JAMDA 24 (2023) 1484–1489

JAMDA

journal homepage: www.jamda.com

Original Study

Oral Anticoagulant Therapy and Risk of Admission to Long-Term Care in patients With Atrial Fibrillation: A Nationwide Cohort Study

Konsta Teppo MD [a,*], K.E. Juhani Airaksinen MD, PhD [a], Olli Halminen PhD [b], Miika Linna PhD [b,c], Jussi Jaakkola MD, PhD [a], Jari Haukka PhD [d], Jukka Putaala MD, PhD [e], Pirjo Mustonen MD, PhD [a], Ville L. Langén MD, PhD [f], Janne Kinnunen MD [e], Juha Hartikainen MD, PhD [c,g], Mika Lehto MD, PhD [h,i]

[a] *Heart Centre, Turku University Hospital and University of Turku, Turku, Finland*
[b] *Department of Industrial Engineering and Management, Aalto University, Espoo, Finland*
[c] *University of Eastern Finland, Kuopio, Finland*
[d] *University of Helsinki, Helsinki, Finland*
[e] *Neurology, Helsinki University Hospital, and University of Helsinki, Helsinki, Finland*
[f] *Department of Medicine, Turku University Hospital, Turku, Finland*
[g] *Heart Centre, Kuopio University Hospital, Kuopio, Finland*
[h] *Heart and Lung Centre, Helsinki University Hospital and University of Helsinki, Helsinki, Finland*
[i] *Department of Internal Medicine, Jorvi Hospital, Helsinki and Uusimaa Hospital District, Espoo, Finland*

Keywords:
Atrial fibrillation
long-term care
anticoagulation
direct oral anticoagulants
nursing homes

A B S T R A C T

Objectives: The impact of oral anticoagulants (OACs) on the need of long-term care (LTC) in the aging and multimorbid population of patients with atrial fibrillation (AF) is unknown. We conducted a nationwide cohort study to evaluate the effect of OACs on the need of LTC.
Design: Retrospective nationwide cohort study.
Setting and Participants: The registry-based FinACAF cohort study covers all patients with incident AF from all levels of care in Finland from 2007 to 2018, as well as all their OAC purchases, LTC admissions, and information on previous home care acuity.
Methods: Incidence rate ratios (IRRs) of LTC admission were calculated using Poisson regression models with a Lexis-type data structure based on 3 time scales: follow-up time from AF diagnosis, calendar year, and age.
Results: We identified 188,752 patients (49.0% female; mean age 71.4 years; mean follow-up 3.6 years) with incident AF without prior LTC, of whom 143,534 (76.0 %) initiated OAC therapy and 11,775 (6.2 %) were admitted to LTC. OAC therapy was associated with lower rates of LTC admission (adjusted IRR 0.79, 95% CI 0.76-0.82). When compared to warfarin, direct oral anticoagulants (DOACs) were associated with lower LTC admission rate (adjusted IRR 0.69, 95% CI 0.61-0.79). No significant disparities were observed between different DOACs.
Conclusions and Implications: OAC therapy, particularly with DOACs, is associated with a substantially lower risk of admission to LTC in patients with AF. Increasing guideline-based OAC coverage among patients with AF may prevent the need of LTC, lengthen survival at home, and potentially decrease health care costs.

Conflict of Interest Disclosures: Konsta Teppo has received research grants from the Finnish Foundation for Cardiovascular Research, Aarne and Aili Turunen Foundation. Jukka Putaala receives speaker fees from Bayer, Boehringer-Ingelheim, BMS-Pfizer, and Abbott; is on the advisory board of Portola, Novo Nordisk, and Herantis Pharma; is a visiting editor in Terve Media; and owns stock in Vital Signum. Pirjo Mustonen is a consultant for Roche, BMS-Pfizer-alliance, Novartis Finland, Boehringer Ingelheim, and MSD Finland. Jari Haukka is a consultant for Research Janssen R&D and receives speaker from Bayer Finland. Miika Linna receives speaker fees from BMSPfizer-alliance, Bayer, and Boehringer-Ingelheim. Juha Hartikainen receives research grants from the Finnish Foundation for Cardiovascular Research, EU Horizon 2020, and EU FP7; is an advisory board member of BMS-Pfizer-alliance, Novo Nordisk, and Amgen; receives speaker fees from Cardiome and Bayer. Juhani Airaksinen receives research grants from the Finnish Foundation for Cardiovascular Research; speaker fees from Bayer, Pfizer, and Boehringer-Ingelheim and is a member in the advisory boards of Bayer, Pfizer, and AstraZeneca. Mika Lehto is a consultant for BMS-Pfizer-alliance, Bayer, Boehringer-Ingelheim, and MSD; receives speaker fees from BMS-Pfizer-alliance, Bayer, Boehringer Ingelheim, MSD, Terve Media, and Orion Pharma; research grants from Aarne Koskelo Foundation, The Finnish Foundation for Cardiovascular Research, and Helsinki and Uusimaa Hospital District Research Fund, Boehringer-Ingelheim. The other authors declare no conflicts of interest.

Funding/Support: This work was supported by the Aarne Koskelo Foundation, The Finnish Foundation for Cardiovascular Research, and Helsinki and Uusimaa Hospital District Research Fund (TYH2019309).

* Address correspondence to Konsta Teppo, MD, University of Turku, 20500, Turku, Finland.
E-mail address: jkitep@utu.fi (K. Teppo).

https://doi.org/10.1016/j.jamda.2023.05.016

Atrial fibrillation (AF) is the most common sustained arrhythmia with a prevalence of 5.2% in the adult population. The prevalence increases considerably with advancing age and as many as 1 in 4 individuals aged >75 years have AF.[1] The most feared complication of AF is ischemic stroke, which often has devastating consequences on patient's functional capacity in daily activities.[2,3] Hence, stroke prevention with oral anticoagulants (OACs), either with warfarin or direct oral anticoagulants (DOACs), is the cornerstone of contemporary treatment of AF.[4] The impact of OACs on outcomes in patients with AF has been a focus of extensive research in the past decades, but there is a complete paucity of information about their effect on the need of long-term care (LTC) in this aging and multimorbid patient group. Indeed, it is not known whether the effects of OACs on the incidence of ischemic stroke, bleeding, and possibly dementia are reflected as a net benefit on independent functioning and survival at home. Therefore, we conducted a retrospective nationwide cohort study to assess the hypothesis that OAC therapy is associated with lower need of LTC in patients with AF.

Methods

Study Population

The Finnish AntiCoagulation in Atrial Fibrillation (FinACAF) Study (ClinicalTrials Identifier: NCT04645537; ENCePP Identifier: EUPAS29845) is a nationwide retrospective cohort study that includes all patients with a recorded AF diagnosis in Finland from 2004 to 2018.[5] Patients were identified using all available national health care registers (hospitalizations and outpatient specialist visits: HILMO; primary health care: AvoHILMO; and National Reimbursement Register upheld by Social Insurance Institute: KELA). The inclusion criterion for the cohort was an *International Classification of Diseases, Tenth Revision* (*ICD-10*), diagnosis code of I48 (including atrial fibrillation and atrial flutter, together referred to as AF) recorded between 2004 and 2018. The exclusion criteria were permanent emigration abroad before December 31, 2018, and age <20 years at AF diagnosis. The current substudy was conducted within a cohort of patients with incident AF between 2007 and 2018, which was established in previous studies of the FinACAF cohort.[6,7] Patients already admitted to LTC before the first AF diagnosis were excluded. OAC therapy may be withheld in patients with clinically perceived short life expectancy and thus also higher proneness to admission to LTC. This may cause confounding by indication on the analyses on the impact of OAC therapy on the risk of admission to LTC. To account for this bias, we applied a 6-month washout period after the AF diagnosis and included only the patients surviving the washout period without admission to LTC. Follow-up began after the washout period and continued until admission to LTC, death, or the end of observation period on September 30, 2018. We also analyzed separately patients with at least a moderate ischemic stroke risk (men with CHA_2DS_2-VASc score ≥1 and women with CHA_2DS_2-VASc score ≥2), patients with a high ischemic stroke risk (men with CHA_2DS_2-VASc score ≥2 and women with CHA_2DS_2-VASc score ≥3), and patients with age ≥70 years at the time of the first AF diagnosis. Additionally, when comparing the associations of DOACs and warfarin with LTC need, only patients diagnosed with AF from 2015 onward were included in the analyses. Baseline comorbidities were gathered from the aforementioned health care registers from 2004 onward. The cohort construction process is summarized in Supplementary Figure 1, and the codes used for the baseline comorbidities are presented in Supplementary Table 1.

Use of OAC Therapy

Exposure to OAC (warfarin, dabigatran, apixaban, rivaroxaban, or edoxaban) therapy was treated as a time-varying variable, and patients were considered exposed to the treatment after the first OAC purchase after AF diagnosis. This intention-to-treat type of an approach in defining drug exposure after the observed start of the therapy was chosen because several events after OAC initiation may concurrently affect possible treatment discontinuation as well as patients' functional status and the eventual risk of admission to LTC. For example, severe ischemic stroke or intracranial bleeding may lead to poor prognosis, discontinuation of preventive therapies, and need of LTC. Additionally, in sensitivity analyses, OAC exposure was considered to start from the first OAC purchase and continue 180 days from the last purchase. Moreover, we conducted analyses to compare DOACs with warfarin as well as different DOACs with each other. In these analyses, patients were classified to be exposed to the treatment after the first warfarin or DOAC purchase.

Admission to LTC

LTC was defined as an LTC decision made by the municipal social service providers or as inpatient care that lasted >90 days at the primary care ward. The study outcome event, admission to LTC, was considered to occur on the date of the first recorded LTC decision obtained from the national Care Register for Social Welfare upheld by the Finnish Institute for Health and Welfare or on the entry date of the first >90-day primary care inpatient period. Finland has a public, tax-funded health care system with full coverage by public health insurance, and admission to LTC is based on the functional capacity of the individual and is not influenced by personal economic capacity.[8] During the past decades in Finland, national strategies aiming to reduce institutionalization have led to a shift from institutional care toward sheltered housing.[8,9] Therefore, all forms of LTC used during the study period, ranging from long health center inpatient periods and long-term institutional care to regular sheltered housing, were included to account for local and temporal variability in the organizing of LTC services. This definition has also been used in previous studies of LTC utilization in Finland.[10]

Study Ethics

The study protocol was approved by the Ethics Committee of the Medical Faculty of Helsinki University, Helsinki, Finland (nr. 15/2017), and granted research permission from the Helsinki University Hospital (HUS/46/2018). Respective permissions were obtained from the Finnish register holders (KELA 138/522/2018; THL 2101/5.05.00/2018; Population Register Centre VRK/1291/2019-3; Statistics Finland TK-53-1713-18/u1281; and Tax Register VH/874/07.01.03/2019). Patients' identification numbers were pseudonymized, and the research group received individualized but unidentifiable data. Informed consent was waived because of the retrospective registry nature of the study. The study conforms to the Declaration of Helsinki as revised in 2013.

Statistical Analyses

We modeled incidence rates and incidence rate ratios (IRRs) with 95% CIs of LTC admission event using the Poisson regression models with a Lexis-type data structure based on 3 time scales: follow-up time from AF diagnosis, calendar year, and age.[11] The Lexis-type data were further split into intervals based on the initiation of OAC therapy. This statistical approach was chosen to account for patients' age increasing during the relatively long observation period between 2007 and 2018, as well as for temporal differences in the rate of LTC

Table 1
Baseline Characteristics of the Study Cohort at the Time of AF Diagnosis According to OAC Initiation During Follow-up

	No OAC Therapy During Follow-up	OAC Therapy During Follow-up	*P* Value
Number of patients	45,218	143,534	
Calendar year of AF diagnosis, mean (SD)	2012 (3.3)	2013 (3.2)	<.001
Demographics			
Mean age, y (SD)	66.4 (17.5)	73.0 (11.0)	<.001
Female sex	44.4	50.5	<.001
Family caregiver	1.6	1.2	<.001
Home care	9.0	6.8	<.001
Income tertiles			<.001
First (lowest)	32.0	34.3	
Second	28.6	35.0	
Third (highest)	39.4	30.6	
Comorbidities			
Diabetes	15.6	22.3	<.001
Dyslipidemia	34.5	51.7	<.001
Heart failure	12.6	15.6	<.001
Hypertension	63.0	76.8	<.001
Any vascular disease	23.4	27.3	<.001
Prior ischemic stroke	6.2	10.0	<.001
Prior bleeding	11.9	8.7	<.001
Abnormal liver function	0.9	0.3	<.001
Renal failure	4.0	2.9	<.001
Alcohol use disorder	6.9	2.9	<.001
Cancer	18.0	19.2	<.001
Dementia	5.2	2.8	<.001
Psychiatric disorder	16.5	10.9	<.001
Risk scores			
CHA2DS2-VASc score, mean (SD)	2.7 (2.0)	3.4 (1.7)	<.001
Modified HAS-BLED score, mean (SD)	2.2 (1.2)	2.5 (1.0)	<.001

CHA2DS2-VASc, congestive heart failure, hypertension, age ≥75 years, diabetes, history of stroke or transient ischemic attack, vascular disease, age 65-74 years, sex category (female); modified HAS-BLED score, hypertension, abnormal renal or liver function, prior stroke, bleeding history, age >65 years, alcohol use disorder, concomitant antiplatelet and nonsteroidal antiinflammatory drugs (no labile INR, max score 8).
Values denote % unless otherwise specified.

admission. Adjusted IRRs were calculated in two separate models, the first of which included age, sex, calendar year, and OAC use to control for the effects of these demographic factors. To control for differences in comorbidities and socioeconomic status, which may also affect the need for LCT, the following additional baseline variables were included in the second model: heart failure, hypertension, diabetes, prior ischemic stroke, vascular disease, dyslipidemia, prior bleeding, alcohol use disorder, renal failure, liver cirrhosis or failure, cancer, dementia, psychiatric disorders, income level (divided in tertiles), as well as home care acuity level during the year preceding AF diagnosis (divided in 6 categories) and family caregiver prior to AF diagnosis. The χ^2 test and the Student *t* test were used to compare baseline variables. Statistical analyses were performed with the IBM SPSS Statistics software, version 28.0 (IBM Corp), and R, version 4.0.5 (R Core Team; https://www.R-project.org).

Results

We identified 188,752 patients (49.0% female); mean age 71.4 years (SD 13.2) with new-onset AF without prior LTC. The mean follow-up time was 3.6 years (SD 3.0). Altogether, 143,534 patients (76.0 %) started OAC therapy, of whom 71.9% initiated treatment with warfarin and 28.1% with DOACs. Patients initiating OAC therapy had lower prevalence of dementia, psychiatric disorders, and prior home care but were older and had higher CHA_2DS_2-VASc and HAS-BLED scores than those not receiving OAC therapy (Table 1). Overall, 11,775 patients (6.2%) were admitted to LTC during follow-up. A total of 44,365 patients (23.5%) died during follow-up without admission to LTC and 8156 patients (4.3%) died after admission to LTC before the end of the study observation period.

In the unadjusted analyses, OAC therapy was not associated with the LTC admission rate. However, in the adjusted regression models, initiation of OAC therapy was associated with a lower risk of admission to LTC (Table 2). The Kaplan-Meier curves of LTC admission for OAC therapy and no OAC therapy crossed each other during follow-up when all patients were included, but when analyses were limited only to patients with a higher ischemic stroke risk or age at least 70 years, the disparity in LTC admission rate was more evident both in the crude survival curves and in the unadjusted and adjusted rate ratios (Figure 1, Supplementary Table 2). In the sensitivity analyses with OAC exposure considered to last only until 180 days after the last drug purchase, OAC therapy was also associated with a lower LTC admission rate (adjusted IRR 0.67, 95% CI 0.64-0.70).

Table 2
Incidence Rates of Admission to Long-Term Care According to the Initiation of Any Oral Anticoagulant Therapy Between 2007 and 2018

Treatment	P-Years (1000 years)	Events, n	Incidence (per 1000 p-years)	Unadjusted IRR	Adjusted IRR (Model 1)	Adjusted IRR (Model 2)
No OAC	248.8	3851	15.5 (15.0-16.0)	(Reference)	(Reference)	(Reference)
Any OAC	525.6	7924	15.1 (14.7-15.4)	0.97 (0.94-1.01)	0.71 (0.68-0.74)	0.79 (0.76-0.82)

IRR, incidence rate ratio; OAC, oral anticoagulant; P-year, patient-year.
IRRs were estimated with the Poisson regression. Model 1 was adjusted for age, sex, and calendar year and Model 2 additionally with heart failure, hypertension, diabetes, ischemic stroke, vascular disease, dyslipidemia, bleedings, alcohol use disorder, renal failure, liver cirrhosis or failure, cancer, dementia, psychiatric disorders, income, home care acuity level, and family caregiver. Values in parentheses are 95% CIs.

When analyses were restricted to the DOAC era, that is, from 2015 onward, DOAC therapy was associated with a lower rate of LTC admission when compared to warfarin. When compared to no OAC therapy, both warfarin and DOAC therapy were associated with lower admission to LTC. Apixaban, dabigatran, and rivaroxaban were associated with lower LTC admission rate when compared with warfarin, but edoxaban did not significantly differ from warfarin. Significant disparities in the LTC admission rate were not observed between different DOACs (Table 3).

Discussion

This nationwide cohort study demonstrated that OAC therapy is associated with a considerably reduced risk of admission to LTC in patients with incident AF, and the association is most evident among patients with higher age or a higher risk of ischemic stroke. Furthermore, when compared to warfarin, use of DOACs was associated with an approximately 30% reduction in the LTC admission rate. The 4 DOACs evaluated did not differ with respect to the rate of LTC admission.

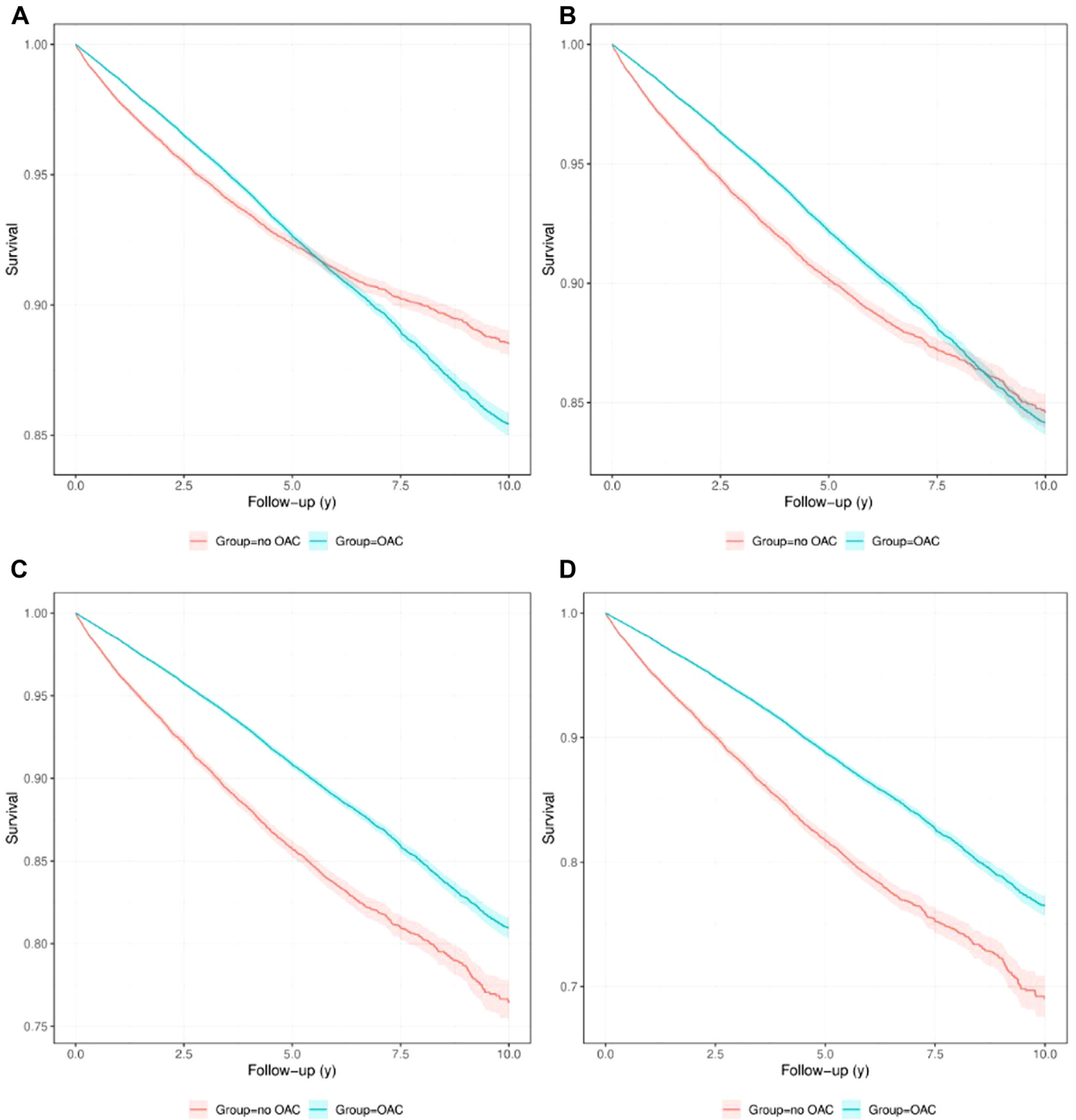

Fig. 1. Kaplan-Meier curves for admission to LTC according to OAC initiation after AF diagnosis in (A) the overall cohort, (B) in patients with at least moderate ischemic stroke risk, (C) in patients with high ischemic stroke risk, and (D) in patients with age ≥70 years at baseline.

Table 3
Incidence Rates of Admission to Long-Term Care According to the Initiation of Different Oral Anticoagulants Between 2015 and 2018

Treatment	P-Years (1000 years)	Events, n	Incidence (per 1000 p-years)	Adjusted IRR (No OAC as Reference)	Adjusted IRR (Warfarin as Reference)	Adjusted IRR (Apixaban as Reference)
All DOACs combined						
No OAC	27.5	458	16.7 (15.2-18.3)	(Reference)	1.35 (1.20-1.52)	N/A
Warfarin	51.5	873	17.0 (15.8-18.1)	0.74 (0.66-0.83)	(Reference)	N/A
Any DOAC	39.5	368	9.3 (8.4-10.3)	0.51 (0.44-0.59)	0.69 (0.61-0.79)	N/A
DOACs separately						
No OAC	27.5	458	16.7 (15.2-18.3)	(Reference)	1.35 (1.20-1.52)	1.85 (1.52-2.24)
Warfarin	51.5	873	17.0 (15.8-18.1)	0.74 (0.66-0.83)	(Reference)	1.37 (1.14-1.64)
Apixaban	11.9	141	11.8 (10.0-14.0)	0.54 (0.45-0.66)	0.73 (0.61-0.88)	(Reference)
Rivaroxaban	18.1	146	8.1 (6.8-9.5)	0.49 (0.41-0.60)	0.67 (0.56-0.80)	0.91 (0.72-1.15)
Dabigatran	9.3	76	8.2 (6.4-10.2)	0.49 (0.38-0.63)	0.66 (0.52-0.84)	0.90 (0.68-1.20)
Edoxaban	0.2	5	22.3 (7.2-52.0)	1.04 (0.43-2.51)	1.40 (0.58-3.38)	1.92 (0.78-4.68)

P-year, patient-year.
IRRs were estimated with the Poisson regression and adjusted for age, sex, calendar year, heart failure, hypertension, diabetes, ischemic stroke, vascular disease, dyslipidemia, bleedings, alcohol use disorder, renal failure, liver cirrhosis or failure, cancer, dementia, psychiatric disorders, income, home care acuity level, and family caregiver. Values in parentheses are 95% CIs.

The current study sheds light to a previously less recognized area in the clinical course of patients with AF. While the benefits of OAC therapy and the associated bleeding risks have been well-established in the previous literature, the impact of OAC therapy on the need of LTC in patients with AF has not been previously investigated.[12-14] In addition to the assessment of hard clinical endpoints, such as death or stroke, it is vital to also acknowledge the impacts of the used treatments on the quality of life and functional status. Our results suggest that OAC therapy can prevent the need of LTC and thus lengthen survival at home in this aging and multimorbid population. These findings are in line with the robust evidence on lower risk of ischemic stroke and mortality associated with OAC therapy.[12] Moreover, DOACs were associated with a lower rate of LTC admission when compared to warfarin, adding to the mounting evidence of the superiority of DOACs in the treatment of AF.[15] Specifically, apixaban, rivaroxaban, and dabigatran seemed all better than warfarin in preventing LTC admission, whereas the small number of patients treated with edoxaban limits the interpretation of its rate estimates.

The prevalence of AF is rising, and in addition to the considerable burden on individual patients, AF places an increasingly critical financial burden on health care systems, with costs largely driven by the long-term disability associated with ischemic strokes.[1,16-18] Reducing the need of LTC, as well as ischemic strokes, by increasing guideline-based OAC use in patients with AF could have a major positive impact on health care costs.[19,20] The reduction in the risk of LTC admission associated with OACs is likely multifactorial and presumably in parts mediated by the lower rate of ischemic strokes. Additionally, preceding OAC therapy, especially with DOACs, in patients suffering an ischemic stroke has been associated with lower stroke severity and better functional outcomes, which could also reflect in our results.[21-23] Other factors underlying the lower need of LTC may be related to the protective role of OACs on cognitive impairment.[24] Furthermore, recent studies have suggested that DOACs may be superior to warfarin in preventing dementia, which may in part explain our results of lower LTC need associated with DOAC therapy.[25,26]

A particular strength of our study is the complete nationwide coverage of the linked national registries. Indeed, the data encompass all patients with AF from all levels of care with virtually no loss to follow-up, all OAC purchases and LTC admissions in Finland, as well as important home care acuity information prior to AF reflecting baseline functional status. Additionally, the statistical model used accounts for temporal differences in the utilization of LTC and for the increase in age during follow-up, which appear to be important factors for LTC admission. Nevertheless, our findings must be interpreted bearing in mind the several limitations of the study, particularly the challenges inherent to retrospective cohort studies based on administrative data. Hence, the findings represent associations and not necessarily causation between OAC therapy and need of LTC. Furthermore, confounding by indication is a common threat to validity in observational studies on treatment effects. However, we attempted to mitigate this bias with the washout period in the patient selection process, as well as with the comprehensive set of variables included in the adjustments. Additionally, information bias may be present because of unmeasured or inappropriately recorded data, although the health care registries used are well-validated and have relatively high diagnostic accuracy, especially regarding cardiovascular diseases.[27,28]

Conclusions and Implications

In conclusion, this nationwide cohort study showed that OAC therapy, especially with DOACs, is associated with a considerably lower risk of admission to LTC in patients with incident AF. Increasing the guideline-based OAC coverage among patients with AF at risk of ischemic stroke may prevent the need of LTC, lengthen survival at home, and potentially decrease health care costs.

References

1. Lehto M, Haukka J, Aro A, et al. Comprehensive nationwide incidence and prevalence trends of atrial fibrillation in Finland. *Open Heart*. 2022;9:e002140.
2. Dhamoon MS, Moon YP, Paik MC, et al. Long-term functional recovery after first ischemic stroke. *Stroke*. 2009;40:2805–2811.
3. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: The framingham study. *Stroke*. 1991;22:983–988.
4. 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 for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2021;42:373–498.
5. Lehto M, Halminen O, Mustonen P, et al. The nationwide finnish anticoagulation in atrial fibrillation (FinACAF): study rationale, design, and patient characteristics. *Eur J Epidemiol*. 2022;37:95–102.
6. Jaakkola J, Teppo K, Biancari F, et al. The effect of mental health conditions on the use of oral anticoagulation therapy in patients with atrial fibrillation: the FinACAF Study. *Eur Heart J Qual Care Clin Outcomes*. 2022;8:269–276.
7. Teppo K, Jaakkola J, Airaksinen KEJ, et al. Mental health conditions and adherence to direct oral anticoagulants in patients with incident atrial fibrillation: a nationwide cohort study. *Gen Hosp Psychiatry*. 2022;74:88–93.
8. Ministry of Social Affairs and Health. *National Framework for High-Quality Services for Older People*. Ministry of Social Affairs and Health publications; 2008.
9. Linnosmaa I, Sääksvuori L. Long-term care policy in Finland: policy brief, country report, CEQUA Study. 2017. Accessed January 25, 2023. http://www.julkari.fi/handle/10024/135807

10. Nihtilä E, Martikainen P. Household income and other socio-economic determinants of long-term institutional care among older adults in Finland. *Popul Stud*. 2007;61:299–314.
11. Plummer M, Carstensen B. Lexis: an R class for epidemiological studies with Long-term follow-up. *J Stat Softw*. 2011;38. https://doi.org/10.18637/jss.v038.i05.
12. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med*. 2007;146:857–867.
13. Connolly SJ, Laupacis A, Gent M, et al. Canadian atrial fibrillation anticoaguiation (CAFA) study. *J Am Coll Cardiol*. 1991;18:349–355.
14. Lip GYH, Edwards SJ. Stroke prevention with aspirin, warfarin and ximelagatran in patients with non-valvular atrial fibrillation: A systematic review and meta-analysis. *Thromb Res*. 2006;118:321–333.
15. Ruff CT, Giugliano RP, Braunwald E, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: A meta-analysis of randomised trials. *Lancet*. 2014;383:955–962.
16. Krijthe BP, Kunst A, Benjamin EJ, et al. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. *Eur Heart J*. 2013;34:2746–2751.
17. Dai H, Zhang Q, Much AA, et al. Global, regional, and national prevalence, incidence, mortality, and risk factors for atrial fibrillation, 1990–2017: results from the Global Burden of Disease Study 2017. *Eur Heart J Qual Care Clin Outcomes*. 2021;7:574–582.
18. Ball J, Carrington MJ, McMurray JJV, Stewart S. Atrial fibrillation: Profile and burden of an evolving epidemic in the 21st century. *Int J Cardiol*. 2013;167:1807–1824.
19. Sussman M, Menzin J, Lin I, et al. Impact of atrial fibrillation on stroke-related healthcare costs. *J Am Heart Assoc*. 2013;2:e000479.
20. Kapiainen S, Väisänen A, Haula T. *Terveyden- Ja Sosiaalihuollon Yksikkökustannukset Suomessa Vuonna 2011*. 2014.
21. Meinel TR, Branca M, De Marchis GM, et al. Prior anticoagulation in patients with ischemic stroke and atrial fibrillation. *Ann Neurol*. 2021;89:42–53.
22. Nakajima M, Inatomi Y, Ueda A, et al. Preceding direct oral anticoagulant administration reduces the severity of stroke in patients with atrial fibrillation – K-PLUS registry. *J Clin Neurosci*. 2021;89:106–112.
23. Xian Y, O'Brien EC, Liang L, et al. Association of preceding antithrombotic treatment with acute ischemic stroke severity and in-hospital outcomes among patients with atrial fibrillation. *JAMA*. 2017;317:1057–1067.
24. Friberg L, Rosenqvist M. Less dementia with oral anticoagulation in atrial fibrillation. *Eur Heart J*. 2018;39:453–460.
25. Kim D, Yang PS, Jang E, et al. Association of anticoagulant therapy with risk of dementia among patients with atrial fibrillation. *Europace*. 2021;23:184–195.
26. Bezabhe WM, Bereznicki LR, Radford J, et al. Oral anticoagulant treatment and the risk of dementia in patients with atrial fibrillation: a population-based cohort study. *J Am Heart Assoc*. 2022;11:e023098.
27. Tolonen H, Salomaa V, Torppa J, Sivenius J, Immonen-Räihä P, Lehtonen A. The validation of the Finnish Hospital discharge register and causes of death register data on stroke diagnoses. *Eur J Cardiovasc Prev Rehabil*. 2007;14:380–385.
28. Sund R. Quality of the Finnish Hospital discharge register: a systematic review. *Scand J Public Health*. 2012;40:505–515.