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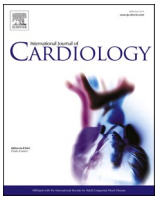

Association of care specialty with anticoagulant prescription and clinical outcomes in newly diagnosed atrial fibrillation: Results from the GARFIELD-AF registry

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A R T I C L E I N F O

Keywords:
Atrial fibrillation
Care specialty
Care setting
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Non-vitamin K oral anticoagulant
Vitamin K anticoagulant

A B S T R A C T

Objective: To determine whether stroke prevention strategy, comorbidity management, and clinical outcome risks differ across atrial fibrillation (AF) care specialties.
Methods: Newly diagnosed non-valvular AF patients enrolled in the international, prospective GARFIELD-AF registry (enrolment: 2010–2016) were analysed. Prescription of oral anticoagulation (OAC) therapy and select comorbidities was assessed by baseline care specialty: cardiology, primary care, or other specialties (internist/neurologist/geriatrician). Associations between care specialty and 2-year clinical outcomes were evaluated using multivariable Cox frailty models to account for within-country homogeneity.
Results: In 52,011 patients, 34,172 (65.7 %) were diagnosed and initially managed in cardiology care, 7396 (14.2 %) in primary care, and 10,443 (20.1 %) in other specialties. The inter-country care specialty distribution varied considerably. Non-vitamin K OAC (NOAC) therapy among CHA_2DS_2-VASc $\geq$2 patients was more common in cardiology care (31.0 %) than primary care (19.8 %) and other specialty care (24.9 %), but comorbidity management was similar across specialties. Compared to cardiology care, primary care was associated with greater non-cardiovascular mortality (1.21 [1.01–1.45]), major bleeding (1.31 [1.05–1.62]), and new/worsening heart failure risk (2.09 [1.69–2.59]). Care in other specialties was associated with greater all-cause (adjusted hazard ratio, 1.19 [95 % CI, 1.09–1.29]), cardiovascular (1.15 [1.01–1.31]), and non-cardiovascular mortality (1.29 [1.13–1.47]), as well as non-haemorrhagic stroke/systemic embolism (1.48 [1.26–1.73]), major bleeding (1.21 [1.02–1.43]), and new/worsening heart failure risk (1.45 [1.21–1.75]) than cardiology care.
Conclusion: Comorbidity management was similar across AF care specialties, but patients outside of cardiology care had fewer NOAC prescriptions and greater risk for most clinical endpoints. Cardiology expertise may have important implications for AF prognosis.
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1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia and is strongly associated with stroke and mortality risk [1]. Early oral anticoagulation (OAC) therapy is critical for reducing stroke risk and improving prognosis [2]. However, prescription of appropriate OAC therapy does not occur for all eligible AF patients, rendering them susceptible to poor clinical outcomes [2,3]. The literature suggests that care specialty at AF diagnosis is a possible predictor for adherence to appropriate OAC prescription in AF patients and, in parallel, for the incidence of future stroke and mortality [4,5].

Analyses of prescription patterns suggest that AF patients in cardiology care are most likely to receive OAC therapy, including non-vitamin K OAC (NOAC) therapy, compared to those in primary care [6]. This trend is consistent with earlier studies on vitamin K antagonist (VKA) prescriptions, which were the standard of care for stroke prevention in AF before the introduction of NOACs [7–10]. Additionally, studies with follow-up data have shown that cardiology care is associated with reduced risk of clinical endpoints, such as stroke and mortality, although the associations with hospitalisation, bleeding, and heart failure (HF) are less consistent [6,7,11].

Together, the evidence suggests that cardiology care is linked to appropriate OAC prescription in AF and prevention of some clinical outcomes. However, previous studies have been limited to retrospective analyses of single-country claims databases or single-country observational studies conducted prior to the widespread use of NOACs in clinical practice. It is it unknown whether the association of care speciality and outcome risk in AF relates to differences in managing conditions commonly comorbid with AF. Therefore, there is a need to examine the relationship of cardiology care, anticoagulant prescription, and clinical outcomes in a large, international patient registry representative of real-world AF patients. This study used the Global Anticoagulation Registry in the FIELD-Atrial Fibrillation (GARFIELD-AF) registry to determine if care specialty is associated with OAC prescription and 2-year clinical outcome risk in patients with newly diagnosed non-valvular AF [12].

2. Methods

2.1. Study design and participants

GARFIELD-AF (NCT01090362) is an international, non-interventional, prospective registry of patients with newly diagnosed non-valvular AF [12]. Adult patients ≥18 years diagnosed with AF and at least one investigator determined risk factor for stroke were consecutively recruited between March 2010 and August 2016 as part of five cohorts across >1000 sites in 35 countries. AF was diagnosed according to local procedures within the six weeks prior to recruitment. The investigation sites reflected the diversity of care specialties and care settings in each country: hospital departments, office-based practice, anticoagulation clinics, and general or family practice. Follow-up time was two years from enrolment. Patients with valvular disease or a transient cause of AF were not included in the registry. Participants with unavailable care setting and follow-up information were excluded from all analyses.

Patients were grouped according to care specialty at AF diagnosis: cardiology, primary care (general practitioner), other specialty care (internist, neurologist, geriatrician) [13]. Given the low number of patients diagnosed and initially managed by neurologists ($n = 872$, 1.7 %) and geriatricians ($n = 201$, 0.4 %), these groups were combined with patients diagnosed by internists ($n = 9370$, 18.0 %). Patients were also grouped according to the care setting of AF diagnosis: hospital, outpatient (offices/anticoagulation centres/thrombosis centres), or emergency room setting.

2.2. Data source

Data was sourced from the electronic case report form (eCRF) of each participant. Data were collected at 4-monthly intervals up to 24 months or until death or loss to follow-up, whichever occurred first. The completeness and accuracy of the captured data was monitored by the coordinating centre (Thrombosis Research Institute, London, UK). Data were examined by an audit and quality control programme, consisting of cross-reference of 20 % of eCRFs in the GARFIELD-AF registry against source documentation at investigation sites [14]. Data for the present analysis were extracted from the final locked registry database in June 2019.

2.3. Ethics statement

Independent ethics committee and hospital-based institutional review board approvals were obtained for the registry protocol. The registry was conducted in accordance with the principles of the Declaration of Helsinki, local regulatory requirements, and the International Conference on Harmonisation–Good Pharmacoepidemiologic and Clinical Practice guidelines. Written informed consent was obtained from all study participants. Participant confidentiality and anonymity was maintained throughout the study.

2.4. Analysis of comorbidity management

Adherence to European Society of Cardiology (ESC) -recommended therapy was determined for the following comorbidities: coronary artery disease, diabetes, congestive HF, hypertension, and peripheral vascular disease [15] (see Table S1 for management guidelines). Patients with none of these comorbidities were excluded from this analysis. Included AF patients were categorised into those with none, some, or all of the eligible comorbidity guideline-adhering therapy.

2.5. Definitions of baseline variables and outcome measures

Vascular disease included patients with coronary artery disease and/or peripheral artery disease. Chronic kidney disease was classified into moderate-to-severe (stages 3–5), mild (stages 1 and 2), or none, according to National Kidney Foundation guidelines. HF was defined as prior or current HF or left ventricular ejection fraction <40 %. AF type was classified according to the European Society of Cardiology guidelines [16]. For assessment of risk, the GARFIELD-AF risk calculator (representing expected occurrence of mortality, ischaemic stroke/transient ischaemic attack (TIA)/systemic embolism (SE) or major bleeding within two years from baseline) [17], CHA_2DS_2-VASc score (HF, hypertension, age ≥ 75 years, diabetes, ischaemic stroke/TIA/SE, vascular disease, age 65–74 years, female sex) [18], and a modified HAS-BLED (systolic blood pressure > 160 mmHg, abnormal renal function, abnormal liver function, stroke history, bleeding history, age > 65 years, use of platelet inhibitors or non-steroidal anti-inflammatory drugs, >8 units of alcohol per week, but not labile international normalized ratio) were calculated [19]. Major bleeding was reported by investigators according to the International Society on Thrombosis and Haemostasis (ISTH) definition [20]. Minor/non-major clinically relevant bleeds that occurred in a critical site or required transfusion were reclassified as major bleeding. Worsening HF was defined as re-stratification into higher New York Heart Association classification after enrolment or acute or progressive decompensation of previous stable HF.

2.6. Statistical analysis

The distribution of variables collected at baseline is reported by care specialty or care setting grouping. Continuous variables are summarised as medians and interquartile range, and categorical variables as frequencies and percentages. Because studies with large sample sizes tend

to produce statistically significant findings in the presence of clinically irrelevant differences, no formal statistical tests were performed for the baseline comparison. Our primary aim was to identify associations between care specialty and selected clinical endpoints: all-cause mortality, cardiovascular mortality, non-cardiovascular mortality, non-haemorrhagic stroke/SE, major bleeding, myocardial infarction/acute coronary syndromes (MI/ACS) and new/worsening HF. Occurrence of clinical outcomes is presented as absolute number of events and event rate per 100 person-years with 95 % confidence intervals (CI). Person-year rates were estimated using a Poisson model. The hazard ratio (HR) for a selected clinical outcome was estimated using multivariable Cox frailty models, incorporating a random effect term to account for within-country homogeneity [21]. The confounding factors include baseline demographics, comorbidities, vital signs, and treatment and are detailed in the results footnotes. Multiple imputation was applied for estimating associations of care specialty with outcomes [22]. Final estimates were obtained by combining results across five imputed datasets. Statistical analyses were carried out using SAS® Enterprise Guide (version 8.1).

3. Results

3.1. Study population

Of the 52,057 patients enrolled in GARFIELD-AF, 46 were excluded from this study due to unavailability of care setting or follow-up information (Fig. S1). Of the 52,011 patients analysed, 34,172 (65.7 %) were diagnosed and initially managed in cardiology care, whereas 7396 (14.2 %) were diagnosed and initially managed in primary care and 10,443 (20.1 %) were diagnosed and initially managed in other specialty care. The baseline characteristics of the care specialty groups are shown in Table 1. Permanent AF was more common in patients in primary care, while persistent AF and paroxysmal AF were more common in patients in cardiology care. AF diagnosis by cardiology or other specialty care was most commonly undertaken in a hospital setting, whereas primary care diagnosis was most common in an outpatient setting. Inter-group differences in medical history were negligible for most comorbidities; although, patients diagnosed in the other specialties care group had an almost two-times higher prevalence of prior stroke/TIA/SE. Median CHA_2DS_2-VASc, HAS-BLED, GARFIELD-AF stroke, and GARFIELD-AF bleeding scores were the similar across care specialties. The GARFIELD-AF death risk score was slightly lower among patients diagnosed in cardiology care.

3.2. Inter-country care specialty and care setting comparison

There was considerable heterogeneity in the distribution of care specialty and care setting type between countries. For instance, AF was diagnosed in cardiology care in over 95 % of AF patients in Turkey, but only 15 % of patients in the United Kingdom (Fig. 1a). Similarly, AF was almost exclusively diagnosed in a hospital care setting in China, whereas in Egypt only 25 % were diagnosed in a hospital setting (Fig. S2).

3.3. Distribution of care specialties throughout follow-up

The overall proportion of patients cared for in cardiology was consistent at about two-thirds of all patients at baseline and at the first and last follow-up visits (Table S2). In contrast, the overall proportion of patients in primary care increased marginally from 14.2 % at baseline to closer to 20 % at first and last follow-up, while those in other specialty care decreased from 20.1 % of patients at baseline to nearly 14 % at first and last follow-up. Of the patients care for in cardiology care at baseline, the majority revisited cardiology care throughout follow-up, with only a small number changing to primary care or other specialty care. Of the patients diagnosed in primary care, approximately 60 % revisited primary care throughout follow-up. The majority that changed care

Table 1
Baseline patient characteristics by care specialty.

Variable	Care specialty		
	Cardiology	Primary care	Other specialty
N	34,172	7396	10,443
Sex, n (%)			
• Male	19,386 (56.7)	4082 (55.2)	5560 (53.2)
• Female	14,785 (43.3)	3314 (44.8)	4883 (46.8)
Age, median (Q1; Q3), years	70.0 (62.0;77.0)	73.0 (65.0;79.0)	72.0 (64.0;79.0)
Ethnicity, n (%)			
• Caucasian	18,414 (55.0)	6010 (85.5)	7571 (73.9)
• Hispanic/Latino	2378 (7.1)	422 (6.0)	593 (5.8)
• Asian	11,955 (35.7)	461 (6.6)	1860 (18.2)
• Afro-Caribbean/Mixed/ Other	723 (2.2)	134 (1.9)	214 (2.1)
Body mass index, median (Q1; Q3), kg/m^2	26.6 (23.7;30.3)	28.2 (25.1;32.0)	27.2 (24.2;31.0)
Systolic blood pressure, median (Q1; Q3), mmHg	130.0 (120.0;144.0)	134.0 (120.0;145.0)	134.0 (120.0;148.0)
Diastolic blood pressure, median (Q1; Q3), mmHg	80.0 (70.0;88.0)	80.0 (71.0;88.0)	80.0 (70.0;90.0)
Pulse, median (Q1; Q3), bpm	84.0 (70.0;105.0)	85.0 (72.0;104.0)	85.0 (72.0;108.0)
Type of atrial fibrillation, n (%)			
• Permanent	3693 (10.8)	1483 (20.1)	1454 (13.9)
• Persistent	5439 (15.9)	929 (12.6)	1385 (13.3)
• Paroxysmal	10,314 (30.2)	1420 (19.2)	2570 (24.6)
• New onset (unclassified)	14,726 (43.1)	3564 (48.2)	5034 (48.2)
Care setting location at diagnosis, n (%)			
• Hospital	22,159 (64.8)	1171 (15.8)	7005 (67.1)
• Outpatient	9017 (26.4)	5194 (70.2)	1707 (16.3)
• Emergency Room	2996 (8.8)	1031 (13.9)	1731 (16.6)
Medical history, n (%)			
• Heart failure	8327 (24.4)	1115 (15.1)	2297 (22.0)
• Acute coronary syndromes	4003 (11.8)	596 (8.1)	934 (9.0)
• Vascular disease	8961 (26.4)	1519 (20.6)	2335 (22.5)
• Carotid occlusive disease	912 (2.7)	201 (2.8)	425 (4.1)
• Pulmonary embolism/DVT	738 (2.2)	255 (3.5)	362 (3.5)
• Prior stroke/TIA/SE	3331 (9.8)	656 (8.9)	1852 (17.9)
• Prior bleeding	815 (2.4)	180 (2.4)	320 (3.1)
• Hypertension	25,776 (75.7)	5651 (76.6)	8177 (78.5)
• Hypercholesterolaemia	13,517 (40.7)	2990 (41.6)	4448 (44.5)
• Diabetes	7445 (21.8)	1552 (21.0)	2545 (24.4)
• Cirrhosis	154 (0.5)	29 (0.4)	110 (1.1)
• Moderate to severe CKD	3080 (9.3)	977 (13.8)	1297 (12.9)
• Dementia	424 (1.2)	96 (1.3)	244 (2.3)
Heavy alcohol consumption, n (%)	627 (2.2)	184 (2.9)	217 (2.5)
Current smoker, n (%)	3613 (11.6)	607 (9.0)	982 (10.4)
Treatment at baseline, n (%)			
• NOAC ± AP	10,122 (30.1)	1492 (20.4)	2498 (24.2)
• VKA ± AP	12,599 (37.5)	3272 (44.7)	4312 (41.7)
• AP only	7017 (20.9)	1581 (21.6)	2163 (20.9)
• None	3889 (11.6)	980 (13.4)	1364 (13.2)
• Risk scores			
CHA_2DS_2-VASc score, median (Q1; Q3)	3.0 (2.0;4.0)	3.0 (2.0;4.0)	3.0 (2.0;5.0)
HAS-BLED score, median (Q1; Q3)[1]	1.0 (1.0;2.0)	1.0 (1.0;2.0)	1.0 (1.0;2.0)
GARFIELD-AF death score[2], median (Q1;Q3)	4.4 (2.4;8.1)	5.3 (3.0;9.3)	5.4 (3.0;9.8)
GARFIELD-AF stroke score[3], median (Q1;Q3)	1.5 (1.0;2.3)	1.6 (1.2;2.4)	1.8 (1.2;2.7)
GARFIELD-AF bleeding score[4], median (Q1;Q3)	1.5 (1.0;2.3)	1.8 (1.1;2.6)	1.7 (1.1;2.6)

DVT: deep vein thrombosis, TIA: transient ischaemic attack, SE: systemic embolism, CKD: chronic kidney disease, NOAC: non-vitamin K oral anticoagulant, AP: anti-platelet therapy, VKA: vitamin K antagonist. [1]The 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). [2]Represents the expected probability of death within two-years follow-up; [3]Represents the expected probability of non-haemorrhagic stroke/SE within two-years follow-

up. [4]Represents the expected probability of major bleeding within two-years follow-up.

specialty during follow-up opted for cardiology care. Of the patients that changed from other baseline specialty care, approximately 30 % visited cardiology care and between 24 and 29 % visited primary care.

3.4. OAC treatment distribution in different care specialties and care settings

In patients at high risk of stroke (CHA_2DS_2-VASc score ≥ 2, excluding sex), the proportion of patients prescribed any OAC increased from cohort one (enrolled in 2010–2011) to cohort five (2015–2016) across all care specialties (Fig. S3). In all patients, NOAC therapy comprised 30.1 % of all OAC prescriptions in cardiology care, and was lower in primary care (20.4 %) and other specialty care (24.2 %, Fig. 1b). Similarly, in patients with CHA_2DS_2-VASc score ≥ 2, NOAC therapy comprised 31.0 % of all OAC prescriptions in cardiology care, and was lower in primary care (19.8 %) and other specialty care (24.9 %) (Fig. 1c).

The baseline characteristics of patient care settings groups is shown in Table S3. The proportion of high-risk AF patients prescribed baseline OAC therapy in a hospital or outpatient setting increased from cohort one to cohort five (Fig. S4). OAC prescription rates in an emergency

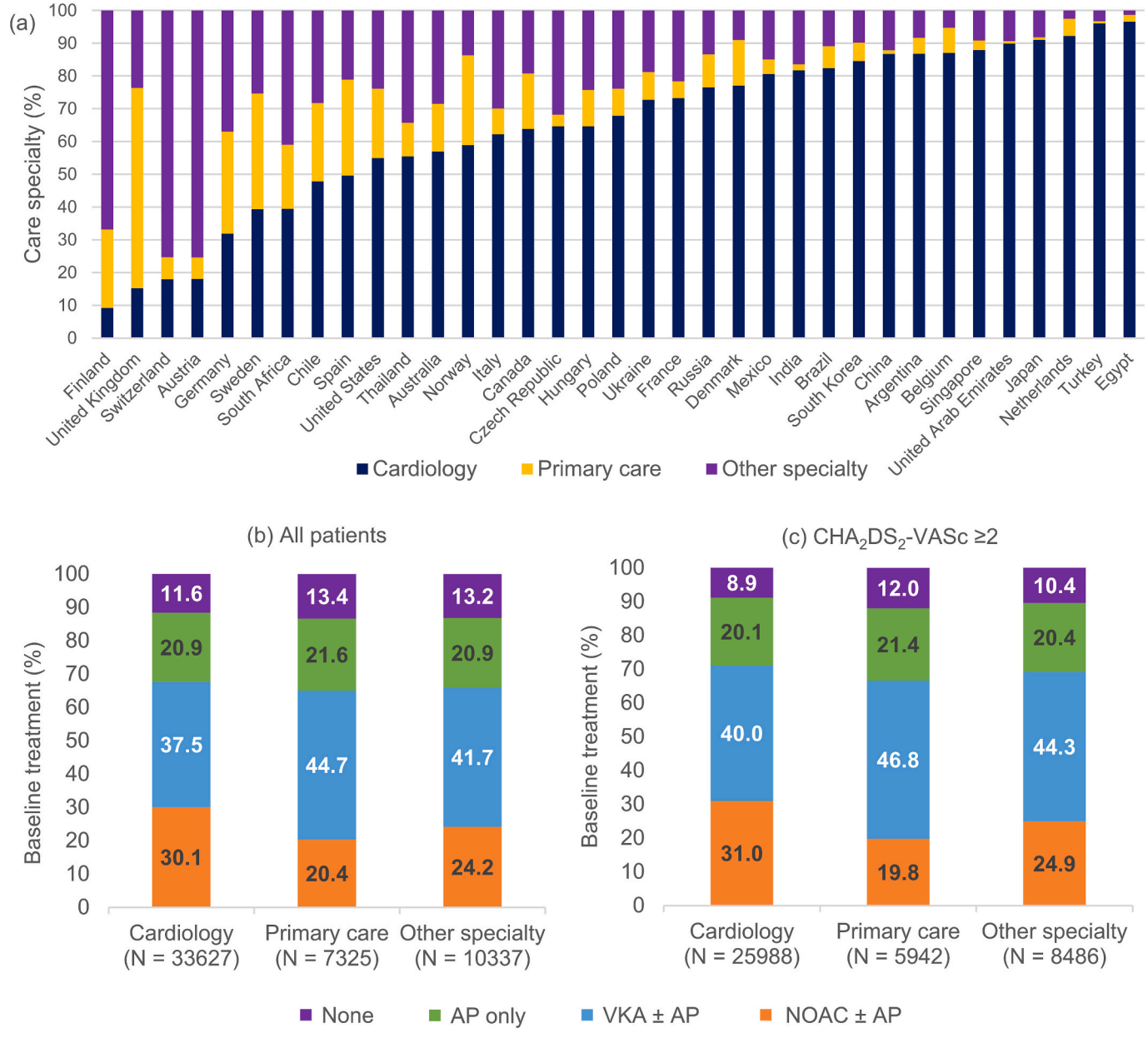

Fig. 1. Relative proportions of atrial fibrillation (AF) care specialty types by country and distribution of baseline treatment types. (a) Data is presented as proportions of AF patients diagnosed and initially managed in cardiology (dark blue), primary care (purple), and other specialty care (yellow) in each country enrolled in the GARFIELD-AF registry. Countries are ordered according to proportion of patients diagnosed in primary care. Relative baseline treatment distributions in all patients and in patients with high stroke risk (CHA_2DS_2-VASc score ≥ 2 (excl. gender)) are shown in panel b and panel c, respectively. Data are presented as percentage of patients in cardiology, primary care, and other specialty care receiving either no treatment (purple), antiplatelet (AP) treatment only (green), vitamin K antagonist (VKA) with or without AP treatment (blue), or non-vitamin K oral anticoagulation (NOAC) with or without AP treatment (orange). Sample sizes are shown in the figure. Patients with unavailable baseline treatment information were excluded ($n = 722$ excluded in all patients; $n = 591$ excluded in patients with high stroke risk). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

room setting were largely similar for each cohort. Prescriptions of any OAC or a NOAC were more common in an outpatient setting than hospital or emergency room settings (Fig. S5).

In patients at high risk for stroke, we then determined the baseline treatment distributions for each care setting *within* each AF care specialty groups (Fig. S6). Among patients diagnosed in cardiology or other specialty care, those seen in an outpatient setting were more commonly prescribed any OAC or a NOAC therapy than those seen in a hospital or emergency room setting (Fig. S6a, b). Among patients diagnosed in a primary care specialty, prescription of any OAC or NOAC therapy was comparable across care settings (Fig. S6c).

3.5. Comorbidity management in different care specialties

We then determined whether ESC guideline-recommended therapy was followed in the treatment of comorbidities in our patient cohort [15]. The proportions of patients receiving all, some, or none of their eligible recommended therapy for the five selected comorbidities was comparable between AF care specialties (Table 2). Similarly, the relative proportions of recommended therapy were comparable between groups when each comorbidity was examined in isolation.

3.6. Association of baseline care specialty with clinical outcomes

The absolute event counts, event rates, and unadjusted and adjusted HRs for the clinical outcomes are shown in Table S4. Baseline primary care was associated with increased non-cardiovascular mortality (aHR 1.21; 95 % CI, 1.01–1.45), major bleeding (aHR 1.31; 95 % CI, 1.05–1.62), and new/worsening HF (aHR 2.09; 95 % CI, 1.69–2.59) compared to cardiology care. Baseline care in another specialty was associated with significantly higher all-cause mortality (aHR 1.19; 95 % CI, 1.09–1.29), cardiovascular mortality (aHR 1.15; 95 % CI, 1.01–1.31), non-cardiovascular mortality (aHR 1.29; 95 % CI, 1.13–1.47), non-haemorrhagic stroke/SE (aHR 1.48; 95 % CI, 1.26–1.73), major bleeding (aHR 1.21; 95 % CI, 1.02–1.43), and new/worsening HF (aHR 1.45; 95 % CI, 1.21–1.75) than baseline cardiology care (Fig. 2). Relative to cardiology care, baseline primary care or other specialty care did not change MI/ACS outcome likelihood.

3.7. Sensitivity analysis

We performed a sensitivity analysis by removing the five countries with less than 20 patients in one or more care specialty groups (Table S5). The results were largely comparable with the main analysis. However, the associations of other specialty care with cardiovascular mortality, non-haemorrhagic stroke/SE, and major bleeding did not reach statistical significance, mainly due to the reduced sample size. In addition, primary care was now associated with significantly higher risk of non-haemorrhagic stroke/SE compared to cardiology care.

4. Discussion

From this analysis of the GARFIELD-AF registry, we found that patients diagnosed with AF in cardiology care are more commonly prescribed appropriate OAC treatment than patients in primary care or other specialty care. Alongside this, care outside of cardiology is associated with greater risk of clinical outcomes, including mortality, non-haemorrhagic stroke/SE, and major bleeding. Importantly, this greater risk of clinical outcomes appears unrelated to differences in comorbidity management, as there was similar adherence to guideline-recommended therapy for five conditions common comorbid with AF. These findings strengthen the relationship between cardiology care, adherence to guideline-recommended pharmacotherapy, and improved outcomes for AF patients.

Table 2
Distribution of guideline-directed medical therapy (GDMT) use by care specialty at baseline.

Comorbidity GDMT use	Care setting specialty		
	Cardiology (*N* = 27,146)	Primary care (*N* = 5784)	Other specialty (*N* = 8390)
All five comorbidities combined			
All of eligible GDMT	12,663 (46.7)	2909 (50.3)	4067 (48.5)
Some of eligible GDMT	8940 (32.9)	1565 (27.1)	2663 (31.7)
None of eligible GDMT	5543 (20.4)	1310 (22.6)	1660 (19.8)
Coronary artery disease	*n* = 6992	*n* = 1090	*n* = 1666
All of eligible GDMT	2702 (38.6)	408 (37.4)	633 (38.0)
Some of eligible GDMT	3835 (54.9)	608 (55.8)	939 (56.4)
None of eligible GDMT	455 (6.5)	74 (6.8)	94 (5.6)
Diabetes	*n* = 6831	*n* = 1405	*n* = 2362
All of eligible GDMT	2492 (36.5)	536 (38.2)	928 (39.3)
Some of eligible GDMT	3047 (44.6)	601 (42.8)	1032 (43.7)
None of eligible GDMT	1292 (18.9)	268 (19.1)	402 (17.0)
Heart failure	*n* = 7512	*n* = 999	*n* = 2091
All of eligible GDMT	3673 (48.9)	435 (43.5)	1035 (49.5)
Some of eligible GDMT	2535 (33.7)	343 (34.3)	693 (33.1)
None of eligible GDMT	1304 (17.4)	221 (22.1)	363 (17.4)
Hypertension	n = 23,865	*n* = 5222	*n* = 7612
All of eligible GDMT	17,452 (73.1)	3753 (71.9)	5620 (73.8)
None of eligible GDMT	6413 (26.9)	1469 (28.1)	1992 (26.2)
Peripheral vascular disease	*n* = 1728	*n* = 328	*n* = 553
All of eligible GDMT	828 (47.9)	157 (47.9)	248 (44.8)
Some of eligible GDMT	384 (22.2)	77 (23.5)	117 (21.2)
None of eligible GDMT	516 (29.9)	94 (28.7)	188 (34.0)

Patients with none of coronary artery disease, diabetes, heart failure, hypertension or peripheral vascular disease are excluded from this analysis. The adopted definitions for GDMT for each comorbidity are reported in Table S1.

4.1. NOACs are more commonly prescribed in cardiology care

In line with previous reports [4,5,13,23,24], we found that OAC prescriptions increased from 2010 to 2016. We now also show that this trend was consistent across all AF care specialties, with about two-thirds of patients prescribed OAC therapy on average. Notably, baseline NOAC prescription was more common in cardiology care in the total cohort and in high-stroke risk patients, with nearly one-third of patients receiving NOAC therapy. Together, these data are indicative of greater adherence to NOAC prescribing guidelines in cardiology care.

Previous studies have also shown similar NOAC prescription patterns in AF care specialties; although, these studies were often limited to single country and retrospective analyses of data from claims databases accessed early in the NOAC era. A large-scale analysis of incident AF prescription records in the USA found that cardiology care is positively associated with NOAC prescription, regardless of patient demographics and comorbidities [5]. Similarly, the TREAT-AF study and the ORBIT-AF and German AFNET registries found greater adherence to OAC prescription guidelines in cardiology care compared to primary care

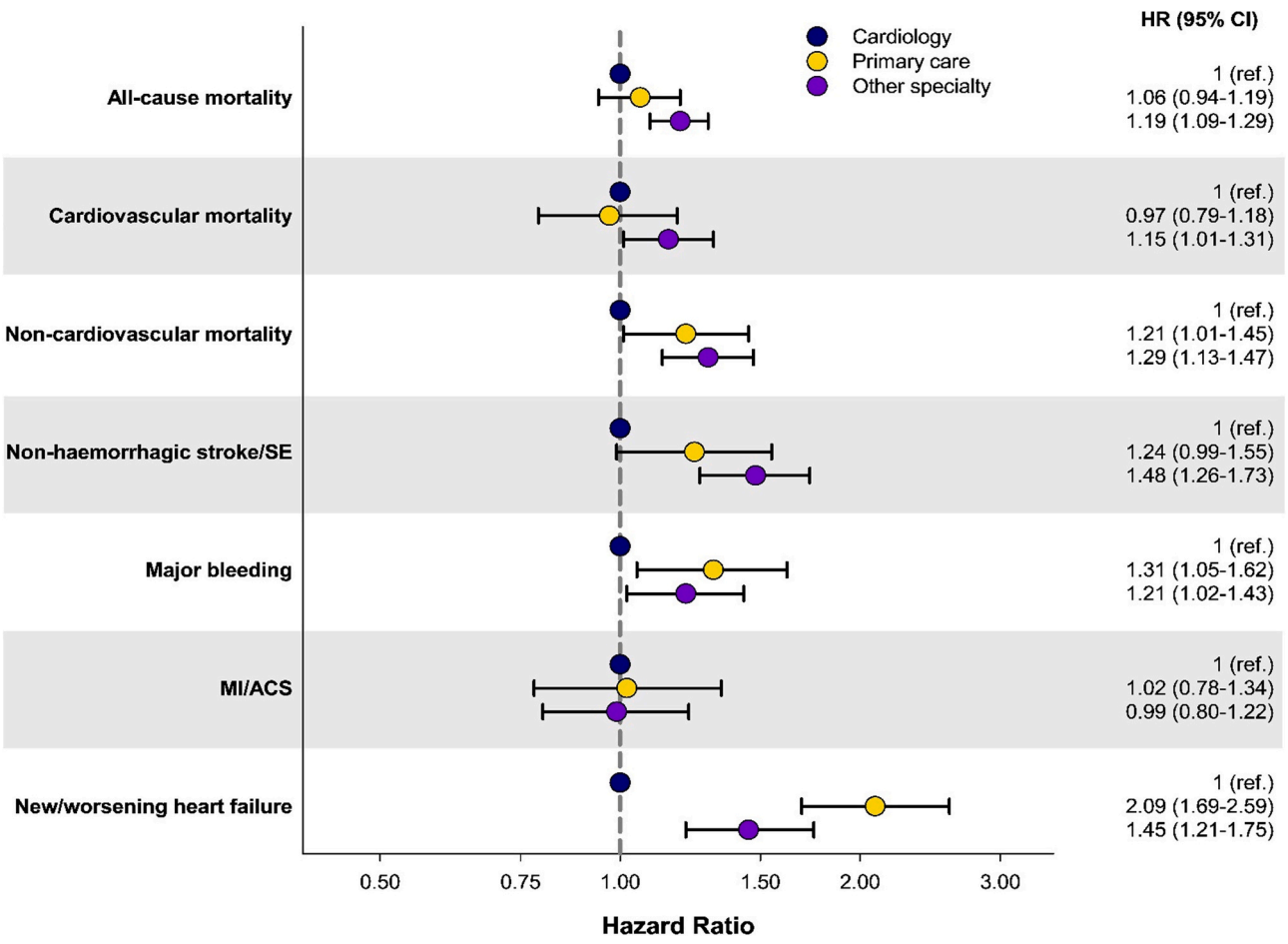

Fig. 2. Adjusted hazard ratios for selected clinical outcomes through 2-year follow-up by care specialty at atrial fibrillation (AF) diagnosis. Data are presented as forest plot with the adjusted hazard ratio (HR) and 95 % confidence interval (CI). Risk for each outcome for patients diagnosed and initially managed in primary care (yellow) and other specialty care (purple) are shown, cardiology care (blue) was used as the reference (ref.). HRs were adjusted by sex, age, race/ethnicity, type of AF, heart failure, vascular disease, hypertension, prior stroke/transient ischaemic attack/systemic embolism (SE), prior bleeding, diabetes, moderate-to-severe CKD, care setting location, and baseline anticoagulation. MI: myocardial infarction, ACS: acute coronary syndrome. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

[7–10]. Our findings, confirm that OAC prescription patterns observed in AF care specialties are consistent in a large, multinational patient registry that is better reflective of the modern era of guideline-recommended NOAC therapy.

4.2. AF diagnosis outside of cardiology is associated with clinical outcome risk

If appropriate OAC is more commonly prescribed in cardiology care, does it relate to clinical outcome risk? Compared to cardiology care, primary care or other specialty care were associated with greater risk of a combination of all-cause, cardiovascular, and non-cardiovascular mortality, as well as stroke/SE, major bleeding, and new/worsening HF. Our findings are consistent with previous analyses of single-country outpatient or emergency care databases that show reductions in stroke or mortality risk in AF patients in cardiology care [6,11]. Furthermore, our results align with the TREAT-AF study, which linked cardiology care to a lower stroke risk and reduced overall and cardiovascular mortality [7].

However, some of our results differ from previous studies, which report that cardiology care, while reducing all-cause mortality and stroke risk, may increase or not affect the risk of bleeding, MI, or HF [6,7,11]. This discrepancy could arise from differences in patient grouping criteria. Our study found non-uniform outcome associations between primary care and other specialty care compared to cardiology care. Therefore, if we included only patients from cardiology and primary care and excluded those in other specialty care, there would have been fewer significant outcome associations found in our analysis, and therefore our conclusions would have been different.

4.3. Other factors that might influence prescription and clinical outcomes

We explored various factors that might influence the associations between care specialty, OAC prescription, and clinical outcomes. Our results suggest that the care setting location impacts OAC prescription for AF patients in each care specialty. For instance, AF patients diagnosed by a cardiology specialist in an outpatient setting were more likely to be receive NOAC therapy than an those diagnosed in hospital or emergency room settings. This finding aligns with a recent report from the GLORIA-AF registry that NOAC prescription is more common in primary care clinics or specialist offices than in university hospitals [4]. Besides care setting, OAC treatment patterns have been linked to geographic factors, with country or continent of enrolment and country healthcare expenditure identified as independent predictors of OAC prescription and likelihood of OAC withholding [4,13]. Given that the GARFIELD-AF registry is international, we applied a multivariable frailty Cox model in our analysis to account for within-country homogeneity when determining the associations of care specialty with clinical outcomes.

AF is often comorbid with other clinical conditions, creating

complexity in treatment decisions [25]. Therefore, differences in comorbidity management in AF care specialties could contribute to the varying clinical outcomes in AF patients observed in our study. We recently showed that adherence to guideline-recommended management of five common AF comorbidities reduces overall mortality risk in AF patients [15]. However, to the best of our knowledge, whether management of comorbidities differs across AF care specialties had not been directly investigated. For our current study, we leveraged the same real-world comorbidity information afforded by GARFIELD-AF registry and found similar adherence to AF comorbidity treatment across AF care specialties. This suggests that the increased clinical outcome risk outside of cardiology care cannot be fully explained by differences in comorbidity management.

4.4. Clinician- and patient-level factors

Several factors have been identified as barriers for adherence to guideline-recommended treatment in AF, potentially contributing to increased clinical outcome risk for patients outside of cardiology care [26]. At the clinician level, barriers include difficulties in interpreting stroke and bleeding risk scores like CHA_2DS_2-VASc and HAS-BLED, lack of knowledge about balancing stroke and bleeding risks, and therapeutic inertia [27,28]. These issues can steer the clinician away from prescribing OAC therapy even when a patient is indicated for it. At the patient level, our research shows that the specialty of care provider influences treatment uptake, with patients outside of cardiology care more likely to refuse treatment [29]. Therefore, it is possible that AF patients in cardiology care are more receptive to treatment uptake. We found that patients diagnosed with AF in cardiology care more commonly returned to their baseline care specialty than those in other care specialties. This exploratory finding could suggest that besides standard referral practices, patients in cardiology are more satisfied with their care and are thus more likely to adhere to prescriptions that reduce outcome risk.

Using data from the largest multinational observational study of real-world AF patients, GARFIELD-AF, our findings indicate that care specialty at diagnosis and initial management influences adherence to guideline-recommended treatment and clinical outcome risk in AF. Importantly, while we have attempted to account for other confounding patient characteristics and treatment of comorbidities, AF is complex and managing AF outcomes and wellbeing is not only determined by baseline anticoagulation. Therefore, our study underscores the need for a holistic approach to pharmacotherapy, lifestyle modification, and clinician and patient education to optimally manage AF [30].

4.5. Limitations

Given the substantial differences in patients' baseline characteristics across care specialties, possible confounding is a limitation of our study. We applied robust statistical methods, including a substantial number of potential confounders in our multivariable models. Nevertheless, we cannot rule out residual, unmeasured confounding, as we were not able to account for factors such as social differences, treatment adherence, follow-up resources, and possible local differences in the package of care. Direct causal links between care specialty and clinical outcomes should not be inferred from these results. Our study was also limited by the unknown subscription to society guidelines for AF management. Our data were collected during the introduction of NOACs into AF care specialties (2010–2016), the associations found in our study might not fully reflect the contemporary AF management landscape. While we did examine the relative proportions of patients visiting each care specialty during follow-up, thorough investigation of longitudinal AF management, such as OAC compliance or switching, was beyond the scope of this study, which focussed on the link between baseline AF care and outcomes.

5. Conclusion

AF patients initially managed in cardiology care more commonly received appropriate OAC therapy than patients diagnosed in primary care or other specialty care. Contemporaneously, care outside of cardiology was associated with increased rates of 2-year clinical outcomes. These findings strengthen the relationship between cardiology care at the time of AF diagnosis and better patient outcomes. We hope these findings generate positive discussion among all AF care providers such that strategies can be implemented to ensure optimal outcomes for patients.

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CRediT authorship contribution statement

C. Fielder Camm: Writing – review & editing, Writing – original draft, Visualization, Supervision, Project administration, Methodology, Conceptualization. **Saverio Virdone:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Formal analysis, Data curation. **Carlos Jerjes-Sánchez:** Writing – review & editing, Investigation. **Seil Oh:** Writing – review & editing, Investigation. **John W. Eikelboom:** Writing – review & editing, Investigation. **Ali Oto:** Writing – review & editing, Investigation. **Keith A.A. Fox:** Writing – review & editing, Investigation, Funding acquisition. **A. John Camm:** Writing – review & editing, Writing – original draft, Supervision, Funding acquisition, Conceptualization. **Karen S. Pieper:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation. **Shinya Goto:** Writing – review & editing, Investigation. **Hany Ragy:** Writing – review & editing, Investigation. **Ajay K. Kakkar:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

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Data availability

Data and analysis presented in this study was derived from the GARFIELD-AF registry, based on accrued eCRF data from 2010 to 2016. Data can be shared upon reasonable request to Svirdone@tri-london.ac.

uk.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2024.132866.

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