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

Leona A. Ritchie (0000-0002-0392-1767)1,2,3, MPharm, Stephanie L. Harrison (0000-0002-8846-0946)1,2,3, PhD, Peter E. Penson (0000-0001-6763-1489)1,3,4, PhD, Ashley Akbari (0000-0003-0814-0801)5,6, MSc, Fatemeh Torabi (0000-0002-5853-4625)5, MSc, Joe Hollinghurst (0000-0002-3556-2017)5, PhD, Daniel Harris (0000-0003-4885-637X)5, PhD, Oluwakayode B. Oke (0000-0003-3964-8667)1,2,3, PhD, Asangaedem Akpan (0000-0002-1764-8669)7,8, MD, Julian P. Halcox (0000-0001-6926-2947)5, MD, Sarah E. Rodgers (0000-0002-4483-0845)9, PhD, Gregory Y.H. Lip (0000-0002-7566-1626)1,2,3,10, MD, Deirdre A. Lane (0000-0002-5604-9378)1,2,3,10, PhD

1Liverpool Centre for Cardiovascular Science, University of Liverpool, Liverpool, L7 8TX, United Kingdom

2Liverpool Heart & Chest Hospital, Liverpool, L14 3PE, United Kingdom

3Department of Cardiovascular and Metabolic Medicine, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, L7 8TX, United Kingdom

4School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University, Liverpool, L3 3AF, United Kingdom

5Population Data Science, Health Data Research UK, Swansea University Medical School, Swansea University, Swansea, Wales, SA2 8PP, United Kingdom

6Population Data Science, Administrative Data Research Wales, Swansea University Medical School, Swansea University, Swansea, Wales, SA2 8PP, United Kingdom

7Musculoskeletal and Ageing Science, Institute of Life Course & Medical Sciences, University of Liverpool, L7 8TX, United Kingdom

8Liverpool University Hospitals NHS Foundation Trust, Liverpool, L9 7AL, United Kingdom

9Department of Public Health, Policy and Systems, Institute of Population Health, University of Liverpool, Liverpool, L69 3GF, United Kingdom

10Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, DK-9220, Denmark

**Corresponding author**

Miss Leona A Ritchie

**Address:** Liverpool Centre for Cardiovascular Sciences, University of Liverpool, William Henry Duncan Building, 6 West Derby Street, Liverpool, L7 8TX, United Kingdom

**E-mail:** Leona.Ritchie@liverpool.ac.uk

**Abstract word count:** 247 (re-submission)

**Main text word count (excluding abstract, additional information, tables and figures):** 2600 (re-submission)

**Number of data elements:** 3 tables, 2 figures

**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 1st January 2003 and 31st 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.1, 2 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%.3-5

Atrial fibrillation increases the risk of stroke four- to five-fold,6 therefore, stroke prevention is the cornerstone of AF management. This focuses on the prescription of oral anticoagulants (OACs),7 however, there is evidence of under-prescribing of OAC in care home residents.3 The prevalence of anticoagulant use for AF in care homes ranged from 17% to 68% across multiple studies.3, 5, 8 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.9, 10 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.11-13

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.7, 14-19 Results from other trials also support the use of warfarin for stroke prevention in people aged ≥75 years with AF.20, 21 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.7 This study aims to elucidate the factors associated with OAC prescription in older people aged ≥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).22

*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.23-25 The data sources included the Welsh Demographic Service Dataset (WDSD),26 the Welsh Longitudinal General Practice (WLGP)27 and the Patient Episode Database for Wales (PEDW).28 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).29 This is linked to anonymised address data for individual participants.30-32 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.33 This threshold was used because conventional significance levels such as 0.05 can fail to identify important variables.34 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 (CHA2DS2-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) CHA2DS2-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 review3 of observational studies in care homes found the majority of studies reported older age,35-40 falls/fall risk,39, 40 and dementia/cognitive impairment36-39, 41 as independent predictors of anticoagulant non-prescription, but a number of studies did not.37, 40-42 Studies also reported previous stroke/TIA35, 36, 38, 39, 43 and VTE35, 36, 39 as independent predictors of anticoagulant prescription, but again, this was not found in all studies.42 Two studies reported no association between anticoagulant prescription and antiplatelet therapy in multivariate analysis,36, 42 but one study reported antiplatelet therapy as an independent predictor of anticoagulant non-prescription.3, 35 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.7 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.7, 44 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.7, 44 Caution should also be applied when prescribing NSAIDs alongside OAC therapy due to the increased risk of bleeding.7 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.45 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 years 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.7 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.7 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]).47 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 to elucidate other barriers to OAC prescription, and further explore temporal associations between OAC prescription and falls, alcohol use and prescription of antiplatelet/NSAID therapy.

**ADDITIONAL INFORMATION**

**Funding**

No specific funding was received for this work. This work was supported by Health Data Research UK [HDR-9006] which receives its funding from the UK Medical Research Council; Engineering and Physical Sciences Research Council; Economic and Social Research Council; Department of Health and Social Care (England); Chief Scientist Office of the Scottish Government Health and Social Care Directorates; Health and Social Care Research and Development Division (Welsh Government); Public Health Agency (Northern Ireland); British Heart Foundation (BHF) and the Wellcome Trust and Administrative Data Research UK which is funded by the Economic and Social Research Council [grant ES/S007393/1]. SER is part-funded by the National Institute for Health Research (NIHR) Applied Research Collaboration North West Coast (ARC NWC). The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

**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.

**Acknowledgements**

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** |
| Age, median (IQR) | 87.0 (82.6, 91.2) | 87.9 (83.4, 92.0) | 86.2 (81.9, 90.2) | <0.001 |
| Age category65-74 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) |
| 85-94 years | 7,859 (54.2) | 4,157 (55.9) | 3,702 (52.5) |
| ≥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 1 (most deprived) | 2,459 (17.1) | 1,270 (17.2) | 1,189 (17.1) | 1.000 |
| 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 deprived) | 2,554 (17.8) | 1,316 (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** |
| CHA2DS2-VASc scoreb, median (IQR) | 4 (3, 5) | 4 (3, 5) | 4 (3, 5) | <0.001 |
| **Bleeding risk** |
| HAS-BLED scoreb, median (IQR) | 3 (2, 3) | 2 (2, 3) | 3 (2, 3) | <0.001 |
| **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-morbiditiesa** |
| 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) | 0.002 |
| Transient ischaemic 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 Pulmonary disease  | 1,794 (12.4) | 811 (10.9) | 983 (13.9) | <0.001 |
| Other pulmonary disease  | 9 (0.1) | <5 (<1) | 7 (0.1) | 0.081 |
| 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 disease  | 855 (5.9) | 352 (4.7) | 503 (7.1) | <0.001 |
| 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 thromboembolism | 464 (3.2) | 93 (1.3) | 371 (5.3) | <0.001 |

AF, atrial fibrillation; CHA2DS2-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 ≥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

\*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

bsee Supplementary Tables S4 and S5 for definitions of the HAS-BLED and CHA2DS2-VASc risk assessment scores used in this study

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

|  |  |
| --- | --- |
|  | **Frailty category on care entrya, n** |
| No frailty,n (%)n=1,864 | Mild frailty,n (%)n=3,714 | Moderate frailty,n (%)n=5,145 | Severe frailty,n (%)n=3,770 |
| **Stroke risk factors on care entryb** |
| Age category65-74 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) |
| Strokec | 331 (17.8) | 761 (20.5) | 1,048 (20.4) | 789 (20.9) |
| **Stroke risk assessment on care entry** |
| CHA2DS2-VASc categoryLow-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) |
| CHA2DS2-VASc score, median (IQR) | 3 (3, 4) | 4 (3, 5) | 4 (3, 5) | 5 (4, 5) |

CHA2DS2-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 ≥75 years

adefined 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

baortic plaque not reported on as a stroke risk factor due to small numbers and risk of resident identification

cincluding 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-valuea** |
| **Demographics** |  |
| Age (per one year increase) | 0.96 (0.96 to 0.97) | 0.96 (0.95 to 0.96) | <0.001 |
| Age category65-74 years | Ref | - |  |
| 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) | - |  |
| Male | 1.26 (1.18 to 1.35) | 1.09 (1.01 to 1.18) | 0.024 |
| WIMD quintile1 (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) | 1.00 (0.90 to 1.12) | - |  |
| **Year of care home entry ≥ 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 entry** |  |
| Smoking history | 1.82 (1.69 to 1.96) | 1.16 (1.06 to 1.26) | 0.001 |
| Harmful alcohol useb | 1.51 (1.34 to 1.70) | 1.00 (0.88 to 1.14) | 0.966 |
| **Medical history prior to care home entry** |  |
| Dementiac | 0.91 (0.81 to 1.03) | - |  |
| Pulmonary diseased | 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) | - |  |
| 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) | - |  |
| 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) | - |  |
| Hypertension | 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) | - |  |
| 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

\*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

cincluding Alzheimer’s disease, vascular dementia, younger onset dementia and other or unspecified dementia

dincluding 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.

First NOAC approved by EMA

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 ≥ 2011 and individual components of CHA2DS2VASc 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

**References**

[1] Karamichalakis N, Letsas KP, Vlachos K*, et al.* Managing atrial fibrillation in the very elderly patient: challenges and solutions. *Vasc Health Risk Manag*. 2015;**11**: 555-562.

[2] Roth GA, Mensah GA, Johnson CO*, et al.* Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update From the GBD 2019 Study. *Journal of the American College of Cardiology*. 2020;**76**: 2982-3021.

[3] Ritchie LA, Oke OB, Harrison SL, Rodgers SE, Lip GYH, Lane DA. Prevalence of atrial fibrillation and outcomes in older long-term care residents: a systematic review. *Age and ageing*. 2021;**50**: 744-757.

[4] Chaskes MJ, Hanner N, Karmilowicz P, Curtis AB. Abstract 14963: Screening for Atrial Fibrillation in High- Risk Nursing Home Residents. *Circulation*. 2018;**138**: A14963-A14963.

[5] O'Caoimh R, Igras E, Ramesh A, Power B, O'Connor K, Liston R. Assessing the Appropriateness of Oral Anticoagulation for Atrial Fibrillation in Advanced Frailty: Use of Stroke and Bleeding Risk-Prediction Models. *J Frailty Aging*. 2017;**6**: 46-52.

[6] Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke*. 1991;**22**: 983-988.

[7] Hindricks G, Potpara T, Dagres N*, et al.* 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *European Heart Journal*. 2020.

[8] Oo W, Kozikowski A, Stein J*, et al.* Antithrombotic Therapy Practices in Older Adults Residing in the Long-Term Care Setting. *Southern Medical Journal*. 2015;**108**: 432-436.

[9] Damanti S, Braham S, Pasina L. Anticoagulation in frail older people. *J Geriatr Cardiol*. 2019;**16**: 844-846.

[10] Sluggett JK, Harrison SL, Ritchie LA*, et al.* High-Risk Medication Use in Older Residents of Long-Term Care Facilities: Prevalence, Harms, and Strategies to Mitigate Risks and Enhance Use. *Sr Care Pharm*. 2020;**35**: 419-433.

[11] Lloyd-Jones D, Adams RJ, Brown TM*, et al.* Executive summary: heart disease and stroke statistics--2010 update: a report from the American Heart Association. *Circulation*. 2010;**121**: 948-954.

[12] Lin HJ, Wolf PA, Kelly-Hayes M*, et al.* Stroke severity in atrial fibrillation. The Framingham Study. *Stroke*. 1996;**27**: 1760-1764.

[13] Reiffel JA. Atrial fibrillation and stroke: epidemiology. *Am J Med*. 2014;**127**: e15-16.

[14] Sardar P, Chatterjee S, Chaudhari S, Lip GY. New oral anticoagulants in elderly adults: evidence from a meta-analysis of randomized trials. *J Am Geriatr Soc*. 2014;**62**: 857-864.

[15] Patel MR, Mahaffey KW, Garg J*, et al.* Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med*. 2011;**365**: 883-891.

[16] Granger CB, Alexander JH, McMurray JJ*, et al.* Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2011;**365**: 981-992.

[17] Connolly SJ, Ezekowitz MD, Yusuf S*, et al.* Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2009;**361**: 1139-1151.

[18] Bauersachs R, Berkowitz SD, Brenner B*, et al.* Oral rivaroxaban for symptomatic venous thromboembolism. *N Engl J Med*. 2010;**363**: 2499-2510.

[19] Schulman S, Kearon C, Kakkar AK*, et al.* Extended use of dabigatran, warfarin, or placebo in venous thromboembolism. *N Engl J Med*. 2013;**368**: 709-718.

[20] Rash A, Downes T, Portner R, Yeo WW, Morgan N, Channer KS. A randomised controlled trial of warfarin versus aspirin for stroke prevention in octogenarians with atrial fibrillation (WASPO). *Age Ageing*. 2007;**36**: 151-156.

[21] Mant J, Hobbs FDR, Fletcher K*, et al.* Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. *The Lancet*. 2007;**370**: 493-503.

[22] Benchimol EI, Smeeth L, Guttmann A*, et al.* The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. *PLoS Med*. 2015;**12**: e1001885.

[23] Lyons RA, Jones KH, John G*, et al.* The SAIL databank: linking multiple health and social care datasets. *BMC Med Inform Decis Mak*. 2009;**9**: 3.

[24] Ford DV, Jones KH, Verplancke JP*, et al.* The SAIL Databank: building a national architecture for e-health research and evaluation. *BMC Health Serv Res*. 2009;**9**: 157.

[25] Jones KH, Ford DV, Jones C*, et al.* A case study of the Secure Anonymous Information Linkage (SAIL) Gateway: a privacy-protecting remote access system for health-related research and evaluation. *J Biomed Inform*. 2014;**50**: 196-204.

[26] Digital Health and Care Wales (DHCW). Secure Anonymised Information Linkage (SAIL) Welsh Demographic Service Dataset (WDSD)

[27] Welsh General Practices. Secure Anonymised Information Linkagae (SAIL) Welsh Longitudinal General Practice Dataset (WLGP) - Welsh Primary Care.

[28] NHS Wales’ Informatics Service (NWIS). Secure Anonymised Information Linkage (SAIL) Patient Episode Dataset for Wales (PEDW).

[29] Hollinghurst J, Akbari A, Fry R*, et al.* Study protocol for investigating the impact of community home modification services on hospital utilisation for fall injuries: a controlled longitudinal study using data linkage. *BMJ Open*. 2018;**8**: e026290.

[30] Rodgers SE, Lyons RA, Dsilva R*, et al.* Residential Anonymous Linking Fields (RALFs): a novel information infrastructure to study the interaction between the environment and individuals' health. *Journal of Public Health*. 2009;**31**: 582-588.

[31] Hollinghurst J, Fry R, Akbari A, Rodgers S. Using Residential Anonymous Linking Fields to Identify Vulnerable Populations in Administrative Data. *International Journal of Population Data Science*. 2018;**3**.

[32] Rodgers SE, Demmler JC, Dsilva R, Lyons RA. Protecting health data privacy while using residence-based environment and demographic data. *Health Place*. 2012;**18**: 209-217.

[33] Bursac Z, Gauss CH, Williams DK, Hosmer DW. Purposeful selection of variables in logistic regression. *Source Code Biol Med*. 2008;**3**: 17.

[34] Mickey RM, Greenland S. The impact of confounder selection criteria on effect estimation. *Am J Epidemiol*. 1989;**129**: 125-137.

[35] Ghaswalla PK, Harpe SE, Slattum PW. Warfarin use in nursing home residents: results from the 2004 national nursing home survey. *American Journal of Geriatric Pharmacotherapy*. 2012;**10**: 25-36.e22.

[36] Gill C. Oral anticoagulation medication usage in older adults with atrial fibrillation residingin long-term care facilities. **Volume 80**: ProQuest Information & Learning, 2019.

[37] Dutcher S. Pharmacotherapeutic management and care transitions among nursing home residents with atrial fibrillation. **Volume 75**: ProQuest Information & Learning, 2015.

[38] Gurwitz JH, Monette J, Rochon PA, Eckler MA, Avorn J. Atrial fibrillation and stroke prevention with warfarin in the long-term care setting. *Arch Intern Med*. 1997;**157**: 978-984.

[39] Frain B, Castelino R, Bereznicki LR. The Utilization of Antithrombotic Therapy in Older Patients in Aged Care Facilities With Atrial Fibrillation. *Clin Appl Thromb Hemost*. 2018;**24**: 519-524.

[40] Bahri O, Roca F, Lechani T*, et al.* Underuse of Oral Anticoagulation for Individuals with Atrial Fibrillation in a Nursing Home Setting in France: Comparisons of Resident Characteristics and Physician Attitude. *Journal of the American Geriatrics Society*. 2015;**63**: 71-76.

[41] Patel AA, Reardon G, Nelson WW, Philpot T, Neidecker MV. Persistence of warfarin therapy for residents in long-term care who have atrial fibrillation. *Clinical Therapeutics*. 2013;**35**: 1794-1804.

[42] Lau E, Bungard TJ, Tsuyuki RT. Stroke Prophylaxis in Institutionalized Elderly Patients with Atrial Fibrillation. *Journal of the American Geriatrics Society*. 2004;**52**: 428-433.

[43] Latif AKA, Peng X, Messinger-Rapport BJ. Predictors of anticoagulation prescription in nursing home residents with atrial fibrillation. *Journal of the American Medical Directors Association*. 2005;**6**: 128-131.

[44] National Institute for Health and Care Excellence. Atrial fibrillation: diagnosis and management. NICE guideline [NG196]. 2021.

[45] Zathar Z, Karunatilleke A, Fawzy AM, Lip GYH. Atrial Fibrillation in Older People: Concepts and Controversies. *Front Med (Lausanne)*. 2019;**6**: 175.

[46] Chao TF, Chiang CE, Chan YH*, et al.* Oral anticoagulants in extremely-high-risk, very elderly (>90 years) patients with atrial fibrillation. *Heart Rhythm*. 2021;**18**: 871-877.

[47] Wilkinson C, Clegg A, Todd O*, et al.* Atrial fibrillation and oral anticoagulation in older people with frailty: a nationwide primary care electronic health records cohort study. *Age Ageing*. 2021;**50**: 772-779.