General Hospital Psychiatry 93 (2025) 116–121

Contents lists available at ScienceDirect

General Hospital Psychiatry

journal homepage: www.elsevier.com/locate/genhospsych

Alcohol use disorder and initiation of oral anticoagulant therapy in patients with atrial fibrillation: A nationwide cohort study

Miika Vanhanen [a,*], Jussi Jaakkola [b], Juhani K.E. Airaksinen [c], Olli Halminen [d], Jukka Putaala [e], Pirjo Mustonen [f], Jari Haukka [g], Juha Hartikainen [h], Alex Luojus [g], Mikko Niemi [g], Miika Linna [d,i], Mika Lehto [d,i,j], Konsta Teppo [c,k]

[a] Faculty of Medicine, University of Turku, Turku, Finland
[b] Cardiac Unit, Department of Internal Medicine, Satasairaala, Pori, Finland
[c] Heart Centre, Turku University Hospital and University of Turku, Turku, Finland
[d] Aalto University, Espoo, Finland
[e] Department of Neurology, Helsinki University Hospital and University of Helsinki, Helsinki, Finland
[f] Turku University Hospital and University of Turku, Finland
[g] University of Helsinki, Helsinki, Finland
[h] Kuopio University Hospital and University of Eastern Finland, Finland
[i] University of Eastern Finland, Kuopio, Finland
[j] Jorvi Hospital, Department of Internal Medicine, HUS Helsinki University Hospital and University of Helsinki, Helsinki, Finland
[k] Biotechnology Unit, Department of Life technologies, University of Turku, Turku, Finland

A B S T R A C T

Objective: Patients with alcohol use disorders (AUD) often receive inferior care for somatic comorbidities. Our objective was to explore whether AUDs influence oral anticoagulant (OAC) initiation for stroke prevention among atrial fibrillation (AF) patients, using a nationwide dataset to assess treatment disparities.
Methods: The Finnish AntiCoagulation in Atrial Fibrillation registry includes data on all 229,565 patients diagnosed with incident AF in Finland during 2007–2018, identified from national registries covering all levels of care. The main outcome was OAC initiation compared between patients with and without AUD.
Results: The patients' mean age was 72.7 years, 50 % were female, 85.0 % were eligible for OAC therapy (CHA_2DS_2-VA score ≥ 1), and 4.7 % had AUD. OAC therapy was initiated in a smaller proportion of patients with AUD compared to those without (52.5 % vs. 71.4 %, $p < 0.001$). This disparity remained significant even after adjusting for comorbidities, socioeconomic status, and laboratory values influencing OAC initiation (adjusted hazard ratio [HR] 0.68; 95 % confidence interval [0.66–0.71]). The absolute difference in OAC initiation between groups stayed consistent at approximately 20 % throughout the study period. Interaction analyses indicated that the association between AUD and lower OAC initiation was stronger in patients with lower income, lower educational attainment, and lower thrombocyte levels, but there was no significant interaction with sex, bleeding history, or hemoglobin levels.
Conclusions: AUDs are associated with a significantly lower rate of OAC initiation even after accounting for comorbidities that influence OAC initiation.

1. Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia affecting up to 5.2 % in the adult population [1], and it is associated with considerably increased risks of ischemic stroke and mortality [2,3]. Although both the risk of stroke and death are effectively mitigated with oral anticoagulant (OAC) therapy, underuse of OAC is common, and substantial disparities in stroke prevention exist between groups defined by characteristics such as age, ethnicity, and socioeconomic status. [4–7].

Alcohol use disorders (AUD) are characterized with compulsive drinking and inability to control alcohol intake despite the resulting harm, and their lifetime prevalence estimates range high as 20 %. [8] Excessive alcohol use confers substantial mortality and morbidity from liver disease, cancer, cardiovascular disease and injuries. [9–11] Moreover, AUDs are often associated with multimorbidity, underscoring the importance of comprehensive treatment of somatic comorbidities, in addition to AUD itself, to reduce mortality and morbidity in these vulnerable patients. [12,13]

Patients affected by mental health disorders and AUD have been reported to receive poorer treatment for their somatic comorbidities compared to individuals without these disorders. [14–16] However,

* Corresponding author at: Faculty of Medicine, Turku University, 20014 Turku, Finland.
E-mail address: miika.h.vanhanen@utu.fi (M. Vanhanen).

https://doi.org/10.1016/j.genhosppsych.2025.01.017
Received 22 December 2024; Received in revised form 27 January 2025; Accepted 27 January 2025
Available online 4 February 2025

data regarding the treatment of AF in patients with AUD is lacking, particularly regarding the utilization of OACs for stroke prevention. Therefore, we conducted a nationwide study to investigate whether the initiation of OAC therapy for AF differs between patients with and without AUD.

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 [17]. Patients were identified from 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 I48 (including atrial fibrillation and atrial flutter, together referred to as AF) recorded between 2004 and 2018. The exclusion criteria were permanent migration abroad before December 31st 2018 and age under 20 years at the time of AF diagnosis. The current substudy was conducted using a cohort of patients with incident AF between 2007 and 2018, established in previous studies of the FinACAF cohort [18–22]. Moreover, in the adjusted analyses using laboratory data, we included only the patients with available laboratory data (50.3 % of patients). Follow-up started on the date of the first AF diagnosis and continued until the initiation of an OAC, death or 31st December 2018, whichever came first. The patient selection process is summarized in Supplementary Fig. 1. Unless otherwise stated, the analyses in this study have been conducted using the entire study population, not limited to patients for whom the CHA_2DS_2-VA score indicates the initiation of anticoagulant therapy.

2.2. Definition of alcohol use disorder

AUDs are frequently underdiagnosed, and even upon diagnosis, the corresponding diagnostic codes may be inadequately recorded in healthcare registries. Therefore, to comprehensively capture patients with probable AUD, we included not only the ICD-10 diagnostic code F10 for AUD but also codes indicating complications of excessive alcohol use (F10, K70, K85.2, K86.00, K86.01, K86.08, I42.6, K29.2, E52, G31.2, G40.51, G62.1, G72.1, Z71.4), as well as the International Classification of Primary Care, Second Edition (ICPC-2) codes P15 and P16 to account for primary care visits. This approach may also mitigate potential sampling bias by not solely focusing on patients actively treated for AUD, a scenario that might have occurred if only F10 ICD-10 codes had been employed. Additionally, we performed sensitivity analyses by including only the F10 codes in the definition of AUD.

2.3. Primary outcome

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. Definition of comorbidities and socioeconomic status

Other comorbidities, laboratory values and socioeconomic status were used in adjustments in analyses. Detailed definitions of the comorbidities can be found in the Supplementary table 2.

Patients were divided into tertiles according to their highest personal annual taxable income and educational level during the FinACAF study's observation period from 2004 to 2018. Annual taxable income was derived from the national Tax Register. The patients' highest achieved educational level categorized according to the International Standard Classification of Education (ISCED) was obtained from Statistics Finland. 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.

2.5. Study ethics

The study protocol was approved by the Ethics Committee of the Medical Faculty of Helsinki University, Helsinki, Finland (nr. 15/2017 and 15/2024) and granted research permission from the Helsinki University Hospital (HUS/46/2018 and HUS/217/2024). 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.

2.6. Statistical analysis

Crude incidence rates of OAC initiation with 95 % confidence intervals were estimated with Poisson regression for patients with and without AUD. Cox proportional hazards regression was used to estimate the unadjusted and adjusted hazard ratios of OAC initiation. The inspection of log-negative log survival curves indicated that the proportional hazards assumption was met. To examine whether possible differences in OAC use were explained by other comorbidities, socioeconomic factors, or pre-existing anemia and thrombocytopenia, the adjusted analyses were performed in three consecutive models. Model 1 included the following variables: age (as categorical variable divided into deciles), sex, calendar year, hypertension, diabetes, heart failure, prior stroke or transient ischemic attack, vascular disease, dementia, prior bleedings, renal failure, liver cirrhosis or failure and depression. In model 2, the regression was further fitted with personal annual income (divided in tertiles), and educational attainment. In addition to the covariates in models 1 and 2, model 3 included also categorical variables for anemia (hemoglobin under 80 g/l, 80–99 g/l, 100–119 g/l and 120 g/l or more) and thrombocytopenia (platelet count under 50 E9/l, 50–99 E9/l, 100–149 E9/l and 150 E9/l or more). Notably, model 3 could include only patients with available laboratory data of both hemoglobin and thrombocytes. Additionally, interactions between socioeconomic variables and AUD, as well as between sex and AUD, were tested to determine whether the impact of AUD on OAC use is modified by patients' socioeconomic status or sex. Similarly, to assess whether prior bleeding events, anemia or thrombocytopenia modified the impact of AUD on OAC initiation, we tested their interactions with AUD. The chi-square test was used to compare differences between proportions, and the independent samples *t*-test to analyze continuous variables. Statistical analyses were performed with the IBM SPSS Statistics software (version 27.0, SPSS, Inc., Armonk, NY) and R (version 4.0.5, https://www.R-project.org).

3. Results

We identified 229,565 patients with incident AF, mean age 72.7 years (SD 13.2); 50.0 % female. Altogether 85.0 % of the patients had at least moderate risk of stroke (CHA_2DS_2-VA -score ≥ 1) and therefore were eligible for OAC therapy. The overall prevalence of AUD at the time of cohort entry was 4.7 %, affecting 10,731 patients, 97.1 % of whom had an ICD-10 code, and 13.1 % an ICPC-2 code for AUD. Patients with

AUD were more often male and had higher prevalence of diabetes, liver failure, renal insufficiency and bleeding history than patients without AUD (Table 1).

Overall, a lower proportion of patients with AUD initiated OAC when compared to patients with no AUD (5636 [52.5 %] vs 156,219 [71.4 %] patients, p ⟨0,001). Among the patients who initiated OAC therapy, NOACs (non-vitamin K oral anticoagulants) were prescribed to 36.2 % of those with AUD, compared to 32.1 % of those without AUD ($p < 0.01$). A continuous increase in the initiation of OACs was observed throughout the study period, with AUD patients consistently being less likely to receive OAC treatment (Fig. 1). The absolute difference in the proportion of patients initiating OACs within one year of follow-up remained steady at approximately 20 % across the study period.

AUD was associated with a lower rate of OAC initiation in Cox regression models before (HR 0.61; 95 % CI 0.59–0.62) as well as after adjusting for confounding variables (HR 0.66; 95 % CI 0.65–0.68). This association remained similar when the regression was further adjusted for socioeconomic factors, and subsequently for the presence of anemia and thrombocytopenia (Fig. 2, Table 2). Furthermore, the association between AUD and lower initiation of OAC was similar in the sensitivity analyses including only ICD-10 diagnosis code F10 as the definition of AUD (Supplementary Table 2). The association also persisted when only patients with at least moderate stroke risk (CHA_2DS_2-VA $\geq$ 1) were included (HR 0.67; 95 % CI 0.65–0.70).

In the interaction analyses, no interaction between sex and AUD on OAC initiation was observed (p-value 0.143), whereas AUD had significant interactions with income tertiles and educational categories (both p-values <0.001). The association between AUD and lower OAC use was more pronounced in patients with lower income and educational attainment (Table 3). AUD had no significant interactions with prior bleeding events ($p = 0.363$) or hemoglobin levels ($p = 0.504$). However, the interaction between AUD and thrombocyte level was significant ($p < 0.001$). The association between AUD and lower OAC initiation was more evident in patients with low thrombocyte levels. (Supplementary Table 3).

Table 1
The baseline characteristics of the study patients, stratified by the history of alcohol use dsorder (AUD).

	AUD ($n = 10,731$)	No AUD ($n = 218,834$)
Baseline characteristics		
Mean age, years (SD)	65 (11.4)	73 (12.8)
Female sex	2190 (20.4)	112,633 (50.4)
Hypertension	7538 (70.2)	162,716 (74.4)
Dyslipidemia	4220 (39.3)	105,432 (48.2)
Heart failure	1897 (17.7)	38,020 (17.4)
Diabetes	2730 (25.4)	46,817 (21.4)
Previous stroke	1279 (11.9)	24,638 (11.3)
Vascular disease	2372 (22.1)	57,401 (26.2)
Renal failure or dialysis	721 (6.7)	8410 (3.8)
Liver cirrhosis or failure	681 (6.3)	479 (0.2)
Bleeding history	2528 (21.4)	26,717 (10.3)
Dementia	557 (5.2)	10,174 (5.1)
Mean CHA_2DS_2-VA -score (SD)	2.3 (1.7)	3.0 (1.7)
Mean CHA_2DS_2-VA Sc -score (SD)	2.5 (1.8)	3.5 (1.8)
Mean modified HAS-BLED -score (SD)	3.3 (1.2)	2.5 (1.0)

Values depict counts (percentages, unless otherwise specified). All differences $p < 0.001$, except for previous stroke $p = 0.002$ and history of heart failure $p = 0.417$. Abbreviations: CHA_2DS_2-VA, congestive heart failure (1 point), hypertension (1 point), age ≥ 75 years (2 points), diabetes (1 point), history of stroke or TIA (2 points), vascular disease (1 point), age 65–74 years (1 point). vascular disease (1 point), age 65–74 years (1 point). modified HAS-BLED score, hypertension, abnormal renal or liver function, prior stroke, bleeding history, concomitant antiplatelet/NSAIDs use, age > 65 years, alcohol abuse (no labile INR, max score 8).

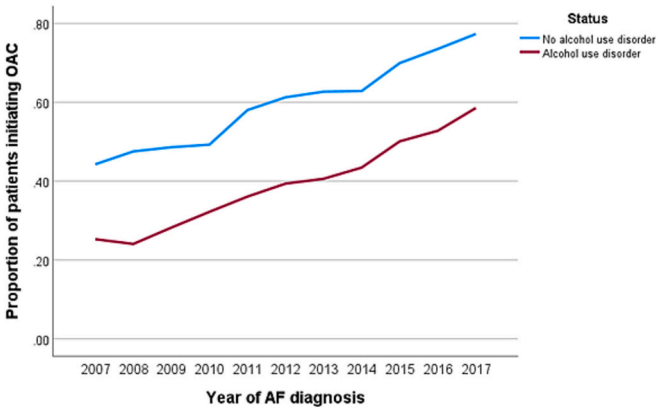

Fig. 1. Proportion of patients initiating oral anticoagulation by 1 year of follow-up according to year of atrial fibrillation diagnosis.

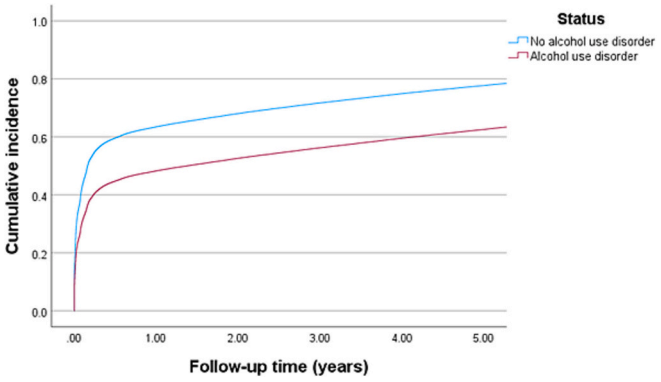

Fig. 2. Cumulative incidence curve of oral anticoagulation initiation in patients with and without alcohol use disorder.

4. Discussion

This study documented that AUD is a frequent comorbidity among patients with AF, affecting nearly one in twenty individuals. AUD was notably associated with over 30 % lower rate of OAC initiation even after extensive adjustments for central bleeding and thrombosis risk factors as well as socioeconomic factors. Although we observed overall favorable OAC initiation trends over time, an approximately 20 % absolute difference between AUD and non-AUD patients persisted throughout the study period.

The relationship between alcohol consumption and AF has been well-documented, with studies showing that alcohol intake increases the risk of AF both in the short and long term [23]. Acute episodes of heavy drinking, or binge drinking, are particularly linked to a higher risk of AF. This phenomenon has led to the widespread use of the term “holiday heart syndrome,” referring to arrhythmias that occur following weekends or holidays [24,25]. In the long term, excessive alcohol use—and even moderate or minimal consumption—has been associated with an increased risk of AF [26]. A dose-response relationship has been identified, where each additional daily drink raises the risk of AF by up to 8 % [27].

AF substantially increases the risk of ischemic stroke, and alcohol consumption further elevates this risk [28]. Studies indicate that even minimal alcohol intake can increase stroke likelihood in AF patients compared to non-drinkers, with the risk escalating proportionally with increasing alcohol consumption. The pathophysiology behind elevated stroke risk due to elevated alcohol consumption involves several interrelated mechanisms. Alcohol can trigger cardiac arrhythmias and abnormalities in cardiac wall motion, which predispose individuals to

Table 2
Initiation of oral anticoagulants according to the presence of alcohol use disorder.

Clinical condition	OAC initiation (*n*)	Proportion of patients with OAC initiation	Patient years	Incidence (per patient-year)	Unadjusted HR	Adjusted HR (model 1)	Adjusted HR (model 2)	Adjusted HR (model 3)
No AUD	156,218	71.4 %	302,171	0.52 (0.51–0.52	(reference)	(reference)	(reference)	(reference)
AUD	5636	52.5 %	19,722	0.29 (0.28–0.29	0.61 (0.59–0.62)	0.66 (0.64–0.68)	0.66 (0.64–0.68)	0.68 (0.66–0.71)

95 % confidence intervals in parenthesis. HR estimated by Cox regression. Model 1 adjusted for age (as categorical variable divided into deciles), sex, calendar year, hypertension, diabetes, heart failure, prior stroke or transient ischemic attack, vascular disease, dementia, prior bleedings, renal failure, liver cirrhosis or failure and depression. In model 2, the regression was further fitted with personal annual income (divided in tertiles), and educational attainment. In addition to the aforementioned variables, model 3 included also categorical variables for anemia and thrombocytopenia. HR, Hazard ratio; AUD, alcohol use disorder.

Table 3
Hazard ratios for the initiation of anticoagulation comparing patients with alcohol use disorder to those without alcohol use disorder in different educational and income categories.

	Unadjusted HR	Adjusted HR (Model 1)	Adjusted HR (Model 2)	Adjusted HR (Model 3)
1st educational category (lowest)	0.57 (0.55–0.59)	0.61 (0.59–0.63)	0.62 (0.59–0.64)	0.65 (0.62–0.69)
2nd educational category	0.60 (0.58–0.63)	0.65 (0.62–0.68)	0.65 (0.62–0.68)	0.67 (0.63–0.71)
1rd educational category (highest)	0.73 (0.69–0.79)	0.73 (0.68–0.77)	0.70 (0.66–0.76)	0.73 (0.68–0.80)
1st Income tertile (lowest)	0.55 (0.52–0.58)	0.55 (0.52–0.58)	0.55 (0.52–0.58)	0.57 (0.53–0.61)
2nd Income tertile	0.57 (0.54–0.59)	0.67 (0.64–0.70)	0.67 (0.64–0.70)	0.70 (0.66–0.74)
3rd Income tertile (highest)	0.77 (0.73–0.80)	0.74 (0.70–0.78)	0.74 (0.70–0.77)	0.75 (0.70–0.79)

ischemic stroke [29]. Chronic alcoholism often leads to secondary non-ischemic cardiomyopathy, increasing the risk of cerebral embolism through rhythm disturbances or the formation of intracardiac thrombi [30]. Furthermore, heavy alcohol consumption is associated with elevated blood pressure, a major risk factor for all types of strokes. Binge drinking appears to be an independent risk factor in young men with cryptogenic ischemic stroke [31]. During binge drinking episodes, alcohol can cause transient spikes in systolic blood pressure, further exacerbating the risk of stroke [32]. Importantly, complete abstinence from alcohol after an AF diagnosis has been shown to significantly reduce stroke risk, underscoring the critical role of lifestyle changes in managing AF and its complications [28].

To the best of our knowledge, no previous study has assessed the issue of OAC initiation in AF patients affected by AUD. However, there are several reports of underutilization of OAC therapy among other vulnerable patient groups, such as patients with mental health disorders or low socioeconomic status. Mental health conditions overall are associated with around 13 % lower incidence of OAC initiation [33]. Similar results also have been reported in patients with lower socioeconomical status. In a prior study, women with higher education level had OAC initiated 14.3 % more often than those with lower education level, and similar pattern was observed in men, though the inequality narrowed over time [34]. These findings are in line with the current study.

The lower rate of OAC initiation in patients with AUD is most likely multifactorial and is partly explained by differences in risk factors of thrombosis and bleeding. Concern of serious bleeding events can be one reason for withholding OAC therapy among AF patients with AUD. Patients with AUD often exhibit an increased risk of hemorrhage mainly due to increased trauma risk and impaired coagulation processes [35,36]. Based on the findings of the current study, physicians appear more likely to withhold OAC therapy due to thrombocytopenia when accompanied by AUD, compared to patients with thrombocytopenia alone. This suggests that factors related to AUD, rather than thrombocytopenia itself, may influence prescribing decisions. Based on the findings of the current study, physicians appear more likely to withhold OAC therapy due to thrombocytopenia in the presence of concomitant AUD, compared to patients with thrombocytopenia without AUD. It has also been documented that alcohol abusers exhibit poorer anticoagulation control compared to those without alcohol abuse [41]. Additionally, the age-adjusted risk of major hemorrhage is significantly higher for alcohol abusers, even after accounting for anticoagulation control and other bleeding risk factors [37]. Furthermore, self-reported alcohol consumption is associated with an increased risk of intracranial hemorrhage in a dose-dependent manner [38]. Alcohol use is also linked to a higher risk of fall-related injuries across all age groups, which may deter OAC initiation in this population [39,40]. Excessive alcohol consumption has also been identified as the strongest individual risk factor for excessive anticoagulation effect of warfarin [41]. However, even though studies show that patients with AUD present higher bleeding risk, in some cases the perceived risk may be based on the treating physician's prejudices or be overestimated. Notably, patients with an estimated high bleeding risk are often also at high risk for ischemic stroke, making stroke prevention measures even more crucial.

In the current study, differences in OAC treatment appeared to be largely influenced by factors other than bleeding and thrombosis risk as even after adjustments for confounding factors, patients with AUD remained more than 30 % less likely to receive OAC therapy. There are several possible explanations for this inequality. Patients with AUD tend to more frequently exhibit other chronic diseases not reflected in thrombosis and bleeding risk scores that may affect OAC initiation. Additionally, those with alcohol-related health problems may often require complex medication regimens that can interact negatively with alcohol and impact OAC initiation. [42]. Moreover, essential support from family and friends, which at times is crucial for good adherence for the used treatments, is often strained by the behavior of the person with AUD. Negative perceptions from physicians towards treating alcohol-related issues can also hinder effective treatment, making it even harder for patients to comply with their treatment plans [43]. Moreover, the lower OAC initiation rate may arise from poorer self-care resources associated with AUDs, potentially leading to reduced adherence and unredeemed prescriptions. Patients with AUD were slightly more likely to be started on NOACs, likely because of their more predictable effects, fewer interactions, and the reduced need for frequent monitoring compared to warfarin. Nonetheless, the gap in OAC use between patients with and without AUD remained similar even in the NOAC era.

Our study, in addition to others, demonstrated that people with AUDs are associated with lower socioeconomic status [6]. Previous reports indicate that higher educational level is associated with a higher likelihood of OAC initiation. The same applies to income levels, and lower income tends to be associated with lower likelihood of OAC initiation [44]. Correspondingly, in the current study, the association between AUD and lower OAC initiation was pronounced in patients with lower socioeconomic status in terms of low income or lower educational

attainment. Indeed, addressing social determinants of health is crucial, as they frequently correlate with one another. Targeting interventions to enhance oral anticoagulant coverage in underserved patient populations could yield substantial improvements in stroke prevention.

The main strength of our study is the nationwide basis and large unselected cohort, covering all levels of healthcare. Importantly, in Finland, all citizens have universal healthcare coverage funded by taxation-based support, ensuring treatment accessibility also for those who experience hardship.

Nevertheless, there are some limitations to this study that must be acknowledged. The primary limitation is the retrospective design and use of register data to define AUD. AUD was identified based on medical history, but alcohol use and its complications are frequently underdiagnosed, meaning that our data likely captured only the more severe cases of AUD. Additionally, changes in alcohol consumption during the study period were not considered. OAC initiation was measured through fulfilled prescriptions, so it is possible that some patients prescribed with OAC therapy never actually took their medication. Although adjustments for baseline variables were made, the possibility of residual confounding cannot be excluded. Also, information bias related to incompletely or inaccurately recorded registry data may also affect the reliability of the study findings.

In conclusion, patients with AF and AUD had a significantly lower rate of OAC initiation compared to those without AUD. This disparity persisted even after adjusting for comorbidities that influence OAC initiation. Future studies should investigate whether rates of AF-related complications differ between these patient groups, and whether the lower use of OACs is reflected in higher burden of stroke in patients with AUDs.

Funding/support

This work was supported by the Aarne Koskelo Foundation, The Finnish Foundation for Cardiovascular Research, Helsinki and Uusimaa Hospital District research fund (TYH2019309), The Finnish Medical Foundation and The Finnish Foundation for Alcohol Studies.

CRediT authorship contribution statement

Miika Vanhanen: Writing – original draft, Visualization, Methodology, Investigation, Formal analysis. **Jussi Jaakkola:** Writing – review & editing, Conceptualization. **Juhani K.E. Airaksinen:** Writing – review & editing, Supervision, Project administration, Conceptualization. **Olli Halminen:** Writing – review & editing, Project administration, Methodology, Data curation, Conceptualization. **Jukka Putaala:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Pirjo Mustonen:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Jari Haukka:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Juha Hartikainen:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Alex Luojus:** Writing – review & editing, Methodology, Conceptualization. **Mikko Niemi:** Writing – review & editing, Methodology, Conceptualization. **Miika Linna:** Writing – review & editing, Methodology, Conceptualization. **Mika Lehto:** Writing – review & editing, Supervision, Project administration, Methodology, Funding acquisition, Conceptualization. **Konsta Teppo:** Writing – review & editing, Supervision, Methodology, Investigation, Data curation, Conceptualization.

Declaration of competing interest

Konsta Teppo: none. Miika Vanhanen: none. Jussi Jaakkola: none. Olli Halminen: none. Jukka Putaala: Speaker: Bayer, Boehringer-Ingelheim, BMS-Pfizer, Abbott; Advisory board: Portola, Novo Nordisk, Herantis Pharma; Visiting editor: Terve Media; Stock ownership: Vital Signum. Pirjo Mustonen: Consultant: Roche, BMS-Pfizer-alliance, Novartis Finland, Boehringer Ingelheim, MSD Finland. Jari Haukka: Consultant: Research Janssen R&D; Speaker: Bayer Finland. Miika Linna: Speaker: BMS-Pfizer-alliance, Bayer, Boehringer-Ingelheim. Juha Hartikainen: Research grants: The Finnish Foundation for Cardiovascular Research, EU Horizon 2020, EU FP7. Advisory Board Member: BMS-Pfizer-alliance, Novo Nordisk, Amgen. Speaker: Cardiome, Bayer. K.E. Juhani Airaksinen: Research grants: The Finnish Foundation for Cardiovascular Research; Speaker: Bayer, Pfizer and Boehringer-Ingelheim. Mika Lehto: Consultant: BMS-Pfizer-alliance, Bayer, Boehringer-Ingelheim, and MSD; Speaker: BMS-Pfizer- alliance, Bayer, Boehringer Ingelheim, MSD, Terve Media and Orion Pharma. Research grants: Aarne Koskelo Foundation, The Finnish Foundation for Cardiovascular Research, and Helsinki and Uusimaa Hospital District research fund, Boehringer-Ingelheim.

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/).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.genhosppsych.2025.01.017.

References

[1] Lehto M, et al. Comprehensive nationwide incidence and prevalence trends of atrial fibrillation in Finland. Open Heart Nov. 2022;9(2):e002140. https://doi.org/10.1136/openhrt-2022-002140.
[2] Björck S, Palaszewski B, Friberg L, Bergfeldt L. Atrial fibrillation, stroke risk, and warfarin therapy revisited: a population-based study. Stroke 2013:44. https://doi.org/10.1161/STROKEAHA.113.002329.
[3] ESC guidelines for the management of atrial fibrillation. Accessed: Nov 09, 2024. [Online]. Available: https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Atrial-Fibrillation.
[4] 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. https://doi.org/10.7326/0003-4819-146-12-200706190-00007.
[5] Essien UR, Kim N, Hausmann LRM, Mor MK, Good CB, Magnani JW, et al. Disparities in anticoagulant therapy initiation for incident atrial fibrillation by race/ethnicity among patients in the veterans health administration system. JAMA Netw Open 2021:4. https://doi.org/10.1001/jamanetworkopen.2021.14234.
[6] Teppo K, Jaakkola J, Biancari F, Halminen O, Linna M, Haukka J, et al. Association of income and educational levels on initiation of oral anticoagulant therapy in patients with incident atrial fibrillation: a Finnish nationwide cohort study. Br J Clin Pharmacol 2023:89. https://doi.org/10.1111/bcp.15501.
[7] Teppo K, Jaakkola J, Biancari F, Halminen O, Linna M, Haukka J, et al. Association of income and educational levels with adherence to direct oral anticoagulant therapy in patients with incident atrial fibrillation: a Finnish nationwide cohort study. Pharmacol Res Perspect 2022;10:e00961. https://doi.org/10.1002/prp2.961.
[8] Carvalho AF, Heilig M, Perez A, Probst C, Rehm J. Alcohol use disorders. The Lancet 2019:394. https://doi.org/10.1016/S0140-6736(19)31775-1.
[9] Centers for Disease Control and Prevention. Deaths from excessive alcohol use in the United States. US Department of Health and Human Services; 2022.
[10] Esser MB, Leung G, Sherk A, Bohm MK, Liu Y, Lu H, et al. Estimated deaths attributable to excessive alcohol use among US adults aged 20 to 64 years, 2015 to 2019. JAMA Netw Open 2022:5. https://doi.org/10.1001/jamanetworkopen.2022.39485.
[11] Kathryn Mchugh R, Weiss RD. Alcohol use disorder and depressive disorders. Alcohol Res 2019;40:e1–8. https://doi.org/10.35946/arcr.v40.1.01.
[12] Tseng PY, Sung FC, Muo CH, Lan YC, Hser YI, Chien SHL, et al. Risk of diabetes and hypertension in a population with alcohol use disorders. BMC Public Health 2024:24. https://doi.org/10.1186/s12889-024-18318-y.
[13] AshaRani PV, Karuvetil MZ, Brian TYW, Satghare P, Roystonn K, Peizhi W, et al. Prevalence and correlates of physical comorbidities in alcohol use disorder (AUD): a pilot study in treatment-seeking population. Int J Ment Health Addict 2023:21. https://doi.org/10.1007/s11469-021-00734-5.
[14] Redelmeier DA, Tan SH, Booth GL. The treatment of unrelated disorders in patients with chronic medical diseases. N Engl J Med 1998:338. https://doi.org/10.1056/nejm199805213382106.

[15] Desai MM, Rosenheck RA, Druss BG, Perlin JB. Mental disorders and quality of diabetes care in the veterans health administration. Am J Psychiatry 2002:159. https://doi.org/10.1176/appi.ajp.159.9.1584.
[16] Druss BG, Bradford DW, Rosenheck RA, Radford MJ, Krumholz HM. Mental disorders and use of cardiovascular procedures after myocardial infarction. JAMA 2000:283. https://doi.org/10.1001/jama.283.4.506.
[17] 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;37:95–102. https://doi.org/10.1007/s10654-021-00812-x.
[18] Teppo K, Jaakkola J, Biancari F, Halminen O, Linna M, Haukka J, et al. Socioeconomic disparities in use of rhythm control therapies in patients with incident atrial fibrillation: a Finnish nationwide cohort study. IJC Heart Vasc 2022; 41:101070. https://doi.org/10.1016/j.ijcha.2022.101070.
[19] Teppo K, et al. Mental health conditions and bleeding events in patients with incident atrial fibrillation: a Finnish nationwide cohort study. Gen Hosp Psychiatry 2022;78:117–22. https://doi.org/10.1016/j.genhosppsych.2022.08.003.
[20] Teppo K, 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. https://doi.org/10.1016/j.genhosppsych.2021.12.012.
[21] Teppo K, Airaksinen KEJ, Jaakkola J, Halminen O, Salmela B, Kouki E, et al. Ischaemic stroke in women with atrial fibrillation: temporal trends and clinical implications. Eur Heart J 2024:ehae198. https://doi.org/10.1093/eurheartj/ehae198.
[22] Teppo K, Langén V, Airaksinen KEJ, Kouki E, Jaakkola J, Halminen O, et al. Temporal trends in hypertension-related ischaemic stroke risk in atrial fibrillation from 2007 to 2018: a nationwide cohort study. Eur J Prev Cardiol 2024. https://doi.org/10.1093/eurjpc/zwae103.
[23] P. Koskinen, M. Kupari, H. Leinonen, and K. Luomanmäki, "Alcohol and new onset atrial fibrillation: a case-control study of a current series," Br Heart J, vol. 57, no. 5, pp. 468–473.
[24] Koskinen P, Kupari M, Leinonen H. Role of alcohol in recurrences of atrial fibrillation in persons less than 65 years of age. Am J Cardiol Oct. 1990;66(12): 954–8. https://doi.org/10.1016/0002-9149(90)90932-q.
[25] Ettinger PO, Wu CF, De La Cruz C, Weisse AB, Ahmed SS, Regan TJ. Arrhythmias and the 'holiday heart': alcohol-associated cardiac rhythm disorders. Am Heart J May 1978;95(5):555–62. https://doi.org/10.1016/0002-8703(78)90296-x.
[26] Alcohol and heart disease - PubMed. Accessed: Oct 10, 2024. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/8941153/.
[27] Larsson SC, Drca N, Wolk A. Alcohol consumption and risk of atrial fibrillation. J Am Coll Cardiol Jul. 2014;64(3):281–9. https://doi.org/10.1016/j.jacc.2014.03.048.
[28] Lee S-R, Choi E-K, Jung J-H, Han K-D, Oh S, Lip GYH. Lower risk of stroke after alcohol abstinence in patients with incident atrial fibrillation: a nationwide population-based cohort study. Eur Heart J Dec. 2021;42(46):4759–68. https://doi.org/10.1093/eurheartj/ehab315.
[29] Gorelick PB. Alcohol and stroke. Stroke Jan. 1987;18(1):268–71. https://doi.org/10.1161/01.STR.18.1.268.
[30] Hillbom M, Numminen H. Alcohol and stroke: pathophysiologic mechanisms. Neuroepidemiology Oct. 1998;17(6):281–7. https://doi.org/10.1159/000026181.
[31] Martinez-Majander N, et al. Association between heavy alcohol consumption and cryptogenic ischaemic stroke in young adults: A case-control study. ffdd9df8–7686-46cb-9d94-377fe7f4b104. Accessed: Dec. 03, 2024. [Online]. Available: https://oulurepo.oulu.fi/handle/10024/50892.
[32] Hillbom M, Saloheimo P, Juvela S. Alcohol consumption, blood pressure, and the risk of stroke. Curr Hypertens Rep Jun. 2011;13(3):208–13. https://doi.org/10.1007/s11906-011-0194-y.
[33] Jaakkola J, 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 Oct. 2021;8(3):269–76. https://doi.org/10.1093/ehjqcco/qcab077.
[34] Lunde ED, et al. Socioeconomic inequality in oral anticoagulation therapy initiation in patients with atrial fibrillation with high risk of stroke: a register-based observational study. BMJ Open May 2021;11(5):e048839. https://doi.org/10.1136/bmjopen-2021-048839.
[35] Chikritzhs T, Livingston M. Alcohol and the risk of injury. Nutrients Aug. 2021;13 (8):2777. https://doi.org/10.3390/nu13082777.
[36] Eismann H, et al. Influence of alcohol consumption on blood coagulation in rotational thromboelastometry (ROTEM): an in-vivo study. Korean J Anesthesiol Aug. 2020;73(4):334. https://doi.org/10.4097/kja.20071.
[37] Efird LM, et al. Identifying the risks of anticoagulation in patients with substance abuse. J Gen Intern Med Oct. 2013;28(10):1333–9. https://doi.org/10.1007/s11606-013-2453-x. May 1987, doi: 10.1136/hrt.57.5.468.
[38] Zirulnik A, et al. Alcohol use is associated with intracranial hemorrhage in older emergency department head trauma patients. J Am Coll Emerg Physicians Open Jul. 2024;5(4):e13245. https://doi.org/10.1002/emp2.13245.
[39] Chen CM, Yoon Y-H. Usual Alcohol Consumption and Risks for Nonfatal Fall Injuries in the United States: results from the 2004–2013 National Health Interview Survey. Subst Use Misuse Jul. 2017;52(9):1120–32. https://doi.org/10.1080/10826084.2017.1293101.
[40] Yuan K, et al. Emergency department visits for alcohol-associated falls among older adults in the United States, 2011 to 2020. Ann Emerg Med Dec. 2023;82(6): 666–77. https://doi.org/10.1016/j.annemergmed.2023.04.013.
[41] Jaakkola S, Nuotio I, Kiviniemi TO, Virtanen R, Issakoff M, Airaksinen KEJ. Incidence and predictors of excessive warfarin anticoagulation in patients with atrial fibrillation—the EWA study. PloS One Apr. 2017;12(4):e0175975. https://doi.org/10.1371/journal.pone.0175975.
[42] Guerzoni S, Pellesi L, Pini LA, Caputo F. Drug-drug interactions in the treatment for alcohol use disorders: a comprehensive review. Pharmacol Res Jul. 2018;133: 65–76. https://doi.org/10.1016/j.phrs.2018.04.024.
[43] Dorrian J. Alcoholism: disease or symptom? The challenges of managing advanced alcoholism and chronic illness. Med J Aust 2010;192(11):661–2. https://doi.org/10.5694/j.1326-5377.2010.tb03671.x.
[44] Collins SE. Associations between socioeconomic factors and alcohol outcomes. Alcohol Res 2016;38(1):83–94.