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ORIGINAL ARTICLE

Association of income and educational levels on initiation of oral anticoagulant therapy in patients with incident atrial fibrillation: A Finnish nationwide cohort study

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Aims: Socioeconomic disparities have been reported in the outcomes of patients with atrial fibrillation (AF). We assessed the hypothesis that AF patients with higher income or educational level are more frequently initiated with oral anticoagulant (OAC) therapy for stroke prevention.

Methods: The nationwide registry-based Finnish AntiCoagulation in Atrial Fibrillation cohort covers all patients with AF from all levels of care in Finland. Patients were divided into income quartiles according to their highest annual income during 2004-2018 and into three categories based on educational attainment. The outcome was the first redeemed OAC prescription.

Results: We identified 239 222 patients (mean age 72.7 ± 13.2 years, 49.8% female) with incident AF during 2007-2018. Higher income was associated with higher OAC initiation rate: compared to the lowest income quartile the adjusted SHRs (95% CI) for OAC initiation were 1.09 (1.07-1.10), 1.13 (1.11-1.14) and 1.13 (1.12-1.15) in the second, third and fourth income quartiles, respectively. Patients in the highest educational category had a slightly lower OAC initiation rate than patients in the lowest educational category (adjusted SHR 0.92 [95% CI 0.90-0.93]). Income-related disparities were larger and education-related disparities only marginal among patients at high risk of ischemic stroke. The socioeconomic disparities in OAC initiation within 1-year follow-up decreased from 2007 to 2018. The adoption of direct OACs as the initial anticoagulant was faster among patients with higher income or educational levels.

Conclusion: These findings highlight potential missed opportunities in stroke prevention, especially among AF patients with low income, whereas the education-related disparities in OAC initiation appear controversial.

KEYWORDS
atrial fibrillation, education, income, oral anticoagulation, socioeconomic factors, stroke prevention

The authors confirm that the Principal Investigator for this paper is Docent Mika Lehto

1 | INTRODUCTION

Atrial fibrillation (AF) is the most common sustained arrhythmia, affecting up to 4.1% of the general population, and is associated with substantially increased risk of ischemic stroke and mortality.[1,2] Fortunately, oral anticoagulant (OAC) therapy effectively reduces the risk of both stroke and death in patients with AF and high stroke risk.[1,3] While vitamin-K antagonists (VKAs) were the cornerstone of stroke prevention for more than 50 years, the emergence of direct oral anticoagulants (DOACs) has revolutionized OAC therapy in patients with AF, and the current guidelines recommend DOACs over VKAs as the first-line anticoagulant in nonvalvular AF due to their superior efficacy and safety profile.[4] Despite the well-established benefits of OAC therapy, its underuse in patients with AF at risk of stroke is common, and clear disparities in stroke prevention have been reported among patient groups defined by characteristics such as age, race, ethnicity, gender and mental health status.[5–12]

Socioeconomic inequalities in health are widespread, and healthcare financing schemes have been shown to affect the magnitude of health disparities.[13–17] Finland, as other Nordic countries, has national publicly funded healthcare, universal coverage of public health insurance and relatively low out-of-pocket health expenditure.[18–20] Notwithstanding, socioeconomic disparities in terms of morbidity, mortality and self-rated health are observed in Finland.[21]

Previous studies have associated lower socioeconomic status with higher incidence of AF as well as with lower use of rhythm control therapies and poorer outcomes in patients with AF.[22–24] However, evidence on the impact of socioeconomic factors on the use of OAC therapy, and particularly on the use of DOACs, is limited. The present nationwide cohort study covering all patients with AF in Finland aimed to assess whether patients' income and educational levels affect the utilization of OAC therapy or the choice of DOAC over VKA as initial anticoagulant.

What is already known about this subject

- Socioeconomic disparities exist in the outcomes of patients with atrial fibrillation (AF).
- Underuse of oral anticoagulant (OAC) therapy for stroke prevention in the presence of AF is common.

What this study adds

- Higher income is associated with higher rate of OAC therapy initiation in patients with AF.
- Educational attainment does not meaningfully affect OAC initiation rate.
- Socioeconomic disparities in the initiation of OAC therapy have decreased during 2007-2017 in Finland.

2 | METHODS

2.1 | Study population

The Finnish AntiCoagulation in Atrial Fibrillation (FinACAF) Study (ClinicalTrials Identifier: NCT04645537, ENCePP Identifier: EUPAS29845) is a nationwide retrospective cohort study including all patients with an AF diagnosis in Finland during 2004-2018.[2] Patients were identified from all available national healthcare registers (hospitalizations and outpatient specialist visits: HILMO, primary health care: AvoHILMO, 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 I48 (including atrial fibrillation and atrial flutter, together referred as AF) recorded between 2004-2018 and cohort entry occurred on the date of the first recorded AF diagnosis. The exclusion criteria were permanent migration abroad before December 31, 2018 and age <18 years at AF diagnosis. Follow-up continued until death or December 31, 2018, whichever occurred first. The current substudy was conducted within a cohort of patients with incident AF between 2007 and 2018, established in previous studies of the FinACAF cohort.[8,25,26] In this cohort, patients with a recorded AF diagnosis during 2004-2006 were excluded because the 2-year medical history was considered too short to exclude the presence of an AF diagnosis before the cohort entry. Additionally, patients who had fulfilled an OAC prescription during 2004-2006 or within a year before the date of first AF diagnosis were excluded since most of them likely had a previous diagnosis of AF. Baseline patient characteristics were gathered from medical records from 2004 until cohort entry. Since OAC therapy is not recommended in AF patients with low risk of stroke, sensitivity analyses were performed among patients with at least intermediate stroke risk as well as among patients with high stroke risk (at least intermediate stroke risk: men with CHA_2DS_2-VASc score ≥1 and women with CHA_2DS_2-VASc score ≥2, high stroke risk: men with CHA_2DS_2-VASc score ≥2 and women with CHA_2DS_2-VASc score ≥3). The patient selection process is summarized in Supporting Information Figure S1.

2.2 | Income and educational levels

The patients' individual highest annual taxable income (to 1000-euro accuracy) during the FinACAF study's observation period from 2004 to 2018 was derived from the national Tax Register. The annual income was capped to a maximum of 100 000 euros to avoid patients' identifiability due to high incomes. To account for changes in income over time and age, patients were divided into age group and AF diagnosis year specific income quartiles, ie, each 10-year age group during each cohort entry year was divided into income quartiles using age group and entry year specific cut-points.[27] The sensitivity analyses'

cohorts were divided into income quartiles in a similar manner. Of note, the median annual income in Finland during the study period was approximately 38 000 euros, and notwithstanding the capping of the income data, the individuals with income capped to 100 000 euros were categorized into the highest income quartile.[28]

The patients' highest achieved educational level categorized according to the International Standard Classification of Education (ISCED) was obtained from Statistics Finland.[29] Educational level was divided into three categories: Category 1: ISCED 0-2 (no registered, preprimary, primary or lower secondary education); Category 2: ISCED 3 (upper secondary or vocational education); Category 3: ISCED 5-8 (tertiary, Bachelor's-level, Master's-level or doctoral level education). ISCED category 4 does not exist in Finland.

Additionally, to investigate income-related disparities in OAC use within the educational categories, patients in the three educational categories were divided separately into halves according to their annual income.

2.3 | Initiation of OAC

The primary outcome was the initiation of OAC therapy, which was considered to occur on the date of first fulfilled OAC (warfarin, apixaban, dabigatran, edoxaban or rivaroxaban) prescription after the cohort entry.

2.4 | 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 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). The patients' identification numbers were pseudonymized, and the research group received individualized, but unidentifiable, data. Informed consent was waived due to the retrospective registry nature of the study. The study conforms to the Declaration of Helsinki as revised in 2013.

2.5 | Statistical analysis

Statistical analyses were performed with the IBM SPSS Statistics software (version 27.0; SPSS, Inc., Armonk, NY, USA) and R (version 4.0.5, https://www.R-project.org). The chi-square test was used to compare differences between proportions, and one-way analysis of variance to analyse continuous variables. Poisson regression was used to estimate the incidence rates of OAC initiation for income quartiles and educational categories. Observation of OAC initiation may be hindered by mortality occurring during the study period, and therefore the Fine-Gray regression with all-cause death as competing event was used to estimate the unadjusted and adjusted subdistribution hazard ratios (SHRs) of OAC initiation for income quartiles and educational categories. Additionally, to determine the factors associated with choosing DOAC over VKA as the initial anticoagulant, a binary logistic regression model was used with DOAC initiation as dependent variable including only patients initiating OAC therapy after 2011 when the first DOAC was approved for stroke prevention in patients with AF. Furthermore, to quantify temporal changes in the magnitude of socioeconomic disparities in overall OAC initiation, interaction terms between socioeconomic categories and cohort entry year as continuous variable were fitted in binary logistic regression models with OAC initiation within 1-year follow-up as the dependent variable. In addition to income and educational levels, the adjusted analyses with the Fine-Gray and binary logistic regression models included the following variables: age, gender, calendar year of AF diagnosis, dementia, cancer, alcohol use disorder, prior bleeding episodes, concomitant use of nonsteroidal anti-inflammatory drugs or antiplatelets, psychiatric disorders, prior stroke or transient ischemic attack, abnormal liver function, abnormal kidney function, diabetes, hypertension, coronary artery disease and heart failure. The definitions of the comorbidities are displayed in Supporting Information Table S1.

3 | RESULTS

We identified 239 222 patients (49.8% female) with incident AF during 2007-2018, the mean age at time of AF diagnosis being 72.7 (SD 13.2) years. Patients with higher income were more often male, had lower stroke risk, higher education and lower prevalence of psychiatric disorders and alcohol abuse than patients with lower income. Similarly, patients with higher education were more often male and had higher income and lower prevalence of comorbidities. Additionally, patients in the lowest educational category were significantly older than patients with higher educational background (Table 1). During the study period, 42.9%, 31.7%, 29.8% and 27.3% of patients died from the lowest to the highest income quartile ($P < .001$). Correspondingly in the educational categories, 43.6%, 22.9% and 19.5% of the patients died from the lowest to the highest category ($P < .001$).

Overall, OAC therapy was initiated in 171 270 (71.6%) patients during the observation period and among them the treatment was initiated with DOAC in 31.0% of patients. When compared to the lowest income quartile, a higher proportion of patients in the higher income quartiles initiated OAC therapy during follow-up (Figure 1). However, notwithstanding this higher proportion of OAC initiators in the higher income quartiles, the crude incidence rate of OAC initiation was lower in the higher income quartiles due to longer follow-up times (Table 2). Patients with higher educational background were less likely to initiate OAC therapy than patients in the lowest educational category during follow-up. Correspondingly, the crude incidence rates of OAC initiation were lower in patients with higher educational levels (Table 2).

TABLE 1 Descriptive characteristics of the cohort according to income and educational levels

	Income quartiles					Educational categories			
	1st (lowest) n = 62 302	2nd n = 57 775	3rd n = 59 670	4th (highest) n = 59 475	*P* value	1st (lowest) n = 125 326	2nd n = 64 675	3rd (highest) n = 49 221	*P* value
Mean annual income (thousands of euros)	2.9 (5.0)	11.6 (9.3)	21.3 (12.4)	51.2 (26.3)	<.001	12.5 (16.9)	22.5 (21.0)	43.5 (27.8)	<.001
Demographics									
Mean age, years	73.6 (13.3)	72.5 (13.3)	72.3 (13.2)	72.3 (13.2)	<.001	77.4 (10.7)	67.4 (13.8)	67.6 (13.8)	<.001
Mean cohort entry year	2013 (3.5)	2013 (3.4)	2013 (3.4)	2013 (3.4)	<.001	2012 (3.4)	2013 (3.4)	2013 (3.4)	<.001
Female sex	38 765 (62.2)	32 209 (55.7)	28 004 (46.9)	20 068 (33.7)	<.001	70 310 (56.1)	29 163 (45.1)	19 573 (39.8)	<.001
Educational categories				<0.001					
1st	42 445 (68.1)	34 241 (59.3)	30 381 (50.9)	18 259 (30.7)		N/A	N/A	N/A	
2nd	16 639 (26.7)	17 793 (30.8)	17 526 (29.4)	12 717 (21.4)		N/A	N/A	N/A	
3rd	3218 (5.2)	5741 (9.9)	11 763 (19.7)	28 499 (47.9)		N/A	N/A	N/A	
Income quartiles									<.001
1st	N/A	N/A	N/A	N/A		42 445 (33.9)	16 639 (25.7)	3218 (6.5)	
2nd	N/A	N/A	N/A	N/A		34 241 (27.3)	17 793 (27.5)	5741 (11.7)	
3rd	N/A	N/A	N/A	N/A		30 381 (24.2)	17 526 (27.1)	11 763 (23.9)	
4th	N/A	N/A	N/A	N/A		18 259 (14.6)	12 717 (19.7)	28 499 (57.9)	
Comorbidities									
Abnormal liver function	433 (0.7)	275 (0.5)	245 (0.4)	234 (0.4)	<.001	545 (0.4)	383 (0.6)	259 (0.5)	<.001
Abnormal renal function	2916 (4.7)	2312 (4.0)	2171 (3.6)	2062 (3.5)	<.001	5816 (4.6)	2205 (3.4)	1440 (2.9)	<.001
Alcohol use disorder	4243 (6.8)	2065 (3.6)	1665 (2.8)	1317 (2.2)	<.001	4261 (3.4)	3488 (5.4)	1541 (3.1)	<.001
Cancer	12 147 (19.5)	11 442 (19.8)	12 218 (20.5)	13 221 (22.2)	<.001	28 349 (22.6)	10 847 (16.8)	9832 (20.0)	
Coronary artery disease	15 419 (24.7)	13 218 (22.9)	13 098 (22.0)	12 208 (20.5)	<.001	33 928 (27.1)	12 210 (18.9)	7805 (15.9)	<.001
Dementia	3944 (6.3)	2951 (5.1)	2739 (4.6)	2381 (4.0)	<.001	8742 (7.0)	1949 (3.0)	1324 (2.7)	<.001
Diabetes	15 686 (25.2)	13 037 (22.6)	12 237 (20.5)	10 732 (18.0)	<.001	30 374 (24.2)	13 293 (20.6)	8025 (16.3)	<.001
Dyslipidemia	29 123 (46.7)	28 178 (48.8)	28 924 (48.5)	28 348 (47.7)	<.001	63 895 (51.0)	29 437 (45.5)	21 241 (43.2)	<.001
Heart failure	14 249 (22.9)	10 412 (18.0)	9209 (15.4)	7826 (13.2)	<.001	27 755 (22.1)	9021 (13.9)	4920 (10.0)	<.001
Hypertension	47 191 (75.7)	43 588 (75.4)	44 083 (73.9)	42 658 (71.7)	<.001	98 067 (78.2)	45 784 (70.8)	33 668 (68.4)	<.001
Prior bleeding	7355 (11.8)	6050 (10.5)	6030 (10.1)	5956 (10.0)	<.001	14 747 (11.8)	6272 (9.7)	4372 (8.9)	<.001
Prior ischemic stroke or TIA	10 670 (17.1)	8922 (15.4)	8617 (14.4)	8304 (14.0)	<.001	21 998 (17.6)	8517 (13.2)	5998 (12.2)	<.001
Prior myocardial infarction	6266 (10.1)	5119 (8.9)	5008 (8.4)	4412 (7.4)	<.001	13 147 (10.5)	4793 (7.4)	2865 (5.8)	<.001
Psychiatric disorder	12 396 (19.9)	7837 (13.6)	6539 (11.0)	5206 (8.8	<.001	16 453 (13.1)	9974 (15.4)	5551 (11.3)	<.001

TABLE 1 (Continued)

	Income quartiles				Educational categories				
	1st (lowest) n = 62 302	2nd n = 57 775	3rd n = 59 670	4th (highest) n = 59 475	*P* value	1st (lowest) n = 125 326	2nd n = 64 675	3rd (highest) n = 49 221	*P* value
Risk scores									
CHA_2DS_2-VASc score	3.8 (1.9)	3.5 (1.9)	3.3 (1.9)	3.1 (1.8)	<.001	4.0 (1.7)	2.9 (1.9)	2.7 (1.8)	<.001
Low stroke risk	3829 (6.1)	4483 (7.8)	5501 (9.2)	5959 (10.0)	<.001	4102 (3.3)	8556 (13.2)	7114 (14.5)	<.001
Intermediate stroke risk	7297 (11.7)	8155 (14.1)	9031 (15.1)	9453 (15.9)	<.001	10 057 (8.0)	13 158 (20.3)	10 721 (21.8)	<.001
High stroke risk	51 176 (82.1%)	45 137 (78.1)	45 128 (75.6)	44 063 (74.1)	<.001	111 167 (88.7)	42 961 (66.4)	31 386 (63.8)	<.001
Modified HAS-BLED score	2.6 (1.1)	2.5 (1.0)	2.5 (1.0)	2.4 (1.1)	<.001	2.7 (1.0)	2.3 (1.1)	2.3 (1.1)	<.001

Note: Values denote n (%) or mean (standard deviation). Low stroke risk: men with CHA_2DS_2-VASc score 0 and women with CHA_2DS_2-VASc score ≤ 1. Intermediate stroke risk: men with CHA_2DS_2-VASc score 1 and women with CHA_2DS_2-VASc score 2. High stroke risk: men with CHA_2DS_2-VASc score >1 and women with CHA_2DS_2-VASc score > 2.

Abbreviations: CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥ 75 years, diabetes, history of stroke or TIA, 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 abuse, concomitant antiplatelet/NSAIDs (no labile INR, max score 8); TIA, transient ischemic attack.

After adjusting for patient characteristics and controlling for mortality differences by considering all-cause death as a competing event in the Fine-Gray regression model, higher income was consistently associated with a higher adjusted rate of OAC initiation. The highest educational category remained associated with a lower OAC initiation rate also in the adjusted competing risk analysis, whereas no difference was observed between the two lowest educational categories (Table 2). Within the educational categories, an association between higher income and OAC use was observed in the two lowest, but not in the highest educational category (Supporting Information Table S4). Similar associations of both income and education with OAC initiation were observed in the adjusted sensitivity analyses including only patients with at least intermediate stroke risk or patients with high stroke risk. However, the higher the stroke risk of the patients, the larger were the observed income-related disparities, whereas the education-related differences attenuated among patients with higher stroke risk. Additionally, in the sensitivity analyses, the crude proportion of patients initiating OACs during follow-up was higher in the higher educational categories than in the lowest category (Supporting Information Table S2).

A steady increase in overall OAC use within the first year after AF diagnosis was observed during 2007-2017. While notable inconsistency in the annual income-related disparities was observed, the overall magnitude of disparities decreased over the study period. Patients with higher education were consistently less likely to initiate OAC therapy across the observation period and a decrease over time was observed also in the differences between educational categories (Figure 2 and Supporting Information Table S3). A clear increase in the share of DOACs as the initial anticoagulant began in 2014, and by 2018 91.9% of the OAC initiations occurred with DOAC. This increase was faster among patients with higher income or education, and a dose-response association was observed between both income and educational levels on the likelihood of DOAC as the first OAC (Figure 2 and Table 3).

4 | DISCUSSION

This nationwide cohort study documented disparities in the initiation of OAC therapy according to income and educational levels in patients with AF. After controlling for differences in mortality and patient characteristics, higher income quartiles were associated with a higher rate of OAC initiation, whereas, interestingly, the highest educational category was associated with a slightly lower OAC initiation rate and no difference was observed between patients in the two lowest educational categories. A significant decrease in the disparities in OAC initiation within the first year after AF diagnosis was observed during the study period. Additionally, among the patients initiating OAC therapy, those with higher income or education were substantially more likely to initiate anticoagulation with DOACs than patients in lower income or educational categories.

Previous research addressing the effect of socioeconomic factors on the use of OAC therapy in patients with AF is limited and has

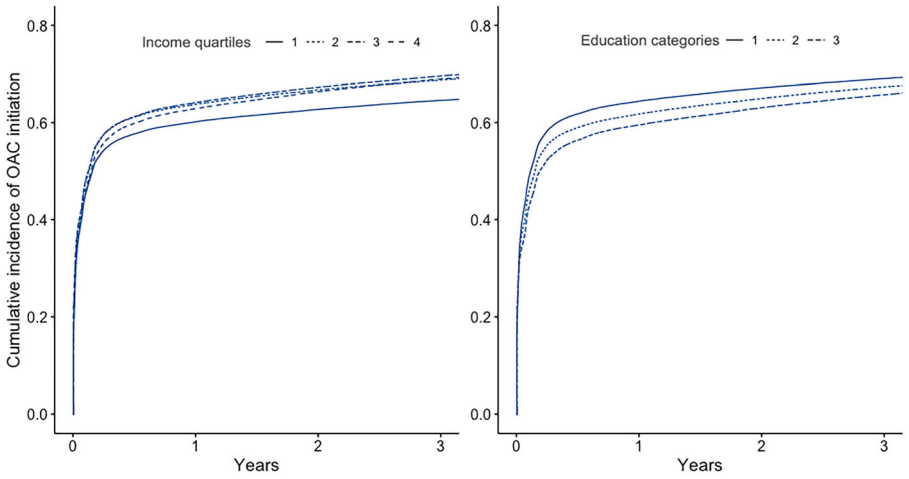

FIGURE 1 Crude cumulative incidence curves of OAC initiation according to income (left panel) and educational levels (right panel)

TABLE 2 Incidence of OAC initiation according to income and educational levels

	Events	Patient years	Incidence (per patient year)	Unadjusted SHR	Adjusted SHR
Income quartile					
1st (lowest)	41 986 (67.4%)	75 019	0.56 (0.55-0.57)	(reference)	(reference)
2nd	41 697 (72.2%)*	75 823	0.55 (0.55-0.56)	1.13 (1.11-1.14)	1.09 (1.07-1.10)
3rd	43 879 (73.5%)*	83 563	0.53 (0.52-0.53)	1.16 (1.15-1.18)	1.13 (1.11-1.14)
4th (highest)	43 708 (73.5%)*	88 730	0.49 (0.49-0.50)	1.14 (1.13-1.16)	1.13 (1.12-1.15)
Educational category					
1st (lowest)	66 798 (53.3%)	134 811	0.67 (0.67-0.68)	(reference)	(reference)
2nd	30 419 (47.0%)*	101 768	0.45 (0.45-0.56)	0.98 (0.96-0.99)	0.99 (0.98-1.01)
3rd (highest)	20 962 (42.6%)*	86 667	0.40 (0.40-0.41)	0.94 (0.93-0.95)	0.92 (0.90-0.93)

Note: 95% confidence intervals in parenthesis. SHRs estimated by Fine-Gray regression with all-cause death as competing event. Adjusted analyses included the following variables: age, gender, calendar year of AF diagnosis, dementia, cancer, alcohol use disorder, prior bleeding episodes, concomitant use of nonsteroidal anti-inflammatory drugs or antiplatelets, psychiatric disorders, prior stroke or TIA, abnormal liver function, abnormal kidney function, diabetes, hypertension, coronary artery disease, heart failure, income quartiles and educational categories.
*$P < .001$ when compared with the lowest category. Abbreviations: SHR, subdistribution hazard ratio; TIA, transient ischemic attack.

demonstrated varying results.[12,30–33] Importantly, these studies have been prone to potential selection, information and confounding biases owing to limited data from only a single level of care, limited follow-up times or insufficient controlling for mortality differences and other confounding factors. Additionally, most previous studies have relied on area-based instead of individual-level socioeconomic data. Therefore, the current study covering uniquely all patients with AF nationwide from all levels of care and individual socioeconomic data substantially expands our understanding of the associations of income and education on the use of OACs. Moreover, as seen in our results, controlling for mortality differences with competing risk models is crucial when assessing differences between socioeconomic levels.

The largest interquartile difference in the adjusted OAC initiation rate was observed between the two lowest income quartiles, and differences between the other income quartiles were marginal. Interestingly, the highest educational category was associated with a lower rate of OAC initiation, a finding somewhat contradictory with previous reports of superior medical treatment in patients with higher educational level.[24,33–36] Yet, observations of similar OAC initiation rate in AF patients from different educational levels can be found from previous literature.[12] Importantly, in the sensitivity analyses among patients with higher stroke risk and therefore a more definite indication for OAC therapy, the income-related differences in OAC initiation were larger than in the main analysis, while the education-related disparities attenuated considerably. Moreover, the income-related disparities were most profound within the lowest educational categories. These findings suggest clinically meaningful income-related inequity in stroke prevention, particularly among patients with low education, which may partly explain the previously reported higher ischemic stroke risk and mortality among patients with AF and low socioeconomic status.[24,37]

Overall, as previously reported by the authors, a substantial and continuous improvement in OAC initiation was observed in Finland during our study period.[8] While the income-related disparities in OAC initiation had large annual variation, the differences between education categories were more profound and consistent across the study

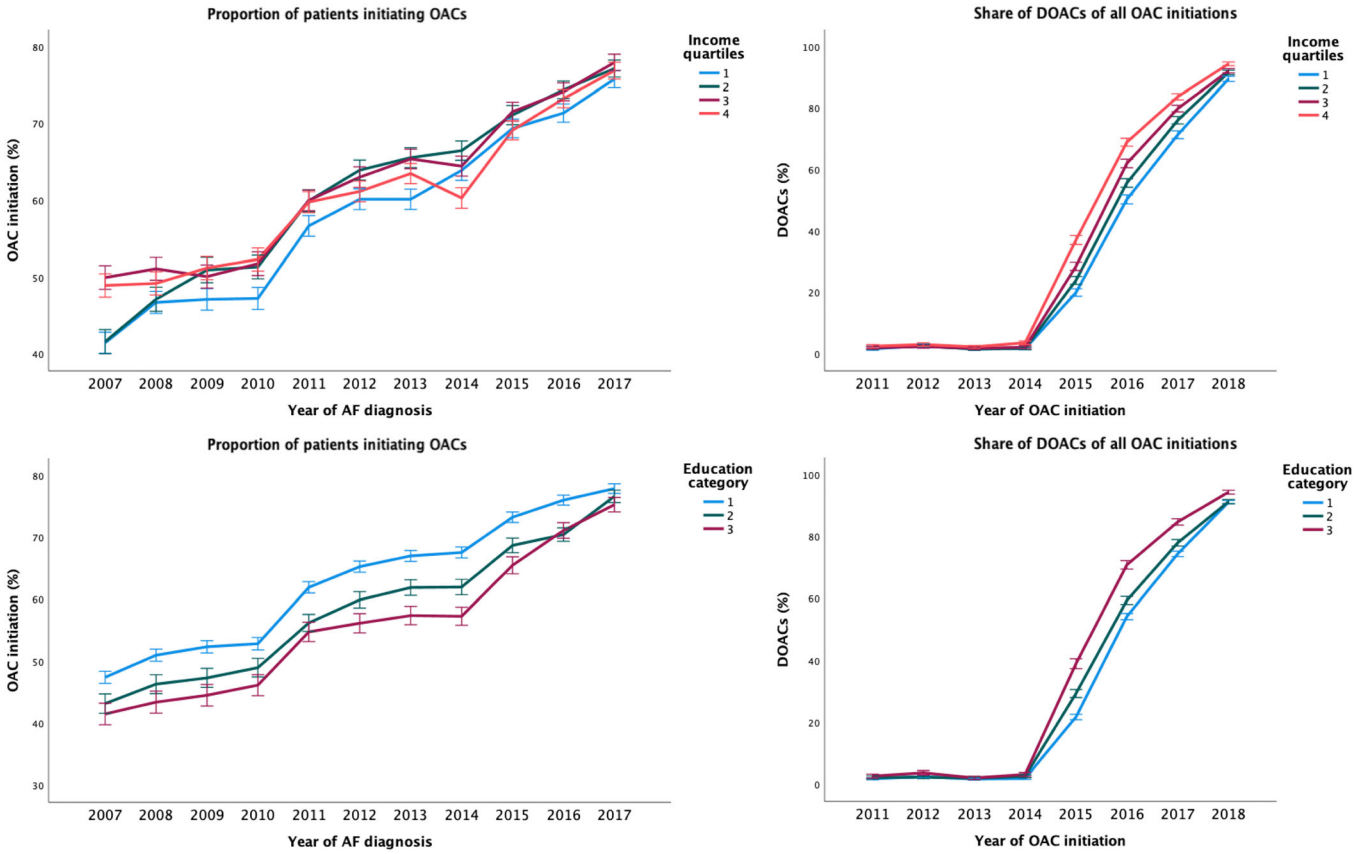

FIGURE 2 Temporal trends in the proportion of patients initiating OAC therapy within 1-year follow-up (left panel) and in the share of DOACs of all OAC initiations (right panel) according to income and educational levels. The 95% confidence intervals are displayed as error bars.

TABLE 3 Proportion of DOAC as the initial anticoagulant during 2011-1018 according to income and educational levels

	DOAC initiations	Unadjusted OR	Adjusted OR
Income quartile			
1st (lowest)	11 425 (34.7%)	(reference)	(reference)
2nd	12 638 (37.1%)*	1.11 (1.08-1.15)	1.16 (1.11-1.21)
3rd	13 717 (39.3%)*	1.22 (1.18-1.26)	1.33 (1.28-1.39)
4th (highest)	15 179 (43.7%)*	1.46 (1.42-1.51)	1.68 (1.60-1.75)
Educational category			
1st (lowest)	23 620 (34.0%)	(reference)	(reference)
2nd	15 659 (41.0%)*	1.35 (1.32-1.39)	1.05 (1.01-1.09)
3rd (highest)	13 680 (47.4%)*	1.76 (1.71-1.81)	1.35 (1.30-1.41)

Note: 95% confidence intervals in parenthesis. Adjusted ORs estimated by binary logistic regression including the following variables: age, gender, calendar year of AF diagnosis, dementia, cancer, alcohol use disorder, prior bleeding episodes, concomitant use of nonsteroidal anti-inflammatory drugs or antiplatelets, psychiatric disorders, prior stroke or TIA, abnormal liver function, abnormal kidney function, diabetes, hypertension, coronary artery disease, heart failure, income quartiles and educational categories.
*P < .001 when compared with the lowest category. Abbreviations: OR, odds ratio; TIA, transient ischemic attack.

period. Importantly, these differences between income and education categories attenuated towards the end of the observation period, corresponding with previous reports of decreasing socioeconomic treatment inequalities in the Nordic countries.[33,38] The increasing awareness of AF and the introduction of the easy-to-use CHA_2DS_2-VASc stroke risk score and systematic clinical guidelines have likely contributed to both the increase in overall OAC use and the decrease in the socioeconomic disparities in OAC coverage. The emergence of DOACs in the mainstream of stroke prevention in patients with AF in Finland occurred during our observation period, particularly during

2014-2018. The adoption of DOACs as the initial anticoagulant was substantially faster among patients with higher income or education. The increase in DOAC use was likely hastened by a number of decisions raising reimbursement rates for DOACs in patients with AF during 2013-2015 in Finland.

The observed disparities in the utilization of OAC therapy between income and educational levels are likely multifactorial. Importantly, although in Finland 42-65% of the costs of DOACs have been reimbursed to AF patients at risk of stroke since 2012, DOACs remain considerably more expensive than VKAs, likely hindering their use in patients with low income. The easier-to-use DOACs may also be initiated with a lower threshold in patients with higher income in situations where the necessary dose monitoring of VKA therapy is seen as cumbersome by the patient or clinician. However, since the inexpensive VKAs would enable affordable stroke prevention for all patients, medicine affordability is unlikely to be the only reason for the observed income-related disparities. Varying levels of health literacy is often proposed as a factor for socioeconomic health disparities, and this may also be reflected in our findings, although, in contrast, higher education was actually associated with lower OAC use in our study.[39,40] Furthermore, differences in trust between patients and clinicians and in patients' preference for OAC therapy, as well as possible systemic biases within the healthcare system and society, may contribute to the observed treatment disparities. Patients with higher education may also make more independent decisions to withhold OAC therapy, regardless of medical advice. Finally, differences in life expectancies as well as in the prevalence of comorbidities and bleeding risk factors among income and educational categories undoubtedly affect the clinical decision making of OAC therapy. Nevertheless, income-related disparities are observed in the initiation of OAC therapy even after adjusting for these differences in patient characteristics, suggesting possible inequity in provided care.

The main limitations of our study are the inherent challenges of register-based retrospective cohort studies, and thus our observations represent associations and not necessarily causation. Importantly, we lacked data on the actual reasons for withholding OAC therapy. Information bias may be present in administrative data due to inaccurate recording of diagnoses, but information on OAC initiation is based on the complete nationwide data of claimed prescriptions, covering all OAC purchases, since OACs are not sold without prescription. Additionally, since our results rely on pharmacy claims, differences in adherence to prescribed OAC therapy may affect the observed OAC initiation rates. Although the analyses were adjusted for both age and cohort entry year, the secular trends in improving educational attainment and educational opportunities may modify the association between education and OAC use. Residual confounding by other unmeasured factors also cannot be excluded. Notwithstanding these limitations, the results of this large nationwide cohort study accentuate disparities in OAC use and emphasize the need for further efforts to ensure adequate and equitable stroke prevention to all patients with AF. Future research is needed to explore the factors underlying the observed differences in the utilization of OAC therapy, and especially whether they reflect clinically well-founded reticence or unfounded inequity in stroke prevention. Whether or not the observed differences in OAC therapy initiation affect outcomes needs to be determined in future studies.

In conclusion, the findings of this nationwide cohort study highlight potential missed opportunities in stroke prevention, especially among AF patients with low income and high risk of ischemic stroke. Overall, the disparities in OAC initiation between income and educational categories decreased over the study period between 2007 and 2018. Additionally, the broad adoption of DOACs as the initial anticoagulant was considerably faster among patients with higher income or educational levels.

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COMPETING INTEREST

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CONTRIBUTORS

Konsta Teppo had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Konsta Teppo, Jussi Jaakkola, Jukka Putaala, Pirjo Mustonen, Jari Haukka, Juhani Airaksinen and Mika Lehto. Acquisition, analysis and interpretation of data: all authors. Drafting of the manuscript: Konsta Teppo. Critical revision of the manuscript for important intellectual content: all authors. Statistical

analysis: Konsta Teppo and Jussi Jaakkola. Obtaining funding: Mika Lehto. Administrative, technical and material support: Jussi Jaakkola, Olli Halminen and Jari Haukka. Supervision: Jussi Jaakkola, Jukka Putaala, Pirjo Mustonen, Jari Haukka, Juhani Airaksinen and Mika Lehto.

DATA AVAILABILITY STATEMENT

Because of the sensitive nature of the data collected for this study, requests to access the dataset 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 Center and Tax Register) through Findata (https://findata.fi/en/).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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