Factors Associated With Oral Anticoagulant Use in Patients With Atrial Fibrillation and Mental Disorders

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Abstract

Objective: This study aims to identify how mental illness severity interacts with oral anticoagulant (OAC) patterns among people with atrial fibrillation (AF).

Methods: AF patients with comorbid mental illness (classified using *ICD-10*) were identified from the South London and Maudsley Biomedical Research Centre Case Register. CHA_2DS_2-VASc and ORBIT scales were used to calculate stroke and bleeding risks, respectively, whereas Health of the Nation Outcome Scales (HoNOS) assessment was used for functional impairment.

Results: Overall, 2,105 AF patients were identified between 2011 and 2019. Serious mental illness (SMI) was associated with lower prescription of any OAC (adjusted risk ratio [aRR]: 0.94; 95% CI, 0.90–0.99). A total of 62% of SMI patients at risk of stroke were not prescribed an OAC. In the AF cohort, alcohol or substance dependence and activities of daily living (ADL) impairment were associated with lower prescription of warfarin (aRR: 0.92; 95% CI, 0.86–0.98 and aRR: 0.96; 95% CI, 0.93–0.99, respectively). Among people with AF and SMI, warfarin was less likely to be prescribed to people with self-injury (aRR: 0.84; 95% CI, 0.77–0.91), hallucinations or delusions (aRR: 0.92; 95% CI, 0.85–0.99), ADL impairment (aRR: 0.91; 95% CI, 0.84–0.99), or alcohol or substance dependence (aRR: 0.92; 95% CI, 0.87–0.98). Among people with AF and comorbid substance use disorder, self-injury (aRR: 0.78; 95% CI, 0.64–0.96), cognitive problems (aRR: 0.84; 95% CI, 0.70–0.99), and other mental illnesses (aRR: 0.83; 95% CI, 0.70–0.99) were associated with lower prescription of warfarin.

Conclusions: An OAC treatment gap for AF patients with comorbid SMI relative to other mental illnesses was identified. The gap was wider in those with dependence comorbidities, positive symptoms, self-injury, or functional impairment.

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Atrial fibrillation (AF) is a common arrhythmia characterized by an irregularly irregular pulse.[1] Compared to the general population, people with AF are 5 to 7 times more likely to have a stroke.[1] Oral anticoagulant (OAC) therapy has been effective in reducing the risk of stroke by 64% and the risk of death by 26% in people with AF.[2] According to the National Institute for Health and Care Excellence (NICE) guidelines, people with AF should be prescribed a direct-acting oral anticoagulant (DOAC) (such as dabigatran, edoxaban, apixaban, or rivaroxaban) or a vitamin K antagonist (VKA) (such as warfarin) when at high risk of stroke as measured by CHA_2DS_2-VASc score.[3,4]

Previous studies[5–7] have shown that people with AF and comorbid mental illness, including depression, anxiety, or serious mental illnesses such as schizophrenia and bipolar disorder, are less likely than those with no mental illness to be prescribed an OAC for AF-related stroke prevention. Similarly, a systematic review[8] assessing the prevalence, safety, and outcomes of OAC use showed that people with dementia had 52% lower odds of being prescribed an OAC compared to people without dementia. Non-initiation of the therapy could be a missed opportunity to prevent stroke occurrence in patients with mental illness who could be safely treated.

The lower rate of OAC in AF patients with comorbid mental illness is multifactorial. People with mental illness may experience cognitive difficulties, impaired self-care, and/or difficulties in adhering to a medication regimen due to the active features of illness.[9–11] Additionally, VKAs such as warfarin require continuous dose titration and monitoring of the international normalized ratio (INR), which can be demanding for people with serious mental illness (SMI) and dementia.[9,12] OAC prescription rates may also be affected by the increased bleeding risk associated with the antithrombotic effect of some

Clinical Points

- Non-initiation of oral anticoagulation therapy among eligible atrial fibrillation (AF) patients with mental illness could be a missed opportunity to prevent stroke occurrence.
- If a patient presents with AF and comorbid mental illness, clinicians should consider assessing the stroke and bleeding risks using the CHA_2DS_2-VASc and ORBIT scales, respectively, to determine if they are eligible for oral anticoagulation therapy.
- When obstacles to indicated anticoagulation are present, such as mental illness–associated factors or high bleeding risk, these should be actively managed.

psychotropic medications, increased rates of alcohol use in people with SMI, or frailty among people with dementia.[9,13] DOACs may be better alternatives as they do not require INR monitoring and have fewer drug, alcohol, and food interactions compared to warfarin.[12] Fragmented medical care could create additional barriers for the management of physical conditions like AF.[14]

The health and social functioning of people with SMI in the United Kingdom is routinely assessed using the Health of the Nation Outcome Scales (HoNOS).[15] Many studies[16–19] have examined the association between the severity of various mental health conditions and all-cause mortality risk including AF-related stroke, but little is known on whether the risk is attributed to lower prescription of antithrombotic treatment.

This study aims to (i) identify the relative rates of recorded prescription of OAC among people with AF and comorbid dementia, SMI, substance use disorder, and other mental illnesses in secondary mental health care; and (ii) evaluate the association between mental illness severity and functional impairment and OAC prescription in eligible patients.

METHODS

Cohort Selection

This retrospective cohort study included patients identified from the South London and Maudsley NHS Foundation Trust (SLM) Biomedical Research Centre (BRC) Clinical Records Interactive Search (CRIS) system.[20] SLM is one of Europe's largest mental health care providers, serving 4 London boroughs (Lambeth, Southwark, Lewisham, and Croydon) with service provision including inpatient and community services. CRIS is an ethically approved data retrieval and extraction platform that allows access to deidentified electronic health records of secondary mental health service users from SLM (excluding patients who opt out from having their records included in CRIS).

The cohort was composed of a defined group of AF patients, aged ≥ 18 years, who were active patients in SLM at any point over a 9-year period between January 1, 2011, and December 31, 2019. *Active* was defined as having at least two face-to-face community contacts or one inpatient admission to SLM during the study period with at least one of the community contacts or admissions being in the 5 years up to window end (from January 1, 2015).

AF was identified by searching for the following keywords in patients' clinical notes: *atrial fibrillation*, *afib*, *a fib*, *A fibrillation*, *irregularly irregular pulse*, *pulse irregularly irregular*, and *irreg irreg*. Identified patients were grouped into diagnostic categories based on the latest mental illness diagnosis (recorded in the structured fields) received during the study period. Using the *ICD-10* classification, the mental illnesses were categorized as follows: dementia (F00–F03); SMI (schizophrenia and other non-mood psychotic disorders [F20–F29], mania [F30], bipolar disorder [F31], and severe depression with psychotic symptoms [F32.3]); substance use disorder (F10–F19); and common mental disorders (depression [F32–F33, except F32.3]; persistent mood affective disorder [F34]; neurotic, stress-related, and somatoform disorders [F40-48]; and disorders of adult personality and behavior [F60–69]).

Study Characteristics

To assess the appropriateness of OAC prescription in people with AF, NICE guidelines recommend a comprehensive assessment of the stroke and bleeding risks using the CHA_2DS_2-VASc and ORBIT scales, respectively.[4] CHA_2DS_2-VASc[21] components include age, sex, history of congestive heart failure, hypertension, stroke, vascular disease, and diabetes, whereas ORBIT[22] components include sex, hemoglobin or hematocrit levels, age, bleeding history, glomerular filtration rate, and treatment with antiplatelet agents.

Physical comorbidities were ascertained from electronic health records' free text during the defined timeframe. Natural language processing (NLP) applications previously validated in SLM were used to detect the presence of physical comorbidities like hypertension, diabetes, and stroke.[23] NLP applications had not been developed for physical conditions like congestive heart failure, vascular disease, and bleeding; thus, these conditions were searched for in the clinical notes using specific keywords. Before calculating CHA_2DS_2-VASc and ORBIT scores, the presence of each physical comorbidity component of the CHA_2DS_2-VASc and ORBIT scales was manually validated on a random sample of 40 patients taken from the cohort. The validation process was conducted by two independent researchers (D.F. and A.D.). The reported similarity was 95.6%.

Psychotropic medications (including non-clozapine oral antipsychotics, long-acting injectable antipsychotics, clozapine, antidepressants, and lithium), antiplatelet agents, and antithrombotic prescriptions of OACs (apixaban, rivaroxaban, dabigatran, edoxaban, warfarin)

Table 1.
Characteristics of Study Cohort[a]

Factor	Dementia (n = 1,013)	SMI (n = 245)	Substance Use Disorders (n = 69)	Common Mental Disorders (n = 778)
Age, mean (SD), y	84.92 (6.74)	65.73 (17.85)	60.43 (12.56)	75.10 (15.73)
Sex, male	438 (43.2)	141 (57.6)	55 (79.7)	370 (47.6)
Ethnicity				
White	773 (76.3)	118 (48.2)	63 (91.3)	599 (77.0)
Black	127 (12.5)	103 (42.0)	3 (4.3)	57 (7.3)
Asian	30 (3.0)	13 (5.3)	1 (1.4)	23 (3.0)
Other	33 (3.3)	6 (2.4)	1 (1.4)	32 (4.1)
Index of Multiple Deprivation score, mean (SD)	23.81 (10.40)	26.73 (9.50)	24.39 (8.91)	24.97 (10.86)
Education, highest level				
A-level	32 (3.2)	34 (13.9)	5 (7.2)	34 (4.4)
GCSE	23 (2.3)	19 (7.8)	2 (2.9)	31 (4.0)
No qualifications	110 (10.9)	21 (8.6)	10 (14.5)	69 (8.9)
University	45 (4.4)	69 (28.2)	7 (10.1)	62 (8.0)
Medication				
Non-clozapine non-depot	215 (21.2)	225 (91.8)	17 (24.6)	207 (26.6)
Non-clozapine depot	34 (3.4)	115 (46.9)	4 (5.8)	23 (3.0)
Clozapine	5 (0.5)	60 (24.5)	1 (1.4)	3 (0.4)
Antidepressant	387 (38.2)	145 (59.2)	42 (60.9)	516 (66.3)
HoNOS Scores				
Overactive, aggressive, disruptive, or agitated behavior				
≤ 1	788 (77.8)	199 (81.2)	18 (26.1)	561 (72.1)
≥ 2	196 (19.3)	39 (15.9)	3 (4.3)	95 (12.2)
Self-injury				
≤ 1	972 (96.0)	231 (94.3)	17 (24.6)	609 (78.3)
≥ 2	12 (1.2)	7 (2.9)	4 (5.8)	46 (5.9)
Problem drinking or drug taking				
≤ 1	968 (95.6)	225 (91.8)	7 (10.1)	609 (78.3)
≥ 2	16 (1.6)	13 (5.3)	14 (20.3)	44 (5.7)
Cognitive problems				
≤ 1	128 (12.6)	159 (64.9)	15 (21.7)	403 (51.8)
≥ 2	856 (84.5)	79 (32.2)	6 (8.7)	248 (31.9)
Physical illness or disability problems				
≤ 1	335 (33.1)	85 (34.7)	9 (13.0)	173 (22.2)
≥ 2	648 (64.0)	153 (62.4)	12 (17.4)	482 (62.0)
Hallucinations and delusions				
≤ 1	877 (86.6)	131 (53.5)	19 (27.5)	582 (74.8)
≥ 2	107 (10.6)	107 (43.7)	2 (2.9)	71 (9.1)
Depressed moods				
≤ 1	845 (83.4)	195 (79.6)	12 (17.4)	440 (56.6)
≥ 2	139 (13.7)	42 (17.1)	9 (13.0)	214 (27.5)
Other mental problems				
≤ 1	662 (65.4)	142 (58.0)	11 (15.9)	340 (43.7)
≥ 2	304 (30.0)	96 (39.2)	10 (14.5)	308 (39.6)
Relationship problems				
≤ 1	838 (82.7)	167 (68.2)	17 (24.6)	504 (64.8)
≥ 2	145 (14.3)	71 (29.0)	4 (5.8)	150 (19.3)
Daily living problems				
≤ 1	338 (33.4)	136 (55.5)	11 (15.9)	288 (37.0)
≥ 2	646 (63.8)	102 (41.6)	10 (14.5)	367 (47.2)
Living conditions problems				
≤ 1	853 (84.2)	196 (80.0)	15 (21.7)	551 (70.8)
≥ 2	116 (11.5)	41 (16.7)	5 (7.2)	99 (12.7)
Occupational problems				
≤ 1	621 (61.3)	167 (68.2)	13 (18.8)	437 (56.2)
≥ 2	361 (35.6)	70 (28.6)	8 (11.6)	214 (27.5)
Total HoNOS score, mean (SD)	11.23 (5.68)	11.27 (6.21)	13.00 (5.11)	11.29 (5.72)

[a]All values are n (%) unless otherwise specified.
Abbreviations: GCSE = General Certificate of Secondary Education, HoNOS = Health of the Nation Outcome Scales, SMI = serious mental illness.

were extracted from free text clinical notes within the defined timeframe using previously validated NLP applications.[23,24]

Mental illness severity was measured using the most recent HoNOS score.[15] The HoNOS are composed of 12 items: agitated behavior, self-injury, alcohol or drug use, cognitive problems, physical illness or disability, hallucinations and delusions, depressed mood, mental and behavioral problems, relationship problems, activities of daily living (ADL) problems, living conditions problems, and occupational problems.[15] The response options follow the format of (0) not a problem, (l) minor problem requiring no action, (2) mild problem but definitely present, (3) moderately severe problem, and (4) severe to very severe problem.[15] In this study, the HONOS items considered relevant were self-injury, alcohol or drug use, cognitive problems, physical illness or disability, hallucinations and delusions, depressed mood, other mental and behavioral problems, and ADL problems. Due to the limited numbers in some categories, the HoNOS items were condensed to 2 response options in the analysis: ≤ 1 representing no problem or minor problem requiring no action, and ≥ 2 representing significant problem.

Statistical Analysis

Descriptive variables are presented in the text and tables. Categorical variables were presented as counts and percentages and compared using a χ^2 test, whereas continuous variables were presented as means and standard deviations and compared using the Student *t* test. Multivariate analyses using a Poisson regression model with a robust error variance were conducted to examine the association between the various mental illnesses (described in the preceding paragraphs) and the prescription of OACs (categorized as DOAC or warfarin) among people with AF. A Poisson regression model was also used to study the association between mental illness severity (as measured by HoNOS) and OAC prescription in the full AF cohort and among the following subgroups: AF with comorbid dementia, AF with comorbid SMI, AF with comorbid substance use disorder,

Table 2.

Stroke and Bleeding Risks for People With Atrial Fibrillation Stratified by Mental Illness Status[a]

Factor	Dementia (n = 1,013)	SMI (n = 245)	Substance Use Disorders (n = 69)	Common Mental Disorders (n = 778)
CHA_2DS_2VASc				
Age, y				
< 65	5 (0.5)	104 (42.4)	45 (65.2)	150 (19.3)
65 to 74	66 (6.5)	50 (20.4)	15 (21.7)	144 (18.5)
≥ 75	942 (93.0)	91 (37.1)	9 (13.0)	484 (62.2)
Hypertension	559 (55.2)	155 (63.3)	30 (43.5)	394 (50.6)
Diabetes	294 (29.0)	128 (52.2)	12 (17.4)	209 (26.9)
Congestive heart failure	311 (30.7)	106 (43.3)	29 (42.0)	300 (38.6)
Stroke	298 (29.4)	72 (29.4)	15 (21.7)	225 (28.9)
Vascular disease	499 (49.3)	163 (66.5)	26 (37.7)	361 (46.4)
CHA_2DS_2VASc score				
0	0 (0.0)	10 (4.1)	15 (21.7)	26 (3.3)
1	4 (0.4)	18 (7.3)	7 (10.1)	45 (5.8)
2	68 (6.7)	27 (11.0)	15 (21.7)	87 (11.2)
3	182 (18.0)	43 (17.6)	13 (18.8)	117 (15.0)
4	224 (22.1)	40 (16.3)	6 (8.7)	164 (21.1)
5	212 (20.9)	37 (15.1)	5 (7.2)	154 (19.8)
6	174 (17.2)	31 (12.7)	7 (10.1)	94 (12.1)
7	104 (10.3)	19 (7.8)	1 (1.4)	57 (7.3)
8	35 (3.5)	13 (5.3)	0 (0.0)	31 (4.0)
9	10 (1.0)	7 (2.9)	0 (0.0)	3 (0.4)
Total CHA_2DS_2VASc score, mean (SD)	4.72 (1.61)	4.21 (2.20)	2.52 (1.98)	4.16 (1.93)
ORBIT				
Age > 74 y	942 (93.0)	91 (37.1)	9 (13.0)	484 (62.2)
Low hemoglobin (< 13 g/dL in males and <12 g/dL in females)	1 (0.1)	6 (2.4)	0 (0.0)	2 (0.3)
Bleeding history	325 (32.1)	85 (34.7)	21 (30.4)	293 (37.7)
eGFR < 60 mL/min/1.73 m^2	22 (2.2)	29 (11.8)	0 (0.0)	14 (1.8)
Antiplatelet	303 (29.9)	88 (35.9)	17 (24.6)	212 (27.2)
ORBIT score				
0	33 (3.3)	68 (27.8)	33 (47.8)	159 (20.4)
1	479 (47.3)	60 (24.5)	12 (17.4)	249 (32.0)
2	187 (18.5)	58 (23.7)	17 (24.6)	133 (17.1)
3	197 (19.4)	31 (12.7)	6 (8.7)	166 (21.3)
4	110 (10.9)	22 (9.0)	1 (1.4)	68 (8.7)
5	7 (0.7)	4 (1.6)	0 (0.0)	3 (0.4)
6	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
7	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Total ORBIT score, mean (SD)	1.89 (1.13)	1.59 (1.41)	0.99 (1.10)	1.67 (1.28)

[a]All values are n (%) unless otherwise specified.
Abbreviations: eGFR = estimated glomerular filtration rate, SMI = serious mental illness.

and AF with comorbid common mental disorders. All relative risks were adjusted for age, sex, and total CHA_2DS_2-VASc and total ORBIT scores. All statistical analyses were performed in R. A P value < .05 was considered significant.

Ethical Approval

This study was conducted using CRIS, an anonymized dataset approved for secondary analyses by the Oxfordshire Research Ethics Committee C (reference 08/H0606/71). The project (ID: 21–047) was approved by the CRIS Oversight Committee.

RESULTS

Cohort Identification

On the basis of the search strategy described in the Methods section, we identified 2,105 active patients with a diagnosis of AF in their electronic mental health record during the study period. Among these patients: 48% were last diagnosed with dementia, 12% with SMI, 3% with substance use disorder, and 37% with a common mental disorder. Table 1 shows the characteristics of the study cohort. Overall, patients with SMI or substance use disorders were younger than those with dementia or common mental disorders. The proportion of people having cognitive problems, physical illness, or ADL impairment was high among the entire AF cohort.

CHA_2DS_2-VASc and ORBIT Scores

Table 2 shows the distribution of AF patients across the various CHA_2DS_2-VASc and ORBIT components stratified by mental health status. The proportion of patients having comorbid hypertension, diabetes, or vascular diseases was significantly higher (P < .001) among patients with SMI compared to those having dementia (despite the younger overall age of people with SMI), substance use disorders, or common mental disorder. However, the mean CHA_2DS_2-VASc score and mean ORBIT score were significantly higher (P < .001) in people with dementia compared to all other categories. The stroke and bleeding scores were significantly lower (P < .001) among people with substance use disorders compared to people with SMI or common mental disorders.

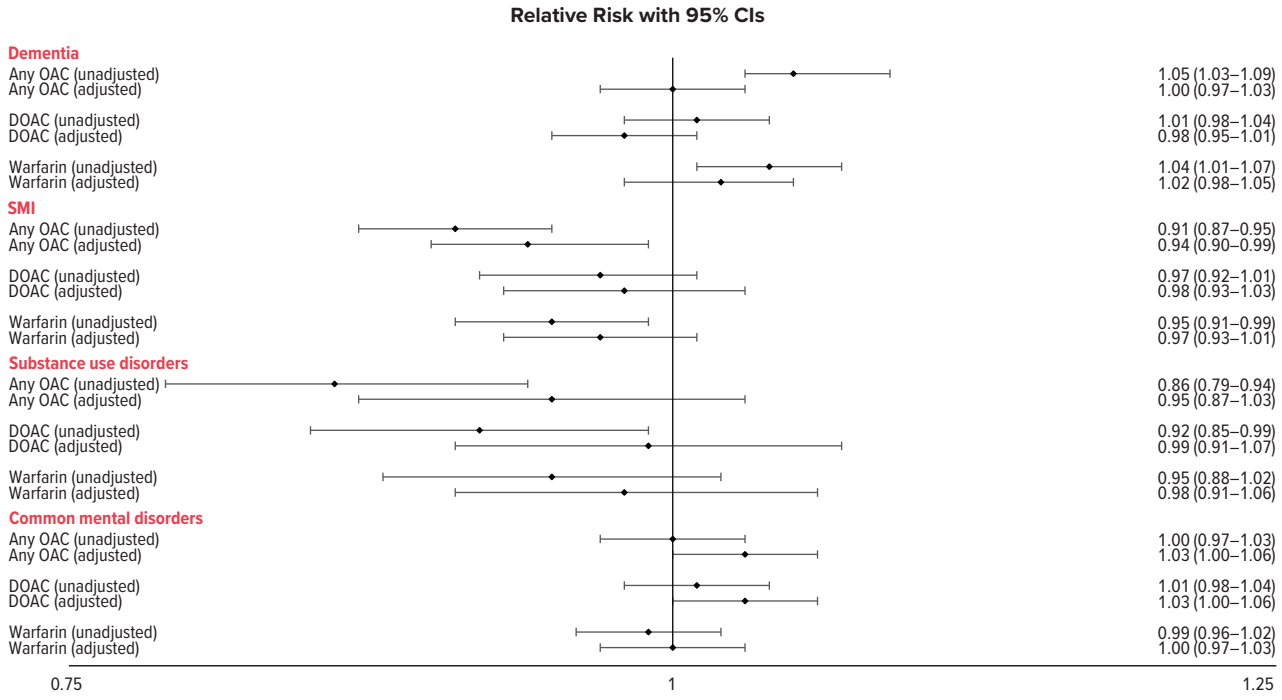
Oral Anticoagulant Prescription

Among AF patients having a CHA_2DS_2-VASc score ≥ 1, 53% of those with dementia, 38% of those with SMI, 37% of those with substance use disorder, and 49% of those with common mental disorders were prescribed an OAC. OAC prescription was significantly lower among people with an SMI diagnosis, compared to a dementia (P < .001) or a common mental disorder (P = .004) diagnosis. Multiple regression analysis using a Poisson regression model with robust standard errors also showed that with adjustment for age, sex, and CHA_2DS_2-VASc and ORBIT scores, SMI compared to non-SMI (dementia, substance use disorders, and common mental disorders) was associated with lower prescription of any OAC (adjusted risk ratio [aRR]: 0.94; 95% CI, 0.90–0.99) (Figure 1).

Noteworthily, among people with AF and dementia, the mean ORBIT score was higher among patients who were not prescribed (vs prescribed) an

Figure 1.

Effect of Mental Illnesses on the Prescription of Oral Anticoagulation Therapy Among People With Atrial Fibrillation[a]



[a]Adjusted estimates are adjusted for age, sex, and total CHA_2DS_2VASc and total ORBIT scores. Estimates are obtained using Poisson regression model with robust standard errors. Dementia is compared to non-dementia (including SMI, substance use disorders, and common mental disorders). SMI is compared to non-SMI (including dementia, substance use disorders, and common mental disorders). Common mental disorders are compared to SMI, substance use disorders, and dementia. Substance use disorders is compared to SMI, dementia, and common mental disorders.
Abbreviations: DOAC = direct-acting oral anticoagulant, OAC = oral anticoagulant, SMI = serious mental illness.

OAC (mean [SD]: 1.98 [1.14] vs 1.81 [1.12], $P = .018$). However, among people with SMI, those not prescribed an OAC had a lower bleeding risk (mean [SD]: 1.40 [1.41] vs 1.98 [1.38], $P = .002$) than those prescribed OAC. No significant difference in the bleeding risk between those prescribed versus not prescribed an OAC was noted among people with substance use disorder or common mental disorder (Table 3).

When analyzing the effect of mental illness severity (measured by HoNOS) on the prescription of OAC in the full AF cohort, we found that alcohol or substance dependency was associated with lower prescription of any OAC, particularly warfarin. Warfarin was also less likely to be prescribed to people with ADL impairment.

When the AF cohort was stratified by mental illness, we found that among people with comorbid SMI, alcohol or substance dependence and ADL impairment were associated with lower prescription of any OAC. Warfarin was also less likely to be prescribed to people with SMI having serious self-injury, alcohol or substance dependency, hallucinations or delusions, or ADL impairment (comparing people with SMI having significant problems related to these domains to those having no or minor problems requiring no action). Among people with

Table 3.

OAC Prescription Rates and Bleeding Risks Among People With AF Who Had a CHA_2DS_2VASc Score ≥ 1, Stratified by Mental Illness[a]

Prescription Variable	Dementia (n = 1,013)	SMI (n = 235)	Substance Use Disorders (n = 54)	Common Mental Disorders (n = 752)
Any OAC	534 (52.7)	90 (38.3)	20 (37.0)	371 (49.3)
Warfarin	214 (21.1)	25 (10.6)	6 (11.1)	127 (16.9)
DOAC	320 (31.6)	65 (27.7)	14 (25.9)	244 (32.4)
No OAC	479 (47.3)	145 (61.7)	34 (63.0)	381 (50.7)
ORBIT score by status of being prescribed any OAC, mean (SD)				
Yes	1.81 (1.12)	1.98 (1.38)	1.05 (1.19)	1.80 (1.23)
No	1.98 (1.14)	1.40 (1.41)	1.18 (1.11)	1.64 (1.30)

[a]All values are n (%) unless otherwise specified.
Abbreviations: AF = atrial fibrillation, DOAC = direct-acting oral anticoagulant, OAC = oral anticoagulant, SMI = serious mental illness.

Table 4.
Association Between the Severity of Mental Illness (Measured by HoNOS Components) and the Prescription of Oral Anticoagulation Therapy Among People With Atrial Fibrillation[a]

HoNOS Component	AF Cohort			AF and Comorbid Dementia			AF and Comorbid SMI			AF and Comorbid Substance Use Disorder			AF and Comorbid Common Mental Disorder		
	Any OAC	DOAC	Warfarin	Any OAC	DOAC	Warfarin	Any OAC	DOAC	Warfarin	Any OAC	DOAC	Warfarin	Any OAC	DOAC	Warfarin
Self-injury	1.01 (0.93–1.09)	1.02 (0.94–1.10)	0.96 (0.89–1.04)	1.01 (0.86–1.20)	1.10 (0.92–1.32)	0.93 (0.78–1.12)	0.90 (0.69–1.19)	0.97 (0.74–1.28)	0.84 (0.77–0.91)	0.86 (0.66–1.11)	0.89 (0.67–1.18)	0.78 (0.64–0.96)	1.04 (0.95–1.15)	1.01 (0.91–1.12)	1.00 (0.90–1.11)
Alcohol or substance dependence	0.92 (0.85–0.99)	0.98 (0.91–1.06)	0.92 (0.86–0.98)	0.91 (0.76–1.10)	0.97 (0.81–1.17)	0.89 (0.76–1.03)	0.87 (0.76–0.99)	0.90 (0.79–1.03)	0.92 (0.87–0.98)	1.05 (0.79–1.40)	0.90 (0.74–1.10)	0.93 (0.71–1.21)	0.95 (0.85–1.06)	1.03 (0.92–1.14)	0.94 (0.85–1.04)
Cognitive problems	0.97 (0.94–1.01)	0.97 (0.93–1.00)	0.99 (0.96–1.02)	0.97 (0.91–1.02)	0.97 (0.91–1.03)	1.01 (0.94–1.07)	0.95 (0.86–1.04)	0.95 (0.86–1.04)	0.94 (0.86–1.03)	0.97 (0.77–1.23)	1.00 (0.81–1.24)	0.84 (0.70–0.99)	0.95 (0.90–1.00)	0.94 (0.89–1.00)	0.98 (0.92–1.03)
Physical illness or disability problems	1.00 (0.97–1.04)	1.03 (0.99–1.06)	0.98 (0.94–1.01)	1.00 (0.96–1.05)	1.03 (0.98–1.08)	0.98 (0.93–1.03)	1.04 (0.94–1.14)	0.98 (0.89–1.09)	1.04 (0.95–1.13)	1.04 (0.83–1.31)	1.00 (0.82–1.23)	0.97 (0.79–1.19)	0.99 (0.93–1.05)	1.02 (0.96–1.09)	0.95 (0.89–1.01)
Hallucinations or delusions	0.97 (0.93–1.01)	0.99 (0.95–1.03)	0.99 (0.95–1.03)	0.96 (0.90–1.03)	0.96 (0.90–1.04)	1.02 (0.95–1.09)	0.96 (0.88–1.05)	1.01 (0.93–1.11)	0.92 (0.85–0.99)	1.24 (1.03–1.51)	1.19 (1.01–1.40)	0.92 (0.82–1.04)	1.04 (0.97–1.12)	1.00 (0.92–1.08)	1.07 (0.99–1.16)
Depressed moods	1.06 (1.03–1.10)	1.07 (1.03–1.11)	1.02 (0.98–1.05)	1.09 (1.03–1.15)	1.09 (1.02–1.16)	1.03 (0.96–1.09)	1.06 (0.95–1.17)	1.10 (0.99–1.23)	1.02 (0.92–1.13)	1.06 (0.86–1.30)	1.11 (0.92–1.34)	0.96 (0.80–1.15)	1.05 (0.99–1.10)	1.04 (0.98–1.10)	1.02 (0.97–1.08)
Other mental problems	1.05 (1.02–1.08)	1.05 (1.01–1.08)	1.00 (0.97–1.04)	1.05 (1.01–1.10)	1.05 (1.00–1.10)	1.01 (0.96–1.06)	1.03 (0.94–1.12)	1.03 (0.94–1.12)	1.00 (0.92–1.09)	1.07 (0.84–1.36)	1.12 (0.90–1.38)	0.83 (0.70–0.99)	1.06 (1.01–1.12)	1.04 (0.98–1.10)	1.01 (0.96–1.07)
Activities of daily living problems	0.98 (0.96–1.02)	1.02 (0.98–1.05)	0.96 (0.93–0.99)	1.00 (0.96–1.05)	1.05 (1.00–1.10)	0.96 (0.92–1.01)	0.90 (0.83–0.98)	0.91 (0.83–1.00)	0.91 (0.84–0.99)	0.99 (0.75–1.32)	0.96 (0.74–1.26)	0.84 (0.67–1.06)	1.00 (0.95–1.05)	1.00 (0.95–1.06)	0.98 (0.93–1.04)

[a]Estimates represent the relative risks with 95% CIs. Estimates are adjusted for age, sex, and total CHA_2DS_2-VASc and total ORBIT scores. Estimates are obtained using Poisson regression model with robust standard errors. For each HoNOS domain, having a significant problem (score ≥ 2) was compared to having no or minor problem requiring no action (score ≤ 1).
Abbreviations: AF = atrial fibrillation, DOAC = direct-acting oral anticoagulant, HoNOS = Health of the Nation Outcome Scales, OAC = oral anticoagulant, SMI = serious mental illness.

AF and comorbid substance use disorder, having significant self-injury problems, cognitive problems, or other mental illnesses was associated with lower prescription of warfarin. No association between these HoNOS components and OAC prescription was noted among people with dementia or common mental disorders (Table 4).

DISCUSSION

This study provides insights into the relationship between mental illness severity and functional impairment and the prescription of OAC, using electronic health records from a secondary mental health service. After adjustment for age, sex, and CHA_2DS_2-VASc and ORBIT scores, patients with AF and comorbid SMI were less likely to be prescribed any OAC compared to those with dementia, substance use disorders, or common mental disorders. Alcohol or substance dependence was associated with lower prescription of any OAC (particularly warfarin) both in the full AF cohort and among people with AF and comorbid SMI. Among the full cohort of AF patients, warfarin was less likely to be prescribed to those having ADL impairment, whereas among the subgroup of AF patients with comorbid SMI, it was less likely to be prescribed to those having serious self-injury, hallucinations or delusions, and ADL impairment. Self-injury, cognitive problems, and other mental illnesses were associated with lower likelihood of warfarin prescription among people with AF and comorbid substance use disorder.

Our findings suggest that 62% of AF patients with SMI considered at high risk of stroke (CHA_2DS_2-VASc score ≥ 1) were not prescribed OAC; surprisingly, this group had a significantly lower mean ORBIT score than those prescribed an OAC. Although this finding could be partly attributed to underrecording of physical conditions in mental health care records (resulting in physical conditions being missed thus a lower ORBIT score), it also tallies with the OAC treatment gap between people with a diagnosis of SMI and the general population previously reported in the literature. A recent study[25] evaluating anticoagulation prescription trends over the past 10 years in a general hospital setting in the UK showed that among AF patients with a CHA_2DS_2-VASc score ≥ 2, those with SMI were less likely than

the general population to be prescribed any OAC (44% vs 54%, $P < .001$) until 2019, although since then the gap has diminished. Højen et al[5] recently reported that among people diagnosed with AF with comorbid schizophrenia, 34% compared to 54% of those without schizophrenia were started on OAC treatment in the first year after diagnosis. Although there was an overall increasing trend over time (2000–2018) in OAC initiation (regardless of schizophrenia status), the disparity remained significant until 2018.[5] Another Danish study[6] showed that schizophrenia and bipolar disorder were significantly associated with lower frequency of OAC among people with AF. This was also confirmed by Jaakkola et al,[7] who reported that any mental health condition, including bipolar disorder and schizophrenia, was associated with lower OAC initiation.

Many studies[16–19] have assessed the effect of mental illness–related symptoms and function on outcomes such as mortality; however, none has looked at their effect on OAC prescription. Hayes et al[16] reported that mortality risk was significantly increased among people with ADL impairment (HoNOS subscale) after controlling for many covariates, including physical health, mental health symptoms and behaviors, and sociodemographic factors. Another study[17] looking at associations between symptoms and mortality in people with SMI reported that mortality was significantly associated with physical illness/disability but not with hallucinations and delusions. The same study[17] reported a positive association between subclinical depression and mortality among people with schizophrenia. Most people with SMI, including bipolar disorder and schizophrenia, do not die from the mental illness itself; instead, increased mortality is due to physical health causes.[26] The association between alcohol or substance dependence and the low prescription of warfarin among people with AF, reported here, could be explained by the fact that warfarin is relatively contraindicated in people with chaotic alcohol or substance dependence, as it may increase patients' bleeding risk.[27] Additionally, the negative association of serious self-injury, hallucinations or delusions, and ADL impairment with warfarin prescription rates among people with SMI could be explained by the fact that it has many interactions and requires continuous monitoring, as well as its toxicity in overdose.

Our study has limitations. First, the analysis is based on data extracted from electronic health records using either an NLP-based or a keyword search approach. Although the major variables were validated, the possibility of having errors in the data cannot be excluded. Second, extracting data from mental health records means that underrecording of physical conditions in the mental health services could have influenced our results. Additionally, we may not have included those for which the medication was listed in primary care only, which could have contributed to underdetection bias. However, our inclusion of only people with at least two contacts or an admission was designed to mitigate this risk. Third, people with schizophrenia, bipolar disorder, mania, and severe depression with psychotic symptoms were grouped under one category (SMI) due to the small number of people diagnosed with each condition. Thus, a comparison between these conditions was not possible. Fourth, findings of this study represent associations between various mental illnesses or mental illness severity with OAC prescription and do not necessarily imply causality. Fifth, it is possible that the low prescription rates of OAC may not universally reflect undertreatment, as they could be related to considered clinical decision making involving other, unquantified, non-modifiable factors. Finally, although findings of this study may be generalizable, particularly as it covers a large population, further research is needed in other geographical areas to confirm generalizability and validate the results or electronic health record searches.

Our study is the first to investigate the association between mental illness severity and the prescription of OAC among people with AF. People with AF and comorbid SMI were less likely to be prescribed any OAC compared to those with dementia, substance use, and common mental disorders, with factors such as alcohol or substance dependence, ADL impairment, self-injury, hallucinations or delusions, and significant cognitive problems negatively influencing the likelihood of indicated OAC prescription. Future studies are required to validate the results and confirm generalizability of the findings in other health care settings.

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