox has received grants and personal fees from Bayer/Janssen and AstraZeneca and personal fees from Sanofi/Regeneron and Verseon outside the submitted work. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Contributors:

PNA contributed to the acquisition, analysis and interpretation of data for the study, and drafted the manuscript. SV contributed to the analysis and interpretation of the data and revised the work critically for intellectual content. FDRH, AJC, and KAAF contributed to the interpretation of the data and revised the work critically for intellectual content. DAF contributed to the acquisition, analysis and interpretation of the data and revised the work critically for intellectual content. FDRH and DAF contributed to the initial methods of GARFIELD-AF in the UK. DAF is also the Principal Investigator and guarantor for the UK study. All authors approved the final version of the manuscript and are accountable for all aspects of the work.

Ethics approval: Independent ethics committee and hospital-based institutional review board approvals were obtained, as necessary, for the registry protocol. The UK study received ethical approval from the South East London Research Ethics Committee 5 (REC 5) on 29 September 2010; REC reference 10/H0805/48.

Funding: This work is supported by KANTOR CHARITABLE FOUNDATION for the Kantor-Kakkar Global Centre for Thrombosis Science. The funding source had no involvement in trial design, collection and analysis of data, or in the writing process of this paper.

Sponsorship was provided by the Thrombosis Research Institute.

Patient and public involvement: There was no direct patient and public involvement in the GARFIELD-AF registry.

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Accepted Manuscript – BJGP – BJGP.2021.0548

Table 1 Baseline characteristics of participants

Variable	Value	%
Age, median (Q1; Q3), years	75.0 (69.0;81.0)	-
Age, years		
<65	471/3574	13.2
65 - 74	1178/3574	32.9
≥75	1925/3574	53.9
Female	1522/3574	42.6
Caucasian race	3441/3483	98.8
BMI, median (Q1;Q3)	28.1 (25.0;32.3)	-
Medical history		
Congestive heart failure	274/3573	7.7
Coronary artery disease	678/3573	19.0
Acute coronary syndromes	363/3561	10.2
Carotid occlusive disease	52/3515	1.5
Prior Stroke/TIA/SE	450/3551	12.7
Vascular disease ¹	760/3551	21.4
History of bleeding	109/3560	3.1
Hypertension	2483/3564	69.7
Hypercholesterolemia	1318/3492	37.7
Diabetes mellitus	629/3573	17.6
Chronic kidney disease (grade ≥3)	896/3499	25.6
Cirrhosis	11/3527	0.3

CHA ₂ DS ₂ -VASc, median (Q1;Q3)	3.0 (2.0;4.0)	-
CHA₂DS₂VASc score categories		
0	89/3528	2.5
1	289/3528	8.2
2	659/3528	18.7
3	972/3528	27.6
4	848/3528	24.0
5	398/3528	11.3
≥6	273/3528	7.7
HAS-BLED ² score, median (Q1;Q3)	2.0 (1.0; 2.0)	-
HAS-BLED² score categories		
0	160/2530	6.3
1	941/2530	37.2
2	950/2530	37.5
3	391/2530	15.5
≥4	88/2530	3.5
Care setting at diagnosis		
Cardiology	544/3573	15.2
Geriatrics	63/3573	1.8
Internal medicine	779/3573	21.8
Neurology	4/3573	0.1
Primary care/general practice	2183/3573	61.1

¹Defined as peripheral artery disease and/or coronary artery disease;

²The risk factor 'Labile INRs' is not included in the HAS-BLED score as it is not collected at baseline. As a result, the maximum HAS-BLED score at baseline is 8 points (not 9)

Table 2. Baseline characteristics by Anticoagulant treatment vs No Anticoagulant treatment

Baseline characteristics	Baseline treatment		P-value ¹
	No OAC (N = 1219)	OAC (N = 2342)	
Sex, n (%)			
Male	719 (59.0)	1324 (56.5)	0.161
Female	500 (41.0)	1018 (43.5)	
Age, median (Q1; Q3), years	75.0 (69.0;82.0)	75.0 (69.0;81.0)	0.353
Ethnicity, n (%)			
Caucasian	1160 (99.0)	2268 (98.7)	0.659
Hispanic/Latino	2 (0.2)	8 (0.3)	
Asian	3 (0.3)	10 (0.4)	
Afro-Caribbean/Mixed/Other	7 (0.6)	12 (0.5)	
Body mass index, median (Q1; Q3), kg/m ²	27.5 (24.6;31.3)	28.4 (25.1;32.7)	0.002
Systolic blood pressure, median (Q1; Q3), mmHg	134.0 (121.0;143.0)	132.0 (120.0;140.0)	0.021
Diastolic blood pressure, median (Q1; Q3), mmHg	79.0 (70.0;84.0)	78.0 (70.0;83.0)	0.127
Pulse, median (Q1; Q3), bpm	82.0 (70.0;102.0)	80.0 (70.0;100.0)	0.033
Type of atrial fibrillation, n (%)			
Permanent	379 (31.1)	852 (36.4)	<0.001
Persistent	65 (5.3)	209 (8.9)	
Paroxysmal	257 (21.1)	392 (16.7)	
New onset (unclassified)	517 (42.4)	889 (38.0)	
Medical history, n (%)			
Heart failure	70 (5.7)	201 (8.6)	0.003
Acute coronary syndromes	114 (9.4)	249 (10.7)	0.224
Vascular disease ²	251 (20.7)	504 (21.7)	0.521
Carotid occlusive disease	14 (1.2)	37 (1.6)	0.294
VTE	40 (3.3)	124 (5.3)	0.007
Prior stroke/TIA/SE	122 (10.1)	328 (14.1)	<0.001
Prior bleeding	69 (5.7)	40 (1.7)	<0.001
Hypertension	810 (66.6)	1664 (71.3)	0.004
Hypercholesterolaemia	429 (36.1)	883 (38.5)	0.172

Diabetes	161 (13.2)	464 (19.8)	<0.001
Cirrhosis	6 (0.5)	5 (0.2)	0.155
Moderate to severe CKD	308 (25.9)	585 (25.5)	0.774
Dementia	8 (0.7)	20 (0.9)	0.529
Heavy alcohol consumption, n (%)	68 (6.3)	58 (2.8)	<0.001
Current smoker, n (%)	87 (7.3)	155 (6.7)	0.554
AP treatment, n (%)	742 (60.9)	447 (19.1)	<0.001
CHA ₂ DS ₂ -VASc score, median (Q1; Q3)	3.0 (2.0;4.0)	3.0 (2.0;4.0)	<0.001
HAS-BLED score ³ , median (Q1; Q3)	2.0 (1.0;3.0)	2.0 (1.0;2.0)	<0.001

¹P-values calculated using t-test or Wilcoxon-Mann-Whitney test for categorical variables and chi-square test or Fisher exact test for categorical variables, as appropriate;

²Defined as peripheral artery disease and/or coronary artery disease;

³The risk factor 'Labile INRs' is not included in the HAS-BLED score as it is not collected at baseline. As a result, the maximum HAS-BLED score at baseline is 8 points (not 9).

Table 3. Two-year event rates per 100 person years in the GARFIELD-AF UK population by treatment at baseline

Treatment at baseline	Outcome					
	All-cause mortality		Non-haemorrhagic stroke/SE		Major bleeding	
	Events	Rate (95% CI)	Events	Rate (95% CI)	Events	Rate (95% CI)
OAC	172	3.89 (3.35-4.52)	46	1.05 (0.79-1.40)	55	1.26 (0.97-1.64)
No OAC	106	4.68 (3.87-5.66)	49	2.21 (1.67-2.92)	25	1.11 (0.75-1.65)
DOAC	52	3.98 (3.03-5.23)	13	1.00 (0.58-1.73)	10	0.77 (0.41-1.43)
VKA	120	3.85 (3.22-4.61)	33	1.07 (0.76-1.51)	45	1.46 (1.09-1.96)
OAC+AP	37	4.43 (3.21-6.11)	6	0.72 (0.32-1.61)	15	1.82 (1.10-3.02)
OAC only	135	3.77 (3.18-4.46)	40	1.13 (0.83-1.54)	40	1.13 (0.83-1.54)
AP only	60	4.35 (3.37-5.60)	35	2.61 (1.87-3.63)	16	1.17 (0.72-1.91)
No OAC nor AP	46	5.19 (3.89-6.93)	14	1.60 (0.95-2.70)	9	1.02 (0.53-1.97)

OAC, anticoagulant; DOAC, direct acting oral anticoagulant; AP, antiplatelet

Figure 1A Treatment at diagnosis by CHA₂DS₂-VASc score

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

Figure 1B. Treatment at diagnosis by HAS-BLED score

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

Figure 2A. Event rates according to CHA₂DS₂-VASc score

Includes only patients with available CHA₂DS₂VASc scores (n=3528)

Figure 2B. Event rates according to HAS-BLED scores

Includes only patients with available HAS-BLED scores (n=2530)

Figure 3. Unadjusted and adjusted¹ hazard ratios of OAC vs No OAC (ref) and corresponding 95% confidence intervals for selected outcomes at two years of follow-up in UK patients

¹Obtained using an overlap-weighted Cox model. Variables included in the weighting scheme are: cohort enrolment, sex, age, ethnicity, type of AF, care setting speciality and location, congestive heart failure, acute coronary syndromes, vascular disease, carotid occlusive disease, prior stroke/TIA/SE, prior bleeding, VTE, hypertension, hypercholesterolemia, diabetes, cirrhosis, moderate to severe CKD, dementia, hyperthyroidism, hypothyroidism, current smoking, heavy alcohol consumption, BMI, heart rate, systolic and diastolic blood pressure at diagnosis, and baseline antiplatelet use.