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#### **Author Accepted Manuscript**

# Anticoagulation in older people with atrial fibrillation moving to care homes: a data linkage study

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#### **ABSTRACT**

**Background** Treatment decisions about oral anticoagulants (OAC) for atrial fibrillation (AF) are complex in older care home residents.

**Aim** To explore factors associated with OAC prescription.

**Design and Setting** Retrospective cohort study set in care homes in Wales, United Kingdom, listed in the Care Inspectorate Wales Registry 2017/18.

**Method** Analysis of anonymised individual-level electronic health and administrative data on people aged ≥65 years entering a care home between 1<sup>st</sup> January 2003 and 31<sup>st</sup> December 2018, provisioned from the Secure Anonymised Information Linkage Databank.

Results Between 2003 and 2018, 14,493 people with AF aged ≥65 years became new residents in care homes in Wales and 7,057 (48.7%) were prescribed OAC (32.7% in 2003 compared to 72.7% in 2018) within six months prior to care entry. Increasing age and prescription of antiplatelet therapy were associated with lower odds of OAC prescription (adjusted odds ratio [aOR] 0.96 per one year age increase [95% confidence interval [CI] 0.95 to 0.96] and aOR 0.91 [0.84 to 0.98], respectively). Conversely, prior venous thromboembolism (aOR 4.06 [3.17 to 5.20]), advancing frailty (mild: aOR 4.61 [3.95 to 5.38]; moderate: aOR 6.69 [5.74 to 7.80]; severe: aOR 8.42 [7.16 to 9.90]) and year of care home entry from 2011 onwards (aOR 1.91 [1.76 to 2.06]) were associated with higher odds of OAC prescription.

**Conclusions** There has been an increase in OAC prescribing in older people newly admitted to care homes with AF. This study provides an insight into the factors influencing OAC prescribing in this population.

# **Keywords**

Atrial fibrillation, nursing homes, anticoagulants, long-term care, practice patterns (physicians'), primary health care

#### How this fits in

Available data on factors that influence the decision to prescribe anticoagulation for atrial fibrillation in care home residents is conflicting. This study adds to the body of evidence to suggest that advancing age and concomitant antiplatelet therapy are barriers to anticoagulant prescription in older people newly admitted to care homes. Targeted educational tools on anticoagulant prescribing in older people with atrial fibrillation and an indication for antiplatelet therapy (e.g. peripheral vascular disease, ischaemic stroke, acute coronary syndrome) are needed.

#### INTRODUCTION

Atrial fibrillation (AF) disproportionately affects older people, with its prevalence increasing in parallel to population growth and ageing.<sup>1,2</sup> Older care home residents represent a growing group of AF patients. Previous estimates for the proportion of older care home residents with a diagnosis of AF have ranged from 7% to 38%.<sup>3-5</sup>

Atrial fibrillation increases the risk of stroke four- to five-fold,<sup>6</sup> therefore, stroke prevention is the cornerstone of AF management. This focuses on the prescription of oral anticoagulants (OACs),<sup>7</sup> however, there is evidence of under-prescribing of OAC in care home residents.<sup>3</sup> The prevalence of anticoagulant use for AF in care homes ranged from 17% to 68% across multiple studies.<sup>3,5,8</sup> With concerns of iatrogenic harm and doubt of the net clinical benefit of treatment, often clinicians face the dilemma of a 'treatment-risk paradox' in this vulnerable group. The risk of adverse events is heightened because of the complex interplay between altered pharmacokinetic and pharmacodynamic profiles, frailty, dementia, falls risk, polypharmacy, multi-morbidity and an exponential increase in stroke and bleeding risk with advancing age.<sup>9</sup> However, the consequences of non-prescription of anticoagulation can be catastrophic; AF-related strokes are often more severe than strokes related to other causes, and people who suffer an AF-related stroke are more likely to die, experience chronic disability and require constant nursing care.<sup>11-13</sup>

The latest European Society of Cardiology (ESC) guidelines on AF state there is sufficient evidence to support OAC prescribing in older people based on a meta-analysis of landmark trials on non-vitamin K antagonist oral anticoagulants (NOACs) including people aged ≥75 years.<sup>7, 14-19</sup> Results from other trials also support the use of warfarin for stroke prevention in

people aged  $\geq$ 75 years with AF.<sup>20, 21</sup> The ESC guidelines also emphasise that frailty, falls risk and multi-morbidity are not sufficient justification for not prescribing OAC in those who are eligible for treatment.<sup>7</sup> This study aims to elucidate the factors associated with OAC prescription in older people aged  $\geq$ 65 years newly admitted to care homes in Wales.

#### **METHODS**

Study design

A retrospective cohort study using anonymised linked data from the Secure Anonymised Information Linkage (SAIL) Databank on CARE home residents with AF (any sub-type or atrial flutter) in Wales (SAIL CARE-AF), following the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) 2015 guidelines (Supplementary Table 1).<sup>22</sup>

#### Data sources

This study utilised anonymised, individual-level population-scale routinely collected electronic health record and administrative data for the population of Wales available within the SAIL Databank.<sup>23-25</sup> The data sources included the Welsh Demographic Service Dataset (WDSD),<sup>26</sup> the Welsh Longitudinal General Practice (WLGP)<sup>27</sup> and the Patient Episode Database for Wales (PEDW).<sup>28</sup> Data were extracted from the PEDW and WLGP using International Classification of Diseases version 10 (ICD-10) and Read version 2 codes, respectively (Supplementary Tables 2 and 3). The WLGP version available to and used by this study contains primary care data with ~80% coverage of patients and general practices in Wales, and PEDW secondary care data with 100% coverage of patients and services.

#### **Participants**

The (CARE) care home data source within the SAIL Databank is derived from care home information available from the Care Inspectorate Wales registry (CIW) with an assigned Residential Anonymous Linking Field (RALF).<sup>29</sup> This is linked to anonymised address data for individual participants.<sup>30-32</sup> The CIW registry 2017/18 was used in this study. Data were extracted for people aged ≥65 years on care home entry with a record of AF (any sub-type or atrial flutter) within the PEDW or WLGP (Supplementary Tables 2 and 3). All participants had a minimum of 12 months data coverage within the WLGP prior to moving to a care home between 1st January 2003 and 31st December 2018. The cohort was restricted to the first care home entry date to prevent participants being accounted for more than once if they moved in and out of different care homes.

#### Co-variates

For information on study covariates, see Supplementary methods.

#### Outcomes

The outcome of interest was OAC prescription or non-prescription between six months before care home entry and the date of care home entry. This was used as a proxy for prescription/non-prescription at the point of care entry.

# Statistical analyses

Unadjusted logistic regression models were used to explore the association between all covariates and OAC prescription or non-prescription. Unadjusted odds ratios [OR] were reported with 95% confidence intervals [CIs] and p-values. Following the process of purposeful selection, any covariate that was not significant at the level 0.1 and not judged to be a potential confounder by the authors (LAR, SLH, DAL, PEP) was excluded from the multivariate

model.<sup>33</sup> This threshold was used because conventional significance levels such as 0.05 can fail to identify important variables.<sup>34</sup> Similar covariates were grouped together and multicollinearity was assessed using the Variance Inflation Factor (see Supplementary methods). Results were reported as adjusted ORs [aOR] with 95% CIs and p-values. For the covariate major bleeding, a sensitivity analysis was carried out to exclude people that had evidence of OAC prescription and a major bleeding event (defined using ICD-10 codes listed in Supplementary Table S2) within six months prior to care entry. This attempted to account for any association that may have arisen because of bleeding caused by OAC. All analyses were completed using Stata v.15 (StataCorp, College Station, Texas 77845, USA).

Research ethics and information governance

For information on research ethics and information governance, see Supplementary methods.

#### **RESULTS**

Characteristics of study cohort on care home entry

Between 2003 and 2018, 14,493 people with AF aged ≥65 years who had at least 12 months of primary care data became new residents in care homes in Wales (Table 1, Supplementary Figure 1). The median (interquartile range, IQR) age (years) of the cohort was 87.0 (82.6-91.2), and 5,103 (35.2%) were males. Of the total cohort with AF, 7,057 (48.7%) had a record of OAC prescription within six months prior to care home entry. There were 5,734 (81.3%) residents on vitamin K antagonist (VKA), 623 (8.8%) on NOAC and 700 (9.9%) that switched between VKA or NOAC therapy in the six months preceding care entry. The proportion of residents prescribed OAC increased from 32.7% in 2003 to 72.7% in 2018 (Figure 1). In 2003, all residents were on VKA. In 2018, 385 (33.0%) were on VKA, 228 (19.5%) were on NOAC and 236 (20.2%) changed between VKA or NOAC prior to care home entry. Residents

prescribed OAC were slightly younger (median age [IQR] 86.2 [81.9-90.2] vs. 87.9 [83.4-92.0]) and a higher proportion were male (37.9% vs. 32.6%). The median [IQR] stroke risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc score 4 [3-5]) at care home entry was the same in residents prescribed OAC and those residents not prescribed OAC, with a slightly higher median [IQR] bleeding risk at care home entry for those prescribed OAC (HAS-BLED score 3 [2-3] vs. 2 [2-3], respectively). There was a greater proportion of residents not prescribed OAC on care home entry who were classified as non-frail (21.5% vs. 3.7%), whereas more residents categorised as moderate (39.9% vs. 31.3%) or severe frailty (34.1% vs. 18.4%) were prescribed OAC. Severely frail residents more commonly had a history of stroke, transient ischaemic attack (TIA), myocardial infarction, hypertension, heart failure (HF), peripheral vascular disease (PVD), venous thromboembolism (VTE) and diabetes compared to those who were mildly or moderately frail. This translated into a higher median (IQR) CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 5 (4-5) for severely frail residents compared to 4 (3-5) for mild or moderately frail residents (Table 2).

# Factors associated with OAC prescription

From unadjusted analyses (Table 3), factors associated with OAC non-prescription included increasing age and prescription of antiplatelet therapy. Conversely, stroke risk factors such as prior stroke (ischaemic, haemorrhagic and stroke of unknown origin), TIA, hypertension, HF, smoking history, VTE, diabetes and PVD were associated with OAC prescription. Male sex, advancing frailty, harmful alcohol use, major bleeding, cancer, pulmonary disease, renal disease, prescription of non-steroidal anti-inflammatory drugs (NSAIDs) and care home entry from 2011 were also associated with OAC prescription. All variables had a significance level <0.05.

In the multivariate model (Table 3 and Figure 2), advancing age (aOR 0.96 per one-year increase [95% CI 0.95 to 0.96], p<0.001) and prescription of antiplatelet therapy remained as factors significantly associated with OAC non-prescription (aOR 0.91 [95% CI 0.84 to 0.98], p=0.014). Prior VTE (aOR 4.06 [95% CI 3.17 to 5.20], p<0.001), ischaemic stroke (aOR 1.51 [95% CI 1.37 to 1.67], p<0.001) and HF (aOR 1.46 [95% CI 1.35 to 1.58], p<0.001) were the stroke risk factors most strongly associated with OAC prescription. Dyslipidaemia, smoking history, stroke of unknown origin and TIA were also other stroke risk factors independently associated with OAC prescription. There was no significant association found between hypertension and OAC prescription. Other independent predictors of OAC prescription included male sex (aOR 1.09 [95% CI 1.01 to 1.18], p=0.024), advancing frailty (mild: aOR 4.61 [95% CI 3.95 to 5.38], p<0.001; moderate: aOR 6.69 [95% CI 5.74 to 7.80], p<0.001; severe: aOR 8.42 [95% CI 7.16 to 9.90], p<0.001), major bleeding (aOR 1.35, 95% CI 1.23 to 1.48, p<0.001), prescription of NSAIDs (aOR 1.75 [95% CI 1.51 to 2.02], p<0.001) and care home entry from 2011 onwards (aOR 1.91 [95% CI 1.76 to 2.06], p<0.001). The Variance Inflation Factor was <1.5 for all covariates (Supplementary Table 6). When age was included as a categorical variable, the same covariates were identified as predictors of OAC prescription or non-prescription (Supplementary Table 7). When people who had a major bleeding event and evidence of OAC prescription within six months prior to care entry were excluded, the positive association between OAC prescription and major bleeding was attenuated (aOR 1.12 [95% CI 1.01 to 1.23], p=0.028) (Supplementary Figure 2).

#### DISCUSSION

Summary

This study found that between 2003-2018, less than half of new care home residents with AF aged ≥65 years were prescribed OAC. The proportion of new residents prescribed OAC within six months before care entry more than doubled from 2003 to 2018. Increasing age and prescription of antiplatelet therapy were independently associated with OAC non-prescription. In contrast, advancing frailty, prior VTE and year of care home entry after 2011 were the strongest predictors independently associated with OAC prescription.

#### Strengths and limitations

To our knowledge, this is one of the largest population studies conducted exclusively in new care home residents that aims to elucidate the factors associated with OAC prescription for AF. Study limitations pertain to the observational design and use of routinely collected data. Data can only give insight into association rather than causation, and the direction of causality cannot be conferred. It is possible that some diagnoses were missed using ICD-10 codes, or classified incorrectly. We would anticipate there to be a greater proportion of residents with dementia than were actually reported, and the number of people with uncontrolled hypertension may have been over-estimated using the study's definition. Investigation of the temporal association between major bleeding and OAC prescription was limited because we could not confirm whether OAC was prescribed before or after the major bleeding event, or what time elapsed between the two. It was not possible to explore temporal associations between NSAID prescription or harmful alcohol use and OAC prescription as this data is not available in SAIL.

#### Comparison with existing literature

When comparing our findings to other care home studies, some of the results are conflicting. One systematic review<sup>3</sup> of observational studies in care homes found the majority of studies reported older age,<sup>35-40</sup> falls/fall risk,<sup>39, 40</sup> and dementia/cognitive impairment<sup>36-39, 41</sup> as

independent predictors of anticoagulant non-prescription, but a number of studies did not.<sup>37, 40-42</sup> Studies also reported previous stroke/TIA<sup>35, 36, 38, 39, 43</sup> and VTE<sup>35, 36, 39</sup> as independent predictors of anticoagulant prescription, but again, this was not found in all studies.<sup>42</sup> Two studies reported no association between anticoagulant prescription and antiplatelet therapy in multivariate analysis,<sup>36, 42</sup> but one study reported antiplatelet therapy as an independent predictor of anticoagulant non-prescription.<sup>3, 35</sup> Inconsistencies in results likely relate to differences in study methods to establish residents' medical and medication history. Another explanation is diversity across care home settings, where resident characteristics, clinical practice and perception of OAC use will differ.

Over the last decade, guidance on stroke prevention management for AF has changed. NOACs became available in Europe in 2011, and are now recommended in preference to VKA therapy. Devoid of complex monitoring requirements, NOACs have improved accessibility to OAC therapy and this is reflected in the study results; people who entered a care home in the post-NOAC era (from 2011 onwards) were significantly more likely to be prescribed OAC therapy. The standpoint on concomitant prescription of antiplatelet and OAC has remained unchanged, with guidelines advising against this to minimise the risk of bleeding. An exception to this is in the event of acute coronary syndrome or percutaneous coronary intervention where antiplatelet therapy is indicated alongside OAC for up to 12 months post-event. At Caution should also be applied when prescribing NSAIDs alongside OAC therapy due to the increased risk of bleeding. Whilst the results of this study suggest an aversion to concomitant prescription of OAC and antiplatelet therapy, this does not appear to be the case for NSAID therapy. NSAIDs are usually prescribed for a short duration to manage acute pain arising from inflammatory conditions. Without being able to distinguish residents prescribed an acute course of NSAID from those regularly prescribed NSAID alongside their OAC therapy, the

findings must be interpreted cautiously. Concomitant prescription is not an absolute contraindication, so it is possible the results reflect an acceptance to prescribe short courses of NSAID alongside OAC therapy in some individuals.

The study finding that each one year age increase is associated with a 4% reduction in OAC prescription verifies ongoing concerns about under-prescribing in older people because of misperceptions of the risk of adverse effects.<sup>45</sup> Ageing is a prominent non-modifiable risk factor for stroke, 6, 7 and any reduction in OAC prescription as a result of older age will have clinical consequences. Recently, a large registry study verified OAC safety in people aged >90 vears with a history of chronic kidney disease and intracranial haemorrhage. 46 There is considerable overlap between bleeding and stroke risk factors, and people with AF and a history of bleeding or intracranial haemorrhage remain at a high ischaemic stroke risk.<sup>7</sup> This may explain the positive association found between major bleeding and OAC prescription. Although this study found an expected rise in OAC prescribing for increasingly frail people, further work is needed to investigate the interaction with deprivation and other socio-economic and demographic factors to assess potential inequalities in prescribing across these groups. Nevertheless, this finding provides an interesting insight on prescribing patterns before definitive guidance on OAC prescription in people with frailty was provided by the ESC in 2020, which states that frailty should not be a barrier to OAC prescription.<sup>7</sup> Another electronic health record study of 58,204 people with AF aged ≥65 years in England also reported a positive association between advancing eFI frailty category and OAC prescription (aOR [95%] CI] mild: 1.84 [1.72 to 1.96]; moderate 2.34 [1.18–2.50] and severe 2.51 [2.33–2.71]).<sup>47</sup> One explanation may be that frailer adults are more frequently reviewed by clinicians, so there are less likely to be omissions in OAC prescribing.

#### *Implications for research and practice*

This study provides an important insight into the factors that influence OAC prescribing for new care home residents with AF, a high-risk group that is under-represented in research. The proportion of new residents prescribed OAC therapy has increased with the introduction of NOACs, but OAC prescription rates are still sub-optimal. There is a need for future research compo de la composición del composición de la co to elucidate other barriers to OAC prescription, and further explore temporal associations between OAC prescription and falls, alcohol use and prescription of antiplatelet/NSAID

#### ADDITIONAL INFORMATION

#### **Funding**

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### **Ethical approval**

The study received Information Governance Review Panel (IGRP) approval (project 0912) before data were made available within the SAIL Databank.

#### **Competing Interests**

SLH has received an investigator-initiated grant from Bristol-Myers Squibb (BMS); GYHL has been a consultant and speaker for BMS/Pfizer, Boehringer Ingelheim and Daiichi-Sankyo, no fees are received personally; DAL has received investigator-initiated educational grants from Bristol-Myers Squibb (BMS), has been a speaker for Bayer, Boehringer Ingelheim, and BMS/Pfizer and has consulted for BMS, and Boehringer Ingelheim; DH reports grants and speaker fees from BMS/Pfizer, outside the submitted work and PEP owns four shares in

AstraZeneca PLC and has received honoraria and/or travel reimbursement for events sponsored by AKCEA, Amgen, AMRYT, Link Medical, Napp, Sanofi. LAR, AAkb, FT, JH, AAkp, OO, SER and JPH have no competing interests to report.

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This study makes use of anonymised data held in the Secure Anonymised Information Linkage (SAIL) Databank. We would like to acknowledge all the data providers who make anonymised data available for research. All research conducted has been completed under the permission and approval of the SAIL IGRP (project number: 0912).

## **Contributions**

SLH, DAL, GYHL, OO, JPH and SER initiated the study. LAR, SLH, DA, PEP, GYHL, AAkp and DH were responsible for compilation and review of ICD-10 and Read code lists for the purpose of data extraction. FT, AAkb and JH were responsible for data processing and preparation within the SAIL Databank. LAR, SLH, DAL led the data analysis and drafting of the paper. All authors reviewed the manuscript contents and approved the submission of the current version of the manuscript. The corresponding author (LAR) attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

**Table 1.** Characteristics of adults with atrial fibrillation aged ≥65 years on care home entry (2003-2018) within the SAIL Databank, by prescription of oral anticoagulation.

Characteristics	All participants with AF, n (%) (n=14,493)	Participants with AF not prescribed OAC, n (%) (n=7,436)	Participants with AF prescribed OAC*, n (%) (n=7,057)	P- value
Demographics		( ) /	( ) )	C
Age, median (IQR)	87.0 (82.6, 91.2)	87.9 (83.4, 92.0)	86.2 (81.9, 90.2)	< 0.001
Age category		, , , , , , , , , , , , , , , , , , ,		
65-74 years	770 (5.3)	341 (4.6)	429 (6.1)	< 0.001
75-84 years	4,682 (32.3)	2,117 (28.5)	2,565 (36.3)	<i>)</i> "
85-94 years	7,859 (54.2)	4,157 (55.9)	3,702 (52.5)	7
≥95 years	1,182 (8.2)	821 (11.0)	361 (5.1)	
Male	5,103 (35.2)	2,427 (32.6)	2,676 (37.9)	< 0.001
WIMD quintile			A. V. *	
1 (most			, ( <b>5</b> y	1.000
deprived)	2,459 (17.1)	1,270 (17.2)	1,189 (17.1)	
2	3,053 (21.3)	1,567 (21.2)	1,486 (21.4)	
3	3,435 (23.9)	1,774 (24.0)	1,661 (23.9)	
4	2,842 (19.8)	1,468 (19.9)	1,374 (19.8)	
5 (least	2 554 (17.9)	1,316 (17.8)	1 220 (17 9)	
deprived)	2,554 (17.8)	1,310 (17.8)	1,238 (17.8)	
Frailty				
No frailty	1,864 (12.9)	1,600 (21.5)	264 (3.7)	< 0.001
Mild	3,714 (25.6)	2,142 (28.8)	1,572 (22.3)	
Moderate	5,145 (35.5)	2,329 (31.3)	2,816 (39.9)	
Severe	3,770 (26.0)	1,365 (18.4)	2,405 (34.1)	
Stroke risk				
CHA <sub>2</sub> DS <sub>2</sub> -VASc score <sup>b</sup> ,	4 (3, 5)	4 (3, 5)	4 (3, 5)	< 0.001
median (IQR)	CA			
Bleeding risk				
HAS-BLED scoreb,	3 (2, 3)	2(2, 3)	3 (2, 3)	< 0.001
median (IQR)	- (-,-)	- (-, -)	- (-,-)	*****
Social history				
Smoking history	3,996 (27.6)	1,620 (21.8)	2,376 (33.7)	< 0.001
Alcoholism	1,223 (8.4)	513 (6.9)	710 (10.1)	< 0.001
Heavy drinker	224 (1.5)	118 (1.6)	106 (1.5)	0.680
Co-morbidities <sup>a</sup>				
Any stroke	2,929 (20.2)	1,248 (16.8)	1,681 (23.8)	< 0.001
Stroke (unknown origin)	618 (4.3)	266 (3.6)	352 (5.0)	< 0.001
Ischaemic stroke	2,232 (15.4)	932 (12.5)	1,300 (18.4)	< 0.001
Haemorrhagic stroke	336 (2.3)	144 (1.9)	192 (2.7)	0.001
Transient ischaemic	330 (2.3)	177 (1.7)	172 (2.7)	
attack	796 (5.5)	361 (4.9)	435 (6.2)	< 0.001
Myocardial infarction	1,131 (7.8)	560 (7.5)	571 (8.1)	0.210
Heart failure	4,204 (29.0)	1,796 (24.2)	2,408 (34.1)	< 0.001
Alzheimer's disease	162 (1.1)	93 (1.3)	69 (1.0)	0.120
Vascular dementia	552 (3.8)	275 (3.7)	277 (3.9)	0.480
	( -)		( )	-

Other dementia or unspecified	542 (3.7)	306 (4.1)	236 (3.3)	0.014
Asthma	1,214 (8.4)	512 (6.9)	702 (9.9)	< 0.001
Chronic Obstructive	1,794 (12.4)	811 (10.9)	983 (13.9)	< 0.001
Pulmonary disease				
Other pulmonary	9 (0.1)	<5 (<1)	7 (0.1)	0.081
disease	7 (0.1)	3 (1)	7 (0.1)	0.001
Peptic ulcer	422 (2.9)	215 (2.9)	207 (2.9)	0.880
Diabetes	728 (5.0)	299 (4.0)	429 (6.1)	< 0.001
Renal disease	1,052 (7.3)	457 (6.1)	595 (8.4)	< 0.001
Liver disease	45 (0.3)	25 (0.3)	20 (0.3)	0.570
Cancer	2,236 (15.4)	1,055 (14.2)	1,181 (16.7)	< 0.001
Hypertension	6,967 (48.1)	3,125 (42.0)	3,842 (54.4)	< 0.001
Dyslipidaemia	1,765 (12.2)	679 (9.1)	1,086 (15.4)	< 0.001
Peripheral vascular	855 (5.9)	352 (4.7)	503 (7.1)	< 0.001
disease	, ,	· · ·		
Aortic plaque	8 (0.1)	<5 (<1)	5 (0.1)	0.430
Major bleeding	2,635 (18.2)	1,095 (14.7)	1,540 (21.8)	< 0.001
Venous	161 (2.2)	02 (1.2)	271 (5.2)	<0.001
thromboembolism	464 (3.2)	93 (1.3)	371 (5.3)	< 0.001

AF, atrial fibrillation;  $CHA_2DS_2$ -VASc, stroke risk assessment scoring 1 point each for female sex, age 65-74 years, history of heart failure, diabetes, hypertension, vascular disease, and 2 points each for history of stroke/transient ischaemic attach/venous thromboembolism and age  $\geq$ 75 years; HAS-BLED, bleeding risk assessment scoring 1 point each for age >65 year, uncontrolled hypertension, liver disease, renal disease, harmful alcohol use, stroke history, prior major bleeding or a predisposition to bleeding, labile international normalised ratio and medication usage predisposing to bleeding; IQR, interquartile range; OAC, oral anticoagulation; WIMD, Welsh Index of Multiple Deprivation

<sup>\*</sup>prescription within six months prior to care entry used as a proxy for prescription at the point of care home entry ayounger onset dementia not reported on due to small numbers and risk of resident identification

<sup>&</sup>lt;sup>b</sup>see Supplementary Tables S4 and S5 for definitions of the HAS-BLED and CHA<sub>2</sub>DS<sub>2</sub>-VASc risk assessment scores used in this study

**Table 2.** Advancing frailty and the prevalence of stroke risk factors in care home residents aged  $\geq$ 65 years with atrial fibrillation.

	Frailty category on care entry <sup>a</sup> , n			
	No frailty,	Mild	Moderate	Severe
	n (%)	frailty,	frailty,	frailty,
	n=1,864	n (%)	n (%)	n (%)
		n=3,714	n=5,145	n=3,770
Stroke risk factors on care entry <sup>b</sup>				
Age category				
65-74 years	109 (5.8)	253 (6.8)	242 (4.7)	166 (4.4)
75-84 years	638 (34.2)	1,249 (33.6)	1,603 (31.2)	1,192 (31.6)
85-94 years	962 (51.6)	1,899 (51.1)	2,856 (55.5)	2,142 (56.8)
≥95 years	155 (8.3)	313 (8.4)	444 (8.6)	270 (7.2)
Male	641 (34.4)	1,375 (37.0)	1,854 (36.0)	1,233 (32.7)
Heart failure	297 (15.9)	731 (19.7)	1,525 (29.6)	1,651 (43.8)
Hypertension	258 (13.8)	1,480 (39.8)	2,810 (54.6)	2,419 (64.2)
Diabetes	46 (2.5)	83 (2.2)	215 (4.2)	384 (10.2)
Myocardial infarction	135 (7.2)	188 (5.1)	380 (7.4)	428 (11.4)
Peripheral vascular disease	36 (1.9)	142 (3.8)	287 (5.6)	390 (10.3)
Venous thromboembolism	38 (2.0)	82 (2.2)	171 (3.3)	173 (4.6)
Transient ischaemic attack	85 (4.6)	165 (4.4)	267 (5.2)	279 (7.4)
Stroke <sup>c</sup>	331 (17.8)	761 (20.5)	1,048 (20.4)	789 (20.9)
Stroke risk assessment on care en	try			
CHA <sub>2</sub> DS <sub>2</sub> -VASc category				_ ,_ ,
Low-moderate	24 (1.3)	42 (1.1)	22 (0.4)	9 (0.2)
Moderate-high	1840 (98.7)	3672 (98.9)	5123 (99.6)	3761 (99.8)
CHA <sub>2</sub> DS <sub>2</sub> -VASc score, median (IQR)	3 (3, 4)	4 (3, 5)	4 (3, 5)	5 (4, 5)

 $CHA_2DS_2$ -VASc, stroke risk assessment scoring 1 point each for female sex, age 65-74 years, history of heart failure, diabetes, hypertension, vascular disease, and 2 points each for history of stroke/transient ischaemic attack/venous thromboembolism and age  $\geq$ 75 years

 $<sup>^</sup>a defined using the electronic Frailty Index (eFI): no frailty (eFI 0-0.12); mild (eFI > 0.12-0.24); moderate (eFI > 0.12-0.24) or severe (eFI > 0.36) frailty \\$ 

<sup>&</sup>lt;sup>b</sup>aortic plaque not reported on as a stroke risk factor due to small numbers and risk of resident identification <sup>c</sup>including ischaemic, haemorrhagic stroke and stroke of unknown origin

**Table 3.** Association between care home resident characteristics and the prescription of oral anticoagulation for atrial fibrillation\*.

Characteristics of residents with atrial fibrillation	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)	P- value <sup>a</sup>
Demographics			
Age (per one year increase)	0.96 (0.96 to 0.97)	0.96 (0.95 to 0.96)	< 0.001
Age category			
65-74 years	Ref	-	Ç.,,
75-84 years	0.96 (0.83 to 1.12)	-	
85-94 years	0.71 (0.61 to 0.82)	-	
≥95 years	0.35 (0.29 to 0.42)	<b>≠</b> **	
Male	1.26 (1.18 to 1.35)	1.09 (1.01 to 1.18)	0.024
WIMD quintile	1.20 (1.10 to 1.50)	1.05 (1.01 to 1.10)	0.02.
1 (most deprived)	Ref		
2	1.01 (0.91 to 1.13)	~ / -	
3	1.00 (0.90 to 1.11)	_ ^ / / _	
4	1.00 (0.90 to 1.11)	_	
5 (least deprived)	` ,		
3 (least deprived)	1.00 (0.90 to 1.12)	O <sup>2</sup> 2 -	
Year of care home entry $\geq 2011$	2.27 (2.12 to 2.43)	1.91 (1.76 to 2.06)	< 0.001
Frailty			
No frailty	Ref	Ref	-
Mild	4.45 (3.85 to 5.14)	4.61 (3.95 to 5.38)	< 0.001
Moderate	7.33 (6.36 to 8.44)	6.69 (5.74 to 7.80)	< 0.001
Severe	10.68 (9.23 to 12.36)	8.42 (7.16 to 9.90)	< 0.001
Social history prior to care home ent	rv		
Smoking history	1.82 (1.69 to 1.96)	1.16 (1.06 to 1.26)	0.001
Harmful alcohol use <sup>b</sup>	1.51 (1.34 to 1.70)	1.00 (0.88 to 1.14)	0.966
Medical history prior to care home e	ntrv		
Dementia <sup>c</sup>	0.91 (0.81 to 1.03)	_	
Pulmonary disease <sup>d</sup>	1.38 (1.26 to 1.50)	0.94 (0.85 to 1.03)	0.191
Peptic ulcer	1.01 (0.84 to 1.23)	-	0.171
Cancer	1.22 (1.11 to 1.33)	1.04 (0.94 to 1.15)	0.401
Dyslipidaemia	1.81 (1.63 to 2.00)	1.13 (1.02 to 1.27)	0.025
Haemorrhagic stroke	1.42 (1.14 to 1.76)	1.18 (0.93 to 1.50)	0.183
Ischaemic stroke	1.58 (1.44 to 1.73)	1.51 (1.37 to 1.67)	< 0.001
Stroke of unknown origin	1.42 (1.20 to 1.67)	1.32 (1.10 to 1.58)	0.002
Transient ischaemic attack	1.29 (1.12 to 1.49)	1.22 (1.04 to 1.43)	0.012
Myocardial infarction	1.08 (0.96 to 1.22)	1.22 (1.01 to 1.13)	0.012
Heart failure	1.63 (1.51 to 1.75)	1.46 (1.35 to 1.58)	< 0.001
Diabetes	1.54 (1.33 to 1.80)	1.05 (0.88 to 1.24)	0.603
Renal disease	1.41 (1.24 to 1.60)	0.96 (0.84 to 1.11)	0.582
Liver disease	0.84 (0.47 to 1.52)	0.70 (0.04 10 1.11)	0.362
	` ,	1.05 (0.09 + 2.1.12)	0.176
Hypertension Peripheral vescular disease	1.65 (1.54 to 1.76)	1.05 (0.98 to 1.13)	0.176
Peripheral vascular disease	1.54 (1.34 to 1.78)	1.09 (0.93 to 1.26)	0.293
Aortic plaque	1.76 (0.42 to 7.35)	1 25 (1 22 += 1 40)	<0.001
Major bleeding	1.62 (1.48 to 1.76)	1.35 (1.23 to 1.48)	< 0.001
Venous thromboembolism	4.38 (3.48 to 5.51)	4.06 (3.17 to 5.20)	< 0.001

# Medication history within six months prior to care home entry

Prescription of antiplatelet(s) without NSAID(S)	0.88 (0.83 to 0.95)	0.91 (0.84 to 0.98)	0.014
Prescription of NSAID(s) without antiplatelet(s)	2.05 (1.80 to 2.33)	1.75 (1.51 to 2.02)	< 0.001

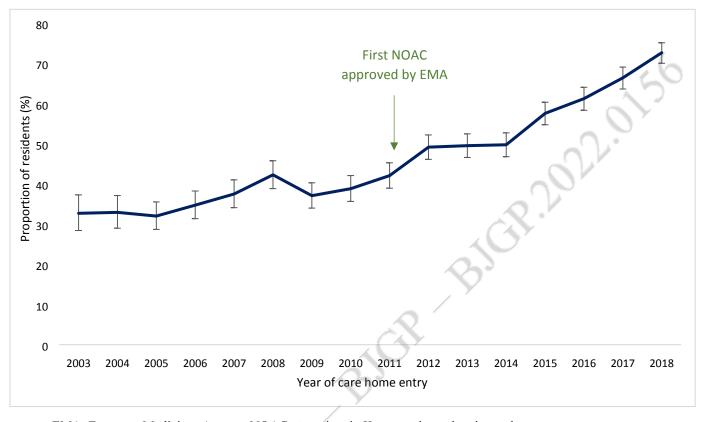
CI, confidence interval; NSAID, non-steroidal anti-inflammatory drug; WIMD, Welsh Index of Multiple Deprivation

<sup>\*</sup>prescription within six months prior to care entry used as a proxy for prescription at the point of care home entry areported for adjusted odds ratio

bincluding alcoholism and heavy drinker

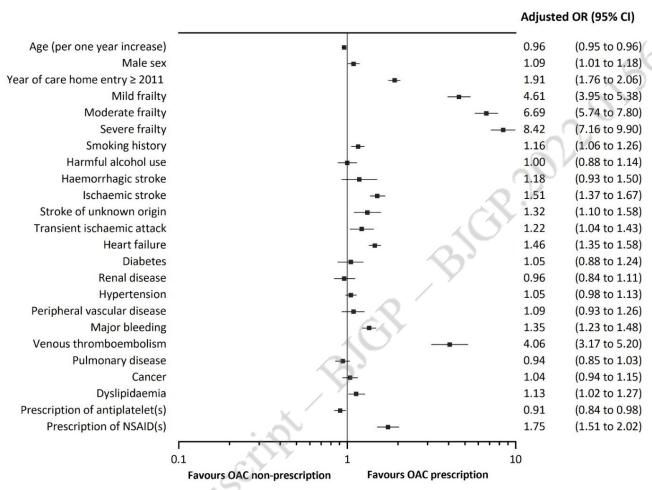
<sup>&</sup>lt;sup>c</sup>including Alzheimer's disease, vascular dementia, younger onset dementia and other or unspecified dementia <sup>d</sup>including asthma, chronic obstructive pulmonary disease and other pulmonary

**Figure 1.** Proportion of care home residents aged ≥65 years with atrial fibrillation prescribed an oral anticoagulant within six months prior to care home entry between 2003-2018.



EMA, European Medicines Agency; NOAC, non-vitamin K antagonist oral anticoagulant

**Figure 2.** Factors associated with prescription of oral anticoagulation\* in new care home residents aged ≥65 years with atrial fibrillation, using a multivariable adjusted model.



Note: reference for frailty categories is no frailty. Multivariate model adjusted for dyslipidaemia, smoking history, cancer diagnoses, year of care home entry  $\geq 2011$  and individual components of CHA<sub>2</sub>DS<sub>2</sub>VASc and HAS-BLED risk assessment scores.

CI, confidence interval; NSAID, non-steroidal anti-inflammatory drug; OAC, oral anticoagulant; OR, odds ratio \*prescription within six months prior to care entry used as a proxy for prescription at the point of care home entry

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