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ORIGINAL RESEARCH ARTICLE

Cost Differences Between Oral Anticoagulation Therapies in Patients with Atrial Fibrillation in Finland

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Abstract

Background The cost burden of new-onset atrial fibrillation (AF) has not previously been studied with unselected nationwide data.

Objective We analyzed differences in the distribution and time course of costs from all categories of healthcare services in patients receiving direct oral anticoagulants (DOACs), warfarin, or no anticoagulation during the first year following diagnosis of AF.

Methods This sub-study of the Finnish AntiCoagulation in Atrial Fibrillation (FinACAF) project comprised all new-onset AF patients from 2011 to 2017 in Finland with an indication for oral anticoagulation treatment. The registry data included information on primary and secondary care services as well as social care services, drug purchases, laboratory data, and reimbursed private care and travel services. We report inverse probability of treatment weighted average costs for different pharmaceutical groups with bootstrapped confidence intervals.

Results In total, 130,745 patients (66,610 on warfarin, 32,996 on DOACs) were included. Weighted first-year costs after onset of AF were €11,364 for rivaroxaban (n = 13,230), €12,642 for apixaban (n = 11,886), €11,403 for dabigatran (n = 7514), and €10,752 for edoxaban (n = 366). Costs were clustered near the diagnosis of AF. Costs for warfarin patients were inversely related to the quality of anticoagulation therapy. Average first-year costs for warfarin patients were €15,860, higher than for patients on DOACs by €3218–€5108. Patients without any oral anticoagulation had the highest first-year costs, €17,682. Patients with high risk of stroke had higher total costs, both in patients using DOACs and warfarin.

Conclusions DOACs had lower total costs than warfarin despite higher drug expenses. Patients without any oral anticoagulation had the highest costs.

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Key Points

Patients with new-onset atrial fibrillation (AF) receiving direct oral anticoagulants (DOACs) have lower total costs of care than patients receiving warfarin.

Total social and healthcare costs during the first year of AF are €10,752–€12,642 for patients receiving different DOACs and €15,860 for patients receiving warfarin.

Low time in therapeutic range is associated with the highest costs of care in new-onset AF patients receiving warfarin.

1 Introduction

Atrial fibrillation (AF) is the most common sustained arrythmia, estimated to affect 5.2% of the adult population [1]. Along with aging populations, both the prevalence of AF patients and associated healthcare costs are predicted to increase. For instance, evidence from the UK suggests that direct costs of AF will more than double by the year 2040 [2]. AF is often associated with other comorbidities, and the patients typically use a wide range of healthcare services. AF is a major risk factor for stroke, the prevention of which necessitates continuous oral anticoagulation (OAC) therapy.

Previously, the only options for OAC were vitamin K antagonists (of which warfarin is the most used), which are cheap but require regular monitoring in the form of international normalized ratio (INR) measurements. Recently, warfarin has been mostly replaced with newer direct oral anticoagulants (DOACs) apixaban, dabigatran, edoxaban, and rivaroxaban, which are more costly but do not necessitate INR monitoring. Patients using DOACs also have a lower risk of stroke or bleeding than patients on warfarin [3]. Since the use of DOACs became widespread relatively recently, there is still scarce research on their impact on health service usage and care costs.

According to a recent systematic review, the first-year costs after a new-onset AF have not been comprehensively studied with non-selected nationwide registry data [4], although some of the related matters, such as the effect of delayed OAC prescription on the costs of incident AF patients has been studied since [5]. Social and healthcare costs of prevalent AF patients (without attention to a time point of AF incidence) were recently studied in a nationwide register study in Finland [6]. Additionally simulations, in majority Markov chain analyses, have been performed, based on selected data from randomized controlled trials (e.g., ARISTOTLE, AVERROES, RE-LY, ROCKET AF) [7–11]. Simulations often make extrapolations based on limited data and might not fully reflect the differences between OACs on healthcare costs and service use in a real-life environment. To our knowledge, this is the first study to give a real-world data-based estimation of incident cost burden of new-onset AF patients. Analysis of new-onset AF is especially relevant when comparing the cost burden of different anticoagulation therapies, as decisions on starting an OAC therapy are typically done at the time of incidence of AF.

In this study, we utilize comprehensive real-world data to compare all the social and healthcare costs of Finnish patients with AF using different OACs in the first year after AF onset. We employ inverse probability of treatment weighting to mitigate the selection bias inherent in registry-based studies. We also analyze how the costs are distributed between different sectors of services and how they develop in time both before and after diagnosis of AF.

2 Data and Methods

2.1 Research Data and Variables

The Finnish AntiCoagulation in Atrial Fibrillation (FinACAF) study is a nationwide register study that covers all patients with AF during 2004 to 2018 in Finland. The present sub-study is focused on patients with new-onset AF during the years 2011–2017, to ensure that each patient has sufficient history data and 1 year of follow-up data after the cohort entry. FinACAF links individual-level data from comprehensive national registers on patients' primary, secondary, and tertiary care and social care services, as well as laboratory measurements, mortality, and socioeconomic status. A comprehensive list of used registers and acquired data is presented in the electronic supplementary material (Table S1). The study rationale and design have been previously reported [1].

Patients were identified based on all nationwide healthcare registers: Care Register for Health Care (Terveys-Hilmo) for hospitalizations and outpatient specialist visits; Register of Primary Health Care Visits (AvoHilmo) for primary healthcare; and National Reimbursement Register upheld by Social Insurance Institute (Kela). The inclusion criterion was an International Classification of Diseases, 10th Revision (ICD-10) code I48 in these registries during the study period, with the first of these diagnoses marking the time of cohort entry.

The cohort of this sub-study excluded patients if they were under 20 years old during cohort entry, moved permanently abroad during the study period, had any use of OAC medication 365 days before the cohort entry, had warfarin prescriptions during 2004–2006, or were diagnosed with AF

before 2011 or after 2017. Patients with a CHA_2DS_2-VA (congestive heart failure, hypertension, age over 75, diabetes, prior stroke or TIA or thromboembolism, 65 vascular disease, age to 74) score of 0 were also excluded from all analyses due to anticoagulation treatment not being recommended in these patients [12]. The flow-chart of the selection of the study population is presented in Fig. 1.

Employing an intention-to-treat approach, the study patients were grouped, based on the OAC regimen they started, into groups of warfarin, dabigatran, rivaroxaban, and apixaban users. The DOAC users were further divided into those receiving standard-dose (150 mg for dabigatran, 20 mg for rivaroxaban, 5 mg for apixaban, and 60 mg for edoxaban) and low-dose treatment (110 mg for dabigatran, 15 mg for rivaroxaban, 2.5 mg for apixaban, and 30 mg for edoxaban).

Individual time in therapeutic range (TTR) values were calculated for the warfarin patients for a time period determined by the drug exposure. The TTR period began 7 days after the first purchase that had an INR measurement within 30 days prior. The period ended 60 days after the last INR measurement if no new measurements were made in that period and also when 180 days passed from the last warfarin purchase if no new purchases were made. The TTR period was also terminated upon the purchase of any DOAC, when 730 days had passed from the start or at the end of the study period on December 31st, 2018. The TTR was then calculated with the Rosendaal method [13] as the percentage of time the interpolated INR value was between 2.0 and 3.0. The TTR was calculated for patients who had three or more INR measurements in the TTR period, and these patients were divided into quartiles based on estimated TTR.

The five components of cost analysis included (1) secondary and tertiary care services, including hospital outpatient care episodes, inpatient care episodes at hospital and health

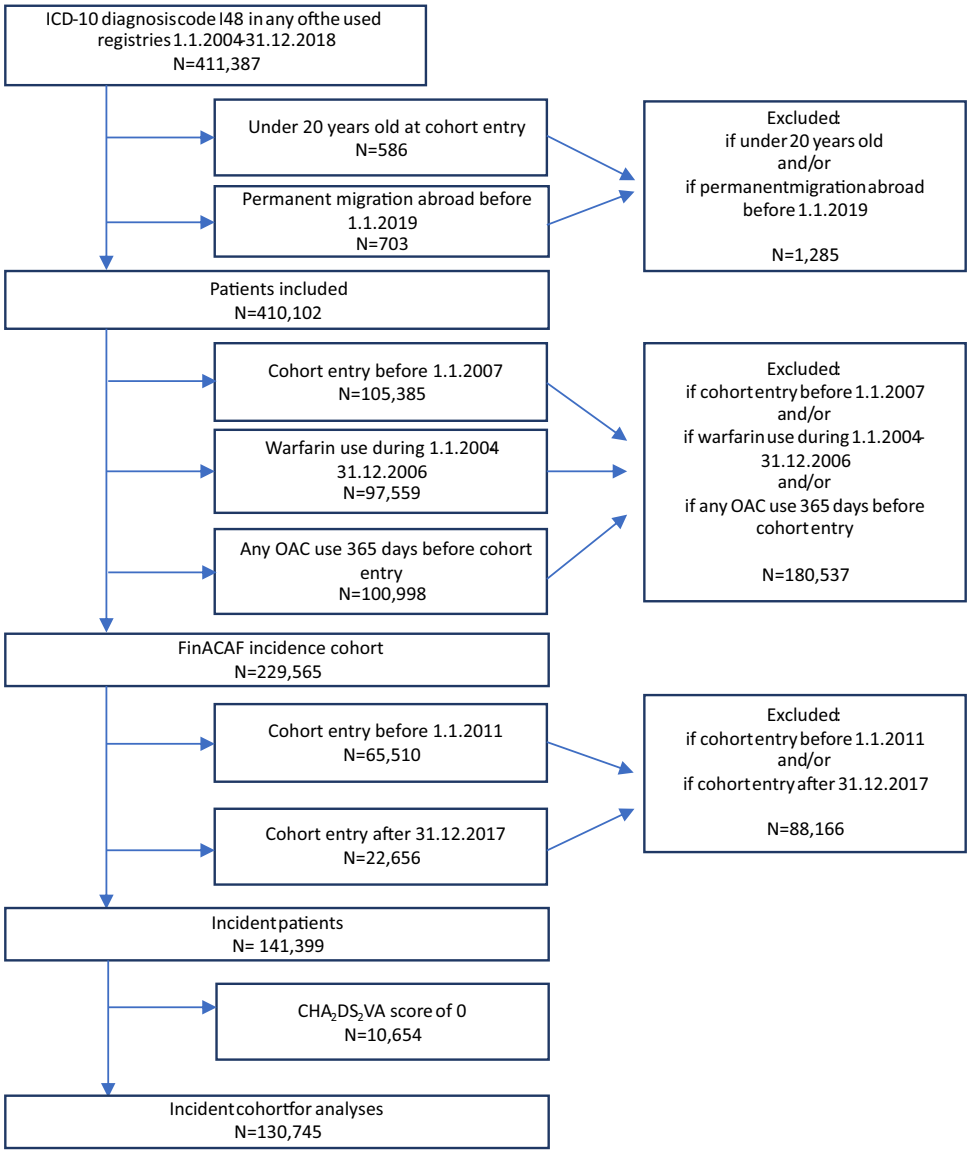

Fig. 1 Patient selection flow-chart of the study. *CHA_2DS_2-VA* Congestive heart failure, Hypertension, Age over 75, Diabetes, Prior stroke or TIA or thromboembolism, Vascular disease, Age 65 to 74, *FinACAF* Finnish AntiCoagulation in Atrial Fibrillation, *ICD-10* International Classification of Diseases 10th revision, *OAC* oral anticoagulation, *TIA* transient ischemic attack

center wards, and emergency department visits, as recorded in the Terveys-Hilmo register; (2) primary healthcare outpatient care episodes, including visits for INR measurements, registered in AvoHilmo; (3) long-term social care service episodes registered in Care Register for Social Welfare (SosiaaliHILMO), including service housing facilities for older people with on-call or 24/7 nurse availability, institutional elderly care facilities, and, to a marginal extent, living facilities and institutional care for disabled people and mental health rehabilitation; (4) prescription drug purchases; and (5) reimbursed travel costs to public or private care or rehabilitation facilities, and reimbursed out-of-pocket costs for care services in a private setting given due to illness, pregnancy, or childbirth, and excluding occupational care services.

The costs of care events were calculated using diagnoses related to the patient grouping and national standard rates. The costs for hospitalizations and outpatient hospital visits, recorded in Terveys-Hilmo, were based on the Nord-DRG (diagnosis-related group) patient grouping definitions, which use the ICD-10 codes and the Finnish version of the Nordic Classification of Surgical Procedures (NCSP) codes for diagnostic and treatment procedures. The cost weights for DRG-based hospital discharges and outpatient hospital visits were calculated using large national samples of individual-level cost accounting data from Finnish hospitals by the national authorities. Services (e.g., surgeries, ward stay) produced in hospital service units had their costs allocated to the patients' hospital episode using the causality principle. Costs from administration were allocated according to the reciprocal method. Primary care contacts were costed based on both the type of provider (general practitioner [GP], nurse, other healthcare professionals) and the mode of delivery (online, in-person, or home visit). Each primary care contact type was priced according to the national price list for unit costs [14].

The per diem cost estimates for long-term social care services were derived from the national standard price lists for unit costs of healthcare services in Finland and used with the individually calculated length-of-stay data. Prescription drug purchase and private care and travel reimbursement information was provided by Kela.

2.2 Ethical Considerations

The study at hand only included previously collected registry information, and thus the patients were not contacted at any point. The data were pseudonymized, and the patients could therefore not be directly identified. The ethical permission was permitted by the ethical committee of the Medical Faculty of Helsinki University, Helsinki Finland (nr. 15/2017 and 15/2024), and the study obtained permission from the Helsinki University Hospital (HUS/46/2018 and HUS/217/2024).

2.3 Statistical Methods

In order to estimate the effect of the treatment, an inverse-probability-of-treatment weighting (IPTW) was applied to the patient groups on different OACs and patients not on OAC. IPTW can mitigate the confounding caused by indication of treatment in situations with several treatment alternatives [15, 16]. The weighting used a generalized boosted model with 10,000 regression trees [17]. Covariates used for the weighting were age, sex, CHA_2DS_2-VA score, modified HAS-BLED (Hypertension, Abnormal renal and liver function, Stroke, Bleeding, Labile INR, Elderly, Drugs or alcohol) score, and categorical variables for ischemic stroke (IS) or transient ischemic attack (TIA), vascular disease, hypertension, diabetes, or cancer before AF onset.

Healthcare costs are reported as the IPTW-weighted average cost per person over the year before and 1 year following the cohort entry, marked by the first AF diagnosis. Costs for hospital care, primary care, social care, and medication are also reported separately, categorized according to the registry source. Confidence intervals for the means were calculated using a bootstrap method with 1000 samples. More detailed information on healthcare costs during the year following the first AF diagnosis are provided, including the separated costs for hospital outpatient care visits, hospital ward treatment, health center ward treatment, emergency department visits, home care services, and other primary care services, as well as costs for OAC and other medication (see the electronic supplementary material, Table S3).

The temporal distribution of total social and healthcare costs, including hospital care, primary care, drug purchases, and social care services, surrounding AF diagnosis are reported on a monthly basis, both before and after the cohort entry. The costs of extended care periods were divided evenly over their duration for the purpose of determining monthly costs. Private care and travel costs were not allocated, as the annual level data were not conducive to monthly level analysis.

Health and social care costs were compared between patients receiving different OACs, as well as patients who did not receive any OAC during the study period. Within warfarin users, the costs were compared according to TTR quartiles as well as patients for whom TTR was not possible to define due to lack of sufficient INR measurements. To assess the cost differences between the high-risk and low-risk patients, we compared the costs of patients with a CHA_2DS_2-VA score of 1 against patients with a score of 2 or more across both different OACs and TTR quartiles of warfarin patients. In the electronic supplementary material, we compared patients on standard doses of DOACs (dabigatran

150 mg, rivaroxaban 20 mg, apixaban 5 mg, and edoxaban 60 mg) against warfarin patients, and patients on low-dose DOACs (dabigatran 110 mg, rivaroxaban 15 mg, apixaban 2.5 mg, and edoxaban 30 mg) against warfarin patients.

To assess the effect of the IPTW on the costs, we compared the average total costs of each medication category with and without the weighting (included in the electronic supplementary material). We also include the raw, unweighted 1-year costs by cost category for each medication group in the supplement.

The statistical analyses were conducted using R version 4.3.2, and with the IBM SPSS Statistics software (Version 27.0, SPSS, Inc., Armonk, NY). The figures were created using the ggplot2 library in R version 4.3.2 and Excel.

3 Results

Between 2011 and 2017, we identified 141,399 patients with newly diagnosed AF. After removing patients with a CHA_2DS_2-VA score of 0, the number of patients was 130,745, of which 66,610 received warfarin, 7514 dabigatran, 13,230 rivaroxaban, 11,886 apixaban, 366 edoxaban, and 31,139 received no OAC during the study period, with average social and healthcare costs of €15,103 in the year following AF onset.

A TTR value was determined for 41,535 (62.4%) of the warfarin patients, with a mean TTR of 66.4%. The average TTR (range) in the TTR quartiles was 33% (0–56.1%) for the lowest quartile, 65.0% (56.1–71.9%) for the second quartile, 77.4% (71.9–82.7%) for the third quartile, and 89.8% (82.7–100%) for the highest quartile.

The average age was 74.8 years, and 51.8% of patients were female (Table 1). The most common comorbidities were hypertension (82.2%), hyperlipidemia (54.1%), and vascular disease (29%). Differences between patients receiving different OACs and warfarin patients with different TTR levels were minor. After applying IPTW, the baseline characteristics are mostly similar between patients receiving different OAC medications (supplementary Table S2; see the electronic supplementary material). Some comorbidities, such as dementia and congestive heart failure, are still more highly represented in patients with no OAC medication in the weighted population.

Cumulative monthly total healthcare costs from a year before AF diagnosis to a year after, calculated with IPTW, are presented in Fig. 2. The average cumulative costs for the whole 2-year period were €15,395 for dabigatran, €15,712 for rivaroxaban, €17,786 for apixaban, and €14,998 for edoxaban. The costs for warfarin patients were €29,337 for the lowest TTR quartile, €23,519 for the second quartile, €18,333 for the third quartile, €14,997 for the highest quartile, and €21,582 for the patients with no valid TTR value. Patients with no OAC medication had an average cumulative healthcare cost of €31,161. Patients on DOACs had costs of similar magnitude compared to each other, with patients on apixaban having slightly higher costs. Lower TTR values in warfarin patients correspond to higher healthcare costs, with the highest quartile having costs comparable to the DOACs. Patients with no OAC medication had healthcare costs comparable to the lowest TTR quartile and were thus more expensive than DOAC patients and most of patients on warfarin. The results, along with 95% confidence intervals, are included in the supplementary material (Table S4).

The weighted average social and healthcare costs in the year following AF onset for patients who received dabigatran, rivaroxaban, or edoxaban were similar at €11,403, €11,364, and €10,752, respectively. Patients on apixaban had slightly higher costs at €12,642 (Figure 3). Warfarin patients had higher costs than DOAC patients at €15,860, with lower TTR corresponding to higher costs. Patients who received no OAC were costlier than warfarin at €17,682. The results, along with 95% confidence intervals, are included in the electronic supplementary material (Table S3).

The largest cost drivers for AF healthcare costs in the year following AF onset were hospital care at €9383 (64.9%) and primary care at €2686 (18.6%). Drug purchases and social care services contributed less to the total at €1075 (7.4%) and €797 (5.5%), respectively. DOAC patients had comparably higher drug costs than warfarin patients due to the higher prices of DOACs (cost difference €496–€625 for different DOAC groups). Warfarin patients respectively had higher primary care costs, driven by the required INR measurements (difference €985–€1315 for different DOAC groups), as well as higher hospital care costs (difference €3218–€5108 for different DOAC groups). For warfarin patients, the different categories of costs increased along with decreasing TTR, with the exception of primary care costs not being increased for the lowest TTR quartile. Elevated hospital care and social care costs were the main contributors for the higher costs of patients who received no OAC.

When the total IPTW-weighted healthcare costs in the first year after AF onset were compared between patients with a CHA_2DS_2-VA score of 1 and patients with a score of 2 or higher, patients with higher scores had higher costs, ranging from less than double in the dabigatran (€7120 vs €12,128), rivaroxaban (€7177 vs €12,068), apixaban (€8181 vs €13,379), and warfarin (€10,185 vs €16,804) groups to more than double in the edoxaban group (€5338 vs €11,536) (Fig. 4). The difference was largest in patients who received no OAC, where CHA_2DS_2-VA scores higher than 1 corresponded to triple the average costs. In warfarin patients, the comparative difference between a CHA_2DS_2-VA score of 1 and higher scores was higher for patients with lower TTR values. The results, along with

Table 1 Patient characteristics at the time of new atrial fibrillation onset

		Total	Warfarin, lowest TTR quartile	Warfarin, second TTR quartile	Warfarin, third TTR quartile	Warfarin, highest TTR quartile	Warfarin, TTR not available
n		130,745	10,199	10,499	10,485	10,352	25,075
Sex, *n* (%)	Male	63,075 (48.2)	5067 (49.7)	4722 (45.0)	4586 (43.7)	4917 (47.5)	11,863 (47.3)
	Female	67,670 (51.8)	5132 (50.3)	5777 (55.0)	5899 (56.3)	5435 (52.5)	13,212 (52.7)
Age, years	Mean (SD)	74.8 (11.4)	74.6 (11.1)	75.7 (10.0)	75.4 (9.4)	74.4 (9.3)	75.5 (10.2)
	65–74	39,433 (30.2)	2861 (28.1)	3170 (30.2)	3480 (33.2)	3823 (36.9)	7582 (30.2)
	Over 75	68,365 (52.3)	5393 (52.9)	5892 (56.1)	5669 (54.1)	5080 (49.1)	13,838 (55.2)
	Under 65	22,947 (17.6)	1945 (19.1)	1437 (13.7)	1336 (12.7)	1449 (14.0)	3655 (14.6)
CHA_2DS_2-VA	1	19,170 (14.7)	1292 (12.7)	1053 (10.0)	1152 (11.0)	1398 (13.5)	2916 (11.6)
	2+	111,575 (85.3)	8907 (87.3)	9446 (90.0)	9333 (89.0)	8954 (86.5)	22,159 (88.4)
Dementia (%)		7598 (5.8)	539 (5.3)	492 (4.7)	415 (4.0)	316 (3.1)	1181 (4.7)
Cancer (%)		29,400 (22.5)	2286 (22.4)	2428 (23.1)	2283 (21.8)	2117 (20.5)	4966 (19.8)
Congestive heart failure (%)		24,337 (18.6)	2546 (25.0)	2304 (21.9)	1750 (16.7)	1361 (13.1)	4938 (19.7)
Ischemic stroke or TIA (%)		22,797 (17.4)	1758 (17.2)	1898 (18.1)	1845 (17.6)	1721 (16.6)	4419 (17.6)
Diabetes (%)		32,360 (24.8)	2917 (28.6)	2934 (27.9)	2551 (24.3)	2294 (22.2)	6232 (24.9)
Abnormal renal function (%)		6129 (4.7)	679 (6.7)	431 (4.1)	329 (3.1)	261 (2.5)	1022 (4.1)
Hyperlipidemia (%)		70,756 (54.1)	5732 (56.2)	6138 (58.5)	6002 (57.2)	5689 (55.0)	13,782 (55.0)
Hypertension (%)		107,439 (82.2)	8405 (82.4)	8683 (82.7)	8653 (82.5)	8352 (80.7)	20,508 (81.8)
Vascular disease (%)		37,960 (29.0)	3262 (32.0)	3157 (30.1)	3010 (28.7)	2657 (25.7)	7377 (29.4)
Abnormal liver function (%)		737 (0.6)	60 (0.6)	49 (0.5)	33 (0.3)	26 (0.3)	66 (0.3)
Bleeding (%)		15,683 (12.0)	1232 (12.1)	1094 (10.4)	947 (9.0)	848 (8.2)	2580 (10.3)
		Dabigatran	Rivaroxaban	Apixaban	Edoxaban	No OAC	
n		7514	13,230	11,886	366	31,139	
Sex (%)	Male	3857 (51.3)	6803 (51.4)	5711 (48.0)	182 (49.7)	15,367 (49.3)	
	Female	3657 (48.7)	6427 (48.6)	6175 (52.0)	184 (50.3)	15,772 (50.7)	
Age, years	Mean (SD)	72.9 (9.8)	73.0 (9.9)	75.5 (10.2)	74.4 (9.6)	74.8 (14.8)	
	65–74	2941 (39.1)	5182 (39.2)	3836 (32.3)	135 (36.9)	6423 (20.6)	
	Over 75	3185 (42.4)	5649 (42.7)	6393 (53.8)	179 (48.9)	17,087 (54.9)	
	Under 65	1388 (18.5)	2399 (18.1)	1657 (13.9)	52 (14.2)	7629 (24.5)	
CHA_2DS_2-VA	1	1161 (15.5)	2099 (15.9)	1391 (11.7)	46 (12.6)	6662 (21.4)	
	2+	6353 (84.5)	11,131 (84.1)	10,495 (88.3)	320 (87.4)	24,477 (78.6)	
Dementia (%)		208 (2.8)	408 (3.1)	482 (4.1)	15 (4.1)	3542 (11.4)	
Cancer (%)		1474 (19.6)	2638 (19.9)	2706 (22.8)	89 (24.3)	8413 (27.0)	
Congestive heart failure (%)		731 (9.7)	1527 (11.5)	1856 (15.6)	46 (12.6)	7278 (23.4)	
Ischemic stroke or TIA (%)		1374 (18.3)	1780 (13.5)	2117 (17.8)	43 (11.7)	5842 (18.8)	
Diabetes (%)		1827 (24.3)	3264 (24.7)	3197 (26.9)	97 (26.5)	7047 (22.6)	
Abnormal renal function (%)		130 (1.7)	303 (2.3)	533 (4.5)	17 (4.6)	2424 (7.8)	
Hyperlipidemia (%)		4332 (57.7)	7451 (56.3)	7171 (60.3)	221 (60.4)	14,238 (45.7)	
Hypertension (%)		6277 (83.5)	10,992 (83.1)	9970 (83.9)	297 (81.1)	25,302 (81.3)	
Vascular disease (%)		1784 (23.7)	3275 (24.8)	3432 (28.9)	87 (23.8)	9919 (31.9)	
Abnormal liver function (%)		16 (0.2)	31 (0.2)	38 (0.3)	3 (0.8)	415 (1.3)	
Bleeding (%)		731 (9.7)	1323 (10.0)	1347 (11.3)	47 (12.8)	5534 (17.8)	

CHA_2DS_2-VA Congestive heart failure, Hypertension, Age over 75, Diabetes, Prior stroke or TIA or thromboembolism, Vascular disease, Age 65 to 74, *OAC* oral anticoagulation, *TIA* transient ischemic attack, *TTR* time in therapeutic range

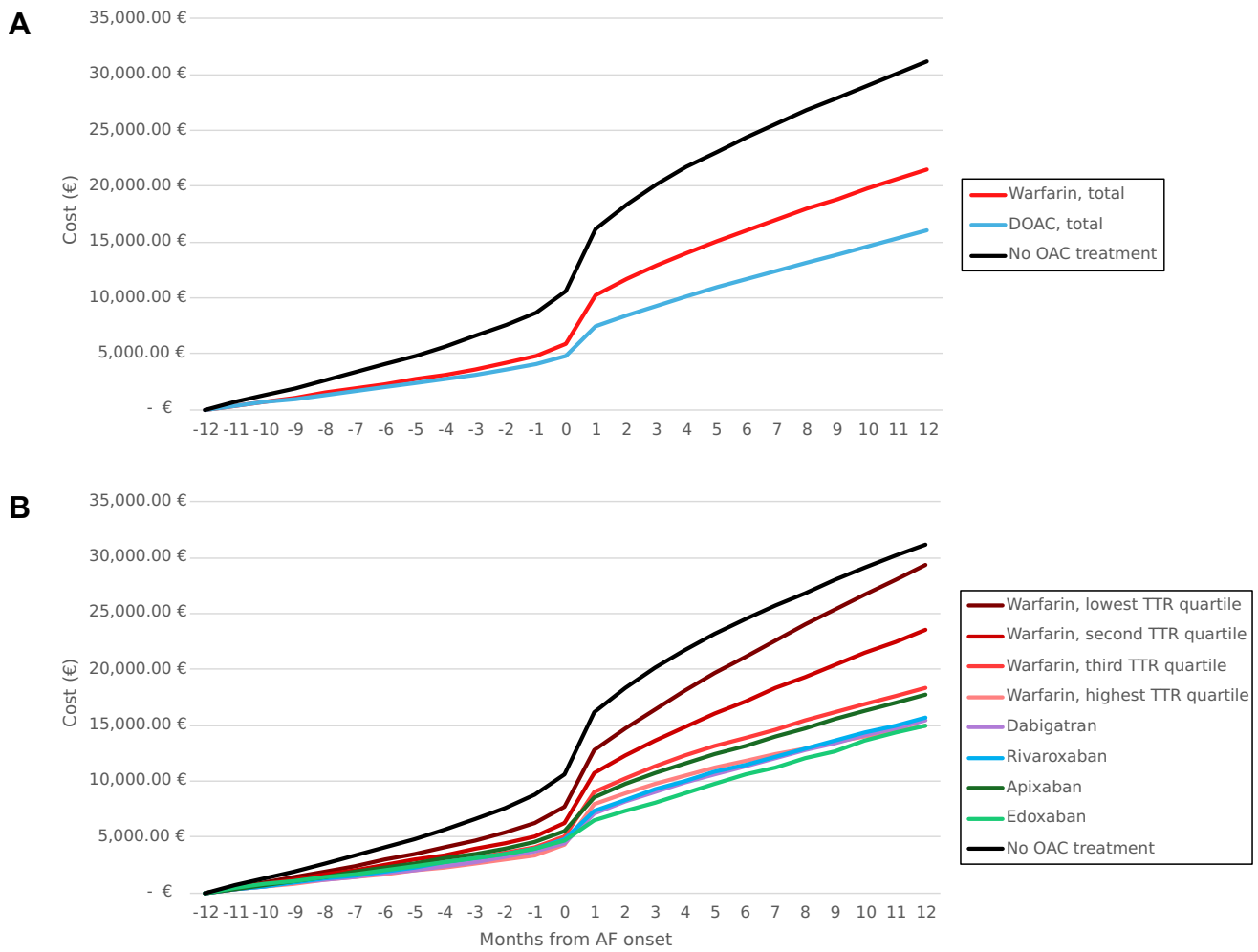

Fig. 2 Weighted total social and healthcare costs 12 months before and after a new-onset atrial fibrillation (AF) diagnosis for all warfarin patients, all direct oral anticoagulation (DOAC) patients, and patients without oral anticoagulation (OAC) (**A**) and for time in therapeutic range (TTR) quartiles of warfarin patients and patients using individual DOACs (**B**)

95% confidence intervals, are included in the electronic supplementary material (Table S5).

In a separate analysis of total costs of DOAC patients who received standard doses, the difference in costs between apixaban and other DOAC groups was reduced (supplementary Figure S1 and Table S6). In patients receiving low-dose DOACs, the differences between DOACs were pronounced (supplementary Figure S2 and Table S7). Additionally, a comparison of IPTW-weighted and unweighted 1-year costs after AF onset showed that the comparisons between OAC medication groups are mostly the same regardless of weighting, with the minor exception of the different DOAC groups having costs closer to each other after IPTW (supplementary Figure S3 and Table S8). Similar results were seen for the unweighted costs of different service types (supplementary Figure S4 and Table S9).

4 Discussion

In our study, we found (1) patients starting a DOAC had lower social and healthcare costs during the 2-year period around the onset of AF, (2) lower TTR in AF patients using warfarin was associated with higher social and healthcare costs, (3) hospital care was the largest cost component in newly diagnosed AF patients, followed by primary care, and (4) AF patients at an increased risk of stroke, identified by a CHA_2DS_2-VA score of 2 or higher, had the highest costs.

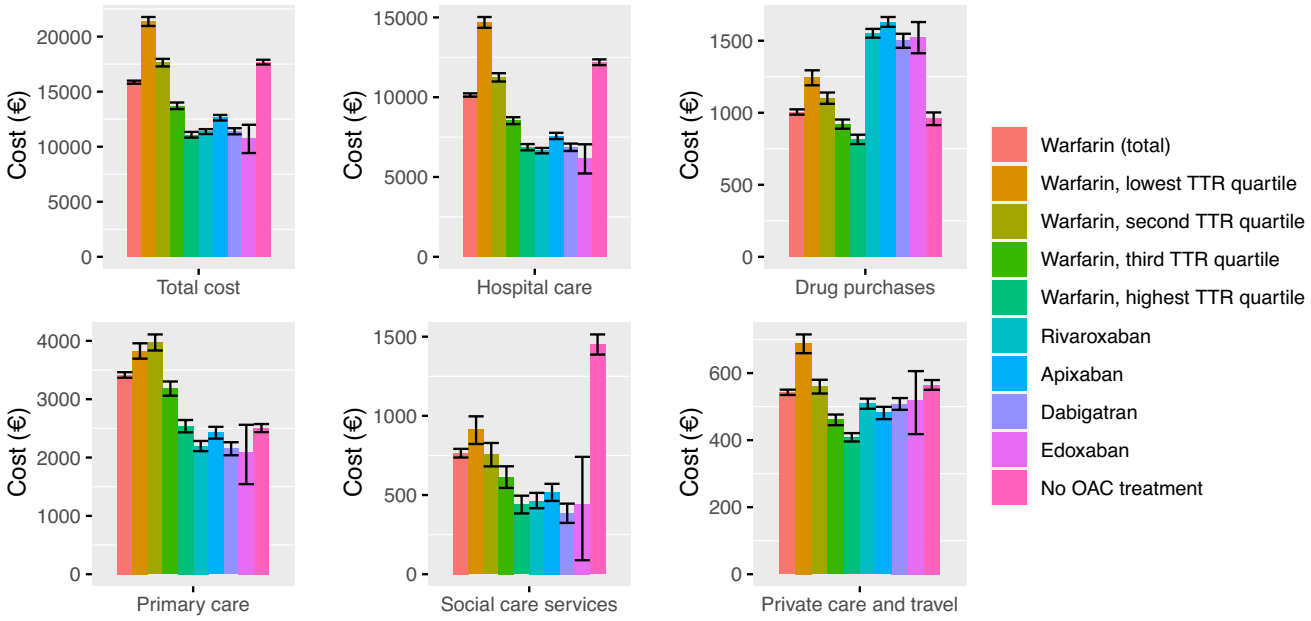

Fig. 3 Weighted accumulated costs by medication group and service type in the 12 months after a new-onset atrial fibrillation diagnosis. *OAC* oral anticoagulation, *TTR* time in therapeutic range

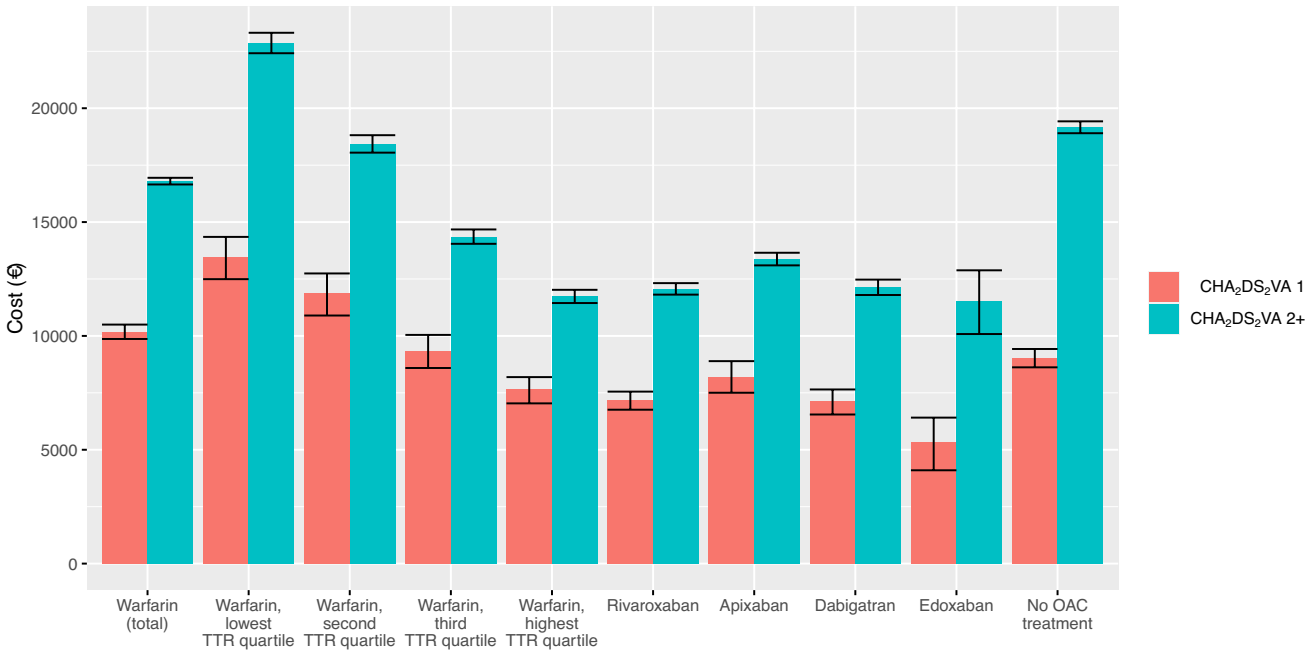

Fig. 4 Weighted accumulated costs by medication group and CHA_2DS_2-VA score in the 12 months after a new-onset atrial fibrillation diagnosis. *CHA_2DS_2-VA* congestive heart failure, hypertension, age over 75, diabetes, prior stroke or TIA or thromboembolism, disease vascular, age 65 to 74, *OAC* oral anticoagulation, *TIA* transient ischemic attack, *TTR* time in therapeutic range

After IPTW, the total social and healthcare costs during the first year after AF onset ranged from €10,752 to €15,860 for patients receiving different OACs. These costs were more than double the costs of the previous year before AF in each medication group. To our knowledge, our study is the first comparing the first-year costs of different OAC therapies. A previous study [18] found a similar increase in hospital and clinical cost associated with AF onset. The costs of AF have been studied in prevalent patient populations [4, 19], with yearly costs ranging from

$18,545 (2002 US dollars) to $39,877 (2010 Canadian dollars) depending on geographic location, organization of healthcare, types of costs included, and choice of study population. The social and healthcare costs of prevalent Finnish AF patients using different OACs have been previously reported in [6]. The study at hand with incident patients found slightly higher costs, possibly due to interventions associated with the diagnosis of AF.

We found costs of patients using different DOACs to be close to each other after applying IPTW, with apixaban patients being slightly more costly. Patients using warfarin had on average 37% higher social and healthcare costs than patients using any of the DOACs, likely due to higher risk of complications. This higher rate of complications has been extensively reported elsewhere, both in relation to standard-dose DOACs [3] and reduced-dose DOACs [20]. In the IPTW setting, this cost difference can be interpreted as the potential savings if the entire warfarin patient population were treated with DOACs. Previous studies with real-world data have found patients using rivaroxaban [21] or dabigatran [22, 23] have total healthcare costs comparable to warfarin patients, and patients using apixaban [24] have lower costs than warfarin patients.

Several simulation studies using Markov models and lifetime follow-up have found DOACs to be cost-effective when compared to warfarin [25–28], while others found the incremental cost of DOAC patients to be higher than desirable [29]. Patients who received no anticoagulation were the most expensive, but these patients are a heterogeneous group, and it is very important that the analyses are performed separately in high and low stroke risk groups, like in the present study.

The costs of warfarin patients correlated with TTR levels, with the lowest TTR group having almost twofold higher total social and healthcare costs than the highest quartile. The highest TTR quartile, where warfarin treatment was most successful, had costs comparable to DOAC users. A similar association between TTR and healthcare costs has been noticed in previous register studies [30, 31]. Previous simulation studies also suggest that warfarin patients with high TTR can have competitive cost-effectiveness when compared to DOAC patients, but when compared to patients with low TTR, DOAC patients are cost-effective [32–34]. However, the TTR of individual patients cannot be reliably predicted, and thus the average cost should be considered in comparisons between medications [3].

The largest contributors to the costs of AF patients were hospital costs and primary care costs, with drug purchases and social care representing smaller contributions. This distribution is similar to those presented in earlier reports [4]. The cost distribution was mostly similar across medication groups. The proportion of primary care is emphasized in warfarin patients, which reflects the need for regular INR monitoring. DOAC patients have higher total drug costs than warfarin patients, which corresponds to estimates of yearly cost of DOAC medication. This difference is likely to diminish with the introduction of generic DOAC alternatives. The cost differences in both primary care and drugs are smaller than the difference in hospital costs, which suggests that the cost differences between warfarin and DOAC patients are mainly driven by differences in hospitalizations rather than the need for INR measurements or higher drug costs. The focus on patients with prevalent AF in prior research is reflected in a patient cohort older than that in this study, which further explains the larger cost contributions of residential care and home care [6].

High risk of stroke, identified by a CHA_2DS_2-VA score of 2 or higher, corresponded to increased healthcare costs in all medication groups compared to patients with low stroke risk. The increases ranged from 64% to 116%, with the highest difference being in patients using edoxaban, followed by patients with no OAC medication. This suggests that patients with no OAC are polarized between healthy patients with no need for OACs and patients who for other medical reasons, e.g., severe renal dysfunction, did not receive OACs or would not benefit from them. An association between high risk of stroke and healthcare costs in AF patients is in line with previous research [35].

The costs were temporally associated with the onset of AF. Previous studies have found temporal associations between IS and AF, and myocardial infarction and AF, which all contribute to the cost effect [36, 37]. Additionally, diagnostic procedures and treatments, such as acute cardioversion, performed in the temporal vicinity of AF onset might increase the costs.

The patients receiving lower doses of DOACs had higher costs altogether. Lower doses, especially of apixaban, are typically prescribed to patients with a higher age and higher number of comorbidities.

The main strength of this study was the comprehensive nationwide dataset that covers all levels of care and includes social care, laboratory data, and drug purchases. The study setting enables a focus on new-onset AF and costs after AF diagnosis. A long study period allows for establishment of a baseline before AF onset, including relevant comorbidities. Additionally, the widespread adoption of DOAC usage in Finland coincides with the study period, which is ideal for comparing between new warfarin and DOAC patients.

This study does not cover the monetary impact of lost work time, although the impact would likely be low due to the average age of the cohort being over 70 years. The registry data are based on administrative recording and can thus be subject to inconsistent documentation practices. Absolute cost numbers presented in this study may not be

applicable to other countries due to differences in prices, practices, and organization of care services, but the relative differences between patient groups are most probably generalizable.

5 Conclusions

Patients on DOACs had lower total social and healthcare costs compared to warfarin users despite the higher cost of medication. DOACs are currently preferred over warfarin due to their clinical effectiveness, and the results support this practice from the cost perspective. When assessing treatment options, it is vital to consider both total costs as well as the effect on resource usage, as these are key factors in assessing cost-effectiveness. Further research will be conducted on the social and healthcare costs of AF patients following typical complications such as IS and intracranial hemorrhage.

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Declarations

Conflict of interest K.E.J.A.: Grants: The Finnish Foundation for Cardiovascular Research; Speaker: Bayer, Pfizer, Boehringer-Ingelheim. Ja.H.: Research grants: EU Horizon 2020, EU FP7; Speaker: Bayer. J.P.: Grants: Academy of Finland, Finnish Foundation for Cardiovascular research, Sigrid Juselius Foundation, Helsinki and Uusimaa Hospital District; Consultant: Herantis Pharma, Novo Nordisk; Speaker: Abbott, BMS-Pfizer, Bayer. P.M.: Consultant: Roche, BMS-Pfizer-alliance, Novartis Finland, Boehringer Ingelheim, MSD Finland, Bayer. K.T.: Grants: The Finnish Foundation for Cardio vascular Research. A.L.A.: Grants: Finnish Foundation for Cardiovascular Research, Sigrid Juselius Foundation; Speaker: Abbott, Johnson & Johnson, Sanofi, Bayer, Boehringer-Ingelheim. Ju.H.: Grants: Finnish Foundation for Cardiovascular Research, EU Horizon 2020; Speaker: Novo Nordisk. M.Le.: Consultant and speaker: BMS-Pfizer-alliance, Bayer, Boehringer-Ingelheim, MSD; Grants: Boehringer-Ingelheim. M.Li.: Speaker: BMS-Pfizer alliance. All other authors declare they have no conflicts of interest.

Authors' contributions Conceptualization: Olli Halminen, K.E. Juhani Airaksinen, Jari Haukka, Jukka Putaala, Pirjo Mustonen, Aapo L. Aro, Juha Hartikainen, Mika Lehto, Miika Linna. Data curation: Olli Halminen, Ossi Lehtonen, Jari Haukka, Miika Linna. Formal analysis: Ossi Lehtonen, Olli Halminen, Miika Linna. Funding acquisition: Mika Lehto. Methodology: Olli Halminen, Miika Linna. Visualization: Ossi Lehtonen, Olli Halminen. Writing—original draft: Ossi Lehtonen. Writing—review and editing: Olli Halminen, K.E. Juhani Airaksinen, Jari Haukka, Jukka Putaala, Pirjo Mustonen, Aapo L. Aro, Juha Hartikainen, Mika Lehto, Miika Linna, Konsta Teppo, Elis Kouki. All authors read and approved the final version.

Ethics approval The ethical permission is permitted by the ethical committee of the Medical Faculty of Helsinki University, Helsinki Finland (nr. 15/2017 and 15/2024), and study permission was obtained from the Helsinki University Hospital (HUS/46/2018 and HUS/217/2024).

Consent to participate The study at hand only included previously collected registry information, and thus the patients were not contacted at any point. The data were pseudonymized, and the patients could therefore not be directly identified. Informed consent was waived because of the retrospective design of the study.

Consent for publication Not applicable.

Code availability Code is available from the corresponding author on a reasonable request.

Data availability The data underlying this article cannot be shared publicly due to its sensitive nature and in accordance with the agreements made with the Finnish registries. Requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the Finnish national register holders (KELA, Finnish Institute for Health and Welfare, Population Register Centre, and Tax Register).

References

1. Lehto M, Halminen O, Mustonen P, Putaala J, Linna M, Kinnunen J, et al. The nationwide Finnish anticoagulation in atrial fibrillation (FinACAF): study rationale, design, and patient characteristics. Eur J Epidemiol. 2022;37(1):95–102.
2. Burdett P, Lip GYH. Atrial fibrillation in the UK: predicting costs of an emerging epidemic recognizing and forecasting the cost drivers of atrial fibrillation-related costs. Eur Heart J Qual Care Clin Outcomes. 2020;8(2):187–94.
3. Lehto M, Luojus A, Halminen O, Haukka J, Putaala J, Linna M, et al. Time-in-therapeutic-range defined warfarin and direct oral anticoagulants in atrial fibrillation: a nationwide cohort study. Ann Med. 2024;56(1):2364825.
4. Wodchis WP, Bhatia RS, Leblanc K, Meshkat N, Morra D. A review of the cost of atrial fibrillation. Value Health. 2012;15(2):240–8.
5. Mulholland RJ, Ciminata G, Quinn TJ, Pollock KG, Lister S, Geue C. Delay and pay? Healthcare costs associated with late oral anti-coagulant prescribing in people with atrial fibrillation. Pharmacoeconomics. 2024;42(11):1241–53.
6. Rissanen A, Herse F, Rossi J, Säävuori N, Roine RO, Pakarinen S. Eteisvärinää sairastavien potilaiden antikoagulaatiohoito ja palveluiden käyttö Suomessa. Suomen lääkärilehti. 2021.

7. Athanasakis K, Boubouchairopoulou N, Karampli E, Tarantilis F, Savvari P, Bilitou A, et al. Cost effectiveness of apixaban versus warfarin or aspirin for stroke prevention in patients with atrial fibrillation: a Greek perspective. Am J Cardiovasc Drugs. 2017;17:123–33.
8. Wei H, Cui C, Cui X, Liu Y, Li D. Cost-effectiveness analysis of dabigatran, rivaroxaban and warfarin in the prevention of stroke in patients with atrial fibrillation in China. BMC Health Serv Res. 2021;21:1–10.
9. Kim H, Kim H, Cho SK, Kim JB, Joung B, Kim C. Cost-effectiveness of rivaroxaban compared to warfarin for stroke prevention in atrial fibrillation. Korean Circ J. 2019;49(3):252.
10. Kasmeridis C, Apostolakis S, Ehlers L, Rasmussen LH, Boriani G, Lip GY. Cost effectiveness of treatments for stroke prevention in atrial fibrillation: focus on the novel oral anticoagulants. Pharmacoeconomics. 2013;31:971–80.
11. Ferreira J, Mirco A. Systematic review of cost-effectiveness analyses of novel oral anticoagulants for stroke prevention in atrial fibrillation. Revista Portuguesa de Cardiologia (Engl Ed). 2015;34(3):179–91.
12. Van Gelder IC, Rienstra M, Bunting KV, Casado-Arroyo R, Caso V, Crijns HJGM, et al. 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): Developed by the task force for the management of atrial fibrillation of the European Society of Cardiology (ESC), with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Endorsed by the European Stroke Organisation (ESO). Eur Heart J. 2024;45(36):3314–414.
13. Rosendaal F, Cannegieter S, van der Meer F, Briët E. A method to determine the optimal intensity of oral anticoagulant therapy. Thromb Haemost. 1993;69(3):236–9.
14. Mäklin S, Kokko P. Terveyden-ja sosiaalihuollon yksikkökustannukset Suomessa vuonna 2017. 2021;
15. Robins JM, Hernan MA, Brumback B. Marginal structural models and causal inference in epidemiology. Epidemiology. 2000;11(5):550–60.
16. Stürmer T, Wyss R, Glynn RJ, Brookhart MA. Propensity scores for confounder adjustment when assessing the effects of medical interventions using nonexperimental study designs. J Intern Med. 2014;275(6):570–80.
17. McCaffrey DF, Griffin BA, Almirall D, Slaughter ME, Ramchand R, Burgette LF. A tutorial on propensity score estimation for multiple treatments using generalized boosted models. Stat Med. 2013;32(19):3388–414.
18. Delaney JA, Yin X, Fontes JD, Wallace ER, Skinner A, Wang N, et al. Hospital and clinical care costs associated with atrial fibrillation for Medicare beneficiaries in the Cardiovascular Health Study and the Framingham Heart Study. Sage Open Med. 2018;6:2050312118759444.
19. Biskupiak J, Ghate SR, Jiao T, Brixner D. Cost implications of formulary decisions on oral anticoagulants in nonvalvular atrial fibrillation. J Manag Care Pharm. 2013;19(9):789–98.
20. Luojus A, Lehto M, Halminen O, Lehtonen O, Niemi M, Teppo K, et al. Reduced dose direct oral anticoagulants and time-in-therapeutic-range defined warfarin in new-onset atrial fibrillation: a report from the nationwide FinACAF study. Eur Heart J Open. 2025;5(3):oeaf046.
21. Laliberté F, Cloutier M, Crivera C, Nelson WW, Olson WH, Schein J, et al. Effect of rivaroxaban versus warfarin on health care costs among nonvalvular atrial fibrillation patients: observations from rivaroxaban users and matched warfarin users. Adv Ther. 2015;32(3):216–27.
22. Bancroft T, Lim J, Wang C, Sander SD, Swindle JP. Health care resource utilization, costs, and persistence in patients newly diagnosed as having nonvalvular atrial fibrillation and newly treated with dabigatran versus warfarin in the United States. Clin Ther. 2016;38(3):545–56.
23. Reynolds SL, Ghate SR, Sheer R, Gandhi PK, Moretz C, Wang C, et al. Healthcare utilization and costs for patients initiating Dabigatran or Warfarin. Health Qual Life Outcomes. 2017;15(1):128.
24. Deitelzweig S, Luo X, Gupta K, Trocio J, Mardekian J, Curtice T, et al. Effect of apixaban versus warfarin use on health care resource utilization and costs among elderly patients with nonvalvular atrial fibrillation. J Manag Care Spec Pharm. 2017;23(11):1191–201.
25. Greenspon AJ. An economic analysis of stroke and atrial fibrillation. In: Flaker G, editor. Stroke prevention in atrial fibrillation. United States: Elsevier; 2018. pp. 1–10.
26. Hallinen T, Soini E, Asseburg C, Linna M, Eloranta P, Sintonen S, et al. Cost-effectiveness of apixaban versus other direct oral anticoagulants and warfarin in the prevention of thromboembolic complications among Finnish patients with non-valvular atrial fibrillation. Clinicoecon Outcomes Res. 2021;13:745–55.
27. Hallinen T, Soini EJ, Linna M, Saarni SI. Cost–effectiveness of apixaban and warfarin in the prevention of thromboembolic complications among atrial fibrillation patients. Springerplus. 2016;5(1):1–9.
28. Wouters H, Thijs V, Annemans L. Cost-effectiveness of dabigatran etexilate in the prevention of stroke and systemic embolism in patients with atrial fibrillation in Belgium. J Med Econ. 2013;16(3):407–14.
29. Canestaro WJ, Patrick AR, Avorn J, Ito K, Matlin OS, Brennan TA, et al. Cost-effectiveness of oral anticoagulants for treatment of atrial fibrillation. Circ Cardiovasc Qual Outcomes. 2013;6(6):724–31.
30. Deitelzweig S, Evans M, Hillson E, Trocio J, Bruno A, Tan W, et al. Warfarin time in therapeutic range and its impact on healthcare resource utilization and costs among patients with nonvalvular atrial fibrillation. Curr Med Res Opin. 2016;32(1):87–94.
31. Silva P, Sznejder H, Vasconcellos R, Charles GM, Mendonca-Filho HTF, Mardekian J, et al. Anticoagulation therapy in patients with non-valvular atrial fibrillation in a private setting in Brazil: a real-world study. Arq Bras Cardiol. 2020;114(3):457–66.
32. You JH. Novel oral anticoagulants versus warfarin therapy at various levels of anticoagulation control in atrial fibrillation—a cost-effectiveness analysis. J Gen Intern Med. 2014;29:438–46.
33. Amin A, Deitelzweig S, Jing Y, Makenbaeva D, Wiederkehr D, Lin J, et al. Estimation of the impact of warfarin's time-in-therapeutic range on stroke and major bleeding rates and its influence on the medical cost avoidance associated with novel oral anticoagulant use-learnings from ARISTOTLE, ROCKET-AF, and RE-LY trials. J Thromb Thrombolysis. 2014;38:150–9.
34. Janzic A, Kos M. Cost effectiveness of novel oral anticoagulants for stroke prevention in atrial fibrillation depending on the quality of warfarin anticoagulation control. Pharmacoeconomics. 2015;33:395–408.
35. Coyle D, Coyle K, Cameron C, Lee K, Kelly S, Steiner S, et al. Cost-effectiveness of new oral anticoagulants compared with warfarin in preventing stroke and other cardiovascular events in patients with atrial fibrillation. Value Health. 2013;16(4):498–506.
36. Karlsson E, Kiviniemi T, Halminen O, Lehtonen O, Haukka J, Mustonen P, et al. Temporal relation of disease onsets in patients with acute myocardial infarction and atrial fibrillation-results from a nationwide registry study. Europace. 2023;25(Supplement_1):euad122-024.
37. Putaala J, Teppo K, Halminen O, Haukka J, Tiili P, Jaakkola J, et al. Ischemic stroke temporally associated with new-onset atrial fibrillation: a population-based registry-linkage study. Stroke. 2024;55(1):122–30.