STROKE PREVENTION IN PATIENTS WITH ATRIAL FIBRILLATION AND COMORBID PHYSICAL AND MENTAL HEALTH PROBLEMS

Farran, Dina

Awarding institution:
King's College London

STROKE PREVENTION IN PATIENTS WITH ATRIAL FIBRILLATION AND CO-MORBID PHYSICAL AND MENTAL HEALTH PROBLEMS

Dina Farran

Thesis submitted for the degree of

Master/Doctor of Philosophy (MPhil/PhD)

Institute of Psychiatry, Psychology and Neuroscience

King's College London

May 2024

ABSTRACT

Background

Atrial fibrillation (AF), the most prevalent cardiac arrhythmia, is associated with an increased risk of stroke leading sometimes to disability and death. In this project, we aim to improve patient safety by screening for stroke risk among people with AF and co-morbid mental illness.

Methods

(a) Conducted a systematic review and meta-analysis on prevalence, management, and outcomes of AF in people with Serious Mental Illness (SMI) versus the general population.

(b) Evaluated oral anticoagulation (OAC) prescription trends in people with AF and co-morbid SMI in King's College Hospital.

(c) Identified the recorded rates of OAC prescription among people with AF and various mental illnesses and evaluated the association between mental illness severity and OAC prescription in eligible patients in South London and Maudsley (SLaM) NHS Foundation Trust.

(d) Implemented an electronic clinical decision support system (eCDSS) consisting of a visual prompt on patient electronic Personal Health Record to screen for AF-related stroke risk in three Mental Health of Older Adults wards at SLaM.

(e) Assessed the feasibility and acceptability of the eCDSS by qualitatively investigating clinicians' perspective of the potential usefulness of the eCDSS (pre-intervention) and their experiences and their views regarding its impact on clinicians and patients (after intervention).

Results

(a) People with SMI had low reported rates of AF. AF patients with SMI were less likely to receive OAC than the general population. When receiving warfarin, people with SMI, particularly bipolar disorder, experienced poor anticoagulation control compared to the general population. Meta-analysis showed that SMI was not significantly associated with an increased risk of stroke or major bleeding when adjusting for underlying risk factors.

(b) Among AF patients having a high stroke risk, those with co-morbid SMI were less likely than non-SMI patients to be prescribed any OAC, particularly warfarin (but not DOACs). However, there was no evidence of a significant difference between the two groups since 2019.

(c) Adjusting for age, sex, stroke and bleeding risk scores, patients with AF and co-morbid SMI were less likely to be prescribed any OAC compared to those with dementia, substance use disorders or common mental disorders. Among AF patients with co-morbid SMI, warfarin was less likely to be prescribed to those having alcohol or substance dependency, serious self-injury, hallucinations or delusions and activities of daily living impairment.
(d) Clinicians were asked to confirm the presence of AF, clinically assess stroke and bleeding risks, record risk scores in clinical notes and refer patients at high risk of stroke to OAC clinics.
(e) Clinicians reported that the eCDSS saved time, prompted them towards guidelines, boosted their confidence, and identified patients at risk. Perceived barriers to using the tool included low admission rate of AF cases, low or insufficient visibility of the alert/awareness of the tool, and impact of the eCDSS on workload.

Conclusions

This study presents a unique opportunity to quantify AF patients with mental illness who are at high risk of severe outcomes, using electronic health records. This has the potential to improve health outcomes and therefore patients' quality of life.

ACKNOWLEDGEMENTS

First and foremost, I would like to thank my supervisors Professor Fiona Gaughran and Professor Mark Ashworth for their continuous support and guidance throughout my PhD journey. Your expertise and insights have been invaluable in shaping this PhD project. I have greatly enjoyed working under your supervision.

I am incredibly grateful to my family and friends who have been very supportive and understanding during this journey. Your love and encouragement have powered me through tough times.

I would like to thank my PhD friend, Dr Dipen Patel, whose pioneering efforts set the foundation for the implementation of similar eCDSSs in SLaM. Your support has been greatly appreciated. I would like to extend my sincere thanks to all the psychiatrists, cardiologists, general practitioners (GPs), pharmacists, nurses, professors, IT teams who contributed to data extraction, design of the eCDSS, or participated in the interviews. Your insights and collaboration have been critical to the success of this project.

Lastly, a huge thank you to the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust and the Centre for Doctoral Training (CDT) in Data-Driven Health at King's College London (KCL) for funding this work. This project could not have been done without your support.

TABLE OF CONTENTS

LIST OF FIGURES & TABLES

LIST OF ABBREVIATIONS

ADL: Activity of Daily Living
AF: Atrial Fibrillation
ALT: Alanine Aminotransferase
AOR: Adjusted Odd Ratio
AP: Alkaline Phosphatase
aPD: adjusted Proportion Difference
ARC: Applied Research Collaboration
aSHR: adjusted Subdistribution Hazard Ratio
AST: Aspartate Aminotransferase
BD: Bipolar Disorder
BRC: Biomedical Research Centre
CCIO: Chief Clinical Information Officer
CDT: Centre for Doctoral Training
CHD: Coronary Heart Disease
CRIS: Clinical Records Interactive Search
DOACs: Direct Oral Anticoagulants
eCDSS: electronic Clinical Decision Support System
eGFR: estimated Glomerular Filtration Rate
EHR: Electronic Health Records
EKG or ECG: Electrocardiogram
ePHR: electronic Personal Health Record
ePJS: electronic Patient Journey System
ePMA: electronic Prescribing and Medicines Administration
GCSE: General Certificate of Secondary Education
GP: General Practitioner
HoNOS: Health of the Nation Outcome Scales
HR: Hazard Ratio
INR: International Normalised Ratio
IT: Information Technology
KCH: King's College Hospital
KCL: King's College London
KERRI: King's Electronic Records Research Interface
MAUD: Maudsley intranet
MHC: Mental Health Condition
MHOA: Mental Health of Older Adult
NICE: National Institute for Health and Care Excellence
NIHR: National Institute for Health Research
NLP: Natural language processing
NOAC: Non-vitamin K antagonist oral anticoagulant
NOS: Newcastle-Ottawa Scale
NSAIDs: nonsteroidal anti-inflammatory drugs
OAC: Oral Anticoagulation
OAT: Oral Anticoagulation Therapy
OR: Odds Ratio

PHH: Physical Health Hub
PPI: Patient and public involvement
PT: Prothrombin Time
PTSD: Post-Traumatic Stress Disorder
RD: Risk Difference
RR: Relative Risk
SCZ: Schizophrenia
SD: Standard Deviation
SLaM: South London and Maudsley
SMI: Serious Mental Illness
SWIFT: What-If Technique
TIA: Transient Ischemic Attack
TTR: Time in Therapeutic Range
UAT: User Acceptance Testing
VHA: Veterans Health Administration
VKA: Vitamin K Antagonist

STATEMENT OF PERSONAL CONTRIBUTION

I led all five studies under the supervision and guidance of Professor Fiona Gaughran and Professor Mark Ashworth.

In the systematic review and meta-analysis (paper 1), I searched the databases for relevant articles, extracted and analysed data, assessed the risk of bias, and wrote the manuscript. A second reviewer (Olwyn Feely) worked independently on data extraction and analysis to help ensure the risk of bias is kept minimal.

In the first observational study (paper 2), Daniel Bean did the data extraction because I did not have permission to access King's College Hospital patient data. However, I did participate in data analysis and wrote the manuscript.

In the second observational study (Paper 3), Matthew Broadbent helped with data extraction; however, I conducted the entire data analysis and wrote the manuscript.

For the development of the electronic clinical decision support system, I drafted the clinical and intervention protocols with the guidance of psychiatrists, cardiologists, GPs, nurses, and the Information Technology (IT) team. I also submitted the proposal for ethical clearance, developed all the training material for clinicians to perform the required clinical assessment, and informed clinicians about the digital tool. Additionally, I supervised the implementation process and tested the intervention. In collaboration with the digital health lead nurse and the Chief Clinical Information Officer (CCIO), I evaluated the clinical safety of the digital tool, and developed a clinical risk management plan.

In the last two studies (Paper 4 &5), I developed the surveys, questionnaires for interviews and all the study materials required including consent form and participant information sheet. Additionally, I collected data (through surveys and interviews), analysed them, and wrote the manuscripts. In paper 4, a Master student independently worked on data extraction and analysis to ensure that more than one reviewer is checking the data, thus reducing the risk of bias. Due to time limitation, this was not done for paper 5.

All manuscripts were circulated to co-authors upon completion for their input.

PREFACE

This thesis follows the "thesis incorporating publications" format. A number of chapters are composed of published, peer-reviewed, journal articles of which I am first author. This thesis includes five journal articles which have been reproduced in full. Three papers are published, one paper is 'under review', and one paper is 'in preparation' (will be submitted to a peer reviewed journal soon), these include:

- Farran, D., Feely, O., Ashworth, M., & Gaughran, F. (2022). Anticoagulation therapy and outcomes in patients with atrial fibrillation and serious mental illness: A systematic review and meta-analysis. Journal of Psychiatric Research. https://doi.org/10.1016/j.jpsychires.2022.11.002
- Farran, D., Bean, D., Wang, T., Msosa, Y., Casetta, C., Dobson, R., Teo, JT., Scott, P., Gaughran, F. (2022). Anticoagulation for atrial fibrillation in people with serious mental illness in the general hospital setting. *Journal of Psychiatric Research*, *153*, 167-173. https://doi.org/10.1016/j.jpsychires.2022.06.044

- Farran D, Broadbent M, Dima A, Ashworth M, Gaughran F. Factors Associated With Oral Anticoagulant Use in Patients With Atrial Fibrillation and Mental Disorders. The Journal of clinical psychiatry. 2024 Jan 3;85(1):50936. https://doi.org/10.4088/JCP.23m14824

- Farran D, Cheang H, Onwumere J, Ashworth M, Gaughran F. Electronic Clinical Decision Support System to Screen for Stroke Risk among Patients with Atrial Fibrillation: Perspectives of Clinicians in a Mental Healthcare Setting. Submitted to BMC psychiatry.

- Farran D, Onwumere J, Funnell N, Bishara D, Tiedt T, Larkin D, Arroyo B, Ashworth M, Gaughran F. Clinicians' Experience with an Electronic Clinical Decision Support System to Screen for Stroke Risk in a Mental Healthcare Setting.

OUTLINE OF THESIS

- Chapter 1 provides a general introduction to mental and physical health of people with major mental illness.
- Chapter 2 presents findings of a systematic review and meta-analysis on the prevalence, management, and outcomes of atrial fibrillation (AF) in people with serious mental illness [Paper 1].
- Chapter 3 describes findings of an observational study aiming to understand trends of oral anticoagulation prescription among patients with AF admitted to King's College Hospital [Paper 2].
- Chapter 4 presents the results of another observational study aiming to investigate rates of oral anticoagulation prescription and association between mental illness severity and oral anticoagulation prescription in South London and Maudsley (SLaM) NHS foundation trust [Paper 3].
- Chapter 5 gives an overview of electronic Clinical Decision Support Systems (eCDSS) and their effectiveness in the management of stroke related to AF.
- Chapter 6 summarises the protocols used to design, implement, and evaluate the acceptability of an eCDSS to screen for stroke risk among people with AF in a mental healthcare setting.
- Chapter 7 presents findings of a mixed method study assessing clinicians' perception of an eCDSS to screen for stroke risk associated with AF in SLaM [Paper 4].
- Chapter 8 describes findings of a mixed method study evaluating clinicians' experience with an eCDSS to screen for stroke risk associated with AF in SLaM [Paper 5].
- Chapter 9 provides a general discussion. It summarises the findings, discusses the research and clinical implications, and highlights the strengths and limitations of the project studies.

PART 1- MENTAL AND PHYSICAL HEALTH OF PEOPLE WITH MAJOR MENTAL ILLNESS

CHAPTER 1- GENERAL INTRODUCTION

1.1 Major mental illness

The term mental illness refers to a range of complex psychiatric conditions that significantly affect an individual's emotional, cognitive and behavioural functioning (1,2). These conditions often result in a substantial impairment in activities of daily living, as well as difficulties in fulfilling responsibilities and engaging in educational, vocational, and social activities within the community (1,2).

Many mental health conditions are considered chronic in nature with symptoms persisting for extended periods of time and often requiring long-term management (3). Examples of major mental health conditions include bipolar disorder, schizophrenia spectrum disorder, major depressive disorder and dementia (3).

Bipolar disorder is a mood disorder characterised by fluctuations in mood, energy levels and activity (4). The condition comprises manic or hypomanic episodes and depressive episodes. Manic episodes consist of an irritable or elevated mood, increased energy, and grandiosity or a high self-esteem (4,5). Other characteristic features include racing thoughts, rapid speech, engaging in high risk or impulsive behaviours, and decreased need for sleep (4,5). Hypomanic episodes are less intense and do not lead to significant impairment in social or occupational functioning (4,5). On the other hand, during depressive episodes, people experience persistent feelings of hopelessness, sadness, and loss of pleasure or interest in activities (4,5). Other common symptoms include fatigue, changes in sleep patterns and appetite, difficulty concentrating, feelings of guilt or worthlessness, and in extreme cases suicidal thoughts (4,5). Psychotic symptoms such as delusions (fixed false beliefs out of keeping with the person's culture or background) and hallucinations (a perception in the absence of a real stimulus) are much more frequent in manic than depressive episodes (4,5).

Schizophrenia spectrum disorder encompasses a group of conditions including schizophrenia, schizoaffective disorder, delusional disorder, schizotypal personality disorder, schizophreniform disorder, and brief psychotic disorder (6). These conditions may include both "positive" and "negative" symptoms (6). Positive psychotic symptoms of schizophrenia include hallucinations, delusions, disorganised thinking/incoherent speech, and disorganised or abnormal motor behaviour (6). Negative symptoms involve reduction or loss of normal functioning and include reduced emotional expression, reduced speech output, decreased ability to experience pleasure, and loss of motivation (6).

Major depressive disorder comprises one or more depressive episodes lasting for at least two weeks (7,8). It is characterised by lack of pleasure or interest in activities, and a pervasive and profound feeling of sadness (7,8). It is classified as mild, moderate and severe and may be accompanied by psychotic symptoms.

Finally, dementia is a term referring to a broad range of symptoms related to a decline in the cognitive function interfering with one's ability to perform daily activities (9). The most common type of dementia is Alzheimer's disease although there are many others including Lewy body disease, vascular dementia, and frontotemporal dementia (9). The main characteristics of dementia include memory impairment (difficulty remembering), cognitive decline (difficulty judging, reasoning, problem solving), communication problems (difficulty in expressing coherently), disorientation (confusion about time, place, and identity), impaired motor function, and loss of independence (9).

1.2 Health of the Nation Outcome Scales (HoNOS)

The Health of the Nation Outcome Scales (HoNOS) is a standardised tool for assessing the severity and outcomes of mental health conditions (10). It provides a multidimensional evaluation of an individual's mental health status, functioning and progress over time (10). The scale includes 12 items grouped into four subscales: behaviour (items 1-3), impairment (items 4-5), symptoms (items 6-8) and social functioning (items 9-12) (10,11). The behaviour subscale examines the

presence and severity of challenging behaviours (aggressive or self-harming) (10,11). Impairment subscale assesses a person's level of impairment in various areas of functioning including physical, cognitive, and social aspects (10,11). The symptoms subscale evaluates psychiatric indications such as delusions, hallucinations, anxiety, and depression (10,11). Finally, social functioning focuses on a person's ability to manage daily living tasks, to engage in social relationships, and to maintain educational activities and employment (10,11). Each item of the HoNOS is rated on a scale from 0 to 4 with 4 representing greater severity (10,11). The sum of the item scores gives a total score ranging from 0 to 48. Interpretation of results can be done on item, subscale, or total score level (10, 11).

1.3 Cardiovascular and cerebrovascular diseases in people with major mental illness

Compared to the general population, people with bipolar disorder, schizophrenia, major depressive disorder, and dementia have a shorter life expectancy (12,13,14). Although this is partly attributable to suicide, literature has shown that physical diseases account for most premature deaths (15,16,17). Among these physical conditions, cardiovascular and cerebrovascular diseases are the main contributors to early mortality in this population (16,17).

A large-scale meta-analysis of more than 3 million patients with serious mental illness (SMI) (schizophrenia, bipolar disorder or major depressive disorder), reported that in cross sectional studies the pooled prevalence of cardiovascular diseases was 10% in people with SMI with an individual rate of 8% in people with bipolar disorder, 12% in those with schizophrenia and 12% in those with major depressive disorder (18).

Adjusting for confounders, SMI patients had significantly higher odds of cardiovascular (odds ratio, OR 1.53, 95% CI: 1.27-1.83; 11 studies), and cerebrovascular diseases (OR 1.42, 95% CI: 1.21-1.66) compared to controls (18). Specifically, people with major depressive disorder were found to be at high risk of coronary heart disease whereas those with schizophrenia were found to be at high risk of cerebrovascular disease, coronary heart disease and congestive heart failure (18). Similarly, in longitudinal studies, a higher incidence of cardiovascular (hazard ratio, HR 1.78, 95%

CI: 1.60-1.98) and cerebrovascular diseases (HR 1.64, 95% CI: 1.26-2.14) was noted in SMI patients vs controls (18). People with schizophrenia, bipolar disorder and depressive disorder were all at elevated risk of cardiovascular-related death compared to controls (18).

As for dementia, two meta-analyses reported a significant association between all-cause dementia and coronary heart diseases (Relative Risk, RR = 1.26, 95% CI; 1.06–1.49 and OR = 1.45, 95% CI; 1.21–1.74) (19,20). The relationship between dementia and cardiovascular diseases is bidirectional with cardiovascular risk factors leading to the development and progression of both cardiovascular diseases and dementia (21,22). Cerebrovascular diseases are major contributors to dementia accounting for around 20% of cases with atherosclerotic and arteriolosclerotic mechanisms being the most common (21).

Major mental health conditions are associated with a high prevalence of modifiable cardiovascular risk factors (23,24). People living with schizophrenia, bipolar disorder, major depressive disorder and dementia are more likely to live a sedentary lifestyle, smoke, have obstructive sleep apnoea, and/or follow a poor diet (23-26). There is 2- to 4- fold increase in the rate of diabetes, hypertension, dyslipidaemia, and metabolic syndrome among people with major mental illness compared to the general population (27,28,29). Other factors such as active features of illness, antipsychotic therapies, substance use disorders, medication nonadherence, poor health literacy, low socioeconomic status, and disparities in healthcare access could also worsen the cardiovascular outcomes among this population (30-34).

1.4 Atrial Fibrillation

Atrial fibrillation (AF) is a type of arrhythmia characterised by an irregularly irregular heart rhythm (35). During an episode of AF, abnormal uncoordinated electrical impulses fire in the atria (upper chambers of the heart) leading to a poor blood flow to the ventricles (lower chambers) and a chaotic heart rhythm (35). Although AF can be asymptotic in many people, it can cause fast, fluttering or pounding heartbeats, chest pain, shortness of breath, dizziness, light-headedness, and fatigue (35). AF is typically diagnosed through physical examination, electrocardiogram (EKG or ECG) to

monitor the heart's electrical activity over a certain period and echocardiogram to identify problems with blood flow and heart muscle contractions (36).

There are three main types of atrial fibrillation: paroxysmal, persistent, and long-standing persistent. Paroxysmal AF refers to episodes of AF that are intermittent and self-terminating (36). They last less than a week and usually stop on their own without any medical intervention (36). Persistent AF is characterised by episodes of AF lasting more than seven days and requiring medical intervention to restore the sinus rhythm (36). Finally, long-standing persistent AF is a more chronic condition that persists more than one year and is sometimes hard to treat (36).

1.4.1. Stroke prevention in people with atrial fibrillation

AF is associated with a 5-fold increase in the risk of stroke (37). The rapid and irregular heartbeats related to AF can cause blood stasis, or pooling, within the atria, increasing the risk of blood clot formation in the heart. These clots can travel to the brain and block the blood flow, potentially resulting in a stroke (37). To mitigate this risk, people with AF are usually prescribed oral anticoagulation (OAC) therapy (37).

There are two main classes of oral anticoagulants: vitamin K antagonist (VKA) and non-vitamin K antagonist oral anticoagulants (NOACs) also known as direct oral anticoagulants (DOACs) (38). Among VKAs, warfarin is the most commonly used (38). It works by interfering with the action of vitamin K considered essential in the production of specific clotting factors (38). To adjust for VKA dosage, the coagulation status is usually monitored by the international normalised ratio (INR) test (39). INR is calculated from the ratio of the patient's prothrombin time (PT) (time in seconds to form a clot) to a control PT (39). The therapeutic INR range for stroke prevention in patients with AF typically lies between 2.0 and 3.0, with INR values below 2 indicating an increased risk of stroke, and values above 3 indicating an increased risk of bleeding (39). AF is also associated with an increased risk of myocardial infarction (MI) (40); however, with an INR value below the therapeutic range, a clot resulting from AF is far more likely to travel through the large arteries to the brain, leading to a stroke, rather than to the coronary ostia to cause an MI (37,41). Notably, current evidence suggests that optimal INR management for stroke prevention may not necessarily confer the same benefits for MI prevention (42). INR management is also

complex in people on warfarin, as it can be affected by co-morbidities, medications, and diet, making it challenging to optimise the patient's time in therapeutic range (TTR) (39).

Warfarin has several contraindications and clinical considerations (43). It is contraindicated in patients with hypersensitivity to warfarin or its components, active hemorrhagic conditions such as gastrointestinal bleeding or cerebral aneurysm, recent or planned surgeries involving the eye or central nervous system, and those undergoing procedures with significant bleeding risk (43). Additionally, it is not recommended for individuals with bleeding tendencies from conditions like ulceration, central nervous system hemorrhage, or severe liver disease, or for those with high non-adherence potential (43). Clinically, elderly patients using warfarin require close monitoring due to an increased risk of bleeding complications associated with age-related factors like falls, drug interactions, and cognitive status. In patients with renal impairment, warfarin may accumulate, increasing bleeding risk (43). Hepatic impairment can also enhance warfarin's anticoagulant effects, necessitating careful monitoring of the INR (43). Dietary intake of vitamin K can decrease warfarin's effectiveness, so patients should maintain a consistent intake of vitamin K-rich foods like spinach and kale (43). Consumption of grapefruit juice, cranberry juice, and alcohol can enhance warfarin's effects, increasing bleeding risk, and should be limited (43). Warfarin also has numerous drug interactions that can either potentiate bleeding risk or reduce anticoagulation effectiveness, particularly with medications such as antiplatelets, NSAIDs, and certain antimicrobials (43). Close monitoring, dose adjustments, and alternative therapies may be needed when warfarin is combined with other drugs (43).

DOACs are medications that directly target specific clotting factors and consist of two main classes: oral direct factor Xa inhibitors (such as rivaroxaban, apixaban, edoxaban) and direct thrombin inhibitors (such as dabigatran) (44). The oral direct factor Xa inhibitors prevent the action of factor Xa involved in the cascade of blood clotting whereas direct thrombin inhibitors inhibit the activity of thrombin, considered a key clotting factor (44).

DOACs also have specific contraindications including active major bleeding and conditions associated with a high risk of bleeding, such as recent gastrointestinal bleeding or significant bleeding disorders (45). DOACs are also contraindicated in patients with severe renal impairment, as the kidneys are primarily responsible for eliminating these drugs, and impaired renal function

can lead to accumulation and an increased risk of bleeding (45). Additionally, patients with mechanical heart valves or moderate to severe mitral stenosis should not use DOACs due to the lack of evidence supporting their efficacy and safety in these conditions (45). DOACs have fewer drug and food interactions than warfarin, but certain situations still demand careful monitoring (45). Concomitant use of strong inhibitors of both P-glycoprotein (P-gp) and cytochrome P450 3A4 (CYP3A4), such as ketoconazole, itraconazole, ritonavir, and others, can increase the blood levels of certain DOACs, thereby elevating the risk of bleeding (45). Similarly, strong inducers of P-gp and CYP3A4, like rifampin and carbamazepine, can reduce DOAC efficacy by decreasing their blood concentrations, potentially leading to thrombotic events (45). Patients with moderate renal impairment or mild to moderate hepatic impairment require increased monitoring due to potential alterations in drug metabolism and excretion (45). DOACs are increasingly used for stroke prevention in patients with AF due to their efficacy, safety profile, and the advantage that they do not require regular INR monitoring, unlike VKAs (46).

The choice of oral anticoagulant depends on many factors including the patient's medical history, potential drug interactions and the preference of both the healthcare provider and the patient.

1.4.2 Assessment of stroke and bleeding risks in people with AF

To determine the need for OAC therapy, people with AF should undergo a stroke and bleeding risk assessment (47). CHA2DS2-VASc is the most commonly used tool to evaluate the risk of stroke whereas HASBLED or ORBIT are mostly used for the bleeding risk (Table 1) (47).

CHA2DS2-VASc estimates the annual risk of stroke in patients with AF (48). The score is calculated by assigning points to each of the following components: congestive heart failure history; hypertension history; diabetes mellitus history; stroke, transient ischemic attack (TIA), or thromboembolism history; vascular disease history; age; and sex (48). The sum of the points associated with each risk factor forms the CHA2DS2-VASc score which can range from 0 to 9 (48). A score of 0 represents a low risk of stroke, 1 represents a moderate risk except if the point is attributed based on sex alone (female aged less than 65 with no other risk factors), and any score above 1 is considered high risk (48).

The decision to prescribe OAC is usually guided by the CHA2DS2-VASc score (47). In general, the therapy should be recommended for patients having a score greater or equal than 2 and should be considered for males having a CHA2DS2-VASc of 1 (47). Although the tool identifies the stroke risk, it does not necessarily dictate the appropriate treatment strategy (47). Other factors such as bleeding risk, patient preference and clinical judgement should be also considered (47).

This requires a collaborative effort between the healthcare provider and the patient to weigh the benefits and potential risks of OAC therapy based on the patient's characteristics and medical history (47).

Age	<65 **0**	65-74 **+1**	≥75 **+2**
Sex	Male **0**	Female **+1**	
Congestive heart failure history	No **0**	Yes **+1**	
Hypertension history	No **0**	Yes **+1**	
Stroke/ transient ischemic attack (TIA)/thromboembolism history	No **0**	Yes **+1**	
Vascular disease history prior myocardial infarction, peripheral artery disease or aortic plaque	No **0**	Yes **+1**	
Diabetes history	No **0**	Yes **+1**	

Table 1. CHA_2DS_2-VASc Scale for Atrial Fibrillation Stroke Risk

HASBLED is a tool that has been used for some time to help healthcare providers assess the risk of bleeding in patients with AF (Table 2) (47). Components of the HASBLED are hypertension, renal disease, liver disease, stroke history, prior major bleeding or predisposition to bleeding, labile

INR, age > 65, medication usage predisposing to bleeding, and alcohol use (49). Each component is assigned a score of 1 (49). The sum of points attributed to each risk factor forms the HASBLED score which could range between 0 and 9 (49). A score of 0 or 1 represents a low bleeding risk, a score of 2 represents a moderate risk and a score greater or equal to 3 represents high risk (49). When the risk is low, OAC therapy can be initiated or continued however, when the risk is moderate or high, careful consideration of the benefits and potential risks associated with OAC therapy is required (47). Additionally, modifiable risk factors should be managed, and a close monitoring of the patient should be warranted (47).

Hypertension Uncontrolled, >160mmHg systolic	No **0**	Yes **+1**
Renal disease Dialysis, transplant, Creatinine>2.26 mg/dL or >200 µmol/L	No **0**	Yes **+1**
Liver disease Cirrhosis or bilirubin >2x normal with AST/ALT/AP >3x normal	No **0**	Yes **+1**
Stroke history	No **0**	Yes **+1**
Prior major bleeding or predisposition to bleeding	No **0**	Yes **+1**
Labile INR Unstable/high INRs, time in therapeutic range <60%	No **0**	Yes **+1**
Age > 65	No **0**	Yes **+1**
Medication usage predisposing to bleeding Aspirin, clopidogrel and nonsteroidal anti-inflammatory drugs (NSAIDs))	No **0**	Yes **+1**
Alcohol use ≥8 units/week	No **0**	Yes **+1**

*AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, AP: Alkaline Phosphatase

Table 2. HASBLED Scale for Major Bleeding Risk

ORBIT is another, more recent, tool recommended by the National Institute for Health and Care Excellence (NICE) to assess the bleeding risk in people with AF (Table 3) (47). ORBIT has a higher accuracy in predicting bleeding risk compared to other tools, including HASBLED (47). Components of ORBIT include anaemia, age>74 years, bleeding history, glomerular filtration rate, and treatment with antiplatelet agents (50). Each component is assigned points, and the sum of all points forms the ORBIT score which could range from 0 to 7 (50). An ORBIT score <3 is considered low, a score equals to 3 is medium risk, and any score above 3 is considered high risk (50). Like any other clinical tool, ORBIT can help in guiding healthcare providers about safety and effectiveness of OAC therapy, however, the tool is most helpful when a comprehensive assessment of the patient's characteristics and medical history is considered (47).

Anaemia Haemoglobin <13g/dl and haematocrit <40% for males or haemoglobin <12g/dl and haematocrit <36% for females	No **0**	Yes **+2**
Age >74 years	No **0**	Yes **+1**
Bleeding history Any history of gastrointestinal bleeding, intracranial bleeding, or haemorrhagic stroke	No **0**	Yes **+2**
Glomerular filtration rate <60mL/min/1.73 m^2	No **0**	Yes **+1**
Treatment with antiplatelet agents	No **0**	Yes **+1**

Table 3. ORBIT Bleeding Risk Scale for Atrial Fibrillation

1.5 Management of physical conditions among people with major mental illness

Compared to the general population, people with mental illness have poorer health outcomes and increased mortality (18). Mental illness may impact the management of physical conditions in different ways.

People with mental illness may struggle to adhere to medication for various reasons, including lack of insight about their health conditions, disorganisation, or negative attitudes towards medication and its efficacy (51,52). This may result in poorer health outcomes or more complex presentations requiring more therapeutic procedures, and sometimes hospitalisation (51,52). Non-adherence is not only restricted to disruption in treatment regimen but also comprises failure to follow up and to perform additional diagnostic tests (51,52).

The active features of illness may also result in difficulties engaging in self-care practices required for managing physical health conditions. Depression, denial of illness, fatigue, lack of motivation, and suicidal thoughts may all interfere with the ability of people with mental illness to engage in healthy lifestyle choices which could aggravate physical health problems (53).

Similarly, cognitive impairment may impact diagnosis and treatment of physical health conditions (54). People with mental illness may have difficulties concentrating, understanding medical instructions, managing appointments, communicating with healthcare providers, and making decisions that affect their life (54). The presence of mental and physical comorbidities often necessitates coordination between multiple healthcare providers and complex treatment plans that could be challenging for people with cognitive impairment.

Disparities in healthcare access form another barrier for the management of physical health conditions among people with mental illness. Social determinants such as housing, education and employment may drive inequalities in physical healthcare among people with mental illness compared to the general population (55). Disparities may also arise from a combination of factors including financial barriers, mental-illness related stigma, and fragmented medical care which may result in a lack of communication and coordination between mental and physical healthcare providers (55, 56, 57, 58). Diagnostic overshadowing also results in missed opportunities for the

identification of physical health conditions, delayed or inadequate treatment, increased health risks and poorer health outcomes (59).

1.6 Thesis aims

This thesis is divided into four parts.

In Part 1, the mental and physical health of people with major mental illness is reviewed. This chapter is a general introduction. It summarises and defines major mental illnesses and their severity and includes an overview of the cardiovascular and cerebrovascular diseases in this population. AF and its associated stroke risk, stroke and bleeding risk assessment tools, and OAC therapy for stroke prevention among people with AF are also outlined. The last part of this chapter gives an overview on the factors affecting the management of physical conditions among people with major mental illnesses. Chapter 2 presents a systematic review and meta-analysis on OAC therapy and outcomes in patients with AF and SMI (paper 1) (60). The aim of this review is to determine prevalence of AF among people with SMI, identify whether there is a disparity in the prescription of OAC therapy among people with AF and SMI compared to the general population, identify the time spent outside the INR therapeutic range among those receiving warfarin, and identify outcomes of AF in people with SMI (60).

Part 2 explores stroke prevention in people with AF and co-morbid SMI in two different healthcare settings using observational data. Chapter 3 describes an analysis of OAC therapy for AF among people with SMI in a general hospital setting, King's College Hospital (paper two) (61). The aim of this study is to evaluate OAC (DOACs and warfarin) prescription trends over the past 10 years in people with AF and SMI who meet the criteria for OAC treatment (61). Chapter 4 describes the rates of recorded prescription of OAC therapy among people with AF and co-morbid dementia, SMI, substance use disorder and other common mental illnesses in a secondary mental healthcare setting, South London and Maudsley (SLaM) NHS Foundation Trust (paper 3) (62). The study also evaluates the association between mental illness severity/functional impairment and OAC prescription in eligible patients (62).

Part 3 describes an electronic clinical decision support system (eCDSS) for the screening of AF-related stroke risk. This part is divided into three chapters. Chapter 5 gives an overview of what an eCDSS is and reviews previous research on the feasibility and acceptability of eCDSSs for the management of physical health conditions in both general and mental healthcare settings. The next chapter (chapter 6) outlines the implementation of an eCDSS to screen for stroke risk among people with AF in a mental healthcare setting (SLaM). The digital, clinical and research protocols are all detailed in this section. In chapter 7, clinicians' perception of the digital tool (pre-implementation) in mental health of older adults (MHOA) wards is investigated. Chapter 8 investigates the experiences of clinicians with the tool (after implementation of the eCDSS), their views regarding its impact on clinicians and patients, and their perspective on its effectiveness (paper 5).

Part 4 of this thesis consists of a general discussion. Chapter 9 summaries all the findings described in parts 1 to 3, provides an overview of future implications, discusses the strengths and limitations, and provides a conclusion for the entire piece of work.

CHAPTER 2- ANTICOAGULATION THERAPY AND OUTCOMES IN PATIENTS WITH ATRIAL FIBRILLATION AND SERIOUS MENTAL ILLNESS: A SYSTEMATIC REVIEW AND META-ANALYSIS - Paper 1 (60)

Dina Farran [a, *], Olwyn Feely [b], Mark Ashworth [c], Fiona Gaughran [a, d]

- *a- Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK*
- *b- School of Medicine, Trinity College Dublin, Dublin, Ireland*
- *c- School of Life Course and Population Sciences, King's College London, London, UK*
- *d- South London and Maudsley NHS Foundation Trust, London, UK*

** Corresponding author. Institute of Psychiatry, Psychology and Neuroscience, King's College London, 16 De Crespigny Park, London, SE5 8AB, UK. E-mail address: dina.1.farran@kcl.ac.uk (D. Farran).*

Farran, D., Feely, O., Ashworth, M., & Gaughran, F. (2022). Anticoagulation therapy and outcomes in patients with atrial fibrillation and serious mental illness: A systematic review and meta-analysis. Journal of Psychiatric Research. https://doi.org/10.1016/j.jpsychires.2022.11.002

Abstract

Objective

A systematic review was conducted to investigate prevalence, management and outcomes of atrial fibrillation (AF) in people with Serious Mental Illnesses (SMI) versus the general population.

Data sources

MEDLINE, EMBASE, and PsycINFO were searched for primary research written in English and published between 2004 and 2022.

Study selection

A total of 1459 studies were identified in the initial search of which 16 met the inclusion criteria. Studies (n = 4) reporting on ischaemic stroke and major bleeding events were included in the meta-analysis.

Data extraction

Two independent reviewers extracted data and assessed risk of bias using the Newcastle-Ottawa Scale. Discrepancies were resolved by consulting a third reviewer.

Results

Low rates of AF were reported among people with SMI suggesting under-recognition or recording gaps. People with SMI and AF were less likely to receive oral anticoagulation therapy compared to the general population. When receiving warfarin, those with bipolar disorder experienced poor anticoagulation control as measured by time in INR therapeutic range. Pooled analysis of risk estimates showed that in patients with identified AF, SMI was not significantly associated with an increased risk of stroke (HR: 1.09; 95%CI: 0.85 to 1.40; I2 = 60%, p = 0.04) or major bleeding (HR: 1.11; 95%CI: 0.95 to 1.28; I2 = 57%, p = 0.03) when adjusted for underlying stroke and bleeding risks using the CHA2DS2VASc and HASBLED scales respectively.

Conclusion

More research is needed to examine the prevalence, management and outcomes of AF in this population, and to evaluate the effect of the introduction of the novel anti-coagulants on these metrics over time.

Keywords

Atrial fibrillation, serious mental illness, oral anticoagulation therapy, ischaemic stroke, bleeding

1. Introduction

Atrial Fibrillation (AF) is the most prevalent cardiac arrhythmia. AF is associated with heart failure and a fivefold increase in the risk of stroke, leading sometimes to death (Kirchhof et al., 2016). People diagnosed with serious mental illnesses (SMI) such as schizophrenia or bipolar disorder have a high prevalence of physical health conditions, reducing their life span by 10–20 years (Walker et al., 2015). Cardiovascular diseases (CVD) are the main contributors to this excess mortality (Correll et al., 2017).

Oral anticoagulation reduces ischaemic stroke risk in AF by about two thirds, but the therapy is associated with an increased risk of bleeding in patients with contributing risk factors (Kirchhof et al., 2016; Redelmeier et al., 1998). Therefore, guidelines recommend a comprehensive assessment of the benefits and risks for each person with AF to assess the appropriateness of prescription of an oral anticoagulant (Jones et al., 2014). CHAD2AD2-VASc and HAS-BLED have been the tools used to assess the risk of thromboembolic and bleeding events respectively, although a newer bleeding event risk assessment tool, ORBIT is now recommended (Gallego et al., 2012; Odum et al., 2012; Perry et al., 2021).

For anticoagulation in AF, patients are prescribed either a vitamin K antagonist (VKA) (usually warfarin) or one of the newer direct oral anticoagulants (DOACs) (e.g. dabigatran, rivaroxaban, apixaban or edoxaban) (Jones et al., 2014). In large randomised controlled trials, patients receiving DOACs have similar or lower rates of ischaemic stroke and major bleeding to those receiving warfarin (Ruff et al., 2014). DOACs offer practical advantages over VKAs as they are not susceptible to such a wide range of dietary or drug interactions. Neither do they have the narrow therapeutic range of VKAs, the latter requiring regular dose titration and monitoring of the international normalised ratio (INR) (Ruff et al., 2014). However, to achieve stroke prevention, adherence with the treatment regimen is necessary for both classes of oral anticoagulants.

Despite evidence supporting the benefits of oral anticoagulation in AF, underuse is consistently reported, particularly in those with SMI(Fenger-Grøn et al., 2021; Jaakkola et al., 2021; Schmitt et al., 2015). Fragmented medical care, poor treatment adherence, drug-drug interactions, along

with barriers to medical care and social deprivation have been identified as factors contributing to increased risk of poor outcomes in this vulnerable population (Hudson, 2005; Kennedy et al., 2013; Lawrence and Kisely, 2010; Orensky and Holdford, 2005; Platt et al., 2008; Trivedi, 2006). A recent meta-analysis showed that a diagnosis of any mental health condition was an independent risk factor for stroke and major bleeding in people with AF and was linked with lower anticoagulant use. The study included a broad range of mental illnesses including alcohol or substance abuse, anxiety, post-traumatic stress disorder, depression, and psychotic disorders (Teppo et al., 2021). Given the poor health outcomes experienced particularly by people with psychotic disorders such as bipolar disorder and schizophrenia (Correll et al., 2017), more detailed enquiry into the prevalence, management, and outcomes of AF in this population is key to inform preventive strategies.

The aim of this review is to (a) determine the prevalence of AF in people with SMI; (b) determine the prescription rate of oral anticoagulants (DOAC vs warfarin) in AF patients with SMI; (c) determine whether oral anticoagulant (OAC)-eligible patients with SMI are less likely to receive OACs compared to general population; (d) identify among SMI patients receiving warfarin the proportion where the INR is outside the defined therapeutic range; and (e) identify the outcomes of AF in people with SMI.

2. Methods

We conducted a systematic review of studies reporting on the prevalence, management and outcomes of AF in people with SMI. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were used to undertake this review (PRISMA, 2021). The full protocol of the review was submitted (20/01/2021) to the International Prospective Register of Systematic Reviews (PROSPERO, 2021). The registration number of the review is: CRD42021231365.

2.1. Search strategies

Studies were identified through systematic searches in MEDLINE, EMBASE, and PsycINFO databases using the following keywords (Appendix A):

- Atrial fibrillation: “atrial fibrillation”
- Serious mental illness: “serious mental illness”, “severe mental illness”, “schizophrenia”, “bipolar affective disorder”, “schizoaffective disorder”, “non-organic psychosis”.
- Oral anticoagulant: “non-vitamin K antagonist oral anticoagulants”, “Direct Oral Anticoagulant”, “DOAC”, “Novel Oral Anticoagulant”, “NOAC”, “dabigatran”, “rivaroxaban”, “apixaban”, “edoxaban”, “vitamin K antagonist”, “warfarin”.
- Anticoagulation control: “Therapeutic range”, “International Normalized Ratio”, “International Normalised Ratio” “INR”, “prothrombin time”.
- Outcomes: “cerebrovascular accident”, “cerebral thrombosis”, “haemorrhage”, “hemorrhage”, “cerebral infarct”, “cerebral infarction”, “bleeding”, “stroke”, “mortality” and “death”.

Additional articles were identified by screening the reference lists of the retrieved studies. The search was restricted to articles written in English and published between 2004 and 2022 (only articles published after 2004 were considered because roughly as of this date aspirin, which was commonly used for the management of AF-related stroke, was no longer considered an effective treatment (Van Walraven et al., 2002)).

2.2. Eligibility criteria

Studies were eligible if they included the following SMI conditions: schizophrenia, bipolar affective disorder, schizo-affective disorder, or non-organic psychosis. Studies reporting on mental health conditions in general without presenting SMI-specific data were excluded. We excluded articles reporting on arrhythmias or cardiovascular diseases in general, where AF was not specifically identified. Studies reporting on the use of oral anticoagulants to treat various conditions including AF in people with SMI were also included in the review. The population of interest was restricted to people aged above 18 years. We excluded reviews, commentaries, case reports, and conference abstracts.

2.3.Data extraction

The titles and abstracts of all retrieved articles were reviewed by two independent researchers (DF and OF). A list of articles meeting the inclusion criteria was then prepared for full assessment. A standardized data extraction form was used to extract the following information: citation details (title, author and year), study setting, design, aim, participant details (age, sex, ethnicity, socioeconomic status, mental health conditions, and exposure to oral anticoagulants), comparator, and outcomes. Two independent reviewers (DF and OF) extracted the data. Discrepancies were resolved by consulting a third reviewer (FG).

2.4.Assessment of bias

The risk of bias in each study was assessed using the Newcastle-Ottawa Scale (NOS) (Wells et al., 2000). For cohort studies, the tool consists of variables falling under three domains: selection (representativeness of the cohort, selection of the non-exposed cohort, ascertainment of exposure, demonstration that the outcome of interest was accounted for or not present at start of study), comparability (comparability of cohorts on the basis of the design or analysis), and outcome (ascertainment of outcome, was followed-up long enough for outcomes to occur, adequacy of follow-up of cohorts).

The same domains are used to assess the risk of bias in cross-sectional studies, however variables falling under these domains are different (selection: representativeness of the sample, sample size, non-respondents, and ascertainment of the exposure; comparability: subjects in different outcome groups are comparable based on the study design or analysis, and confounding factors are controlled; and outcome: assessment of the outcome and statistical test). A study can be awarded a maximum of nine stars: one star for each variable under selection and outcome domains and a maximum of two stars for comparability. A higher number of stars indicates less risk of bias. Two independent reviewers (DF and OF) assessed the risk of bias. Discrepancies were resolved by consulting a third reviewer (FG).

2.5. Statistical analysis

Articles reporting on ischaemic stroke and bleeding risks in people with AF and co-morbid SMI were included in the meta-analysis. Data on different SMI groups within the same study were presented separately. Hazard ratios were log transformed and standard errors calculated from the 95% confidence intervals. Pooled analysis was conducted using random effects model with estimates greater than 1 indicating higher risk. Forest plots were used to visualise the variation between studies and I^2 statistics to quantify heterogeneity. A p-value less than 0.05 was considered statistically significant. All statistical analyses were conducted in R using 'meta' package.

3. Results

A total of 1459 studies were identified in the initial search (Fig. 1). After title and abstract screening, 1407 were excluded as they did not meet inclusion criteria. The remaining 52 studies were fully assessed. Thirty-six publications were further excluded because the study did not report on SMI (n = 14), reported on arrhythmia but not specifically AF (n = 12), reported on cardiovascular diseases but not specifically AF (n = 9) or because the study did not answer any of the research questions proposed in this review (n = 1). Finally, a total of 16 studies were included. No additional articles were identified after screening the reference lists of the retrieved studies (Fig. 1).

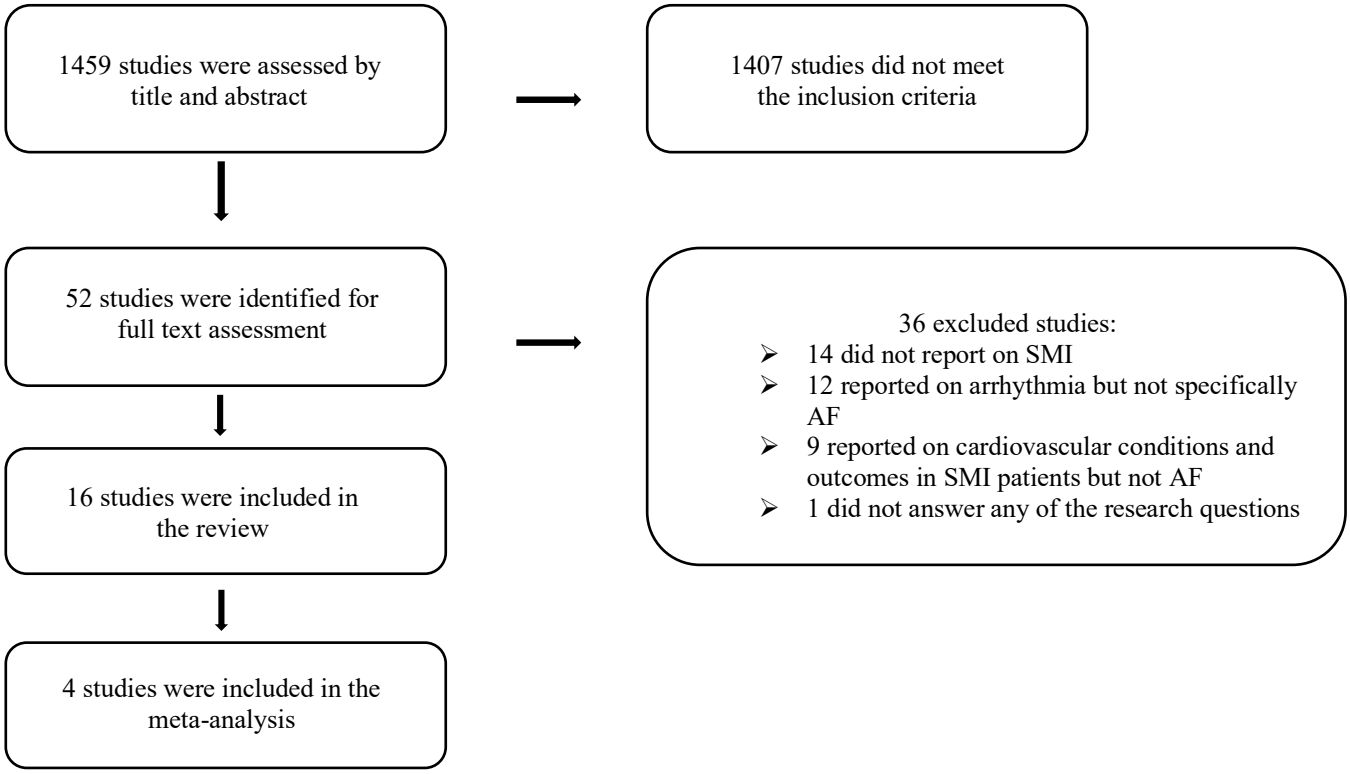


Figure 1. Flowchart of study selection

3.1.Study characteristics

Studies included in the final review were conducted in the United States (n = 7) (Chamberlain et al., 2017; Khalid et al., 2019; Paradise et al., 2014; Razouki et al., 2014; Rose et al., 2010; Schauer et al., 2005; Schmitt et al., 2015), United Kingdom (n = 3) (Farran et al., 2013b, 2022; Smith et al., 2013a; 2013b), Denmark (n = 3) (Højen et al., 2022; Fenger-Grøn et al., 2021; Søgaard et al., 2017), Finland (n = 2) (Teppo et al., 2022; Jaakkola et al., 2021), and Taiwan (n = 1) (Yang et al., 2014). Among these studies, fourteen were of cohort design, and two cross-sectional (Smith et al., 2013a; 2013b). The publication years ranged from 2005 to 2022. Three studies focused on the prevalence of AF among people with schizophrenia or bipolar disorder (Yang et al., 2013b, 2014), five on anticoagulation rates in oral anticoagulant eligible patients with SMI compared to those in the general population (Farran et al., 2022; Højen et al., 2022; Fenger-Grøn et al., 2021; Jaakkola et al., 2021; Schmitt et al., 2015), while three reported on anticoagulation control represented by

time within or outside the INR therapeutic range (Paradise et al., 2014; Razouki et al., 2014; Rose et al., 2010) and six described the outcomes of AF in people with SMI (Teppo et al., 2022; Chamberlain et al., 2017; Khalid et al., 2019; Paradise et al., 2014; Schauer et al., 2005; Søgaard et al., 2017). As for the oral anticoagulants used, twelve studies included warfarin, and seven additionally included DOACs (Farran et al., 2022; Højen et al., 2022; Teppo et al., 2022; Fenger-Grøn et al., 2021; Jaakkola et al., 2021; Khalid et al., 2019; Søgaard et al., 2017). The sample size of the studies ranged between 121 and 1.75 million. The Veterans Health administration was the most frequently used database among the retrieved studies (N = 4) (Table 1). Among the studies included in the review, eleven were rated as good quality, three as fair, and two as poor quality using NOS (Table 2).

	Study			Patients' characteristics				OAC	Comparator	Findings
Author (year)	Setting	Design	Aim	Age (mean (SD) unless otherwise mentioned)	Sex (Male)	Ethnicity	MHC			
Yang et al. (2014)	Taiwan National Health Insurance nationwide database (N: 927,915)	Observational study	Evaluate whether gender modulates the impacts of different psychoses on the occurrence of AF.	-General population: 32 (20) -SCZ: 39 (14) -SCZ & AF: 60 (19) -BD: 46 (17) -BD & AF: 66 (12)	-General population:50% -SCZ: 56% -SCZ + AF: 57% -BD: 38% -BD+ AF: 44%	NA	-BD (n=5112) -SCZ (n=2963)	NA	General population	*Prevalence of AF: -General population 7.8 ‰ (8.5‰ in males and 7.2‰ in females) -SCZ 2.4‰ (2.4 ‰ in males and 2.3 ‰ in females) -BD 14.3‰ (16.5‰ in males and 12.9‰ in females) *Recorded AF prevalence was higher in people with a diagnosis of BD than SCZ and than the general population (p<0.001 for both).
Smith et al. (2013)	Primary Care Clinical Informatics Unit at the University of Aberdeen, UK (consisting of all registered patients who were alive and permanently registered with 314 general practices on 31 March 2007) (N= 1,751,841)	Cross- sectional study	To examine the nature and extent of physical comorbidities in individuals with BD within primary care	-With BD: 54.5 years (15.3) -W/O BD: 47.9 (18.2)	-With BD: 39.5% -W/O BD: 49.1%	NA	BD (n=2582)	NA	People with no BD	* The prevalence of AF was 1.4% in people with BD vs 1.7% in controls (p=0.02) *People with BD had lower recorded rates of AF (OR 0.68, 95% CI 0.45 to 0.94) compared to controls after adjusting for age and gender.
Smith et al. (2013)	Primary Care Clinical Informatics Unit at the University of Aberdeen (which consists of patients registered with	Cross-sectional study	To assess the nature and extent of physical-health comorbidities in people with SCZ and related psychoses compared with controls.	-SCZ: 51.6 years (16.5) -Controls: 48 (18.3)	-SCZ: 51.5% -Controls: 49.1%	NA	SCZ or related non-organic psychosis (n=9677)	NA	People with no SCZ	* The prevalence of AF was 1.4% in people with SCZ vs 1.7% in controls (p<0.001) *People with SCZ had lower recorded rates of cardiovascular disease, including AF (OR 0.62, 95% CI 0.51 to 0.73) after

	314 primary care practices in Scotland). (N= 9677 patients with schizophrenia and 1414701 controls)									adjusting for age, gender, and deprivation score.
Farran et al. (2022)	Electronic health records of patients admitted to King's College Hospital (from January 1 2011 to August 1 2020) (N= 16 916)	Retrospective cohort study	To evaluate anticoagulation prescription trends in people with both AF and comorbid SMI who met the CHAD2AD2-VASc criteria for anticoagulation treatment.	*SMI: 71.88 (13.92) *Non-SMI: 75.72 (12.95)	* SMI: 55.7% *Non-SMI: 55.8%	NA	SMI including: bipolar disorder, schizophrenia, severe depression, psychosis, delusional disorder or mania (n= 465)	Warfarin, DOACs	AF patients with no SMI	*Compared to non-SMI patients, those with SMI had significantly higher CHA2DS2-VASc (mean (SD): 5.3 (1.96) vs 4.7 (2.08), $p < 0.001$) and HASBLED scores (mean (SD): 3.2 (1.27) vs 2.5 (1.29), $p < 0.001$). *Among AF patients having a CHA2DS2-VASc ≥2, those with co-morbid SMI were less likely than non-SMI patients to be prescribed an OAC (44% vs 54%, $p < 0.001$).
Hojen et al. (2022)	Nationwide Danish Health Registries : National Patient Register, National Prescription Registry, Danish Civil Registration System (from January 1 2000 to 31 December 2017) (N= 192 434)	Retrospective cohort study	To examine OAC initiation in patients with schizophrenia diagnosed with incident AF	*SCZ: 69.5 (11.6) *Without SCZ : 69.6 (11.5)	* SCZ: 49.7% *Without SCZ: 49.5%	NA	SCZ (n= 662)	VKA, DOACs	Matched AF patients without SCZ	*Among patients with SCZ 33.7% initiated OAC within the first year after AF diagnosis, compared with 54.4% of patients without SCZ, corresponding to an adjusted Risk Difference (RD) of −20.7 (95% confidence interval [CI]: −24.7 to −16.7). * During 2000–2011, 18.3% of patients with SCZ and 42.9% without SCZ initiated OAC (adjusted RD −23.6%, 95% CI −28.8 to −18.6). *During 2012–2018, this was 48.5% and 65.7%, respectively (adjusted RD −14.4%, 95% CI −20.4 to −8.4).

Fenger-Grøn et al. (2021)	Nationwide Danish registries (from January 1, 2005, to December 31, 2016) (Incident AF-N= 147 810; Prevalent AF-N=199 219)	A nationwide cohort study	To assess whether BD or SCZ is associated with a lower rate of oral anticoagulation therapy (OAT) initiation in patients with incident AF and lower prevalence of OAT in those with prevalent AF.	*Age in treatment initiation group: -General population: 76.9 (10.1) - BD: 74.55 (10.27) - SCZ: 69.26 (12.37) *Treatment prevalence group: -General population: 75.85 (10.26) -BD:73.99 (10.37) -SCZ: 67.46 (12.82)	*Treatment initiation group -General population: 46.8% - BD: 35% - SCZ: 37.9% *Treatment prevalence group - General population: 51.3% -BD:40.5% -SCZ: 43.8%	NA	* Treatment initiation group -BD (n=1208) -SCZ (n=572) *Treatment prevalence group -BD (n=7954) -SCZ (n=3259)	VKA, DOACs	AF patients with no BD and SCZ	*Accounting for age, sex, and calendar time, BD and SCZ were associated with significantly lower frequency (aPD) of OAT initiation within 90 days after incident AF (BD: −12.7% (95% CI: −15.3% to −10.0%); SCZ: −24.5% (95% CI, −28.3% to −20.7%) and lower OAT prevalence in patients with prevalent AF (BD: −11.6% (95% CI: −13.9% to −9.3%); SCZ: −21.6% (95% CI, −24.8% to −18.4%). *Adjusting for socioeconomic factors and other comorbid conditions attenuated these associations, particularly for patients with BD, however SCZ continued to be associated with a lower rate (aPD) of OAT initiation (−15.5%, 95% CI, −19.3% to −11.7%) and a lower OAT prevalence (−12.8%, 95% CI, −15.9% to −9.7%). *The SCZ- associated deficits in OAT initiation and prevalence remained significant After the introduction of DOACs (aPD in 2013-2016 alone: −12.4%; 95% CI, −18.7% to −6.1% for initiation and −10.1%; 95% CI, −13.8% to −6.4% for prevalence), whereas this was not the case for the OAT initiation deficit associated with BD (aPD in 2013-2016: −2.0%; 95% CI, −6.4% to 2.3%).

Jaakkola et al.(2021)	Three national healthcare registers in Finland covering primary to tertiary care and drug purchases (from 2007 to 2018) (N= 239 222)	A nationwide cohort study	* To determine whether the presence of MHCs affects the rate of initiation of OAC therapy in AF patients. * To determine whether the introduc-tion of NOACs has improved OAC coverage among patients with AF and MHCs.	-Any MHC: 72.8 years (14.2) -BD: 64.2 (13.0) -SCZ: 69.6 (11.7)	-Any MHC: 40.5% -BD: 53.7% -SCZ: 47.2%	NA	-Any MHC (n= 47 547) -BD (n=1129) -SCZ (n= 1560)	Warfarin and DOACs	AF patients with no mental health conditions	*Lower adjusted rates of initiation of OAC in: BD (aSHR: 0.838; 95% CI: 0.824 to 0.852), and SCZ (aSHR: 0.838; 95% CI: 0.824 to 0.851). Covariates included age, sex, hypertension, dyslipidaemia, heart failure, diabetes, prior stroke or transient ischaemic ischaemia, vascular disease, renal failure or dialysis, liver cirrhosis or failure, alcohol abuse, prior bleeding episodes and dementia. *Any MHC remained associated with impaired incidence of OAC initiation in the DOAC era during 2015–18 (aSHR: 0.821; 95% CI 0.805 to 0.837).
Schmitt et al. (2015)	Veterans Health Administration (N=125 670)	Retrospective cohort study	Determine: *Whether AF patients with versus without MHCs differ in eligibility for anticoagulation *Whether, among AF patients eligible for warfarin, rates of warfarin receipt differ for patients with versus without MHC.	-No MHC:75.5 years (7.6) -MHC: 73.4 (9.8)	-No MHC: 98.7% -MHC: 97.9%	-White, non-Hispanic: No MHC (94.7%), MHC (93.3%) -African American: No MHC (3.8%), MHC (4.8%) -Asian: No MHC (0.2%), MHC (0.2%) -North American Native: No MHC (0.1%), MHC (0.2%)	Psychotic disorders (n=122)	Warfarin	Warfarin eligible patients with no mental health conditions.	*High stroke risk and contraindications to anticoagulation were both more common in patients with MHC than controls: 1.4% versus 0.6% had a history of intracranial hemorrhage; 27% versus 20% had a history of other hemorrhage; 17% versus 3% had a history of dementia; 2% versus 1% had a history of cirrhosis; and 0.6% versus 0.5% had a history of end-stage renal disease (P <.05 for all comparisons). *Among warfarin eligible patients, those with psychotic disorders were less likely to receive warfarin than those without these

						-Hispanic: No MHC (1.0 %), MHC (1.5 %) -Other/ unknown: No MHC (1.0 %), MHC (1.0 %)				conditions (AOR: 0.77; 95% CI, 0.65 to 0.90). *When stratified by CHADS2 score, people with psychotic disorders having a CHADS2 score between 2 and 3 were less likely than controls to receive warfarin (AOR: 0.75; 95% CI, 0.59 to 0.96).
Razouki et al. (2014)	100 Veterans Health Administration (VHA) sites (N=103 897)	Observational study	*To illustrate different patterns of anticoagulation control *To identify patient-level factors that are associated with each pattern	*20-54 years (7.1%) *55-59 (11.1%) *60-64 (12.2%) *65-69 (11.2%) *70-74 (16.3%) *>=75 (42.1%)	male: 98.1%	-Non-Hispanic white (85.2%) -Non-Hispanic black (9.2%) -Hispanic (3.1%) -Asian (0.4%) -Native American (0.4%) - Other/unknown (1.7%)	-BD (n=1629) -SCZ (n=911) -ther psychotic disorders (n=830)	Warfarin	NA	*Among patients with poor control (n=44 086) (TTR)< 60%): 50% had a unidirectional INR pattern below the target range of 2-3 in more than 75% of their out-of-range time. 20% evidenced a unidirectional high tendency (> 75% of out-of-range time > 3). The remaining 30% showed neither a high nor a low tendency and were assumed to have erratic control. *Adjusting for multiple variables including age, sex, ethnicity, mental and physical conditions, BD was significantly associated with more time below therapeutic range (3.2%, p<0.001). *SCZ and other psychotic disorders did not predict more time above or below therapeutic range.
Rose et al. (2010)	Veterans Health Administration	Observational study	To identify patient-level predictors of oral anticoagulation	*Inception period (first 6 months of warfarin therapy):	*Inception period - male: 97.3%	*Inception	Inception:	Warfarin	NA	*During the inception period, BD was significantly

	(N= 124 619)		control in the outpatient setting.	20-54 years old: 12.7% 55-59:16.2% 60-64: 16.7% 65-69: 11.0% 70-74: 13.7% ≥75: 29.7% *Experienced period (after the first 6 months of warfarin therapy): 20-54: 7.1%; 55-59:11.1%; 60-64: 12.2%; 65-69: 11.2%; 70-74: 16.3%; ≥ 75: 42.1 %	*Experienced period-male: 98.1%	-Non-Hispanic White 73.9% -Non-Hispanic Black 11.3% -Hispanic 2.9% -Asian 0.3% -Native American 0.4% -other 11.2% *Experienced -Non-Hispanic White 77.2% -Non-Hispanic Black 8.5% -Hispanic 2.8% -Asian 0.3% -Native American 0.3% -other 10.9 %	*Bipolar disorder (n=1279) *Schizophrenia (n=701) Experienced: *Bipolar disorder (n=2386) *Schizophrenia (n=1263)			associated with less TTR (−2.9%; 95%CI: -4.5 to -1.4; p<0.001) after adjusting for multiple variables (including age, sex, ethnicity, mental and physical conditions). SCZ was not significantly associated with percent TTR (-0.7%; 95%CI: -2.7 to 1.3) *During the experienced period, BD was significantly associated with less TTR (-1.8%; 95%CI: -2.7 to -1.0; p<0.001) whereas SCZ was not associated with percent TTR (0.8%, 95%CI: -0.4 to 2.0).
Teppo et al. (2022)	Three national healthcare registers: hospitalizations and outpatient specialist visits: HILMO; primary health care: AvoHILMO; and National Reimbursement Register upheld by Social Insurance Institute: KELA (from 2004 to 2018)	Retrospective Nationwide registry-based cohort study	* To assess the incidence of first-ever ischaemic stroke in patients with and without MHCs and the independent effect of different MHCs on stroke risk in patients with incident AF. *To assess all-cause mortality rates in AF patients with and without MHCs and whether differences in OAC use affect outcomes in these patients.	*BD : 62.8 (12.8) *SCZ: 68.8 (11.7)	*BD: 55.8% *SCZ: 39.8%	NA	*BD (n= 933) *SCZ (n= 1329)	VKA, DOACs	Matched pairs without MHCs	* After propensity score (calculated using a regression model including: age, gender, calendar year of AF diagnosis, hypertension, dyslipidaemia, heart failure, diabetes, vascular disease, renal failure or dialysis, liver cirrhosis or failure, alcohol abuse, income, CHA_2DS_2-VASc score and modified HAS-BLED score) matching and adjusting for OAC use, no MHC group was associated with increased ischaemic stroke risk (aSHRs (95% CI): BD 1.398 (0.947–2.006), SCZ 0.803 (0.594–1.085).

	(N= 203 154)									* SCZ was associated with higher all-cause mortality (adjusted HRs (95% CI): 1.543 (1.352–1.761)).
Søgaard et al. (2017)	Three well-established Danish registries nationwide: the National Patient Register, the National Prescription Registry and the Civil Registration System- Denmark (N=253 741)	Nationwide registry-based cohort study	To compare rates of stroke, fatal thromboembolic events and bleeding in patients with AF with and without mental disorders	-Control: 73.3 years (13.1) -SCZ: 64.5 (13.7) -BD: 73.0 (11.2)	-Control: 53.3 % -SCZ: 54.3% -BD: 40.4%	NA	-SCZ (n=534) -BD (n= 569)	NOACs, non-vitamin K oral anticoagulant	AF cohort with no diagnosis of SCZ, or BD	*Compared with matched comparisons, crude 5-year HRs of ischaemic stroke were 1.37 (95% CI 0.88 to 2.14) for SCZ, and 1.04 (95% CI 0.69 to 1.56) for BD. After adjusting for risk factors, comorbidity and the use of oral anticoagulants, these HRs declined towards the null. *Crude HRs of fatal thromboembolic events were 3.16 (95% CI 1.78 to 5.61) for SCZ, and 1.53 (95% CI 0.93 to 2.53) for BD. *Rates of major bleeding were increased in patients with SCZ (crude HR 1.37, 95% CI 0.99 to 1.90) but not BD (HR 0.82, 95% CI 0.58 to 1.15). * Adjustment for the components of the CHA_2DS_2-VASc and HAS-BLED scores attenuated the risk of bleeding in patients with SCZ (HR 1.17; 95%CI: 0.83 to 1.63) * Patients with BD were significantly less likely to experience bleeding when adjusting for comorbidities, CHA_2DS_2-VASc and HAS-BLED scores (HR 0.67; 95%CI: 0.47 to 0.95)

Paradise et al. (2014)	Veterans Health Administration (N=103,897)	Retrospective cohort study	*To examine the association of specific MHCs with anticoagulation control and major hemorrhage *To determine the portion of risk for hemorrhage attributable to poor anticoagulation control	* MHC: 20-54 years old (12.0%), 55-59 (18.9%), 60-64(15.9%), 65-69(9.8%), 70-74(12.1%), 75+(31.3%) *No MHC: 20-54 (5.2%), 55-59 (8.1%), 60-64(10.8%), 65-69(11.7%), 70-74(17.9%), 75+(46.2%)	male: -MHC: 96.9% -No MHC: 98.6%	*MHC: -Non-Hispanic white (83.9%) -Non-Hispanic black (10.0%) -Others (6.1%) *No MHC: -Non-Hispanic white (85.6%) -Non-Hispanic black (8.9%) -Others (5.4%)	-BD (n= 2102) -SCZ (n=847) -other psychotic disorders (n=1909)	Warfarin	Patients on OAC (as primary indication for AF) with no mental health conditions	*The mean TTR was 63.2% in controls, 53.1% in BD, 54.1% in SCZ and 54% in other psychotic disorders. *After controlling for demographic information, comorbid conditions, date of warfarin inception, indication for warfarin therapy, and the number of non-warfarin medications and hospitalizations: -BD was significantly associated with less TTR (-2.63%, p<0.001). -SCZ was not associated with percent TTR (-0.36, p-value not significant) . -Other (than SCZ) psychotic disorders were associated with less TTR (-2.92 %, p <0.001). *Patients (on warfarin) having other psychotic disorders had an increased hazard for major hemorrhage (HR 1.25,95%CI: 1.05 to 1.49; p<0.05) after controlling for covariates (age, TTR, hypertension, stroke, chronic liver disease, chronic kidney disease, alcohol abuse, and non-alcohol substance abuse).
Sidra et al. (2019)	NA (N=121)	retrospective cohort study	To evaluate the bleeding risk and thromboembolic events on oral anticoagulation with warfarin versus rivaroxaban for AF in bipolar patients.	-Warfarin median age (range): 64.5 (40.6-90.2) -Rivaroxaban: 66.8 (39.1-89.0)	-Warfarin: Male (51.1%), -Rivaroxaban: Male (48.2%)	*Warfarin: -White (82.6%) -Other (17.4%)	-BD on rivaroxaban (n= 29) -BD on warfarin (n= 92)	Warfarin, Rivaroxaban	AF patients with bipolar disorder on warfarin vs rivaroxaban	*With a median follow-up of 35.6 months, the estimated cumulative incidence of any bleeding at 3 years in patients who received warfarin or rivaroxaban was 14.3% [95% CI: 5.6 to 23.1] and 7.9%,

						*Rivaroxaban -White (86.2%) -Other (13.8%)				respectively (95% CI: 4.3 to 18.4), (p = 0.36). *The estimated cumulative incidence of cerebrovascular accident at 3 years in patients who received warfarin or rivaroxaban was 5.9% (95% CI: 0.07 to 0.12) and 0%, respectively
Schauer et al. (2005)	Ohio Medicaid administrative database (N=9 345)	Retrospective cohort analysis	To determine whether substance abuse, psychiatric disease, and the social factors, perceived barriers to adherence, increase the risk of both thromboembolic and hemorrhagic events in patients with atrial fibrillation	-Control: 72 years (14.4) -Psychiatric illness: 73 (10.7)	-Control: 34 % -Psychiatric illness: 31%	White: -Control: 85% -Psychiatric illness: 86%	*Psychiatric illness (n= 2108) defined as SCZ, affective psychosis (including major depressive disorder, manic disorder, and BD), paranoia, or other nonorganic psychosis.	warfarin	Atrial fibrillation patients receiving warfarin with no psychiatric illness	*Subjects with psychiatric illness had an adjusted risk ratio of 1.5 (95% CI: 1.04 to 2.1) for intracranial hemorrhage while receiving warfarin. *Subjects with psychiatric illness had an adjusted risk ratio of 1.4 (95% CI: 1.1 to 1.7) for stroke. *People with psychiatric illness receiving warfarin were at a significantly increased risk of gastrointestinal bleeding (1.2; 95%CI: 1.0 to 1.4).
Chamberlain et al. (2016)	Rochester Epidemiology Project-Olmsted County, Minnesota (N= 1430 AF patients and community controls matched 1:1 on age and sex)	Cohort study	*To compare the prevalence and duration of 19 comorbid conditions in patients with AF and in population controls. *To determine the associations of comorbidities with hospitalization and death	-AF cases: 73.6 years (13.8) -Controls 72.7 (13.5)]	Male: 48.6% (full cohort)	NA	*SCZ (n= 48)	NA	Patients with AF	There was no excess of SCZ in people with AF (n=48) and controls (n=31) (p=0.052) *After adjustment for age, sex, and other comorbidities, the risk of hospitalization of AF patients with comorbid SCZ was 1.22 (95% CI: 0.98 to 1.52), and the risk of death of AF patients with comorbid SCZ was 1.19 (95% CI: 0.92 to 1.54).

Table1. Characteristics and findings of included studies

Abbreviations' key:
OR: odd ratio, AOR: adjusted odd ratio, HR: hazard ratio, CI: confidence interval, aPD: adjusted proportion difference, aSHR:djusted subdistribution hazard ratio, RD: risk difference, VHA: Veterans Health Administration, SCZ: schizophrenia, BD: bipolar disorder, AF: atrial fibrillation, PTSD: post-traumatic stress disorder, CHD: coronary heart disease, OAT: oral anticoagulation therapy, OAC: oral anticoagulant, VKA: vitamin K antagonist, NOAC: non-vitamin K antagonist oral anticoagulant, MHC: mental health condition, INR: international normalized ratio, TTR: time in therapeutic range, SMI: serious mental illness.

Cohort studies									
Study ID	**Selection**				**Comparability**	**Outcome**			**Total (9⋆)**
	Representativeness of exposed cohort (⋆)	Selection of the non- exposed cohort (⋆)	Ascertainment of exposure (⋆)	Demonstration that outcome of interest was not present at start of study (⋆)	(⋆⋆)	Assessment of outcome (⋆)	Was follow-up long enough for outcomes to occur (⋆)	Adequacy of follow up for cohorts (⋆)	
Yang et al. (2014)	⋆	_	⋆	-	- -	⋆	⋆	⋆	5⋆ P
Farran et al. (2022)	⋆	⋆	⋆	-	⋆⋆	⋆	⋆	⋆	8⋆ G
Hojen et al. (2022)	⋆	⋆	⋆	-	⋆⋆	⋆	⋆	⋆	8⋆ G
Fenger-Grøn et al. (2021)	⋆	⋆	⋆	-	⋆⋆	⋆	⋆	⋆	8⋆ G
Jaakkola et al.(2021)	⋆	⋆	⋆	-	⋆⋆	⋆	⋆	⋆	8⋆ G
Schmitt et al. (2015)	⋆	⋆	⋆	-	⋆⋆	⋆	⋆	⋆	8⋆ G
Razouki et al. (2014)	⋆	-	⋆	-	⋆⋆	⋆	⋆	⋆	7⋆ F
Rose et al. (2010)	⋆	-	⋆	-	⋆⋆	⋆	⋆	⋆	7⋆ F
Teppo et al. (2022)	⋆	⋆	⋆	-	⋆⋆	⋆	⋆	⋆	8⋆ G
Søgaard et al. (2017)	⋆	⋆	⋆	_	⋆⋆	⋆	⋆	⋆	8⋆ G
Paradise et al. (2014)	⋆	⋆	⋆	-	⋆⋆	⋆	⋆	⋆	8⋆ G
Sidra et al. (2019)	⋆	-	⋆	-	- -	⋆	⋆	⋆	5⋆ P
Schauer et al. (2005)	⋆	⋆	⋆	-	⋆⋆	⋆	⋆	⋆	8⋆ G
Chamberlain et al. (2016)	⋆	–	⋆	-	⋆⋆	⋆	⋆	⋆	7⋆ F

Cross-sectional studies								
Study ID	**Selection**				**Comparability**	**Outcome**		**Total (8⋆)**
	Representativeness of the sample (⋆)	Sample size (⋆)	Non-respondents (⋆)	Ascertainment of the exposure (⋆)	(⋆⋆)	Assessment of outcome (⋆)	Statistical test (⋆)	
Smith et al. (2013)-a	⋆	⋆	⋆	⋆	⋆⋆	⋆	⋆	8⋆ G
Smith et al. (2013)-b	⋆	⋆	⋆	⋆	⋆⋆	⋆	⋆	8⋆ G

Table 2. Quality assessment of studies using a modified Newcastle-Ottawa scale

3.2.Prevalence of atrial fibrillation in people with serious mental illness

Yang et al. (2014) compared the prevalence of AF in people with schizophrenia or bipolar disorder to that of the general population by gender in a sample of 927 915 Taiwanese residents (from 2001 to 2008); the recorded prevalence of AF was 2.4‰ among people with schizophrenia (n = 2963), and 14.3‰ among those with bipolar (n = 5112). Compared to the general population prevalence of 7.8‰, unadjusted AF prevalence was higher in bipolar patients ($p < 0.001$) but lower in those with schizophrenia ($p < 0.001$) (Yang et al., 2014). AF patients with bipolar disorder were older than those with schizophrenia and had a high prevalence of relevant co-morbidities including cerebrovascular diseases, lipid metabolism disorders and thyroid disorders, while low numbers of co-morbidities were recorded in those with schizophrenia (Yang et al., 2014). The study did not examine for differences in AF prevalence between the two groups adjusting for these covariates (Yang et al., 2014).

Smith et al. (2013) assessed the likelihood of having physical comorbidities in people with bipolar disorder compared to controls in a cross-sectional study including 1.75 million patients registered in 314 UK general practices. The prevalence of AF was 1.4% in people with bipolar disorder (n = 2582) vs 1.7% in controls ($p = 0.02$) (Smith et al., 2013a). Adjusting for age and gender, lower recorded rates of AF were reported among people with bipolar disorder (OR 0.68; 95% CI: 0.45 to 0.94) (Smith et al., 2013a). A second study of 9677 people with schizophrenia and 1.41 million controls from the same database, yielded similar findings, with adjusted rates of AF lower in patients than controls (OR 0.62; 95% CI: 0.51 to 0.73, $p < 0.001$) (Smith et al., 2013b). A meta-analysis on these findings was not feasible due to insufficent comparable data.

3.3.Oral anticoagulant use among people with serious mental illness

Five studies assessed oral anticoagulation therapy in AF patients with SMI compared to the general population (Farran et al., 2022; Højen et al., 2022; Fenger-Grøn et al., 2021; Jaakkola et al., 2021; Schmitt et al., 2015). Using electronic health records of patients admitted to a large hospital in London (n = 16 916) between 2011 and 2020, Farran et al. (2022)evaluated anticoagulation prescription trends in people with both AF and co-morbid SMI (including bipolar disorder, schizophrenia, severe depression, psychosis, delusional disorder or mania) who met the CHAD2AD2-VASc criteria for anticoagulation treatment. Compared to non-SMI patients, those with SMI had significantly higher CHA2DS2-VASc (mean (SD): 5.3 (1.96) vs

4.7 (2.08), p < 0.001) and HASBLED scores (mean (SD): 3.2 (1.27) vs 2.5 (1.29), p < 0.001). Among AF patients having a CHA2DS2-VASc ≥2, those with co-morbid SMI were less likely than non-SMI patients to be prescribed an OAC (44% vs 54%, p < 0.001). However, there was no evidence of a significant difference between the two groups since 2019 (Farran et al., 2022).

In a recent Danish nationwide cohort study (n = 192 434), Højen et al. (2022) reported that among patients with AF and schizophrenia 33.7% initiated OAC within the first year after AF diagnosis, compared to 54.4% of patients without schizophrenia, corresponding to an adjusted risk difference (RD) of −20.7 (95% CI: −24.7 to −16.7) (rates were adjusted for individual factors included in the CHA2DS2VASc and HASBLED).OAC initiation increased over time regardless of co-morbid schizophrenia status. During 2000–2011, 18.3% of patients with schizophrenia and 42.9% without schizophrenia initiated OAC (adjusted Risk Difference (RD) −23.6%, 95% CI −28.8 to −18.6). During 2012–2018, the corresponding figures were 48.5% and 65.7%, respectively (adjusted RD −14.4%, 95% CI −20.4 to −8.4) (Højen et al., 2022). Another Danish nationwide cohort study (n = 147 810) similarly reported that people with bipolar disorder (n = 1208) and schizophrenia (n = 572) were less likely to be initiated on oral anticoagulation when newly diagnosed with AF than the general population (aPD BD: −12.7%; 95% CI: −15.3% to −10.0%; SCZ: −24.5%; 95% CI:−28.3% to −20.7%) with a corresponding lower OAC prevalence among those with prevalent AF (BD: −11.6%; 95% CI: −13.9% to −9.3%; SCZ: −21.6%; 95% CI: −24.8% to −18.4%) after adjusting for multiple variables including age and sex. Further adjustments for comorbidities and socioeconomic factors attenuated these associations particularly among bipolar patients (Fenger-Grøn et al., 2021). After introduction of DOACs, anticoagulation treatment gap remained significant among people with a diagnosis of schizophrenia but not among those with bipolar disorder (Fenger-Grøn et al., 2021).

In Finland, a nationwide cohort study (n = 239 222) reported that, after adjusting for confounders such as age, sex, stroke and bleeding risk factors, any mental health condition was associated with lower rate of oral anticoagulation therapy in AF patients (adjusted subdistribution hazard ratio (aSHR): 0.867; 95%CI: 0.856 to 0.880) (Jaakkola et al., 2021). When stratified by mental health condition, similar associations were reported in people with bipolar disorder (n = 1129) (aSHR: 0.838; 95% CI 0.824 to 0.852), and schizophrenia (n = 1560) (aSHR 0.838; 95% CI 0.824 to 0.851) (Jaakkola et al., 2021). No improvement in anticoagulation treatment gap was detected after the introduction of DOACs (between 2015

and 2018) among people with any mental health condition (aSHR 0.821; 95% CI 0.805 to 0.837) (Jaakkola et al., 2021).

In a retrospective cohort study of the Veterans Health Administration database (n = 12 190), Schmitt et al. (2015) found that warfarin eligible patients with psychotic disorders (n = 122) were 77% as likely to receive warfarin as controls (AOR 0.77; 95% CI, 0.65–0.90) adjusting for age, sex, race/ethnicity, CHADS2 stroke risk (precursor to the CHAD2AD2-VASc score (Lip et al., 2010)) and physical comorbidity index. When further stratified by stroke risk, people with psychotic disorders having a CHADS2 score between 2 and 3 were less likely to receive warfarin (AOR: 0.75; 95% CI 0.59 to 0.96) than were controls (Schmitt et al., 2015).

Overall, all five studies reported that AF patients with SMI were less likely to receive oral anticoagulation therapy than the general population. Findings of these studies were not pooled in a meta-analysis because the data presented were not directly comparable, comprising proportions (Farran et al., 2022), risk difference (Højen et al., 2022), proportion difference (Fenger-Grøn et al., 2021), hazard ratios (Jaakkola et al., 2021) and odd ratios (Schmitt et al., 2015).

3.4.International normalised ratio in people with serious mental illness

Three studies reported on the international normalised ratio (INR) in people with SMI (Paradise et al., 2014; Razouki et al., 2014; Rose et al., 2010). In a sample of 103 897 patients receiving warfarin with a target INR of 2–3, Razouki et al. (2014) reported that among 44 086 patients overall with poor anticoagulation control (time in therapeutic range <60%), 50% had unidirectional INR patterns below 2.0 (spend more than 75% of their time outside the therapeutic range with an INR below 2), 20% unidirectional INR patterns above 3.0 (spend more than 75% of their out-of-range time with an INR above 3), and the remaining 30% had a directionless pattern (erratic-do not fit into either of these categories). Adjusting for multiple covariates, bipolar disorder (n = 1629) predicted more time spent below therapeutic range (3.2%, $p < 0.001$) whereas diagnoses of schizophrenia (n = 911) or other psychotic disorders (n = 830) did not predict more time above or below the goal range (Razouki et al., 2014).

Rose et al. (2010) showed in a sample of 124 619 Veterans Health Administration patients receiving warfarin that adjusting for age, sex, ethnicity, mental and physical conditions, the percentage time in therapeutic range was negatively affected by a diagnosis of bipolar disorder during both the inception period (first six months of warfarin use) (n = 1279) (−2.9, 95% CI: 4.5 to −1.4) and anytime thereafter (n = 2386) (−1.8%; 95%CI: 2.7 to −1.0; $p < 0.001$). In contrast, schizophrenia (n = 701 in inception period and n = 1263 in experienced period (after the first 6 months of warfarin therapy) was not statistically associated with time in therapeutic range during either period (Rose et al., 2010).

Similarly, Paradise et al. (2014) reported in a sample of 103 897 Veterans Health Administration patients on warfarin a decrease of 2.63% ($p < 0.001$) and 2.92% ($p < 0.001$) in time spent in therapeutic range among people with bipolar disorder (n = 2102) and psychotic disorders (n = 1909) (other than schizophrenia (n = 847)) respectively.

Overall, the papers consistently reported that people with SMI, particularly bipolar disorder, although not schizophrenia, spend less time in therapeutic range compared to the general population. A meta-analysis on these findings was not feasible due to insufficent comparable data.

3.5.Outcomes of atrial fibrillation in people with serious mental illness

Outcomes of AF in people with SMI were assessed in six studies (Teppo et al., 2022; Chamberlain et al., 2017; Khalid et al., 2019; Paradise et al., 2014; Schauer et al., 2005; Søgaard et al., 2017). Adjusting for multiple covariates, Chamberlain et al. (2017) reported that a diagnosis of schizophrenia (n = 48) was not significantly associated with hospitalization (OR 1.22; 95% CI: 0.98 to 1.52), nor death (OR1.19; 95% CI: 0.92 to 1.54) in people with AF.

In a recent study, Teppo et al. (2022) reported that diagnoses of bipolar disorder (n = 933) and schizophrenia (n = 1329) were not associated with increased risk of ischaemic stroke among people with AF (adjusted SHRs (95% CI): 1.398 (0.947–2.006) and 0.803 (0.594–1.085) respectively) after propensity score matching (calculated using a regression model including: age, gender, calendar year of AF diagnosis, hypertension, dyslipidaemia, heart failure, diabetes, vascular disease, renal failure or dialysis, liver cirrhosis or failure, alcohol abuse, income, CHA_2DS_2-VASc score and modified HAS-BLED score) and adjusting for OAC use.

Schizophrenia was, however, associated with higher all-cause mortality (adjusted HRs:1.543 (1.352–1.761)). In a sample of 253 741 patients with AF, Sogaard et al.(2017) reported that people with schizophrenia (n = 534) had a crude 5-year hazard ratio (HR) of 3.16 (95% CI 1.78 to 5.61) for fatal thromboembolic events. The risk decreased to 2.88 (95% CI 1.57 to 5.28) after adjusting for oral anticoagulation therapy and CHA2DS2VASc and HASBLED scores. Compared to controls, the same study reported a crude 5-year HR of 1.37 (95% CI 0.88 to 2.14) for ischaemic stroke in people with schizophrenia and 1.04 (95% CI 0.69 to 1.56) in those with bipolar disorder (n = 569) (Søgaard et al., 2017). Adjusting for risk factors and oral anticoagulation therapy, the estimates declined to 1.16 (95% 0.72 to 1.87) and 0.85 (95% CI 0.55 to 1.29) respectively (Søgaard et al., 2017). Additionally, Schaeur et al. (2005)reported that people with psychiatric illness (n = 2108) (defined as schizophrenia, affective psychosis, paranoia or non-organic psychosis) had an adjusted HR of 1.36 (95% CI 1.06 to 1.74) for ischaemic stroke.

Major bleeding in people with AF and co-morbid SMI was assessed in three studies (Paradise et al., 2014; Schauer et al., 2005; Søgaard et al., 2017). Eligible bleeding events included intracranial, gastrointestinal and major bleeding in various anatomical positions. One study reported adjusted hazard ratios of 1.46 (95%CI 1.04 to 2.05) and 1.19 (95%CI 1.03 to 1.39) for intracranial and gastrointestinal bleeding respectively among people with psychiatric illness (n = 2108) (Schauer et al., 2005). Adjusting for bleeding risk factors, Paradise et al. (2014) showed that people with psychotic disorders (n = 1909) (other than schizophrenia) were at increased risk of major bleeding (adjusted HR: 1.25; 95%CI 1.05 to 1.49), whereas those with bipolar disorder (n = 2102) (adjusted HR: 1.10; 95% CI 0.91 to 1.34) and schizophrenia (n = 847) (adjusted HR: 0.89; 95%CI 0.61 to 1.16) were not. Similarly, Søgaard et al. (2017) reported no significant increase in the risk of bleeding among people with schizophrenia (n = 534) (HR:1.22; 95%CI 0.87 to 1.72) nor bipolar disorder (n = 569) (HR:0.72; 95%CI 0.51 to 1.02) once adjusted for oral anticoagulation therapy, and stroke and bleeding risk factors.

Regarding specific OACs, a retrospective cohort study (n = 121) reported no significant difference in the cumulative incidence of thromboembolic and bleeding events (type unspecified) among AF patients with bipolar disorder receiving rivaroxaban (n = 29) versus warfarin (n = 92) (Khalid et al., 2019).

3.6.Meta-analysis

The risk of ischaemic stroke in people with AF and co-morbid SMI was reported in three studies (Teppo et al., 2022; Schauer et al., 2005; Søgaard et al., 2017). Schauer et al. (2005) assessed stroke risk in people with SMI, while Søgaard et al. (2017) and Teppo et al. (2022) assessed it in people with bipolar disorder and schizophrenia separately. The three studies were observational (cohort studies), reported on the same population (people with AF and co-morbid SMI) and controls (people with AF and no SMI), had similar objectives (evaluate the association between SMI and ischaemic stroke), used the same statistical model in their analyses (Cox proportional hazard regression) and adjusted for almost the same confounders (Søgaard et al. (2017) adjusted for comorbidities, oral anticoagulation therapy and CHA2DS2VASc and HASBLED scores, Teppo et al. (2022) matched propensity score and adjusted for OAC use, whereas Schauer et al. (2005) adjusted for all factors significant at $p < 0.05$ in the unadjusted model (which included hypertension, diabetes mellitus, chronic heart failure, liver disease, and renal disease, and deep vein thrombosis)) (Teppo et al., 2022; Schauer et al., 2005; Søgaard et al., 2017). Noteworthy, in the Søgaard et al. (2017)and Teppo et al. (2022) studies, people with AF were included in the analysis regardless of their anticoagulation status, whereas in Schaeur et al. (2005) only people receiving warfarin were included. Pooled analysis of the adjusted risk estimates (using random effect models) showed that among people with AF, SMI was not significantly associated with an increased risk of stroke (pooled adjusted HR: 1.09; 95%CI: 0.85 to 1.40; $I^2 = 60\%$; $p = 0.04$) (Fig. 2a).

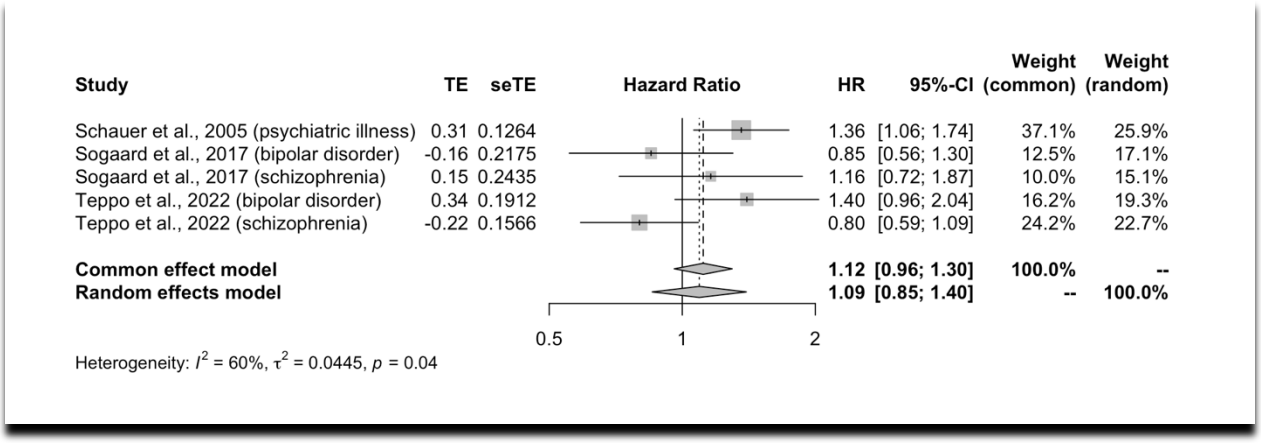


Figure 2a. Forest plot of pooled risk estimates of ischaemic stroke in people with atrial fibrillation and serious mental illnesses

The risk of major bleeding in people with AF and co-morbid SMI was reported in three studies (Paradise et al., 2014; Schauer et al., 2005; Søgaard et al., 2017). Schaeur et al. (2005) assessed the risk of intracranial and gastrointestinal bleeding separately in anticoagulated people SMI, whereas Søgaard et al. (2017) and Paradise et al. (2014)assessed the risk of major bleeding in people with bipolar disorder and schizophrenia. The effect of 'other psychotic disorders' was additionally studied in the latter (Paradise et al., 2014). The Paradise et al. (2014)study was similar to the other two (Schauer et al., 2005; Søgaard et al., 2017) in terms of study design (cohort study), objectives (evaluate the association between SMI and major bleeding), statistical analysis (Cox proportional hazard regression), and confounders (bleeding risk factors using HASBLED risk assessment model). The population in Paradise et al. (2014) consisted of people on warfarin (as a primary indication for AF) with and without SMI. Pooled analysis of the adjusted risk estimates (using random effect models) showed that among people with AF, SMI was not significantly associated with an increased risk of major bleeding (pooled adjusted HR: 1.11; 95%CI: 0.95 to 1.28; I^2 = 57%; p = 0.03) (Fig. 2b).

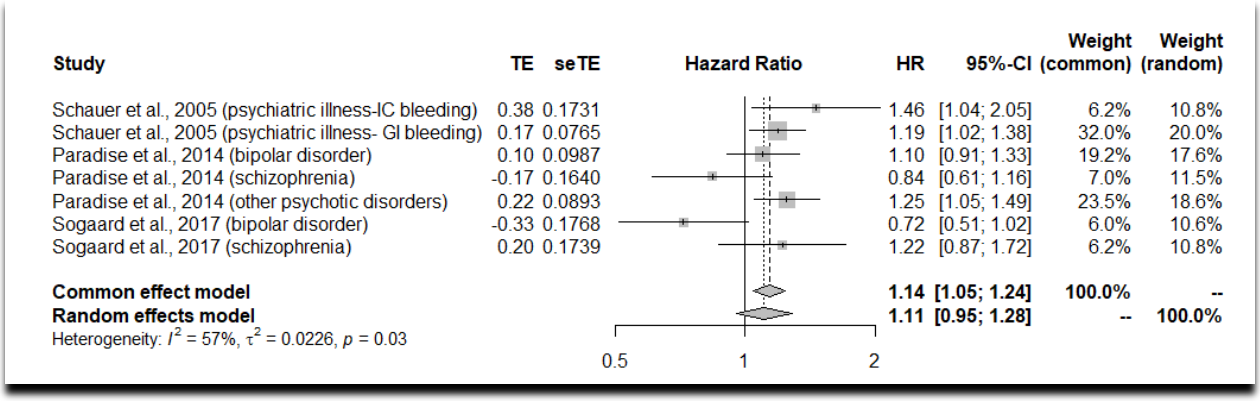


Figure 2b. Forest plot of pooled risk estimates of major bleeding in people with atrial fibrillation and serious mental illnesses

4. Discussion

This systematic review demonstrated lower recorded prevalence of AF among people with bipolar disorder and schizophrenia compared to the general population. SMI was associated with lower rates of oral anticoagulation therapy in people with AF. Among people receiving warfarin, those with bipolar disorder experienced poor anticoagulation control as measured by

time in INR therapeutic range. The meta-analysis showed no significant association between SMI and ischaemic stroke or major bleeding after controlling for risk factors.

4.1.Prevalence of atrial fibrillation in people with serious mental illness

People with SMI are at increased risk of physical morbidities with a 78% higher risk of developing cardiovascular diseases than the general population (Correll et al., 2017; Momen et al., 2020). In this review, lower rates of AF were reported among people with schizophrenia or bipolar disorder compared to the general population after controlling for age and sex (Smith et al., 2013a; 2013b; Yang et al., 2014). Of note, these studies did not adjust for ethnicity which could be an important factor explaining the low rates of AF in the SMI population. A recent meta-analysis found that Black ethnic groups have a significantly increased risk of being diagnosed with schizophrenia and affective psychoses compared to the general population (Halvorsrud et al., 2019), while studies on the prevalence of AF by ethnic groups reported a low prevalence of AF among Black patients compared to White patients (Mathur et al., 2013; Shen et al., 2010).

However, the low recorded rates of AF in people with SMI may also reflect possible under-recognition or under-recording of AF in this group especially since included papers reflected routinely collected clinical data which may have exhibited recording bias. People may be less likely to seek medical help for cardiovascular conditions if their mental health is compromising motivation, executive function, capacity or trust, and lack of awareness or denial of illness can have an important effect (De Hert et al., 2011). Disparities are not only seen at the health care access and utilization level but also in healthcare provision. Healthcare fragmentation between primary and mental health services may result in an uncertainty regarding which provider is responsible for the physical healthcare of people with mental illness which may result in missed opportunities for identification and documentation of modifiable risk factors, such as AF. Additionally, diagnostic overshadowing has been reported as a potential barrier to physical health care in people with SMI as symptoms (like palpitations or breathlessness) may be misinterpreted by clinicians or patients (Nash, 2013).

Interventions aiming to improve the communication of physical conditions and risks between physical and mental health services offer an opportunity for better identification, risk stratification and, where needed, implementation of effective preventive measures.

4.2.Anticoagulation therapy in people with serious mental illness

Despite good evidence of substantial net benefit from OAC in the general population, people with SMI and AF were less likely to receive oral anticoagulation therapy even after adjusting for age (Farran et al., 2022; Højen et al., 2022; Fenger-Grøn et al., 2021; Jaakkola et al., 2021; Kirchhof et al., 2016; Schmitt et al., 2015). Fenger-Grøn et al. (2021)reported an increase in OAC initiation and prevalence among people with schizophrenia and bipolar disorder after the introduction of DOACs in 2008 (analysis performed between 2013 and 2016) although a significant anticoagulation treatment deficit remained for those with schizophrenia. Another Danish study also found that initiation of OAC was substantially lower among patients with AF and schizophrenia compared to matched AF peers despite the increase in OAC use noted among people with schizophrenia (Højen et al., 2022). Farran et al. (2022) reported a significant difference in OAC prescription (any OAC or warfarin (but not DOACs)) between SMI and non-SMI patients only before 2019, after that no evidence of a significant difference (in warfarin, DOACs, or any OAC) was noted between the two groups. An increasing trend of DOAC use and decreasing trend of warfarin use among both SMI and non-SMI patients were reported between 2011 and 2020 (Farran et al., 2022).

All studies assessing anticoagulation control in people with SMI reported that bipolar disorder was associated with more time outside the anticoagulant therapeutic range, however, this was not the case for schizophrenia (Paradise et al., 2014; Razouki et al., 2014; Rose et al., 2010). Given that people with schizophrenia also experience poor clinical outcomes (if not worse) (Momen et al., 2020), the difference could be due to sample size or selection bias with the number of people with bipolar disorder almost twice that of people with schizophrenia in all three studies (Paradise et al., 2014; Razouki et al., 2014; Rose et al., 2010).

Oral anticoagulation therapy can be challenging in people with SMI as active features of illness can result in poorer self-management and difficulties adhering to prescribed treatments (Blixen et al., 2016; Levin et al., 2016). The underuse may be also related to concerns about the

increased bleeding risk although no randomised trials have to date demonstrated a benefit of withholding OAC treatment in patients having a high bleeding risk score. There is no clear threshold above which the benefits of OAC are offset by the bleeding risk. Thus, NICE emphasise that it is important to tailor the management plan according to the patients' overall risk factors and mitigate these whenever possible (Rutherford et al., 2018).

4.3.Outcomes of atrial fibrillation in people with serious mental illness

In keeping with the 25% (RR 1.25, 95%CI: 1.08–1.45) excess risk of ischaemic stroke and the 17% (RR 1.17, 95%CI: 1.08–1.27) higher risk of bleeding seen in AF patients with any co-morbid mental illness over those with AF and no mental health conditions (Teppo et al., 2021), we identified six eligible studies, three of which (Paradise et al., 2014; Schauer et al., 2005; Søgaard et al., 2017) were identified in the meta-analysis by Teppo et al. (2021), assessing outcomes of AF in people with SMI. Our findings were not in line with the ones presented by Teppo et al. (2021) as no significant association was detected between SMI and ischaemic stroke or major bleeding in people with AF when adjusting for risk factors. This difference may be explained by the fact that Teppo et al. (2021), included common mental illnesses (such as anxiety, depression and post-traumatic stress disorder) in their study, whereas our inclusion criteria was restricted to people with SMI only. Moreover, the risk estimates included in our meta-analysis were all adjusted for OAC use, stroke and/or bleeding risk factors, whereas Teppo et al. (2021) pooled crude (Søgaard et al., 2017) and adjusted hazard ratios which might have influenced the results.

The risk of adverse outcomes is not surprising in the light of increased prevalence of both stroke and bleeding risk factors as well as a number of other factors common among the SMI population such as smoking, substance use, sub-optimal nutrition, obesity and low physical activity (Goff et al., 2005; Green et al., 2007; Phelan et al., 2001). Although oral anticoagulation therapy increases the risk of bleeding, many bleeding risk factors are modifiable offering an opportunity to reduce this risk. Kirchhof et al. (2020) reported that among people with AF receiving rivaroxaban, 40% of major bleeding events occurred in those with at least one of the three modifiable bleeding risk factors: uncontrolled hypertension, heavy alcohol use, and concomitant treatment with nonsteroidal anti-inflammatory drugs or antiplatelets. The presence of at least one of these risk factors increased the risk of major

bleeding by 2-fold (with an additive effect showed with increasing number of risk factors) (Kirchhof et al., 2020). This implies that it may have been possible to reduce this elevated risk by clinical management, as suggested in our study.

This study has several limitations. All included studies were observational, meaning that they were more prone to confounding and bias, in particular recording bias. The definition of SMI differed to an extent between studies, however, since research investigating the management of AF in this population is limited, we included all the articles that presented SMI-specific data (as defined in our search strategy). Most of the retrieved articles investigated warfarin use whereas research on DOAC use in people with SMI is as yet very limited. The meta-analysis included a limited number of studies, thus, publication bias cannot be excluded. Findings of the meta-analysis may not be generalisable since heterogeneity was high. However, previous research has reported that I^2 could have a substantial bias when the meta-analysis includes a limited number of studies and that the bias is positive when the true fraction of heterogeneity is small (Von Hippel, 2015). This means that I^2 value could be an overestimate when the number of studies included in a meta-analysis is small (Von Hippel, 2015).

Research on management and outcomes of AF in people with SMI is scarce. These people are less likely to receive indicated oral anticoagulation therapy and experience poor anticoagulation control when prescribed warfarin. More research is needed to compare the prescription rates of DOACs vs warfarin in this population to determine whether anticoagulation treatment deficit has narrowed since the introduction of DOACs, as well as to examine difference in outcomes in those prescribed a DOAC rather than warfarin. Additionally, more clinical interventions aiming to risk stratify SMI patients and improve the management of their physical conditions are needed. Managing modifiable bleeding risk factors (such as hypertension, alcohol use, and medication predisposing to bleeding such as nonsteroidal anti-inflammatory drugs (NSAIDs) or antiplatelet agents) could increase the prescription of OACs and reduce the risk of adverse events in this vulnerable population. To ensure that no AF cases are missed, future studies should investigate the effectiveness of AF screening interventions (such as single-lead ECG monitoring device) in people with SMI. Additionally, to guarantee a safe and effective treatment, the feasibily and acceptability of electronic clinical decision support systems (eCDSSs) to improve the recording of physical conditions (such as AF, stroke and bleeding risk factors) in electronic health records of patients with SMI should be evaluated. These studies should be repeated after implementation to detect

changes in the prevalence and/or recording of physical conditions among people with SMI. Future studies related to AF should also consider adjusting for stroke and bleeding risk factors as unadjusted rates are difficult to interpret particularly in people with SMI.

Finally, coordination and collaboration of specialists from different healthcare systems could also optimize healthcare provided to these patients to aid access to integrated care with clear and defined responsibilities, shared patients' records, and programs providing clinical guidelines for the recording and management of physical conditions.

Sources of direct funding, support or sponsorship

DF is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust and by the KCL funded Centre for Doctoral Training (CDT) in Data-Driven Health.
FG is in part supported by the National Institute for Health Research's (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London, by the Maudsley Charityand by the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust.
MA is in part funded by the Guy's and St Thomas' Charity and the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London).
The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

Role of the sponsor

The sponsors had no role in the conduct of the study; design, management, analysis, or interpretation of the data; and preparation, review, or approval of the manuscript.

Declaration of competing interest

DF has no conflict of interest to declare.

FG has received honoraria from Lundbeck and Otsuka.

MA has no conflict of interest to declare.

OF has no conflict of interest to declare.

Acknowledgement

None.

Abbreviations' key

OR: odd ratio

AOR: adjusted odd ratio

HR: hazard ratio

CI: confidence interval

aPD: adjusted proportion difference

aSHR: djusted subdistribution hazard ratio

VHA: Veterans Health Administration

SCZ: schizophrenia

BD: bipolar disorder

AF: atrial fibrillation

PTSD: post-traumatic stress disorder

CHD: coronary heart disease

OAT: oral anticoagulation therapy

OAC: oral anticoagulant

VKA: vitamin K antagonist

NOAC: non-vitamin K antagonist oral anticoagulant

MHC: mental health condition

INR: international normalised ratio

TTR: time in therapeutic range

SMI: serious mental illness

References

Blixen, C.E., Kanuch, S., Perzynski, A.T., Thomas, C., Dawson, N.V., Sajatovic, M., 2016. Barriers to self-management of serious mental illness and diabetes. Am. J. Health Behav. 40, 194–204. https://doi.org/10.5993/ajhb.40.2.4.

Chamberlain, A.M., Alonso, A., Gersh, B.J., Manemann, S.M., Killian, J.M., Weston, S.A., Byrne, M., Roger, V.L., 2017. Multimorbidity and the risk of hospitalization and death in atrial fibrillation: a population-based study. Am. Heart J. 185, 74–84. https://doi.org/10.1016/j.ahj.2016.11.008.

Correll, C.U., Solmi, M., Veronese, N., Bortolato, B., Rosson, S., Santonastaso, P., Thapa-Chhetri, N., Fornaro, M., Gallicchio, D., Collantoni, E., Pigato, G., 2017. Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: a large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls. World Psychiatr. 16, 163–180. https://doi.org/10.1002/ wps.20420.

De Hert, M., Cohen, D.A.N., Bobes, J., Cetkovich-Bakmas, M., Leucht, S., Ndetei, D.M., Newcomer, J.W., Uwakwe, R., Asai, I., Mo¨ller, H.J., Gautam, S., 2011. Physical illness in patients with severe mental disorders. II. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level. World Psychiatr. 10, 138. https://doi.org/10.1002/j.2051-5545.2011.tb00036.x.

Farran, D., Bean, D., Wang, T., Msosa, Y., Casetta, C., Dobson, R., Teo, J.T., Scott, P., Gaughran, F., 2022. Anticoagulation for atrial fibrillation in people with serious mental illness in the general hospital setting. J. Psychiatr. Res. 153, 167–173. https://doi.org/10.1016/j.jpsychires.2022.06.044.

Fenger-Grøn, M., Vestergaard, C.H., Ribe, A.R., Johnsen, S.P., Frost, L., Sandbæk, A., Davydow, D.S., 2021. Association between bipolar disorder or schizophrenia and oral anticoagulation use in Danish adults with incident or prevalent atrial fibrillation. JAMA Netw. Open 4, e. https://doi.org/10.1001/ jamanetworkopen.2021.10096, 2110096-e2110096.

Gallego, P., Roldaʹn, V., Torregrosa, J.M., Gaʹlvez, J., Valdʹes, M., Vicente, V., Marín, F., Lip, G.Y., 2012. Relation of the HAS-BLED bleeding risk score to major bleeding, cardiovascular

events, and mortality in anticoagulated patients with atrial fibrillation. Circulation: Arrhythmia and Electrophysiology 5, 312–318. https://doi. org/10.1161/circep.111.967000.

Goff, D.C., Cather, C., Evins, A.E., Henderson, D.C., Freudenreich, O., Copeland, P.M., Bierer, M., Duckworth, K., Sacks, F.M., 2005. Medical morbidity and mortality in schizophrenia: guidelines for psychiatrists. J. Clin. Psychiatr. 66, 183–194. https:// doi.org/10.4088/jcp.v66n0205.

Green, A.I., Drake, R.E., Brunette, M.F., Noordsy, D.L., 2007. Schizophrenia and co-occurring substance use disorder. Am. J. Psychiatr. 164, 402–408. https://doi.org/ 10.1176/ajp.2007.164.3.402.

Halvorsrud, K., Nazroo, J., Otis, M., Hajdukova, E.B., Bhui, K., 2019. Ethnic inequalities in the incidence of diagnosis of severe mental illness in England: a systematic review and new meta-analyses for non-affective and affective psychoses. Soc. Psychiatr. Psychiatr. Epidemiol. 54, 1311–1323. https://doi.org/10.1007/s00127-019-01758- y.

Højen, A.A., Nielsen, P.B., Riahi, S., Jensen, M., Lip, G.Y., Larsen, T.B., Søgaard, M., 2022. Disparities in oral anticoagulation initiation in patients with schizophrenia and atrial fibrillation: a nationwide cohort study. Br. J. Clin. Pharmacol. https://doi. org/10.1111/bcp.15337.

Hudson, C.G., 2005. Socioeconomic status and mental illness: tests of the social causation and selection hypotheses. Am. J. Orthopsychiatry 75, 3–18. https://doi.org/ 10.1037/0002-9432.75.1.3.

Jaakkola, J., Teppo, K., Biancari, F., Halminen, O., Putaala, J., Mustonen, P., Haukka, J., Linna, M., Kinnunen, J., Tiili, P., Aro, A.L., 2021. The Effect of Mental Health Conditions on the Use of Oral Anticoagulation Therapy in Patients with Atrial Fibrillation: the FinACAF Study. European Heart Journal-Quality of Care and Clinical Outcomes. https://doi.org/10.1093/ehjqcco/qcab077.

Jones, C., Pollit, V., Fitzmaurice, D., Cowan, C., 2014. The management of atrial fibrillation: summary of updated NICE guidance. Br. Med. J. 348 https://doi.org/ 10.1136/bmj.g4440.

Kennedy, W.K., Jann, M.W., Kutscher, E.C., 2013. Clinically significant drug interactions with atypical antipsychotics. CNS Drugs 27, 1021–1048. https://doi.org/10.1007/ s40263-013-0114-6.

Khalid, S., Thapa, B., Wajahat, R., Covut, F., Clark, B.A., Daw, H., 2019. Assessment of bleeding risk and cerebrovascular events in bipolar disorder patients with atrial fibrillation on warfarin versus rivaroxaban. Am. J. Therapeut. 26, e641–e644. https://doi.org/10.1097/mjt.0000000000000842.

Kirchhof, P., Benussi, S., Kotecha, D., Ahlsson, A., Atar, D., Casadei, B., Castella, M., Diener, H.C., Heidbuchel, H., Hendriks, J., Hindricks, G., 2016. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Kardiol. Pol. 74, 1359–1469. https://doi.org/10.5603/kp.2016.0172.

Kirchhof, P., Haas, S., Amarenco, P., Hess, S., Lambelet, M., Van Eickels, M., Turpie, A.G., Camm, A.J., XANTUS Investigators*, 2020. Impact of modifiable bleeding risk factors on major bleeding in patients with atrial fibrillation anticoagulated with rivaroxaban. J. Am. Heart Assoc. 9, e009530 https://doi.org/10.1161/ jaha.118.009530.

Lawrence, D., Kisely, S., 2010. Inequalities in healthcare provision for people with severe mental illness. J. Psychopharmacol. 24, 61–68. https://doi.org/10.1177/ 1359786810382058.

Levin, J.B., Aebi, M.E., Tatsuoka, C., Cassidy, K.A., Sajatovic, M., 2016. Adherence to psychotropic and nonpsychotropic medication among patients with bipolar disorder and general medical conditions. Psychiatr. Serv. 67, 342–345. https://doi.org/ 10.1176/appi.ps.201500010.

Lip, G.Y., Nieuwlaat, R., Pisters, R., Lane, D.A., Crijns, H.J., 2010. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest 137, 263–272. https://doi.org/10.1378/chest.09-1584.

Mathur, R., Pollara, E., Hull, S., Schofield, P., Ashworth, M., Robson, J., 2013. Ethnicity and stroke risk in patients with atrial fibrillation. Heart 99, 1087–1092. https://doi. org/10.1136/heartjnl-2013-303767.

Momen, N.C., Plana-Ripoll, O., Agerbo, E., Benros, M.E., Børglum, A.D., Christensen, M. K., Dalsgaard, S., Degenhardt, L., de Jonge, P., Debost, J.C.P., Fenger-Grøn, M., 2020. Association between mental disorders and subsequent medical conditions. N. Engl. J. Med. 382, 1721–1731.

Nash, M., 2013. Diagnostic overshadowing: a potential barrier to physical health care for mental health service users. Ment. Health Pract. 17 https://doi.org/10.7748/ mhp2013.12.17.4.22.e862.

Odum, L.E., Cochran, K.A., Aistrope, D.S., Snella, K.A., 2012. The CHADS 2 versus the new CHA 2 DS 2-VAS c scoring systems for guiding antithrombotic treatment of patients with atrial fibrillation: review of the literature and recommendations for use. Pharmacotherapy 32, 285–296. https://doi.org/10.1002/j.1875- 9114.2012.01023.x.

Orensky, I.A., Holdford, D.A., 2005. Predictors of noncompliance with warfarin therapy in an outpatient anticoagulation clinic. Pharmacotherapy 25, 801–1808. https://doi. org/10.1592/phco.2005.25.12.1801.

Paradise, H.T., Berlowitz, D.R., Ozonoff, A., Miller, D.R., Hylek, E.M., Ash, A.S., Jasuja, G.K., Zhao, S., Reisman, J.I., Rose, A.J., 2014. Outcomes of anticoagulation therapy in patients with mental health conditions. J. Gen. Intern. Med. 29, 855–861. https://doi.org/10.1007/s11606-014-2784-2.

Perry, M., Betty, S.K., Downes, N., Andrews, N., Mackenzie, S., 2021. Atrial fibrillation: diagnosis and management—summary of NICE guidance. Br. Med. J. 373 https:// doi.org/10.1136/bmj.n1150.

Phelan, M., Stradins, L., Morrison, S., 2001. Physical health of people with severe mental illness: can be improved if primary care and mental health professionals pay attention to it. BMJ 322, 443–444. https://doi.org/10.1136/bmj.322.7284.443.

Platt, A.B., Localio, A.R., Brensinger, C.M., Cruess, D.G., Christie, J.D., Gross, R., Parker, C.S., Price, M., Metlay, J.P., Cohen, A., Newcomb, C.W., 2008. Risk factors for nonadherence

to warfarin: results from the IN-RANGE study. Pharmacoepidemiol. Drug Saf. 17, 853–860. https://doi.org/10.1002/pds.1556.

PRISMA, 2021. Accessed December 6, 2021. http://www.prisma-statement.org.

PROSPERO, 2021. Accessed December 6, 2021. https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=231365.

Razouki, Z., Ozonoff, A., Zhao, S., Rose, A.J., 2014. Pathways to poor anticoagulation control. J. Thromb. Haemostasis 12, 628–634. https://doi.org/10.1111/jth.12530.

Redelmeier, D.A., Tan, S.H., Booth, G.L., 1998. The treatment of unrelated disorders in patients with chronic medical diseases. N. Engl. J. Med. 338, 1516–1520. https://doi.org/10.1056/nejm199805213382106.

Rose, A.J., Hylek, E.M., Ozonoff, A., Ash, A.S., Reisman, J.I., Berlowitz, D.R., 2010. Patient characteristics associated with oral anticoagulation control: results of the Veterans AffaiRs Study to Improve Anticoagulation (VARIA). J. Thromb. Haemostasis 8, 2182–2191. https://doi.org/10.1111/j.1538-7836.2010.03996.x.

Ruff, C.T., Giugliano, R.P., Braunwald, E., Hoffman, E.B., Deenadayalu, N., Ezekowitz, M. D., Camm, A.J., Weitz, J.I., Lewis, B.S., Parkhomenko, A., Yamashita, T., 2014. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet 383, 955–962. https://doi.org/10.1016/s0140-6736(13)62343-0.

Rutherford, O.C.W., Jonasson, C., Ghanima, W., Holst, R., Halvorsen, S., 2018. New score for assessing bleeding risk in patients with atrial fibrillation treated with NOACs. Open heart 5, e000931. https://doi.org/10.1136/openhrt-2018-000931.

Schauer, D.P., Moomaw, C.J., Wess, M., Webb, T., Eckman, M.H., 2005. Psychosocial risk factors for adverse outcomes in patients with nonvalvular atrial fibrillation receiving warfarin. J. Gen. Intern. Med. 20, 1114–1119. https://doi.org/10.1111/j.1525- 1497.2005.0242.x.

Schmitt, S.K., Turakhia, M.P., Phibbs, C.S., Moos, R.H., Berlowitz, D., Heidenreich, P., Chiu, V.Y., Go, A.S., Friedman, S.A., Than, C.T., Frayne, S.M., 2015. Anticoagulation in atrial fibrillation: impact of mental illness. Am. J. Manag. Care 21, e609–e617.

Shen, A.Y.J., Contreras, R., Sobnosky, S., Shah, A.I., Ichiuji, A.M., Jorgensen, M.B., Brar, S.S., Chen, W., 2010. Racial/ethnic differences in the prevalence of atrial fibrillation among older adults—a cross-sectional study. J. Natl. Med. Assoc. 102, 906–914. https://doi.org/10.1016/s0027-9684(15)30709-4.

Smith, D.J., Martin, D., McLean, G., Langan, J., Guthrie, B., Mercer, S.W., 2013a. Multimorbidity in bipolar disorder and undertreatment of cardiovascular disease: a cross sectional study. BMC Med. 11, 1–11. https://doi.org/10.1186/1741-7015-11- 263.

Smith, D.J., Langan, J., McLean, G., Guthrie, B., Mercer, S.W., 2013b. Schizophrenia is associated with excess multiple physical-health comorbidities but low levels of recorded cardiovascular disease in primary care: cross-sectional study. BMJ Open 3, e002808. https://doi.org/10.1136/bmjopen-2013-002808.

Søgaard, M., Skjøth, F., Kjældgaard, J.N., Larsen, T.B., Hjortshøj, S.P., Riahi, S., 2017. Atrial fibrillation in patients with severe mental disorders and the risk of stroke, fatal thromboembolic events and bleeding: a nationwide cohort study. BMJ Open 7, e018209. https://doi.org/10.1136/bmjopen-2017-018209.

Teppo, K., Jaakkola, J., Biancari, F., Halminen, O., Putaala, J., Mustonen, P., Haukka, J., Linna, M., Kinnunen, J., Tiili, P., Kouki, E., 2022. Mental health conditions and risk of first-ever ischemic stroke and death in patients with incident atrial fibrillation: a nationwide cohort study. Eur. J. Clin. Invest., e13801 https://doi.org/10.1111/ eci.13801.

Teppo, K., Jaakkola, J., Lehto, M., Biancari, F., Airaksinen, K.J., 2021. The impact of mental health conditions on oral anticoagulation therapy and outcomes in patients with atrial fibrillation: a systematic review and meta-analysis. Am J. Prevent. Cardiol. 7, 100221 https://doi.org/10.1016/j.ajpc.2021.100221.

Trivedi, J.K., 2006. Cognitive deficits in psychiatric disorders: current status. Indian J. Psychiatr. 48, 10. https://doi.org/10.4103/0019-5545.31613.

Van Walraven, C., Hart, R.G., Singer, D.E., Laupacis, A., Connolly, S., Petersen, P., Koudstaal, P.J., Chang, Y., Hellemons, B., 2002. Oral anticoagulants vs aspirin in nonvalvular atrial fibrillation: an individual patient meta-analysis. JAMA 288, 2441–2448. https://doi.org/10.1001/jama.288.19.2441.

Von Hippel, P.T., 2015. The heterogeneity statistic I 2 can be biased in small meta- analyses. BMC Med. Res. Methodol. 15, 1–8. https://doi.org/10.1186/s12874-015- 0024-z.

Walker, E.R., McGee, R.E., Druss, B.G., 2015. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. JAMA Psychiatr. 72, 334–341. https://doi.org/10.1001/jamapsychiatry.2014.2502.

Wells, G.A., Shea, B., O'Connell, D., Peterson, J., Welch, V., Losos, M., Tugwell, P., 2000. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Accessed December 6, 2021. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

Yang, H.Y., Huang, J.H., Lin, Y.K., Hsu, C.Y., Chen, S.A., Chen, Y.J., 2014. Bipolar disorder and schizophrenia present different risks of atrial fibrillation: a nationwide population-based analysis. Acta Cardiol. Sin. 30, 46.

PART 2- STROKE PREVENTION IN PEOPLE WITH ATRIAL FIBRILLATION AND CO-MORBID MENTAL ILLNESS

CHAPTER 3- ANTICOAGULATION FOR ATRIAL FIBRILLATION IN PEOPLE WITH SERIOUS MENTAL ILLNESS IN THE GENERAL HOSPITAL SETTING - Paper 2 (61)

Dina Farran[a,**,*], Daniel Bean[b,c,*], Tao Wang[b], Yamiko Msosa[b], Cecilia Casetta[a,d], Richard Dobson[b,c,e], James T. Teo[f], Paul Scott[g,1], Fiona Gaughran[a,e,h,1]

[a] *Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK*

[b] *Department of Biostatistics and Health Informatics, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK* [c] *Health Data Research UK London, Institute of Health Informatics, University College London, London, UK*

[d] *Department of Health Sciences, ASST Santi Paolo Carlo, Milano, Italy*

[e] *NIHR Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London, London, UK*

[f] *Department of Neurosciences, King's College Hospital NHS Foundation Trust, Denmark Hill, London, UK*

[g] *Department of Cardiology, King's College Hospital, Denmark Hill, London, UK*

[h] *South London and Maudsley NHS Foundation Trust, London, UK*

** Corresponding author. Institute of Psychiatry, Psychology and Neuroscience, King's College London, 16 De Crespigny Park, London, SE5 8AB, UK.

E-mail address: dina.1.farran@kcl.ac.uk (D. Farran).

*Joint first authors.

[1]Joint senior authors.

Farran, D., Bean, D., Wang, T., Msosa, Y., Casetta, C., Dobson, R., Teo, JT., Scott, P., Gaughran, F. (2022). Anticoagulation for atrial fibrillation in people with serious mental illness in the general hospital setting. *Journal of Psychiatric Research*, *153*, 167-173. https://doi.org/10.1016/j.jpsychires.2022.06.044

Abstract

Objective

People with serious mental illnesses (SMI) have an increased risk of stroke compared to the general population. This study aims to evaluate oral anticoagulation prescription trends in atrial fibrillation (AF) patients with and without a comorbid SMI.

Methods

An open-source retrieval system for clinical data (CogStack) was used to identify a cohort of AF patients with SMI who ever had an inpatient admission to King's College Hospital from 2011 to 2020. A Natural Language Processing pipeline was used to calculate CHA2DS2-VASc and HASBLED risk scores from Electronic Health Records free text. Antithrombotic prescriptions of warfarin and Direct acting oral anticoagulants (DOACs) (apixaban, rivaroxaban, dabigatran, edoxaban) were extracted from discharge summaries.

Results

Among patients included in the study (n = 16 916), 2.7% had a recorded co-morbid SMI diagnosis. Compared to non-SMI patients, those with SMI had significantly higher CHA2DS2-VASc (mean (SD): 5.3 (1.96) vs 4.7 (2.08), $p < 0.001$) and HASBLED scores (mean (SD): 3.2 (1.27) vs 2.5 (1.29), $p < 0.001$). Among AF patients having a CHA2DS2-VASc ≥2, those with co-morbid SMI were less likely than non-SMI patients to be prescribed an OAC (44% vs 54%, $p < 0.001$). However, there was no evidence of a significant difference between the two groups since 2019.

Conclusion

Over recent years, DOAC prescription rates have increased among AF patients with SMI in acute hospitals. More research is needed to confirm whether the introduction of DOACs has reduced OAC treatment gaps in people with serious mental illness and to assess whether the use of DOACs has improved health outcomes in this population.

Keywords

Atrial fibrillation, Serious mental illness, Oral anticoagulation, Warfarin, DOACs

1. Introduction

People suffering from serious mental illnesses (SMI) such as schizophrenia, bipolar disorder and severe depression have a high prevalence of cardiovascular diseases, contributing to 10–20 years of potential life lost (Walker et al., 2015). Atrial fibrillation (AF) is the most prevalent sustained cardiac arrhythmia and is associated with a fivefold increased risk of stroke (Kirchhof et al., 2016). According to the National Institute for Health and Care Excellence (NICE) guidelines, the management of the thromboembolic risk of AF requires a comprehensive assessment of risk factors for thromboembolic (using the CHAD2AD2-VASc tool) and bleeding events (using ORBIT or HASBLED tools), and long-term treatment with oral anticoagulants when appropriate (Linden, 2014; Lip et al., 2010; Rutherford et al., 2018).

Anticoagulation in AF patients is achieved by the prescription of either a vitamin K antagonist (VKA) (eg warfarin) or one of the direct oral anticoagulants (DOACs) (dabigatran, rivaroxaban, apixaban or edoxaban) (Jones et al., 2014). Warfarin and other vitamin K antagonists were the only class of oral anticoagulants available up until 2009, when DOACs were developed. DOACs have a different mechanism of action inhibiting thrombin or activated factor X (factor Xa) and are now considered leading therapeutic alternatives to warfarin (Jones et al., 2014; Ruff et al., 2014). They offer several advantages over vitamin K antagonists, such as not having a narrow therapeutic window requiring frequent International Normalised Ratio (INR) monitoring and dose adjustments, a rapid onset and offset of action, and absence of dietary limitations, making them potentially more suitable for many people with a diagnosis of SMI (Ruff et al., 2014).

Although oral anticoagulation has been effective in reducing the risk of stroke in people with AF, underuse has been sustainably reported, especially in patients with co-morbid SMI (Fenger-Grøn et al., 2021; Jaakkola et al., 2021; Schmitt et al., 2015; Walker et al., 2011). The anticoagulation treatment deficit in people with SMI may be attributed to challenges in self-management and adhering to treatment regimens, drug-drug interactions, bleeding concerns and factors that increase bleeding risk, social deprivation as well as fragmented medical care (Kennedy et al., 2013; Lawrence and Kisely, 2010; Platt et al., 2008).

People with AF and co-morbid SMI are at increased risk of not receiving oral anticoagulation (Teppo et al., 2021), but to date, little is known of whether this has changed since the introduction of DOACs. This study aims to evaluate anticoagulation prescription trends in a

large inner-city hospital, King's College Hospital (KCH), over the past 10 years in people with both AF and comorbid SMI who met the CHAD2AD2-VASc criteria for anticoagulation treatment.

2. Methods

2.1. Cohort selection

We used CogStack, an open-source information retrieval platform for clinical data (Jackson et al., 2018), to identify a cohort of adult patients who ever had an inpatient admission to KCH in the time between 2011-01-01 to 2020-08-01 and in whom AF had been documented in the discharge summary.

The discharge summaries were searched for the exact keywords "AFib", "AF", "PAF" or "Atrial Fibrillation" using our previously validated search strategy (Bean et al., 2019). Patients who were directly discharged from the clinical decision unit or the emergency department were eligible for inclusion in the cohort as they did not have discharge summaries.

We then employed a search strategy in that cohort to identify the presence or absence of any SMI diagnosis recorded anywhere in the clinical records between 2011-01-01 to 2020-08-01. The search algorithm was adapted from our previously published risk scoring algorithm (Bean et al., 2019) to detect the following SMI diagnoses: bipolar disorder, schizophrenia, severe depression, psychosis, delusional disorder or mania, while excluding dementia and conditions secondary to an organic problem or substance use. The risk score pipeline was used to map these general concepts to any specific child term in the Systemized Nomenclature of Medicine – Clinical Terms (SNOMED CT) ontology (El-Sappagh et al., 2018). If any of these terms was detected and not negated it was considered an SMI diagnosis. We used MedCAT (Kraljevic et al., 2021) as the underlying NLP tool to detect mentions of any of these conditions in discharge summaries or clinical notes for the AF patient cohort.

2.2. CHA2DS2-VASc and HASBLED risk scores calculation

To calculate CHA2DS2-VASc and HASBLED risk scores, we used the Natural Language Processing (NLP) pipeline developed by Bean et al. (2019), that allows calculation of the risk

scores from Electronic Health Records (EHR) free text, again, anywhere in the clinical notes within the previously defined timeframe. We used MedCAT (Kraljevic et al., 2021) as the underlying NLP tool for clinical concept annotation and the SNOMED CT ontology for terminology mapping of clinical concepts.

2.3. Oral anticoagulant prescriptions

Antithrombotic prescriptions of oral anticoagulants (OACs) (apixaban, rivaroxaban, dabigatran, edoxaban, warfarin) were extracted from free text discharge summaries within the previously defined timeframe. This was performed using a custom NLP pipeline validated in a previous work (Bean et al., 2019).

2.4. Statistical analysis

Categorical variables were presented as counts and percentages and compared using a Chi-squared test, whereas continuous variables were presented as means and standard deviations and compared using Student *t*-test. All statistical analyses were performed in Python using numpy and statsmodels. A $P < 0.05$ after Bonferroni correction for multiple testing was considered significant. In analysis of prescribing trends, SMI status and OAC prescribing were determined per admission (i.e. individual patients can move from the "non-SMI" to "SMI" category if their SMI diagnosis was not known for earlier admissions). In overall statistics, patients were considered at their last admission to hospital.

Ethical approval

This project was conducted under London South East Research Ethics Committee approval (reference 18/LO/2048) granted to the King's Electronic Records Research Interface (KERRI), project ID 20200201.

3. Results

3.1. Cohort identification

Based on the search strategy described above, we identified 21 546 patients with mentions of AF. After excluding patients based on the admission date, death, and age (<18), we ended up with a cohort of 16 916 adult patients admitted to KCH with a diagnosis of AF, of whom 465

(2.7%) had a recorded comorbid SMI diagnosis. Among AF patients with SMI, 199 were prescribed an oral anticoagulant (Fig. 1). Table 1 shows the characteristics of the study cohort. Overall, patients with SMI were younger and had higher rates of other comorbidities than those without SMI.

3.2. CHA2DS2-VASc and HASBLED scores

Fig. 2 shows the distribution of AF patients across the various CHA2DS2-VASc and HASBLED scores by mental health status. Compared to non-SMI patients, those with SMI had significantly higher CHA2DS2-VASc (mean (SD): 5.3 (1.96) vs 4.7 (2.08), $p < 0.001$) and HASBLED scores (mean (SD): 3.2 (1.27) vs 2.5 (1.29), $p < 0.001$). Among the SMI patients, 96% had a CHA2DS2-VASc≥ 2 and 73% had a HASBLED score ≥3 whereas among non-SMI patients the proportions were 93% and 51% respectively.

3.3. OAC prescription trends

Overall, 54% of AF patients with a CHA2DS2-VASc ≥2 were prescribed an OAC. When stratified by mental health status, a significant difference in overall OAC prescription rate was detected between SMI and non-SMI patients (44% vs 54% respectively, $p < 0.001$). In particular, warfarin was prescribed twice as often to non-SMI than SMI patients ($p < 0.001$) whereas no significant difference in the prescription of DOAC was detected between the two groups ($p = 1.0$) (Table 2). Although there was a significant difference in anticoagulation rates between AF patients with and without SMI in the overall cohort, the trend over time indicated that the overall average was not representative of current clinical practice (Fig. 3a). We therefore split the cohort chronologically into visits before and after January 2019 and analysed the rates separately (Table 2). Although the proportion of AF patients with HASBLED ≥3 was consistently higher in the SMI group (77% vs 61%, $p < 0.001$), from 2019 onwards there was no longer evidence of a significant difference in overall anticoagulation rates between AF patients with and without co-morbid SMI having a CHA2DS2-VASc ≥2 (56% vs 63%, $p = 0.35$) (Table 2). In the non-SMI group, the proportion of patients with a CHA2DS2-VASc ≥2 prescribed any OAC significantly increased between the two timepoints (51%–63%, $p < 0.001$) as did the proportion of patients at high risk of bleeding (52%–61%, $p < 0.001$).

We also split OAC prescribing in each group into warfarin vs DOAC use, finding qualitatively similar trends in both patient groups, with Warfarin use decreasing and DOAC use increasing over time (Fig. 3b). DOAC prescribing rates now exceed warfarin rates in both groups.

Fig 1. Cohort selection.

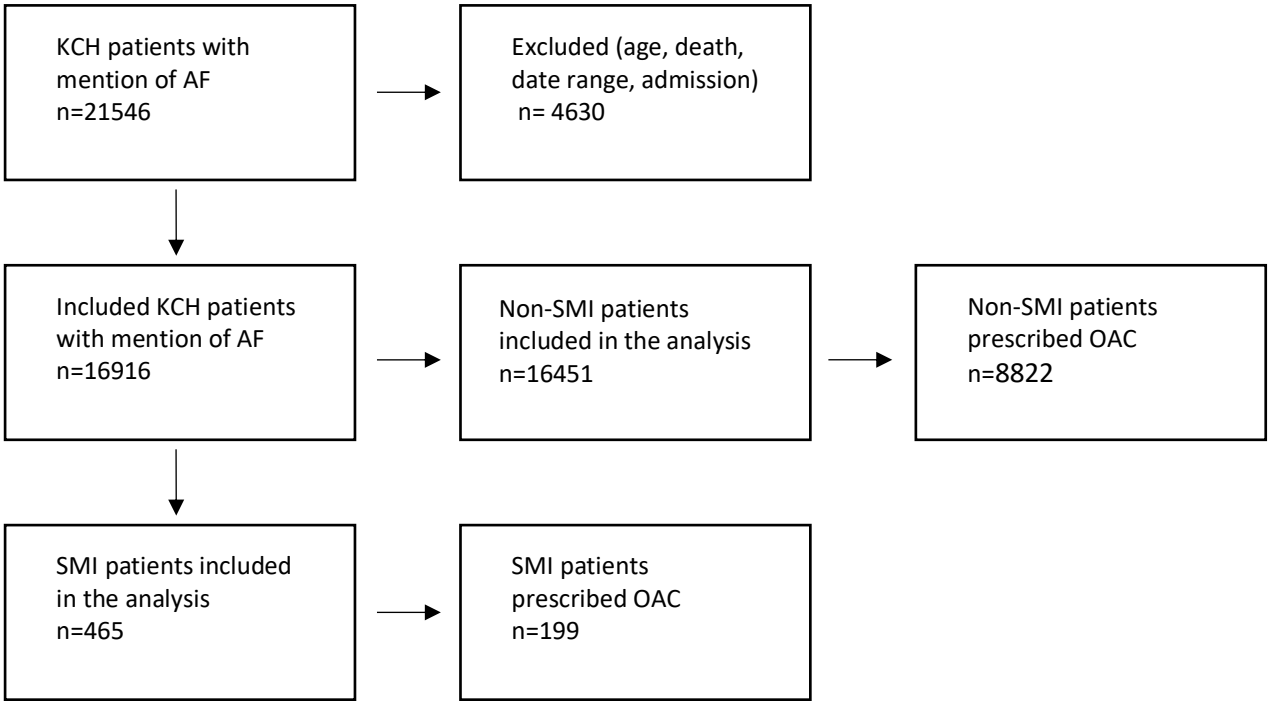


Table 1. Characteristics of study cohort.

Group	Factor	All AF Patients (N=16916)	SMI (N=465)	Not SMI (16451)	P-value
Demographics	**Age**	75.61 (12.99)	71.88 (13.92)	75.72 (12.95)	<0.001
	Male	9443 (55.8%)	259 (55.7%)	9184 (55.8%)	1.0
CHA2DS2-VASc Components	**vascular disease**	6120 (36.2%)	214 (46.0%)	5906 (35.9%)	<0.001
	Age 65-74	3846 (22.7%)	122 (26.2%)	3724 (22.6%)	1.0
	stroke	8637 (51.1%)	312 (67.1%)	8325 (50.6%)	<0.001
	hypertension	12981 (76.7%)	385 (82.8%)	12596 (76.6%)	0.085
	Female	7473 (44.2%)	206 (44.3%)	7267 (44.2%)	1.0
	congestive heart failure	5862 (34.7%)	210 (45.2%)	5652 (34.4%)	<0.001
	diabetes mellitus	6146 (36.3%)	234 (50.3%)	5912 (35.9%)	<0.001
	Age ≥ 75	10053 (59.4%)	230 (49.5%)	9823 (59.7%)	<0.001
HAS-BLED Components	**alcohol**	740 (4.4%)	72 (15.5%)	668 (4.1%)	<0.001
	bleeding	9856 (58.3%)	352 (75.7%)	9504 (57.8%)	<0.001
	drugs increasing bleed risk	659 (3.9%)	21 (4.5%)	638 (3.9%)	1.0
	abnormal renal function	7873 (46.5%)	301 (64.7%)	7572 (46.0%)	<0.001
	uncontrolled hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.0
	stroke	8637 (51.1%)	312 (67.1%)	8325 (50.6%)	<0.001
	abnormal liver function	1696 (10.0%)	83 (17.8%)	1613 (9.8%)	<0.001
HAS-BLED Score	**0**	883 (5.2%)	11 (2.4%)	872 (5.3%)	0.28
	1	2960 (17.5%)	37 (8.0%)	2923 (17.8%)	<0.001
	2	4430 (26.2%)	80 (17.2%)	4350 (26.4%)	<0.001
	3	4419 (26.1%)	144 (31.0%)	4275 (26.0%)	0.75
	4	3249 (19.2%)	123 (26.5%)	3126 (19.0%)	<0.01
	5	862 (5.1%)	64 (13.8%)	798 (4.9%)	<0.001
	6	107 (0.6%)	6 (1.3%)	101 (0.6%)	1.0
	7	6 (0.0%)	0 (0.0%)	6 (0.0%)	1.0
	total	2.55 (1.3)	3.18 (1.27)	2.53 (1.29)	<0.001
CHA2DS2-Vasc Score	**0**	381 (2.3%)	6 (1.3%)	375 (2.3%)	1.0
	1	778 (4.6%)	11 (2.4%)	767 (4.7%)	1.0
	2	1468 (8.7%)	24 (5.2%)	1444 (8.8%)	0.33
	3	2232 (13.2%)	43 (9.2%)	2189 (13.3%)	0.54
	4	2789 (16.5%)	72 (15.5%)	2717 (16.5%)	1.0
	5	2866 (16.9%)	85 (18.3%)	2781 (16.9%)	1.0
	6	2774 (16.4%)	91 (19.6%)	2683 (16.3%)	1.0
	7	2123 (12.6%)	72 (15.5%)	2051 (12.5%)	1.0

	8	1138 (6.7%)	45 (9.7%)	1093 (6.6%)	0.54
	9	367 (2.2%)	16 (3.4%)	351 (2.1%)	1.0
	Total	4.72 (2.08)	5.28 (1.96)	4.7 (2.08)	<0.001
Anticoagulation Status	**Any OAC**	9021 (53.3%)	199 (42.8%)	8822 (53.6%)	<0.001
	Warfarin	4086 (24.2%)	56 (12.0%)	4030 (24.5%)	<0.001
	DOAC	4935 (29.2%)	143 (30.8%)	4792 (29.1%)	1.0

Note: Age, stroke and bleeding total scores are shown as mean (SD) and tested with a t-test, all other values are N (%) and tested with a chi-squared test.

Fig 2. CHA2DS2-VASc and HASBLED scores for the entire AF cohort (SMI and non-SMI) at their most recent hospital admission.

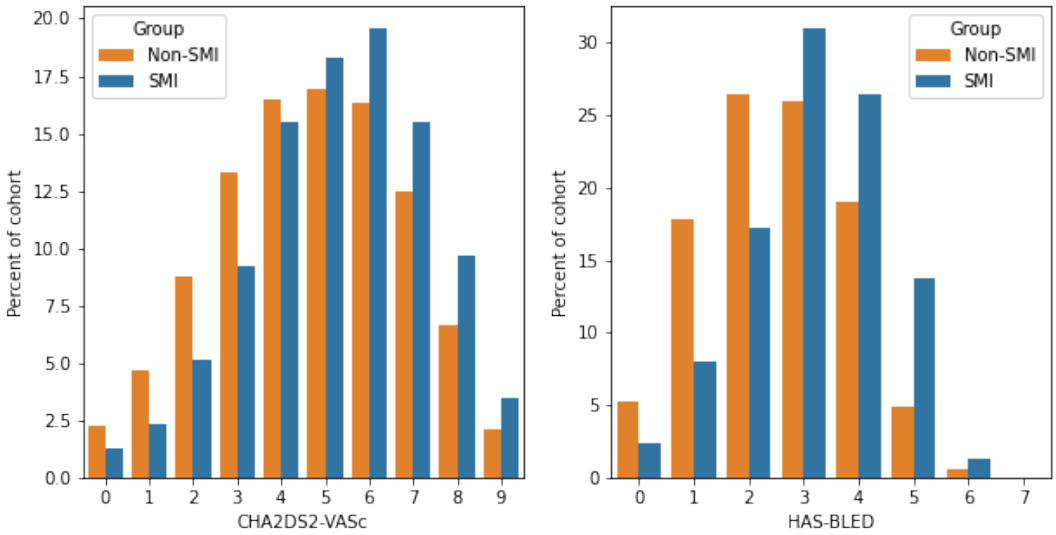
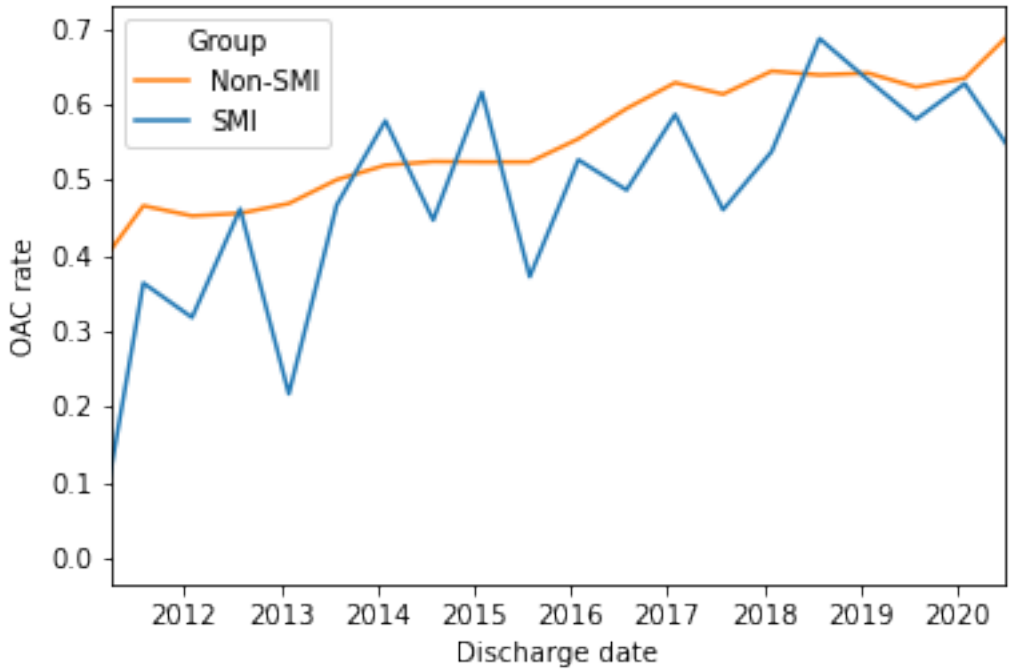


Table 2. Anticoagulation rates for the AF cohort at high risk of stroke, stratified by SMI status and time.

Time	Factor	All AF Patients	SMI	Not SMI	P-value
All	**HAS-BLED ≥ 3**	8582 (54.5%)	334 (74.6%)	8248 (53.9%)	<0.001
	Any OAC	8506 (54.0%)	195 (43.5%)	8311 (54.3%)	<0.001
	Warfarin	3839 (24.4%)	55 (12.3%)	3784 (24.7%)	<0.001
	DOAC	4667 (29.6%)	140 (31.2%)	4527 (29.6%)	1.0
	N	15757	448	15309	
2019-2020	**HAS-BLED ≥ 3**	2409 (61.3%)	119 (76.8%)	2290 (60.6%)	<0.001
	Any OAC	2477 (63.0%)	86 (55.5%)	2391 (63.3%)	0.35
	Warfarin	500 (12.7%)	15 (9.7%)	485 (12.8%)	1.0
	DOAC	1977 (50.3%)	71 (45.8%)	1906 (50.5%)	1.0
	N	3932	155	3777	
2011-2018	**HAS-BLED ≥ 3**	6157 (52.2%)	215 (73.4%)	5942 (51.7%)	<0.001
	Any OAC	6012 (51.0%)	109 (37.2%)	5903 (51.3%)	<0.001
	Warfarin	3334 (28.3%)	40 (13.7%)	3294 (28.6%)	<0.001
	DOAC	2678 (22.7%)	69 (23.5%)	2609 (22.7%)	1.0
	N	11795	293	11502	

Note: only patients with CHA2DS2-VASc ≥ 2 are included. All values are N (%) and tested with a chi-squared test.

Fig 3.a Trend in anticoagulation rate over time by SMI diagnosis for AF patients at high risk of stroke (CHA2DS2-VASc ≥2).



Note: Rates were aggregated on a 6-months level and limited to 2020-06-30 as the last complete six months in the dataset.

Fig 3.b. Trend in anticoagulation rates over time split by SMI diagnosis and type of OAC for AF patients at high risk of stroke (CHA2DS2-VASc≥2).

Note: Rates were aggregated on a 6-months level and limited to 2020-06-30 as the last complete six months in the dataset. DOAC = direct acting oral anticoagulant.

4. Discussion

This study provides insights on the oral anticoagulation (warfarin vs DOACs) prescription rate among AF patients with and without a co-morbid SMI using electronic health records. Compared to non-SMI patients, those with SMI had more comorbidities and significantly higher CHA2DS2-VASc and HASBLED scores. Among AF patients having CHA2DS2-VASc ≥2, those with co-morbid SMI were less likely than non- SMI patients to be prescribed any OAC, particularly warfarin (but not DOACs). However, there was no evidence of a significant difference between the two groups since 2019.

Our findings are in line with previous research showing that there is a treatment gap between SMI and non-SMI patients (Fenger-Grøn et al., 2021; Jaakkola et al., 2021; Schmitt et al., 2015). Using the Veterans Health Administration database (n = 12 190), Schmitt et al. (2015) reported that warfarin eligible patients with psychotic disorders (n = 122) were less likely to receive the treatment compared to controls (AOR 0.77; 95% CI, 0.65–0.90). A nationwide cohort study in Finland (n = 239 222) reported that diagnoses of bipolar disorder (n = 1129) (adjusted subdistribution hazard ratio (aSHR): 0.838; 95% CI 0.824 to 0.852) and schizophrenia (n = 1560) (aSHR 0.838; 95% CI 0.824 to 0.851) were associated with lower rates of oral anticoagulation therapy in AF patients after adjusting for multiple confounders (age, sex, stroke, and bleeding risk factors) (Jaakkola et al., 2021). Similarly, using a Danish nationwide cohort (n = 147 810), Fenger-Grøn et al. (2021) reported that among newly AF diagnosed patients, bipolar disorder (n = 1208) and schizophrenia (n = 572) were associated with a significantly lower frequency of oral anticoagulation therapy initiation adjusting for age and sex (bipolar: − 12.7%, 95% CI: − 15.3% to − 10.0%; schizophrenia: − 24.5% 95% CI: − 28.3% to − 20.7%). Anticoagulation treatment deficit remained significant after the introduction of DOACs (analysis performed between 2013 and 2016) among patients with schizophrenia but not among those with bipolar disorder (Fenger-Grøn et al., 2021).

In this study, we report that there was no evidence of a significant difference in anticoagulation prescription rates between SMI and non-SMI AF patients after 2019 suggesting an improvement in anticoagulation therapy among a population considered at high risk of adverse events. However, the prescription rate of any OAC only reached 44% among SMI patients and 54% among non-SMI patients whose CHA2DS2-VASc ≥2. This means that up until 2020, a large proportion of AF patients was not prescribed an OAC despite being at high risk of stroke. Previous studies have attributed OAC treatment deficit to concerns about the increased

bleeding risk although no previous research has shown that the benefits of the treatment are offset by this risk (Paradise et al., 2014; Rutherford et al., 2018; Schauer et al., 2005).

Instead, according to NICE guidelines, people with high bleeding risk score should be managed for factors increasing the bleeding risk such as uncontrolled hypertension, alcohol, and relevant medications (Linden, 2014). Our findings suggest that clinicians are adhering to these guidelines as despite higher HASBLED scores, there was an increase in OAC prescription rates among AF patients particularly those with co-morbid SMI.

Labile INR is another issue for people on warfarin. People with mental illness on warfarin spend less time in therapeutic range and have a higher proportion of sub- and supra-therapeutic INR values compared to the general population (Maki et al., 2013; Razouki et al., 2014; Rose et al., 2010). Given the larger therapeutic range and the simpler dosing regimen, DOACs may be better alternatives in people with active features of mental illness (January et al., 2019). This was practically noted in our population as DOAC prescribing rate has shown a substantial increase over time (2011–2020) while warfarin use has decreased. Despite being younger, AF patients with SMI had higher stroke and bleeding risks (measured by the CHA2DS2-VASc and HASBLED scores) compared to non-SMI patients, mainly due to the higher prevalence and incidence of physical comorbidities (Correll et al., 2017; Lai et al., 2020, 2022). This is in line with previous studies assessing associations and outcomes of atrial fibrillation in patients with mental illness. In a Danish nationwide cohort study, people with schizophrenia had a crude 5-year hazard ratio (HR) of 3.16 (95% CI 1.78 to 5.61) for fatal thromboembolic events, with trends towards increased risks of bleeding (1.37; 95% CI: 0.99 to 1.90) (Søgaard et al., 2017). Similarly, another study reported that patients with psychiatric illness (including schizophrenia, affective psychosis, and other nonorganic psychosis) receiving warfarin had an increased risk of intracranial haemorrhage (adjusted HR1.5; 95% CI: 1.04, 2.1), gastrointestinal bleeding (adjusted HR 1.2; 95%CI: 1.03, 1.4) and stroke (adjusted HR 1.4; 95% CI: 1.1, 1.7) (Schauer et al., 2005). A recent meta-analysis reported that AF patients with any mental health condition were at 25% higher adjusted ischemic stroke risk (RR 1.25, 95%CI: 1.08–1.45) and 17% higher bleeding risk (RR 1.17, 95%CI: 1.08–1.27) compared to patients without mental illness (Teppo et al., 2021).

Our study has limitations. First, the analysis is based on data extracted from electronic health records using an NLP-based approach. Although the major variables were manually validated

in our analysis (accuracy: 96% for AF, 95% for SMI, 80% for CHA2DS2VASc), and MedCAT (Kraljevic et al., 2021) has been validated in a number of sites for various conditions, it is likely that our automatically extracted variables contain errors. However, the issue of accuracy is not only limited to our approach but is an issue with conventional EHR data, where even in seemingly robust registries data accuracy is not universally high (Faxon and Burgess, 2016; Poulos et al., 2021). Second, the study population was limited to patients admitted to the hospital as they tend to have more accurately recorded data, especially in terms of drug prescription, therefore may not be fully representative of the overall population. Additionally, it was not possible to reliably distinguish whether OAC prescription was from the community or the hospital by searching for data in the discharge summaries as they included information about the medical history and medications prescribed prior to admission. Third, NICE guidelines now recommend ORBIT rather than HASBLED as a bleeding risk assessment tool, however, by the time the new guidelines were released (2021) data extraction and validation were completed. Given that there is little difference in sensitivity and specificity between the two tools we proceeded with HASBLED. Fourth, the co-morbidities captured in this study were restricted to the CHA2DS2-VASc and HAS- BLED components. This approach allowed us to focus on a set of variables for which we could validate our pipeline and are accepted as clinically relevant in this context, but other risk factors associated with increased risk of poor outcomes in AF patients with co-morbid mental illness may not have been recorded. Fifth, rates were aggregated on a 6-months level for the trend analysis with patients contributing only once to the interval (most recent admission within the interval) and more than once to different intervals. Patients with multiple admissions could be a potential cause of bias, however, the risk is low knowing that most patients included in the study had only 1 admission (71% had only 1 admission, 92% had at most 3 admissions and 93% had at most 5 admissions). Finally, this study was conducted over a period of 10 years in one hospital, part of King's Health Partners, an Academic Health Sciences Centre which prioritises mind-body care and awareness of inequities. Although findings of this study may be generalizable, particularly as it covers a large population, further research should be done in other organizations using different electronic health records to validate the data.

In this study, oral anticoagulation prescription rate has shown an increasing trend among both SMI and non-SMI patients with no evidence of a significant difference between the two groups since 2019 in one major London teaching hospital. A substantial rise in DOAC prescription was noted among all AF patients regardless of their SMI status. AF patients with comorbid

mental illness had high stroke and bleeding risks mainly attributed to the increased prevalence and incidence of contributing risk factors. More research is needed to confirm whether the introduction of DOACs has reduced OAC treatment gap between SMI vs non-SMI patients and whether the use of DOACs has improved the health outcomes in people with SMI.

Sources of direct funding, support, or sponsorship

DF is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHSFoundation Trust and by the KCL funded Centre for Doctoral Training (CDT) in Data-Driven Health. DB holds a UKRI Fellowship as part of HDRUK MR/S00310X/1. TW and YM are supported by the Maudsley Charity Grant (No.1517). RD's work is supported by the following: (1) NIHR Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London, London, UK; (2) Health Data Research UK, which is funded by the UK Medical Research Council, Engineering and Physical Sciences Research Council, Economic and Social Research Council, Department of Health and Social Care (England), Chief Scientist Office of the Scottish Government Health and Social Care Directorates, Health and Social Care Research and Development Division (Welsh Government), Public Health Agency (Northern Ireland), British Heart Foundation and Wellcome Trust; (3) The BigData@Heart Consortium, funded by the Innovative Medicines Initiative-2 Joint Undertaking under grant agreement No. 116074. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA; it is chaired by DE Grobbee and SD Anker, partnering with 20 academic and industry partners and ESC; (4) the National Institute for Health Research University College London Hospitals Biomedical Research Centre; (5) the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London; (6) the UK Research and Innovation London Medical Imaging & Artificial Intelligence Centre for Value Based Healthcare; (7) the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust. J.T.T. has received research grant funding support from Innovate UK, NHSX, Office of Life Sciences, National Institutes of Health Research, Bristol Meyers Squibb, and Pfizer. FG is in part supported by the National Institute for Health Research's (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London, by the Maudsley Charity and by the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust.

Role of the sponsor

The sponsors had no role in the in the conduct of the study; design, management, analysis, or interpretation of the data; and preparation, review, or approval of the manuscript.

Author statement

Dina Farran: Investigation, Methodology, Validation, Roles/Writing original draft, Writing review & editing.

Daniel Bean: Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Writing review & editing.

Tao Wang: Data curation, Software, Writing review & editing. Yamiko Msosa: Data curation, Software, Writing review & editing. Cecilia Casetta: Conceptualization, Investigation, Writing review & editing.

Richard Dobson: Conceptualization, Funding acquisition, Resources, Supervision, Writing review & editing.

James T. Teo: Conceptualization, Investigation, Writing review & editing.

Paul Scott: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing review & editing.

Fiona Gaughran: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing review & editing.

Declaration of competing interest

J.T.T. has received speaker honoraria from Bayer, Bristol-Meyers Squibb, Pfizer, and Goldman Sachs; hospitality from iRhythm Technologies; copyright fees from Wiley Blackwell; and owns public shares in Apple, Nvidia, Amazon, and Alphabet.

Acknowledgement

None.

References

Bean, D.M., Teo, J., Wu, H., Oliveira, R., Patel, R., Bendayan, R., Shah, A.M., Dobson, R. J., Scott, P.A., 2019. Semantic computational analysis of anticoagulation use in atrial fibrillation from real world data. PLoS One 14, e0225625. https://doi.org/10.1371/ journal.pone.0225625.

Correll, C.U., Solmi, M., Veronese, N., Bortolato, B., Rosson, S., Santonastaso, P., et al., 2017. Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: a large-sCardiovasc. Intervent.cale meta-analysis of 3,211,768 patients and 113,383,368 controls. World Psychiatr. 16, 163–180. https://onlinelibrary.wiley.com/doi/full/10.1002/wps.20420.

El-Sappagh, S., Franda, F., Ali, F., Kwak, K.S., 2018. SNOMED CT standard ontology based on the ontology for general medical science. BMC Med. Inf. Decis. Making 18, 1–19. https://bmcmedinformdecismak.biomedcentral.com/articles/10.118 6/s12911-018-0651-5.

Faxon, D.P., Burgess, A., 2016. Cardiovascular registries: too much of good thing? Circulation. Cardiovascular Interventions 9, e003866. https://www.ahajournals.or g/doi/abs/10.1161/circinterventions.116.003866.

Fenger-Grøn, M., Vestergaard, C.H., Ribe, A.R., Johnsen, S.P., Frost, L., Sandbæk, A., Davydow, D.S., 2021. Association between bipolar disorder or schizophrenia and oral anticoagulation use in Danish adults with incident or prevalent atrial fibrillation. JAMA Netw. Open 4. https://doi.org/10.1001/ jamanetworkopen.2021.10096 e2110096-e2110096.

Jaakkola, J., Teppo, K., Biancari, F., Halminen, O., Putaala, J., Mustonen, P., Haukka, J., Linna, M., Kinnunen, J., Tiili, P., Aro, A.L., 2021. The Effect of Mental Health Conditions on the Use of Oral Anticoagulation Therapy in Patients with Atrial Fibrillation: the FinACAF Study. European Heart Journal-Quality of Care and Clinical Outcomes. https://doi.org/10.1093/ehjqcco/qcab077.

Jackson, R., Kartoglu, I., Stringer, C., Gorrell, G., Roberts, A., Song, X., Wu, H., Agrawal, A., Lui, K., Groza, T., Lewsley, D., 2018. CogStack-experiences of deploying integrated information retrieval and extraction services in a large National Health Service Foundation Trust hospital. BMC Med. Inf. Decis. Making 18, 1–13. https:// doi.org/10.1186/s12911-018-0623-9.

January, C.T., Wann, L.S., Calkins, H., Chen, L.Y., Cigarroa, J.E., Cleveland, J.C., Ellinor, P.T., Ezekowitz, M.D., Field, M.E., Furie, K.L., Heidenreich, P.A., 2019. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of cardiology/American heart association task force on clinical practice guidelines and the heart rhythm society. J. Am. Coll. Cardiol. 74, 104–132.

Jones, C., Pollit, V., Fitzmaurice, D., Cowan, C., 2014. The management of atrial fibrillation: summary of updated NICE guidance. Bmj 348. https://doi.org/10.1136/ bmj.g4440.

Kennedy, W.K., Jann, M.W., Kutscher, E.C., 2013. Clinically significant drug interactions with atypical antipsychotics. CNS Drugs 27, 1021–1048. https://doi.org/10.1007/ s40263-013-0114-6.

Kirchhof, P., Benussi, S., Kotecha, D., Ahlsson, A., Atar, D., Casadei, B., Castella, M., Diener, H.C., Heidbuchel, H., Hendriks, J., Hindricks, G., 2016. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Kardiol. Pol. 74, 1359–1469. https://doi.org/10.5603/kp.2016.0172.

Kraljevic, Z., Searle, T., Shek, A., Roguski, L., Noor, K., Bean, D., Mascio, A., Zhu, L., Folarin, A.A., Roberts, A., Bendayan, R., 2021. Multi-domain clinical natural language processing with medcat: the medical concept annotation toolkit. Artif. Intell. Med. 117, 102083 https://doi.org/10.1016/j.artmed.2021.102083.

Lai, F.T., Guthrie, B., Mercer, S.W., Smith, D.J., Yip, B.H., Chung, G.K., et al., 2020. Association between antipsychotic use and acute ischemic heart disease in women but not in men: a retrospective cohort study of over one million primary care patients. BMC Med. 18, 1–10. https://bmcmedicine.biomedcentral.com/articles/10. 1186/s12916-020-01765-w.

Lai, F.T., Mercer, S.W., Guthrie, B., Yip, B.H., Chung, G.K., Zou, D., et al., 2022. Sociodemographic moderation of the association between depression and stroke incidence in a retrospective cohort of 0.4 million primary care recipients with hypertension. Psychol. Med. 52, 283–291. https://www.cambridge.org/core/jour nals/psychological-medicine/article/abs/sociodemographic-moderation-of-the -association-between-depression-

and-stroke-incidence-in-a-retrospective-cohort -of-04-million-primary-care-recipients-with-hypertension/ 5055D5F52CB197996EAAF89B8F330C33.

Lawrence, D., Kisely, S., 2010. Inequalities in healthcare provision for people with severe mental illness. J. Psychopharmacol. 24, 61–68. https://doi.org/10.1177/ 1359786810382058.

Linden, B., 2014. Diagnosis and management of atrial fibrillation: the latest NICE guidance. Br. J. Card. Nurs. 9, 372–373. https://doi.org/10.12968/ bjca.2014.9.8.372.

Lip, G.Y., Nieuwlaat, R., Pisters, R., Lane, D.A., Crijns, H.J., 2010. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest 137, 263–272. https://doi.org/10.1378/chest.09-1584.

Maki, E.D., Miesner, A.R., Grady, S.E., Marschall, L.M., 2013. Effects of depressive and other psychiatric disorders on anticoagulation control in a pharmacist-managed anticoagulation clinic. Ann. Pharmacother. 47, 292–1300. https://doi.org/10.1177/ 1060028013503788.

Paradise, H.T., Berlowitz, D.R., Ozonoff, A., Miller, D.R., Hylek, E.M., Ash, A.S., Jasuja, G.K., Zhao, S., Reisman, J.I., Rose, A.J., 2014. Outcomes of anticoagulation therapy in patients with mental health conditions. J. Gen. Intern. Med. 29, 855–861. https://doi.org/10.1007/s11606-014-2784-2.

Platt, A.B., Localio, A.R., Brensinger, C.M., Cruess, D.G., Christie, J.D., Gross, R., Parker, C.S., Price, M., Metlay, J.P., Cohen, A., Newcomb, C.W., 2008. Risk factors for nonadherence to warfarin: results from the IN-RANGE study. Pharmacoepidemiol. Drug Saf. 17, 853–860. https://doi.org/10.1002/pds.1556.

Poulos, J., Zhu, L., Shah, A.D., 2021. Data gaps in electronic health record (EHR) systems: an audit of problem list completeness during the COVID-19 pandemic. Int. J. Med. Inf. 150, 104452. https://www.sciencedirect.com/science/article/pii/ S1386505621000782.

Razouki, Z., Ozonoff, A., Zhao, S., Rose, A.J., 2014. Pathways to poor anticoagulation control. J. Thromb. Haemostasis 12, 628–634. https://doi.org/10.1111/jth.12530.

Rose, A.J., Hylek, E.M., Ozonoff, A., Ash, A.S., Reisman, J.I., Berlowitz, D.R., 2010. Patient characteristics associated with oral anticoagulation control: results of the Veterans AffaiRs Study to Improve Anticoagulation (VARIA). J. Thromb. Haemostasis 8, 2182–2191. https://doi.org/10.1111/j.1538-7836.2010.03996.x.

Ruff, C.T., Giugliano, R.P., Braunwald, E., Hoffman, E.B., Deenadayalu, N., Ezekowitz, M. D., Camm, A.J., Weitz, J.I., Lewis, B.S., Parkhomenko, A., Yamashita, T., 2014. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet 383, 955–962. https://doi.org/10.1016/s0140-6736(13)62343-0.

Rutherford, O.C.W., Jonasson, C., Ghanima, W., Holst, R., Halvorsen, S., 2018. New score for assessing bleeding risk in patients with atrial fibrillation treated with NOACs. Open heart 5, e000931. https://doi.org/10.1136/openhrt-2018-000931.

Schauer, D.P., Moomaw, C.J., Wess, M., Webb, T., Eckman, M.H., 2005. Psychosocial risk factors for adverse outcomes in patients with nonvalvular atrial fibrillation receiving warfarin. J. Gen. Intern. Med. 20, 1114–1119. https://doi.org/10.1111/j.1525- 1497.2005.0242.x.

Schmitt, S.K., Turakhia, M.P., Phibbs, C.S., Moos, R.H., Berlowitz, D., Heidenreich, P., Chiu, V.Y., Go, A.S., Friedman, S.A., Than, C.T., Frayne, S.M., 2015. Anticoagulation in atrial fibrillation: impact of mental illness. Am. J. Manag. Care 21, e609–e617.

Søgaard, M., Skjøth, F., Kjældgaard, J.N., Larsen, T.B., Hjortshøj, S.P., Riahi, S., 2017. Atrial fibrillation in patients with severe mental disorders and the risk of stroke, fatal thromboembolic events and bleeding: a nationwide cohort study. BMJ Open 7, e018209. https://doi.org/10.1136/bmjopen-2017-018209.

Teppo, K., Jaakkola, J., Lehto, M., Biancari, F., Airaksinen, K.J., 2021. The impact of mental health conditions on oral anticoagulation therapy and outcomes in patients with atrial fibrillation: a systematic review and meta-analysis. Am. J. Prevent. Cardiol. 7, 100221 https://doi.org/10.1016/j.ajpc.2021.100221.

Walker, E.R., McGee, R.E., Druss, B.G., 2015. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. JAMA Psychiatr. 72, 334–341. https://doi.org/10.1001/jamapsychiatry.2014.2502.

Walker, G.A., Heidenreich, P.A., Phibbs, C.S., Go, A.S., Chiu, V.Y., Schmitt, S.K., Ananth, L., Frayne, S.M., 2011. Mental illness and warfarin use in atrial fibrillation. Am. J. Manag. Care 17, 617–624.

CHAPTER 4- FACTORS ASSOCIATED WITH ORAL ANTICOAGULANT USE IN PATIENTS WITH ATRIAL FIBRILLATION AND MENTAL DISORDERS -Paper 3 (62)

Dina Farran[1]* (MSc, MPH), **Matthew Broadbent** (MA (hons))[2], **Aikaterini Dima** (MD, MSc)[1,2], **Mark Ashworth**[3](DM), **Fiona Gaughran**[1,2] (MD)

1. Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
2. South London and Maudsley NHS Foundation Trust, London, UK
3. School of Life Course and Population Sciences, King's College London, London, UK

* *Corresponding author. Institute of Psychiatry, Psychology and Neuroscience, King's College London, 16 De Crespigny Park, London, SE5 8AB, UK. E-mail address: dina.1.farran@kcl.ac.uk (D. Farran).*

Farran D, Broadbent M, Dima A, Ashworth M, Gaughran F. Factors Associated With Oral Anticoagulant Use in Patients With Atrial Fibrillation and Mental Disorders. The Journal of clinical psychiatry. 2024 Jan 3;85(1):50936. https://doi.org/10.4088/JCP.23m14824

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. CHA2DS2-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 high 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.

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 CHA2DS2-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.

INTRODUCTION

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 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) 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 standard error 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, 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 DS - 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 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 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).

Table 1. Characteristics of study cohort[a]

Factor	Dementia (N=1013)	SMI (N=245)	Substance Use Disorders (n=69)	Common Mental Disorders (N=778)
Age (mean (SD))	84.92 (6.74)	65.73 (17.85)	60.43 (12.56)	75.10 (15.73)
Sex-Male (number/%)	438 (43.2)	141 (57.6)	55 (79.7)	370 (47.6)
Ethnicity (number/%)				
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 (number/%)				
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 (number/%)				
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 (12 domains; number/%)				
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.*

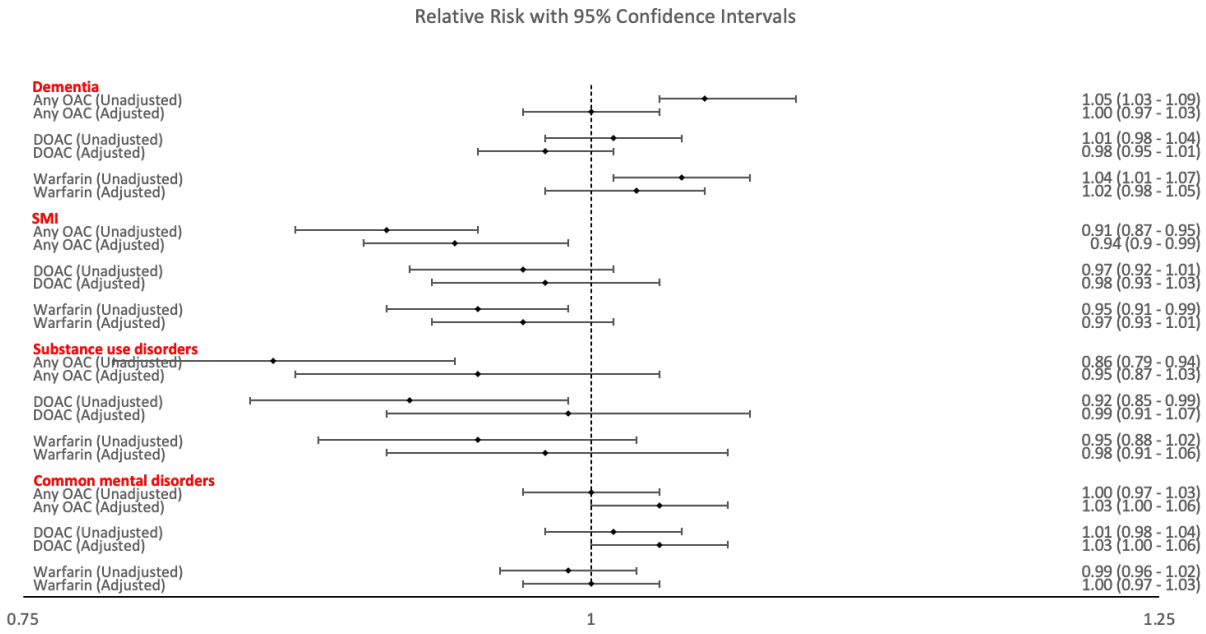
Abbreviations: GCSE = General Certificate of Secondary Education, HoNOS = Health of the Nation Outcome Scales, SMI = serious mental illness.

Table 2. Stroke and bleeding risks for people with atrial fibrillation stratified by mental illness status[a]

Factor	Dementia (N=1013)	SMI (N=245)	Substance Use Disorders (n=69)	Common Mental Disorders (N=778)
CHA_2DS_2VASc				
Age				
<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 scores				
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 (mean (SD))	4.72 (1.61)	4.21 (2.20)	2.52 (1.98)	4.16 (1.93)
ORBIT				
Age >74	942 (93.0)	91 (37.1)	9 (13.0)	484 (62.2)
Low Haemoglobin (<13g/dL in males & <12g/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 scores				
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 (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.

Fig1. 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, total CHA2DS2VASC 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 comprated 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.

Table 3. OAC prescription rates and bleeding risks among AF people having a CHA2DS2VASc >=1 stratified by mental illness [a]

	Dementia (N= 1013)	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 (mean (SD)) of people prescribed any OAC	1.81 (1.12)	1.98 (1.38)	1.05 (1.19)	1.80 (1.23)
ORBIT (mean (SD)) of people NOT prescribed any OAC	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

	AF cohort			AF and co-morbid Dementia			AF and co-morbid SMI		
HoNOS components	**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)
Alcohol or substance dependency	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)
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)
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)
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)
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)
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)
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)

Table 4 continued

	AF and co-morbid Substance Use Disorder			AF and co-morbid Common Mental Disorder		
HoNOS components	**Any OAC**	**DOAC**	**Warfarin**	**Any OAC**	**DOAC**	**Warfarin**
Self-injury	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 dependency	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 (0.77 - 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	1.04 (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	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 (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	1.07 (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	0.99 (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% confidence intervals. Estimates are adjusted for age, sex, total CHA2DS2VASC 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.

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 under recording 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 under recording 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 under detection 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.

Author Affiliations: Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom (Farran, Dima, Gaughran); South London and Maudsley NHS Foundation Trust, London, United Kingdom (Broadbent, Dima, Gaughran); School of Life Course and Population Sciences, King's College London, London, United Kingdom (Ashworth).

Relevant Financial Relationships: The authors have no conflict of interest to declare. The authors report no financial or other relationship relevant to the subject of this article.

Funding/Support: Dr Farran is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust and by the KCL-funded Centre for Doctoral Training (CDT) in Data-Driven Health. Drs Broadbent and Dima are employed by the South London and Maudsley NHS Foundation Trust. Dr Ashworth is in part funded by the Guy's and St Thomas' Charity and the NIHR ARC South London. Dr Gaughran is in part supported by the National Institute for Health Research's (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London, by the Maudsley Charity, and by the NIHR ARC South London at King's College Hospital NHS Foundation Trust.

Role of the Funders/Sponsors: The sponsors had no role in the in the conduct of the study; design, management, analysis, or interpretation of the data; and preparation, review, or approval of the manuscript.

Disclaimer: The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

References

1- Hindricks G, Potpara T, Dagres N et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS) The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. European heart journal. 2021;42(5):373-498.

2- Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Annals of internal medicine. 2007;146(12):857-67.https://doi.org/10.7326/0003-4819-146-12-200706190-00007

3- Odum L, Cochran K, Aistrope D, Snella K. The CHADS2 versus the New CHA2DS2-VASc Scoring Systems for Guiding Antithrombotic Treatment of Patients with Atrial Fibrillation: Review of the Literature and Recommendations for Use. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2012;32(3):285-296. doi:10.1002/j.1875-9114.2012.01023.x

4- Jones C, Pollit V, Fitzmaurice D, Cowan C. The management of atrial fibrillation: summary of updated NICE guidance. BMJ. 2014;348. https://doi.org/10.1136/bmj.g3655

5- Højen AA, Nielsen PB, Riahi S, Jensen M, Lip GY, Larsen TB, Søgaard M. Disparities in oral anticoagulation initiation in patients with schizophrenia and atrial fibrillation: a nationwide cohort study. British Journal of Clinical Pharmacology. 2022. https://doi.org/10.1111/bcp.15337

6- Fenger-Grøn M, Vestergaard C, Ribe A et al. Association Between Bipolar Disorder or Schizophrenia and Oral Anticoagulation Use in Danish Adults With Incident or Prevalent Atrial Fibrillation. JAMA Netw Open. 2021;4(5):e2110096. doi:10.1001/jamanetworkopen.2021.10096

7- Jaakkola J, Teppo K, Biancari F et al. The effect of mental health conditions on the use of oral anticoagulation therapy in patients with atrial fibrillation: the FinACAF

study. European Heart Journal - Quality of Care and Clinical Outcomes. 2021. doi:10.1093/ehjqcco/qcab077

8- Fanning L, Ryan-Atwood TE, Bell JS, Meretoja A, McNamara KP, Dārziņš P, Wong IC, Ilomäki J. Prevalence, safety, and effectiveness of oral anticoagulant use in people with and without dementia or cognitive impairment: a systematic review and meta-analysis. Journal of Alzheimer's Disease. 2018;65(2):489-517.doi:10.3233/JAD-180219

9- Mongkhon P, Alwafi H, Fanning L, Lau WC, Wei L, Kongkaew C, Wong IC. Patterns and factors influencing oral anticoagulant prescription in people with atrial fibrillation and dementia: Results from UK primary care. British Journal of Clinical Pharmacology. 2021;87(3):1056-68. DOI: 10.1111/bcp.14464

10- Levin J, Aebi M, Tatsuoka C, Cassidy K, Sajatovic M. Adherence to Psychotropic and Nonpsychotropic Medication Among Patients With Bipolar Disorder and General Medical Conditions. Psychiatric Services. 2016;67(3):342-345. doi:10.1176/appi.ps.201500010

11- Blixen C, Kanuch S, Perzynski A, Thomas C, Dawson N, Sajatovic M. Barriers to Self-management of Serious Mental Illness and Diabetes. Am J Health Behav. 2016;40(2):194-204. doi:10.5993/ajhb.40.2.4

12- Ruff C, Giugliano R, Braunwald E et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. The Lancet. 2014;383(9921):955-962. doi:10.1016/s0140-6736(13)62343-0

13- Schauer D, Moomaw C, Wess M, Webb T, Eckman M. Psychosocial risk factors for adverse outcomes in patients with nonvalvular atrial fibrillation receiving warfarin. J Gen Intern Med. 2005;20(12):1114-1119. doi:10.1111/j.1525-1497.2005.0242.x

14- Lawrence D, Kisely S. Review: Inequalities in healthcare provision for people with severe mental illness. Journal of Psychopharmacology. 2010;24(4_suppl):61-68. doi:10.1177/1359786810382058

15- HONOS ASSESSMENT (Health of the Nation Outcome Scales). Peardonville house. Accessed January 18, 2023. https://peardonvillehouse.ca/wp-content/uploads/2018/12/Assessments.pdf

16- Hayes RD, Chang CK, Fernandes AC, Begum A, To D, Broadbent M, Hotopf M, Stewart R. Functional status and all-cause mortality in serious mental illness. 2012. https://doi.org/10.1371/journal.pone.0044613

17- Hayes RD, Chang CK, Fernandes A, Begum A, To D, Broadbent M, Hotopf M, Stewart R. Associations between symptoms and all-cause mortality in individuals with serious mental illness. Journal of psychosomatic research. 2012;72(2):114-9. https://doi.org/10.1016/j.jpsychores.2011.09.012

18- Wu CY, Chang CK, Hayes RD, Broadbent M, Hotopf M, Stewart R. Clinical risk assessment rating and all-cause mortality in secondary mental healthcare: the South London and Maudsley NHS Foundation Trust Biomedical Research Centre (SLAM BRC) Case Register. Psychological medicine. 2012;42(8):1581-90. DOI: 10.1017/S0033291711002698

19- Su YP, Chang CK, Hayes RD, Perera G, Broadbent M, To D, Hotopf M, Stewart R. Mini-mental state examination as a predictor of mortality among older people referred to secondary mental healthcare. PLoS One. 2014;9(9):e105312. DOI: 10.1371/journal.pone.0105312

20- Stewart R, Soremekun M, Perera G, Broadbent M, Callard F, Denis M, Hotopf M, Thornicroft G, Lovestone S. The South London and Maudsley NHS foundation trust biomedical research centre (SLAM BRC) case register: development and descriptive data. BMC psychiatry. 2009;9(1):1-2. doi:10.1186/1471-244X-9-51

21- CHA_2DS_2-VASc Score for Atrial Fibrillation Stroke Risk. mdcalc. Accessed January 18, 2023.https://www.mdcalc.com/calc/801/cha2ds2-vasc-score-atrial-fibrillation-stroke-risk

22- ORBIT Bleeding Risk Score for Atrial Fibrillation. mdcalc. Accessed January 18, 2023.https://www.mdcalc.com/calc/10227/orbit-bleeding-risk-score-atrial-fibrillation

23- CRIS NLP Service (2021) Library of production-ready applications, v1. 6. https://www.maudsleybrc.nihr.ac.uk/media/463740/applications-library-v21.pdf. Accessed January 18, 2023.

24- Kadra G, Stewart R, Shetty H, Jackson RG, Greenwood MA, Roberts A, Chang CK, MacCabe JH, Hayes RD. Extracting antipsychotic polypharmacy data from electronic

health records: developing and evaluating a novel process. BMC psychiatry. 2015 ;15(1):1-7. DOI 10.1186/s12888-015-0557-z

25- Farran D, Bean D, Wang T, Msosa Y, Casetta C, Dobson R, Teo JT, Scott P, Gaughran F. Anticoagulation for atrial fibrillation in people with serious mental illness in the general hospital setting. Journal of psychiatric research. 2022;153:167-73. DOI: 10.1016/j.jpsychires.2022.06.044

26- Correll CU, Solmi M, Veronese N, Bortolato B, Rosson S, Santonastaso P, Thapa-Chhetri N, Fornaro M, Gallicchio D, Collantoni E, Pigato G. Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: a large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls. World Psychiatry. 2017;16(2):163-80. https://doi.org/10.1002/wps.20420

27- Roth JA, Bradley K, Thummel KE, Veenstra DL, Boudreau D. Alcohol misuse, genetics, and major bleeding among warfarin therapy patients in a community setting. Pharmacoepidemiology and drug safety. 2015;24(6):619-27. doi: 10.1002/pds.3769

PART 3- ELECTRONIC CLINICAL DECISION SUPPORT SYSTEM (ECDSS) FOR MANAGEMENT OF AF-RELATED STROKE RISK

CHAPTER 5- OVERVIEW OF ECDSS

5.1 Definition of an eCDSS

An electronic clinical decision support system (eCDSS) is a software designed to analyse patient data and accordingly help healthcare providers with clinical decision making (63). It can take the form of an alert or reminder that provides clinicians with evidence-based guidelines towards optimal preventive, diagnostic and treatment strategies (63).

ECDSSs consist of two main types: knowledge based, and non-knowledge-based (64). The difference between the two lies in how information is processed and utilised for clinical decision support (64). An eCDSS that uses a knowledge base to support clinicians relies on medical knowledge mainly the scientific literature, clinical guidelines, and best practices (64). This type of tools often operates under the if-then rule: if a specific scenario appears, an alert is issued (64). However, a non-knowledge-based eCDSS relies more on data-driven approaches by using artificial intelligence, machine learning and statistical modelling (64). This type operates by analysing patterns found in patients' data to determine relationships and accordingly make predictions and recommendations (64).

ECDSSs offer many benefits including improving patient safety (by reducing medication errors, identifying patients at risk, and adhering to clinical guidelines), enhancing the quality of care, spreading knowledge, improving clinical efficiency, ensuring consistency in healthcare provision, and improving documentation of clinical data (65). However, the tool has also some drawbacks such as alert fatigue, overreliance, false positive recommendations, disruption of workflow, and loss of autonomy (65-67). To maximize the benefits and minimize the drawbacks, ongoing monitoring, evaluation, and improvement should be ensured when implementing an eCDSS in a healthcare setting.

5.2 Effectiveness of eCDSSs in the management of AF-related stroke

In a systematic review of 148 randomised controlled trial aiming to assess the effect of CDSSs on healthcare processes, Bright et al. reported an improvement in preventive services (OR 1.42, 95% CI 1.27 to 1.58), and prescription of appropriate therapies (OR 1.57, 95% CI 1.35 to 1.82) (61). The study also reported a significant effect of CDSSs on morbidity (RR 0.88, 95% CI 0.80 to 0.96) but not on mortality ((OR 0.79, 95% CI 0.54 to 1.15) (68). Similar findings were reported by Njie et al. who additionally emphasised on the significant positive effect of CDSSs in treating diseases (69).

ECDSSs for the management of AF and the stroke risk associated with it have been previously assessed for effectiveness in multiple general hospital settings. While certain outcomes may vary based on the healthcare setting and tool design, the cumulative evidence highlights the crucial role of eCDSSs in improving the management of stroke related to AF and the quality of care to those at risk (70-79).

A retrospective cohort study in Ohio involving 6123 patients evaluated a CDSS aiming to improve warfarin prescription (70). The tool recommended the therapy for eligible patients based on a tailored assessment of the risks and benefits (70). Although warfarin was recommended for 49% of patients, only 10% received it (70). However, a trend towards a decreased risk of stroke with the use of warfarin was noted among patients for whom the therapy was recommended, while an increased risk of gastrointestinal bleeding was noted among patients for whom warfarin was given and the CDSS recommended no use of warfarin (70).

Another study aiming to improve anticoagulation therapy through a computer software to support clinical decisions in three primary care trusts in England reported an increase in anticoagulation therapy from 53% to 60% (72). Similarly in Sweden, a cluster randomised trial involving AF patients (n=1857) assessed the effectiveness of a CDSS in improving guideline-based prescription of anticoagulation therapy in 43 primary care clinics (74). A significant increase in prescription of the therapy was observed after 12 months although no effect on strokes, transient ischaemic attack, or systemic embolism was noted in the study timeframe (74). Sheibani et al. also reported a significant increase in guideline adherence regarding anticoagulation therapy (48% to 66%,

p<0.0001) after implementing a CDSS for AF-related stroke management (N=373) (71). The adherence trend was stable even during the post-intervention phase (78).
On the other hand, a Dutch cluster randomised controlled trial assessing a CDSS intended to optimise stroke prevention in general practices by providing recommendations to prescribe oral anticoagulation therapy based on the patient's situation, could not demonstrate effectiveness mainly due to the under use of the tool (73). Similarly, an observational study evaluating the efficacy of a CDSS aiming to improve warfarin use among patients newly diagnosed with AF (n=268), reported no impact of the tool on the behaviour of healthcare providers (71).

No studies have assessed the effectiveness of such digital tools in a mental healthcare setting although research has shown that people with AF and co-morbid mental illness are less likely than the general population to be prescribed oral anticoagulation therapy to reduce the risk of stroke (60). Additionally, in our systematic review we found low recorded rates of AF in people with SMI reflecting possible under-recognition or under-recording of the condition in this group (60). Interventions aiming to improve the communication of physical conditions and risks between physical and mental health services offer an opportunity for better identification, risk stratification and, where needed, implementation of effective preventive measures. In the next chapter, the adoption of an eCDSS to improve the standard of AF screening among people with mental illness across secondary healthcare settings is described.

CHAPTER 6- IMPLEMENTATION OF AN ECDSS TO SCREEN FOR STROKE RISK AMONG PEOPLE WITH AF IN A MENTAL HEALTHCARE SETTING

Strokes associated with AF tend to be more severe and are more likely to cause disability and death compared to non-AF strokes (80). Among people having a stroke history, the risk of subsequent strokes significantly increases if AF is not managed (80).

Strokes can reduce the quality of life on many levels. It can affect the overall cognitive function leading to difficulties performing activities of daily living (81). It can lead to emotional and psychological consequences such as anxiety and depression (81). The ongoing care and the medical expenses may also impose a financial burden on the patients and their carers (81). Thus, preventive measures such as identification of stroke risk and early initiation of anticoagulation therapy (when needed) could reduce morbidity and mortality, preserve cognitive function and improve patients' quality of life.

A digital alerting system to improve screening for stroke risk among people with AF and co-morbid mental illnesses was developed with input from multi-disciplinary healthcare professionals, academic health informatics department, the IT team and digital clinical safety team at the host NHS Trust (SLaM). Mental Health of Older Adults (MHOA) wards at SLaM were chosen for the implementation of the eCDSS as the prevalence of AF is greater in older adults. The intervention was conducted in AL1 ward at Maudsley, Chelsham House at Bethlem and Hayworth ward at Ladywell.

6.1 Clinical protocol

Based on NICE guidelines and inputs from general practitioners, psychiatrists (including juniors and consultants), and pharmacists, a clinical protocol for the management and monitoring of AF-related stroke in SLaM adult inpatients was developed. The protocol highlights possible symptoms of AF and provides guidance on how to diagnose the condition and manage it based on stroke and bleeding risks. The clinical protocol was approved by the SLaM Quality Centre and was posted on the Maudsley intranet (physical health section) as a reference for clinicians dealing with patients having AF (Fig 1).

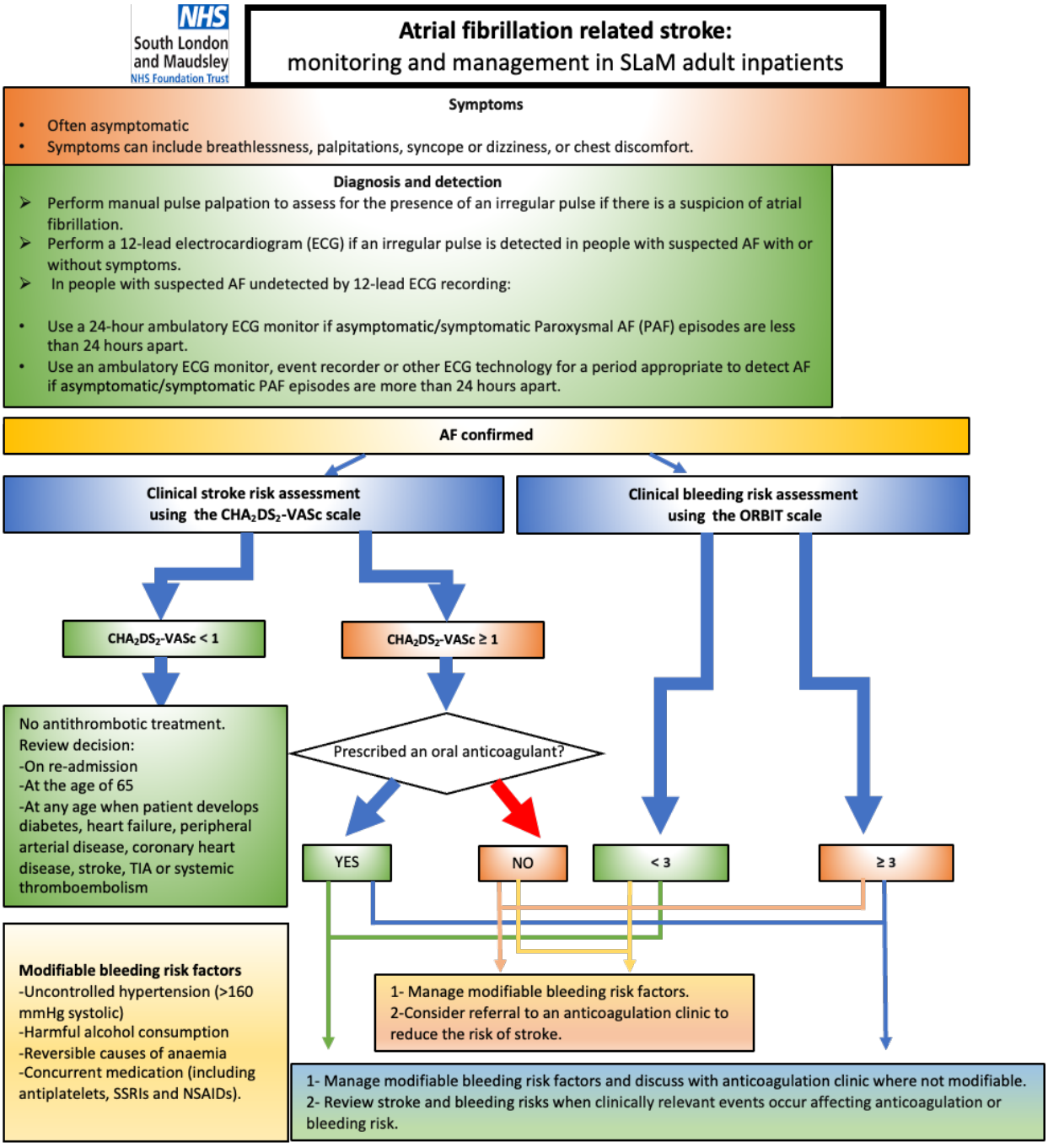


Fig 1. Clinical protocol for the management and monitoring of AF-related stroke in SLaM adult inpatients

6.2 Intervention protocol

The digital tool used for the eCDSS is CogStack which is an open-source information retrieval and extraction system with the capability to offer near real-time natural language processing (NLP) of electronic health records (EHR) (82).

The eCDSS prompts clinicians if patients with documented AF are admitted to the hospital under their care. Alerts are triggered by the presence of old or new diagnosis of AF in clinical notes. The previously developed Medical Concept Annotation Toolkit (MedCAT) was used as the underlying NLP tool to detect mentions of AF in free text clinical notes, clinical document repository or under physical health hub in electronic Patient Journey System (ePJS) (the main electronic patient notes system in SLaM where EHRs are accessed) (83). To ensure that the model is performing well, we conducted a validation exercise. All text documents (N=678,612) for all inpatients (N=699), extracted on March 30, 2023, were annotated. Mentions of AF identified by the model (N=81) were then manually labelled. The model performed reasonably well with metrics of Precision= 0.86, Recall= 0.92, F1= 0.89, and Accuracy= 0.81.

The eCDSS consists of a visual prompt on a patient electronic Personal Health Record (ePHR) (platform connected to ePJS where all alerts are sent and where the Trust's electronic prescribing system (ePMA) is located). The targeted healthcare providers are psychiatrists (junior doctors and consultants) and pharmacists, as they are the ones more likely to action the content of the alert.

Clinicians are prompted to confirm the presence of AF, complete clinical assessment of stroke and bleeding risks using the CHA_2DS_2VASc and ORBIT scales, and record scores in the Physical Health Hub (PHH) on ePJS. If patients are found to be at high risk of stroke, clinicians are prompted to refer them to oral anticoagulation clinics.

The OAC referral pathway for patients identified as high risk for stroke involves several coordinated steps. Clinicians are advised to refer high-risk patients to an appropriate OAC clinic based on the patient's GP address. The OAC clinics are not located within the mental health wards where the digital tool is implemented, meaning patients are typically seen by these clinics after hospital discharge rather than during their admission. The referral process involves sending an email to the OAC clinic, specifying that the patient has been diagnosed with AF and that both stroke and bleeding risks have been assessed using the CHA2DS2-VASc and ORBIT scales.

Additionally, clinicians are required to attach the patient's physical health summary to the referral email. To to facilitate smooth communication and coordination of care, clinicians are provided with the contact details (emails and phone numbers) of all the OAC clinics. In these clinics, a specialist team is responsible for initiating and monitoring anticoagulation treatment, ensuring that patients receive appropriate management based on their assessed risks. This structured pathway aims to streamline the transition from risk assessment to treatment initiation, ensuring that high-risk patients receive timely and effective anticoagulation therapy.

All training materials required to do this task were developed and made available on the MAUD page (intranet page).This included:

- The clinical protocol for the management of AF-related stroke in SLAM adult inpatients (Fig 2).
- Links to the $CHAD_2DS_2VASc$ and ORBIT calculators.
  CHA2DS2-VASc Score for Atrial Fibrillation Stroke Risk- MDCalc
  ORBIT Bleeding Risk Score for Atrial Fibrillation- MDCalc
- NICE guidelines on the diagnosis and management of AF related stroke
  Atrial fibrillation: diagnosis and management
- Step by step guidance on where to find the alerts on ePHR (Appendix B)
- Step by step guidance on how to record the stroke and bleeding risks in ePJS (Appendix C)
- Step by step guidance on how to make a referral to an oral anticoagulation clinic (Appendix C).

The study protocol was published on ClinicalTrials.gov (84).

The digital tool developed in this study does not qualify as a medical device because it does not independently diagnose or recommend a specific medical intervention. Instead, the eCDSS provides clinicians with relevant information and reminders based on existing clinical guidelines, leaving the ultimate decision-making to the healthcare professional. By prompting clinicians to consider stroke risk screening, the eCDSS functions more as a decision-support tool that encourages adherence to best practices (85).

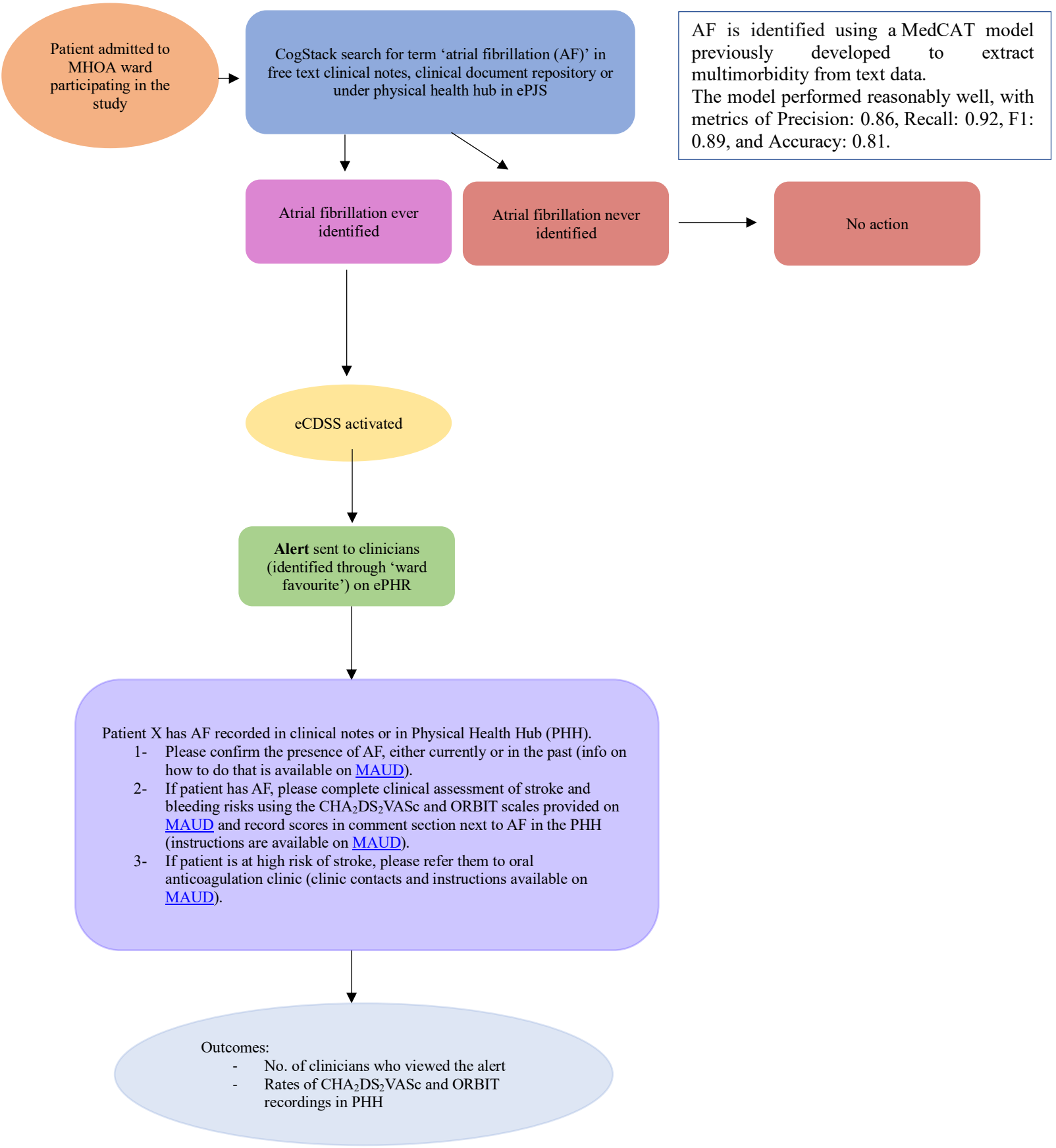


Fig 2. Intervention protocol for the screening of AF-related stroke in SLaM adult inpatients

6.3 Digital clinical safety

In collaboration with the digital health lead nurse and the Chief Clinical Information Officer (CCIO), the clinical safety of the digital tool was evaluated, and a clinical risk management plan was developed.

A workshop took place to develop a hazard log. During the workshop, a hazard identification exercise using the Structured What-If Technique (SWIFT) was performed (86). At each point on the process map the following questions were explored:

- What could go wrong (hazards), how often (likelihood) and how bad could it be (severity) for the patient?
- What causes the hazards?
- What risk controls/mitigation is already in place?
- What (if any) additional risk controls could be put in place?

The criteria that were used for scoring is described in Appendix D. The values obtained for severity and likelihood were then applied to the below matrix to obtain an overall risk score from 1 to 5 (Table 4) (87). Accordingly, 5 represents an unacceptable level of risk, 4 represents a mandatory elimination or control to reduce risk to an acceptable level, 3 represents an undesirable level of risk requiring attempts to control or reduce risk unless impractical, 2 represents an acceptable risk where cost of further reduction outweighs benefits gained, and 1 represents an acceptable risk with no further action required.

Likelihood	Very High	3	4	4	5	5
	High	2	3	3	4	5
	Medium	2	2	3	3	4
	Low	1	2	2	3	4
	Very Low	1	1	2	2	3
		Minor	Significant	Considerable	Major	Catastrophic
		Severity				

Table 4. Risk Estimation Matrix

Table 5 details risks which were deemed to be high or significant (scoring 3 – 5) at the initial risk assessment. For each identified hazard, an estimation of the associated clinical risk was made. Wherever possible, attempts were made to reduce all hazards to as low as reasonably practical.

Summary of hazards and mitigation strategies					
No.	Hazard	Initial Risk	Cause	Control/mitigations	Residual Risk
H01	Staff see the alert but are unsure of the clinical protocol for managing AF.	3	**Human factors:** Clinicians may have very little experience with AF assessments/care due to working in mental health services opposed to acute care	**System Design:** In the alert, there is a link to the MAUD page providing the following: 1. Clinical protocol for the monitoring and management of AF-related stroke in SLAM adult inpatients 2. Links to the $CHAD_2DS_2VASc$ and ORBIT calculators 3. NICE guidelines on the diagnosis and management of AF related stroke 4. Step by step guidance on how to record the stroke and bleeding risks in ePJS 5. Step by step guidance how to make a referral to an oral anticoagulation clinic **Training** - Guidance on where to find the AF alerts in ePHR has been developed. This was used as part of training and is available on MAUD page.	2
H02	CHA_2DS_2VASc and ORBIT calculators are not on clinical systems.	3	**ePJS limitations:** CHA_2DS_2VASc or ORBIT were never requested to be added to ePJS	**System Design:** CHA_2DS_2VASc and ORBIT have been added to MAUD. A link to MAUD has been embedded in the Cogstack alert. **Training**: Training involved showing staff this workflow	2

H03	Staff are unsure of where to record the CHA_2DS_2VASc and ORBIT scores once calculated.	3	**Human factors:** New workflow combined with staff tending to record notes in events rather than the designated sections	**Training:** Training involved showing staff this workflow	2
H04	Staff do not record CHA_2DS_2VASc and ORBIT scores in the ePJS Physical Health Hub	3	**Human factors:** Staff tend to record notes in events rather than the designated sections	**Training:** The project team offered training and support to the 3 piloting wards to establish the workflow and emphasise the benefits of recording information in the correct place.	2
H05	Staff unaware of where to find the alerts / return to alerts later.	3	**Human factors:** Clinicians may not be used to using the ePHR system or are not aware that this is where the alerts are embedded	**Training:** Training materials also showed how to go to alerts section on ePHR	2
H06	Staff not able to see all their patients across different wards / sites	3	**Human factors:** Staff have not set their location(s) in ePHR to see alerts for those patients	**Training:** *'Guidance on where to find the AF alerts in ePHR'* has step by step guide demonstrating how to set your ward location(s).	2

Table 5. Summary of significant hazards and corresponding mitigation strategies

Following the application of the controls mentioned above, all hazards have been reduced to a tolerable level (2 or lower).

User Acceptance Testing (UAT) undertaken on 15 June 2023 showed that the system worked as designed. Further validity testing was conducted on the 3 piloting inpatient wards participating in the study to ensure end to end process for clinical safety and accurateness were in place.

The project got both the CogStack and digital clinical safety approvals.

6.4 Feasibility and acceptability study protocol

Adoption of an eCDSS to improve screening for AF-related stroke in people with a diagnosis of mental illness presents a unique opportunity for early prevention but requires evidence of acceptability and feasibility. In this chapter, we study the feasibility and acceptability of such digital tool in Mental Health of Older Adults inpatient wards. The primary objectives of the study were to understand whether the tool would be successfully implemented, accepted, and used by clinicians.

A member of the research team approached managers of the three wards, discussed the study with them and confirmed that they are agreeable to the ward taking part. Staff on recruited wards were advised by their managers that their ward is participating in the study and were asked whether they would be agreeable to being approached with further information regarding the study by the research team. Clinical staff particularly psychiatrists (including junior doctors and consultants) and ward pharmacists were invited to participate in the study. Interested staff were provided with a participant information sheet (Appendix E) and were asked to sign a consent form (Appendix F).

Pre-intervention, all consenting staff were asked to complete a survey (Appendix G) about the management of stroke risk associated with AF. Additionally, they were asked to complete a 20-minute individual interview (Appendix H) to capture how AF is being managed in secondary mental healthcare settings and to capture healthcare providers understanding of clinical decision support systems and its potential impact on improving the quality of care. During the interview participants were given a chance to raise any concerns or ask further questions related to the study.

After the intervention, healthcare providers on the wards receiving the intervention were asked to complete a follow-up survey (Appendix G) and another 20-minute interview (Appendix H) at least three months after the start of the study. The interview was to to scope their experiences with the digital tool and their attitudes towards use of digital technologies to aid in clinical decision making. At the end of the interview, participants were asked to provide their ward telephone number or email so that the research team can provide them with the results of the study.

Surveys were completed online. Interviews were semi-structured in nature and were conducted remotely via Microsoft teams and recorded onto a secure drive and stored upon secure IT systems.

There were no expected safety risks to staff from participating in the study:

- Participation was voluntary and healthcare providers could choose to withdraw from the study, terminate the interview or the survey at any time point. Participants did not receive any form of financial incentives for their involvement.
- Information gathered in this study remained confidential.
- Participant anonymity was protected and maintained by the research team.
- The duration of the interviews was only for 20 minutes and was conducted at a time that was most convenient for the participant to avoid any interference with other clinical activities.
- Participants were made aware that if any information disclosed put them or any other individual at potential risk of harm, a member of the research team will have a detailed discussion with them based on which they may be advised to speak to their ward manager.

6.4.1 Patient and public involvement

Patient and public involvement (PPI) played a key role in shaping our research project. A discussion of the project's objectives, methodology and anticipated outcomes was conducted with NIHR Applied Research Collaboration (South London) Applied Informatics theme PPI group. Participants demonstrated a keen interest in the research and provided valuable perspectives that enriched our understanding. Additionally, participants offered thoughtful suggestions, emphasizing the importance of keeping alerts simple and straightforward, a reflection of their desire for clear communication. Beyond the immediate scope of the project, participants expressed a genuine interest in remaining engaged, showcasing a commitment to receiving regular updates and contributing further input in the future. This collaborative exchange not only strengthened the transparency of our research but also underscored the significance of ongoing patient and public involvement in shaping the research landscape.

6.4.2 Governance and ethics approvals

Ethical approval was granted by the King's College London Research Ethics Committee, SLaM Capacity and Capability (Trust R&D Reference: R&D2023/004) and NHS Health Research Authority (22/HRA/5452).The study was conducted in accordance with the principles of the Declaration of Helsinki (1996) and all applicable regulatory requirements including but not limited to the UK policy framework for health and social care research, Trust and Research Office policies and procedures and any subsequent amendments. Information gathered in this study were kept confidential and managed based on the Data Protection Act, NHS Caldicott Guardian, The Research Governance Framework for Health and Social Care and HRA Approval.

CHAPTER 7- ELECTRONIC CLINICAL DECISION SUPPORT SYSTEM TO SCREEN FOR STROKE RISK AMONG PATIENTS WITH ATRIAL FIBRILLATION: PERSPECTIVES OF CLINICIANS IN A MENTAL HEALTHCARE SETTING- Paper 4

Dina Farran[1](MPH), **Hou Wang Cheang** [1](MSc)**, Juliana Onwumere** (PhD)[2,3,4], **Mark Ashworth**[5](DM), **Fiona Gaughran**[1,3] (MD)

4. Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
5. Department of Psychology, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
6. South London and Maudsley NHS Foundation Trust, London, UK
7. NIHR Biomedical Research Centre for Mental Health South London and Maudsley NHS, London, UK
8. School of Life Course and Population Sciences, King's College London, London, UK

Corresponding author
Dina Farran
Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
16 De Crespigny Park, London SE5 8AB, UK
+447402011448/ +96170163721
dina.1.farran@kcl.ac.uk

Farran D, Cheang H, Onwumere J, Ashworth M, Gaughran F. Electronic Clinical Decision Support System to Screen for Stroke Risk among Patients with Atrial Fibrillation: Perspectives of Clinicians in a Mental Healthcare Setting. Submitted to BMC psychiatry.

Abstract

Background

Electronic Clinical Decision Support Systems (eCDSSs) have been an integral component of the digital transformation in healthcare. This study aims to explore mental health clinician experience in screening for stroke risk among patients with atrial fibrillation and their perception of the potential impact of an eCDSS in improving care quality.

Methods

A mixed method study, employing a questionnaire and individual semi-structured interviews, was conducted in a large London national health service trust. Interviews were analysed using an inductive thematic approach.

Results

The sample comprised 10 clinicians. Two overarching themes related to prevention of AF-related stroke were identified from interviews: challenges faced on wards and strategies needed to improve practice. Challenges included difficulty identifying relevant medical histories of patients, clinician perceived lack of expertise, fragmented medical care, and mental health symptoms Suggestions to improve clinical practice included clinicians receiving alerts containing the latest guidelines and policies on stroke management, and bespoke training sessions designed to advance the knowledge, competencies and confidence of clinicians.

As for the potential impact of an eCDSS in improving quality of care, two themes emerged: perceived benefits and perceived risks. Potential benefits included enhanced clinical effectiveness, saving time and improved outcomes. Reported perceived risks were rigidity in decision making, annoyance, and increased workload.

Conclusion

A positive attitude towards an eCDSS to screen for stroke risk was identified although some concerns were noted. Understanding clinician perceptions of how an eCDSS may enhance health care and outcomes could serve as a basis for creating impactful digital health tools.

Keywords: atrial fibrillation, mental illness, stroke risk, clinical decision support systems, digital health alerts.

Introduction

Electronic clinical decision support systems (eCDSSs) are software-based tools that analyse patient data locked in electronic health records (EHR) and provide clinicians with relevant clinical support in the form of alerts or reminders (1). Given the increasing volume of clinical information and the rapid advances in the field of medicine, eCDSSs can be pivotal in providing evidence-based clinical guidelines and tailored clinical support with personalised guidance for diagnostic, therapeutic and preventive interventions (1).

eCDSSs have gained substantial attention in recent years. They can assist in selecting appropriate treatment, managing medication (dosing, contraindications, potential interactions, side effects), calculating risk scores, identifying patients at risk, tracking patient progress over time, and collecting, analysing, and documenting clinical data (2). This has the potential to reduce medical errors and enhance health outcomes. However, eCDSSs can also have drawbacks. Alert fatigue can result in healthcare professionals becoming desensitised to notifications and potentially missing important information. This is often the case when the digital tool is overused or poorly designed (2,3,4). Clinicians can report feeling overwhelmed with the volume and frequency of alerts which may, in turn, disrupt workflow resulting in less face-to-face time with patients (2,3,4). Additionally, eCDSSs can lead to incorrect recommendations if the data input is inaccurate or of poor quality (2,3,4).

Many eCDSSs have been developed to help healthcare professionals manage physical health conditions, including atrial fibrillation (AF) and associated stroke risk (5). AF is an arrhythmia characterised by irregular heartbeats. AF disrupts the ability of the heart to pump blood effectively resulting in a higher risk of blood clotting within the left atrium of the heart and an increased risk of stroke (6). Based on the National Institute for Health and Care Excellence (NICE) guidelines, patients with AF should undergo a stroke and bleeding risk assessment using the CHA_2DS_2VASc and ORBIT scales respectively. NICE recommends oral anticoagulation therapy for patients with a CHA_2DS_2VASc score ≥ 2 and asks clinicians to consider anticoagulation for males with a CHA_2DS_2-VASc of 1. When the bleeding risk is low (ORBIT score <3), oral anticoagulation therapy can be initiated or continued; however, when the risk is moderate or high, careful consideration of the benefits and potential risks associated with the therapy is required (7,8,9).

Research assessing the prevalence of AF among people with mental disorders is scarce. A recent nationwide population-based study reported that the risk of AF increased by 2-fold in patients with bipolar disorder or schizophrenia and by 1.5-1.7 fold in those with depression, insomnia and anxiety disorders compared to controls (10). Additionally, people living with a mental illness are at increased risk of cardiovascular disease (including strokes) mainly due to risk factors such as obesity, smoking, diabetes, hypertension, and dyslipidaemia (10). Despite evidence supporting the benefits of oral anticoagulation therapy, people with AF and co-morbid mental health conditions are less likely than the general population to be prescribed oral anticoagulation therapy (11).

Many studies have evaluated the feasibility, acceptability, and effectiveness of eCDSSs in supporting the management of AF and related stroke risk in general acute hospital settings. However, these studies were not conducted in mental healthcare settings (12-21). Implementing an eCDSS that screens for the stroke risk among AF patients admitted to a mental health hospital is key to early prevention and quality of life improvement.

To determine the success of its integration in daily clinical practice, this study sought to explore: (i) clinician experience in the prevention of AF-related stroke in secondary mental healthcare services; (ii) clinician perspectives on the potential impact of an eCDSS in improving the quality of care in mental healthcare services.

Methods

Design

This cross-sectional study employed mixed methods research design, incorporating a short online survey and individual semi-structured interviews.

Study setting and ethical considerations

The study was conducted between March and May 2023 in three mental health of older adult (MHOA) inpatient wards at South London and NHS Foundation Trust (SLaM). Ethical approval was granted by the King's College London Research Ethics Committee, SLaM Capacity and

Capability (Trust R&D Reference: R&D2023/004) and NHS Health Research Authority (22/HRA/5452).

Recruitment

Purposive sampling was used to identify and recruit participants who were likely to provide clinical care for patients with AF and a co-morbid mental health condition.

Senior management on potential wards were first approached by the research team and given brief information regarding the nature of the study and the eCDSS to be implemented. Wards that expressed an interest in the study were provided with further detailed information.

A subgroup of healthcare professionals, including psychiatrists and pharmacists working on recruited wards were all invited to complete a short survey and take part in an individual online interview. Potential participants were given an information leaflet and an opportunity to ask and discuss any further concern regarding the study. If in agreement to enroll, participants were asked to sign a consent form. The number of participants required for this study was not pre-estimated and was fully dependent on theme saturation in the qualitative part.

Intervention

The eCDSS consists of a visual prompt on patient electronic personal health record (ePHR), a platform connected to electronic patient journey system (ePJS) (the main electronic patient notes system where EHRs are accessed) where all alerts are sent. Whenever a patient with documented AF is admitted to the hospital, an alert is sent to clinicians asking them to confirm the presence of AF, complete clinical assessment of stroke and bleeding risks using the CHA_2DS_2VASc and ORBIT scales, and record scores in the ePJS. In cases where patients are found to be at high risk of stroke, clinicians are asked to refer them to oral anticoagulation clinics.

Data collection

All participants were asked to complete a short online survey that collected information about their age, gender, professional background, and years of clinical experience. The survey also asked clinicians to rate the degree to which they were in agreement with a set of brief statements related to their awareness of the guidelines for AF-related stroke prevention, being confident in assessing the stroke and bleeding risks using the CHA_2DS_2VASc and ORBIT scales respectively and being

confident in managing patients at risk. Statements were presented with responses on a Likert scale anchored from strongly disagree to strongly agree. Example statements included:

- "I am confident in identifying atrial fibrillation patients eligible for oral anticoagulation therapy."
- "I am confident in assessing the stroke risk using the CHA_2DS_2VASc tool and the bleeding risk using the ORBIT tool."
- "I am confident in managing atrial fibrillation-related stroke risk in mental healthcare settings."

The interview schedule was designed to capture participants experience of AF-related stroke prevention in secondary mental healthcare services, and on the potential impact of an eCDSSs in improving clinician led care in MHOA wards. The interview topic guide was informed by field experts including psychiatrists and general practitioners. Participants were contacted via email and interview appointments were scheduled based on their availability. Interviews lasted for approximately 20 minutes, were conducted on Microsoft Teams by the same researcher (DF) and followed a semi-structured format with key prompts to direct the discussion. All interviews were audio recorded, transcribed verbatim and de-identified prior to analyses.

Data analysis

A thematic analysis using an inductive approach (22) was conducted by two members of the research team (DF and HC). After data familiarisation, the two researchers descriptively coded all the transcripts independently then developed a coding framework. The framework was further refined after several discussions although no major interpretative differences were noted. Codes were organised into themes that captured significant patterns in the data relevant to the research questions. This process involved ongoing enhancement by looking for similarities and differences within and across transcripts, as well as identifying patterns based on participant characteristics. These themes were then defined, assigned labels, and discussed with clinical experts for inputs.

This study was approached with a solid understanding of applied health informatics and the potential transformative power of eCDSSs which could have introduced bias to the perspective of the researcher working on data collection and analysis (DF). To address this issue, reflexivity was

practiced throughout the whole research process. This was done by frequently questioning preconceptions and recording assumptions and personal biases. Additionally, the in depth understanding of the stroke risk associated with AF and the consequences of missing cases at risk of stroke may have affected the lens through which data was analysed. This was mitigated by involving another researcher (HC) who worked in parallel and independently on data analysis. Both researcher (DF and HC) maintained transparency. By acknowledging positionality and actively engaging in reflexivity, researchers sought to ensure objectivity and credibility of this study.

Results

The sample comprised 10 participants of whom 6 reported their gender as female and 4 as male. Participants age ranged between 25 and 46 years with a mean age of 32. In terms of professional background, a slighter larger number were psychiatrists which included 3 participants at consultant level and 3 at more junior level. The remaining participants (n=4) were pharmacists. The mean years of clinical experience (defined as years a healthcare professional has spent in clinical practice since professional qualification) was 7.25.

Figure 1. Coding tree of themes pertaining to the prevention of AF-related stroke in MHOA ward

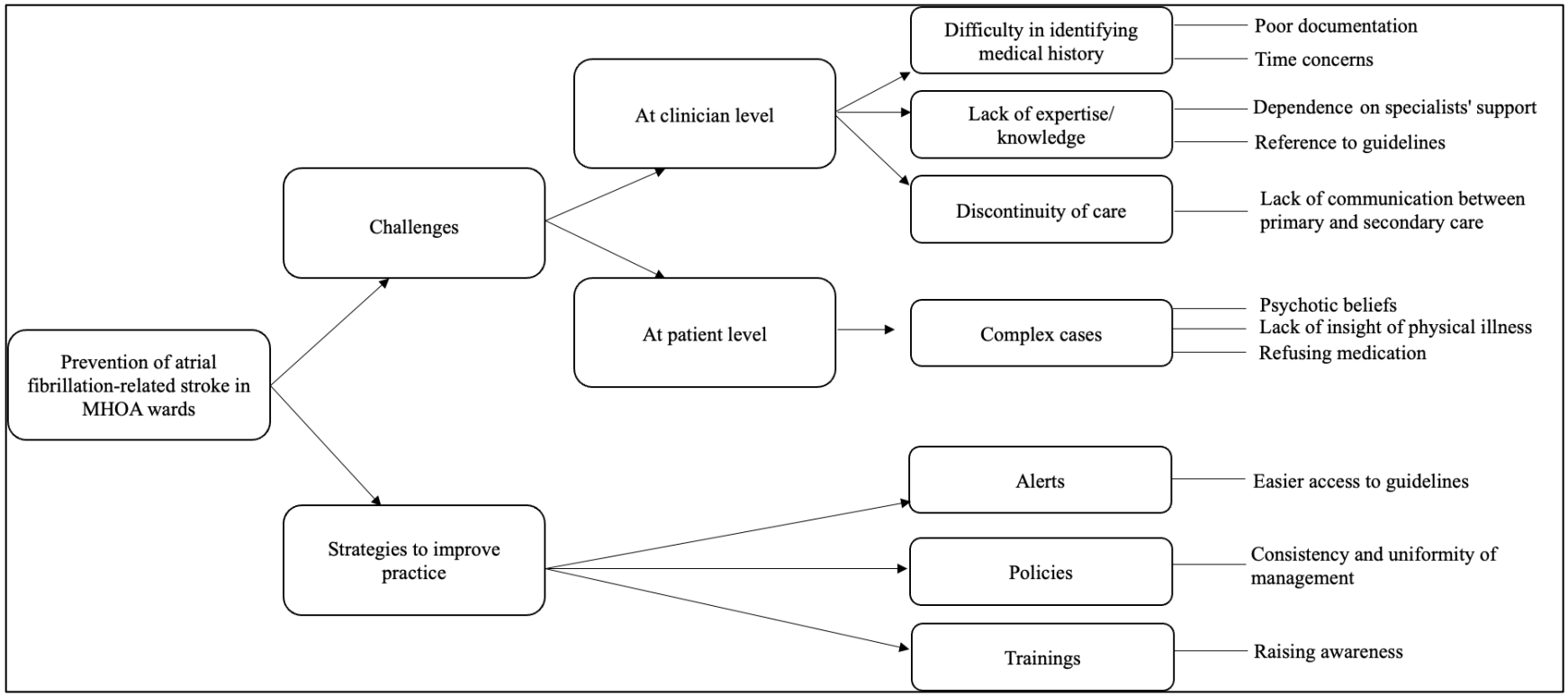
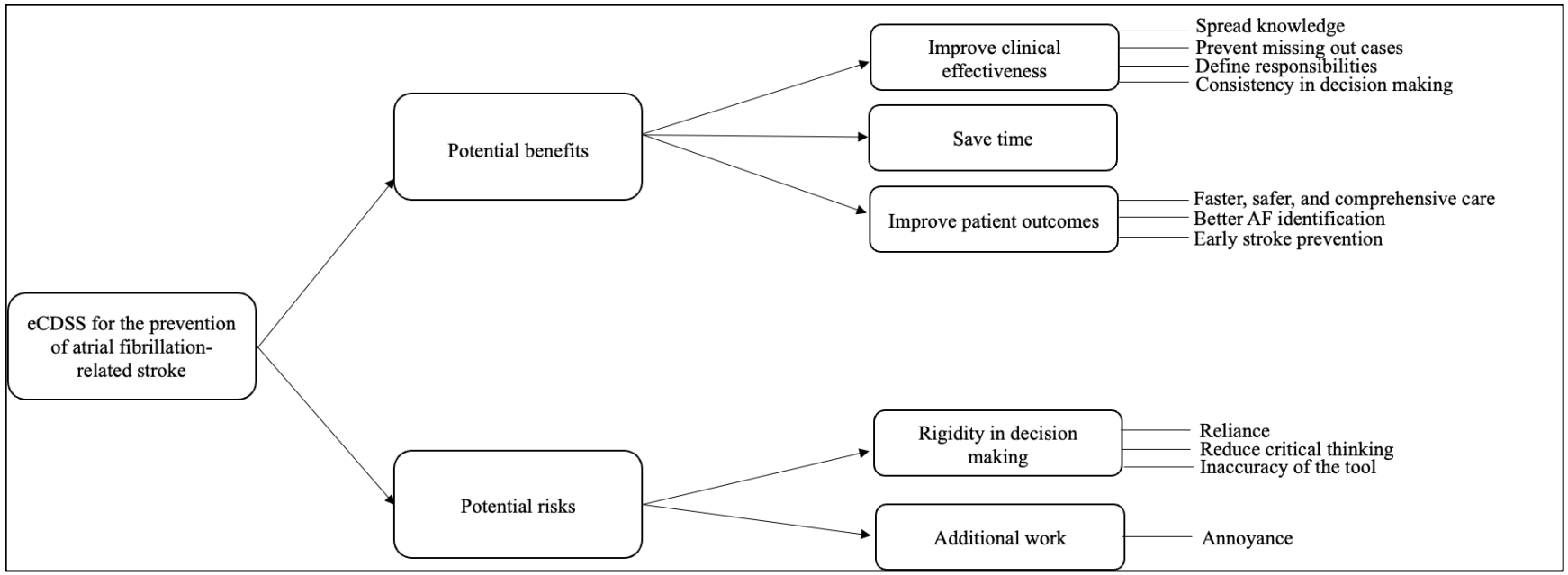


Figure 2. Coding tree of themes pertaining to the potential impact of an eCDSS for the prevention of AF-related stroke in MHOA wards



*eCDSS: electronic clinical decision support system

Fifty percent of participants (n=5) considered that AF-related stroke prevention is sub-optimal on the wards where they work. Half of participants reported being confident or somewhat confident in managing AF-related stroke prevention in mental healthcare settings or in making referrals to oral anticoagulation clinics. Around 60% reported being confident or somewhat confident using the CHA_2DS_2VASc tool to assess the risk of stroke, whereas only 30% reported being confident or somewhat confident using the ORBIT tool to assess the risk of bleeding. Almost all participants strongly agreed that having access to an eCDSS would help them to better assess stroke and bleeding risks in patients with AF.

Thematic analysis of the interviews identified two overarching themes related to prevention of AF-related stroke: (1) challenges faced on wards and (2) strategies needed to improve practice (fig 1). As for the potential impact of an eCDSS in improving quality of care, two themes emerged: (1) perceived benefits and (2) perceived risks (fig 2).

Prevention of AF-related stroke in MHOA wards

Challenges

Participants discussed challenges in the prevention of AF-related stroke in MHOA wards at two levels.

At clinician level, many participants reported that identifying a medical history of AF from the electronic clinical notes is a challenging and time-consuming task. Some of them attributed this to poor documentation of physical health conditions in mental healthcare settings. Another challenge is clinician lack of knowledge and expertise in the management of physical conditions. To optimise management of physical long-term conditions, most clinicians would seek support from specialists or refer to guidelines such as NICE. Discontinuity of care provision and lack of communication between primary and secondary care were also considered obstacles in the prevention of AF-related stroke in MHOA wards. Participants expressed their concerns about the lack of coordination and follow up with general practitioners (GPs) and its effect on the quality of care (fig 1, table 1).

- Subject 1 (psychiatrist): “sometimes it's a bit more difficult to get the appropriate history like have they had any previous strokes, do they have any comorbidities, or do they have any other risk factors, family history of stroke.”

- Subject 2 (psychiatrist): “I'd speak to my medical colleagues or end up looking at guidelines and trying to follow because I wouldn't be kind of regularly checking on what the latest guidance is. So, it'd be something I'd have to refresh myself when the situation comes up.”

- Subject 4 (pharmacist): “I also think the communication between primary and secondary care is probably one of the biggest obstacles.”

At patient level, patients with mental illness admitted to MHOA wards are complex, generally having both physical and mental health diagnoses. Illness related symptoms (e.g. delusional beliefs) and active features of illness may result in patient denial of being physically ill, saying that they want to die or refusing medication (fig 1, table 1).

- Subject 1 (psychiatrist): “Patients refuse to take medications because of their psychotic beliefs or them just having given up, depression, wanting to die, basically, so they don't have the will to get better.”

Strategies to improve practice

To improve AF-related stroke prevention in MHOA wards, most participants suggested sending alerts to clinicians on ePJS containing the latest guidelines, including tools for stroke and bleeding risk assessment, guidance on how to interpret the scores, and guidance on how to refer patients at high risk of stroke to oral anticoagulation clinics. Although most of the information are available online, healthcare professionals highlighted the importance of making them easily accessible when needed to increase efficiency. They also suggested having policies at the system level for AF-related stroke management to ensure consistency and uniformity in healthcare provision. At a more individual level, training sessions for healthcare professionals on the management of AF and how

to perform stroke and bleeding risk assessments based on the latest guidelines were thought helpful (fig 1, table 1).

- Subject 2 (psychiatrist): “having PJS alerts is very key, so something that would prompt people and you know provide a very easy pathway for them to follow the guidance rather than kind of spending time to look things up and then not knowing if it's accurate or if it's appropriate.”

- Subject 9 (psychiatrist): “So I think like very concise and clear guidelines. And probably like a hyperlink to where you can do the CHA_2DS_2VASc and ORBIT scoring and then maybe have the kind of action points for the outcome scores.
- Subject 4 (pharmacist): “maybe just having like policies on how to manage AF and sort of guidance. I know we have like the physical health guidelines here, but yeah, like a clear pathway would be great.”

<u>eCDSS for the prevention of AF-related stroke</u>

Potential benefits

Most healthcare professionals reported that an eCDSS for the prevention of AF-related stroke in MHOA wards would improve clinical effectiveness. This could be through spreading knowledge on the management of the condition among clinicians specialised in mental health, defining responsibilities, and ensuring consistency in decision making. Additionally, participants emphasised on the effectiveness of the tool in saving time and speeding up the clinical assessment process. They also reported that an eCDSS would be helpful in improving patient health outcomes as it will ensure a faster, safer, and more comprehensive care, improve AF identification in MHOA wards, reduce the chances of getting inappropriate treatments, and ensure early stroke prevention (fig 2, table 1).

- Subject 4 (pharmacist): “Prompting clinicians and also alerting them can make people feel comfortable, knowing that they've got, like, some sort of system in place and like everyone know where the responsibilities lie in terms of managing.”

- Subject 3 (psychiatrist): “the benefits can help you achieve something or kind of assessment risks and benefits and things a bit more quickly.”

- Subject 7 (pharmacist): “So enabling better patient care, faster, maybe more comprehensive, maybe just safer basically if it's flagging things up.”

Potential risks

While an eCDSS can be a very helpful tool for healthcare professionals, it may have potential risks; one of these is the rigidity in decision making. Participants reported that they may become over reliant on such digital tools which may influence their critical thinking skills. They also emphasised that errors in the accuracy of the tool may be misleading and could result in wrong recommendations. Participants were kind of worried about the increased workload caused by the digital tool and reported that annoyance and alert fatigue could be other downsides (fig 2, table 1).

- Subject 3 (psychiatrist): “I think the main thing is that people can just become kind of blinkered or rigid in their decision making and kind of forget about the specific individual factors for that patient that may be quite relevant, but don’t necessarily come up on the on the tool.”

- Subject 4 (pharmacist): “Uh harms of this system would be over reliance on electronic systems, we can become a bit over relying I think. A bit of an overreliance sometimes isn't great.”

- Subject 6 (pharmacist): “if the electronic system has any fault to it, then they could potentially lead to a mess.”
- Subject 2 (psychiatrist): “There's lots of things already that we have to do on ePJS and another form is likely, unless it's really prompting, it's likely to get forgotten and avoided actively or found to be quite annoying.”

Table 1. Illustrative quotations for the identified sub-themes

Sub-themes	Examples
Difficulty in identifying medical history	• "sometimes it's a bit more difficult to get the appropriate history like have they had any previous strokes, do they have any comorbidities, or do they have any other risk factors, family history of stroke." • "The recording of ECG in the department sometimes isn't great. Uploading ECG onto our clinical document system doesn't happen a lot of the times, so one of the challenges is to find the ECG initially for people to identify it." • "the doctor usually will read the clinical notes to find out the cardiac history for the patient. This is how we usually identify AF or any stroke history for patient. I guess the challenge is that it's a bit time wasting because the doctors will have to review previous clinical letters or any discharge summary."
Lack of expertise/ knowledge	• "I don't feel very confident at all, to be honest. I did my foundation years ago and like mental health placement before starting psychiatry training. You know, I used to deal with it a bit on the medical take, but I think if I were to identify a new AF on admission, I'd just discuss it with specialists. But independently, if you were like, sort this out yourself I wouldn't feel confident." • "Saddly not knowledgeable, I would immediately go and look up the NICE guidance to see the most up to date guidelines because we don't use it all the time. I probably know when to be worried. I would know where to find the information. But it wouldn't be all in my mind. But I wouldn't say I'm knowledgeable at all." • "Well, I'm aware of the CHA2DS2VASc and ORBIT, but not familiar with their use." • "I'd speak to my medical colleagues or end up looking at guidelines and trying to follow because I wouldn't be kind of regularly checking on what the latest guidance is. So it'd be something I'd have to refresh myself when the situation comes up."
Discontinuity of care	• "I also think the communication between primary and secondary care is probably one of the biggest obstacles." • "The main obstacle I think is the discontinuity of care between secondary care and primary care and also from our side we're a bit of a like mental health setting so when we're starting medications that might increase the bleed risk, I think that's something that we don't have much of a process for here."

Complex cases	• "Patients refuse to take medications because of their psychotic beliefs or them just having given up, depression, wanting to die, basically, so they don't have the will to get better." • "A lot of people at this stage of their dementia lack insight to their physical health." • "If we assess the patient to have a high risk of stroke and we want to start on anticoagulants, a lot of our patients actually refuse medication." • "Patients don't want any of the medication either. They think we're trying to poison them." • "Patients not taking their medication is quite a common scenario on my ward."
Alerts	• "having PJS alerts is very key, so something that would prompt people and you know provide a very easy pathway for them to follow the guidance rather than kind of spending time to look things up and then not knowing if it's accurate or if it's appropriate." • "Reminding people and having these tools easily accessible, you know, so they don't have to look them up so that they're incorporated probably in the notes." • "So I think like very concise and clear guidelines. And probably like a hyperlink to where you can do the CHA2DS2VASc and ORBIT scoring and it would then maybe have the kind of action points for the outcome scores. • "I think more information. I think what would be good obviously is an explanation on why that's being recommended, just so that physicians are aware. It'd be great if they could say like well, if the CHA2DS2VASc is greater than this much in these patients, we recommend that, and for example, if it is recommended that they just get monitored annually. Just a statement saying why". • " So again I I guess the hardest thing with the AF question is that you end up with the CHA2DS2VASc and ORBIT scores or whatever, which is fine. However, you might end up with somebody who you know they score high on CHA2DS2VASc, but then high for ORBIT as well. They obviously have something that flags on, but you don't really know what that means. There's still a judgment involved, I guess. So if it was to help with making that part of the Judgment, that I guess would be helpful." • "I think it would be worth including the e-mail address or way to refer to cardiology and everything you need to action that request. What I think would be most useful is kind of like how to do it, what you're supposed to do with it and how to do what you're supposed to do with it?" • "Well, obviously, where to refer if you need to. Where to refer if you need support or help. And maybe also some contact for local OAC clinics and know where to refer people depending on their GP or their

	home address or their hospital location. Just so we're not kind of running around and we just got kind of single referral point of access."
Policies	• "maybe just having like policies on how to manage AF and sort of guidance. I know we have like the physical health guidelines here, but yeah, like a clear pathway would be great." • "I think having some uniformity of how we address things across different wards would be helpful and would provide consistency." • "at trust level, I guess having a policy. Because at SLaM we have a bit of a problem in that we don't have policies for general health conditions, so I always get calls about where's SLaM's policy for that specific physical health conditions."
Trainings	• "At individual level, probably training for our junior doctors and the rest of the team as well. Yeah, training on kind of recognition, and latest guidelines. Also as I mentioned, kind of what to do in a typical situation which you know we might come into contact with our patient cohort." • "I guess it would be just kind of ongoing training to make sure that we are up to date with guideline changes and things." • "I think improving clinicians knowledge of how to manage it. So more awareness of when anticoagulant has to be indicated, how to manage people on anticoagulants. So yeah, just knowledge and like teaching sessions would be great." • "Perhaps during the induction process, this is one of those things that Drs have to be inducted in the expectation that these are the steps that we need to take if somebody does have AF."
Improve clinical effectiveness	• **"**And then another benefit would be increasing awareness in clinicians about strokes and prevention of strokes especially in elderly patients where these are more common." • "Prompting clinicians and also alerting them can make people feel comfortable, knowing that they've got, like, some sort of system in place and like everyone know where the responsibilities lie in terms of managing." • "I mean, I think if it's consistent, if it's done for all patients, then we'll pick up more patients or less will be missed whether or not patient gonna be compliant is the different thing. But at least we'll pick them up and an attempt to sort of preventing stroke will be made."

Save time	• "The benefits would be to identify, you know information that we want to quickly." • "I guess because it's hard for clinicians to keep track of the patients or like all the patients all the time, I guess it will help to speed up like to help their job a little bit. When they get notified, they can further look into it rather than missing it out completely." • "the benefits can help you achieve something or kind of assessment risks and benefits and things a bit more quickly." • "Then, certainly it would sort of take into account all the guidelines at the same time and point you in the right direction, which just makes you save time and effort."
Improve patient care	• "Starting prevention and treatment earlier." • "The benefits would be that people are appropriately anticoagulated and we avoid strokes especially that we've got lots of people with kind of high physical health care morbidities and vascular risk factors." • **"**Obviously I think it will reduce the number of patients who might not be getting the appropriate treatment or the appropriate prevention, so that would be the main benefit." • "I guess they can help to prioritise workload for them and it will also highlight physical health problems and I think it will help them to make the decision with a more like a well-rounded approach like considering the physical health factors, not just the mental health." • "So enabling better patient care, faster, maybe more comprehensive, maybe just safer basically if it's flagging things up." • It "will improve the safety in a tremendous amount to be honest"
Rigidity in decision making	• "I think the main thing is that people can just become kind of blinkered or rigid in their decision making and kind of forget about the the specific individual factors for that patient that may be quite relevant, but don't necessarily come up on the on the tool." • "we can start to think that's the only thing that matters. So like with AF preventing stroke they might just care about the CHA2DS2VASc and ORBIT scores and see what the decision tool makes and they might not be looking at what other things are happening with the patients" • "as long as it's a suggestion and It's not going to prevent sort of clinical decision making, it is fine. And I think we need to make sure that yes, it is a prompt and everything but at the end of the day the clinician has to make a decision based on what they believe is appropriate even if it's not exactly what the tool says. It should be fine as long as we don't take the thinking out of it and it's sort of like a tool rather than mandatory in a sense."

	• "You know automated system can never replace a human you know, because the human person takes into account the individual with their specific circumstances. So most people will probably fit into that system, but there will be others that require more individualized approach." • "there may be mistakes I guess from the electronic system and identifying the wrong thing or misleading us. And I worry that maybe at some point clinicians will just think that if it's not been highlighted to me electronically, I don't need to think about it. I think there's always a danger of that for anything so." • "if the electronic system has any fault to it, then they could potentially lead to a mess." • "Uh harms of this system would be over reliance of electronic systems, we can become a bit over relying I think. A bit of an overreliance sometimes isn't great." • "It might cause dependency. Clinicians could be just relying on the screening of the electronic system rather than themselves reading into the history." • "I think maybe the disadvantages are that clinicians will be relying on electronic decision support system rather than thinking for themselves or trying to find their information"
Additional work	• "There's lots of things already that we have to do on ePJS and another form is likely, unless it's really prompting, it's likely to get forgotten and avoided actively or found to be quite annoying." • "The harm is I don't know how the tool is. If it's going to pick up, if it's going to be accurate and picking up what it picks up, if it's going to end up more work for the NHS because they're scrolling through lots of data." • "I guess maybe more paperwork." • "because there's no more time in the day, you know, like there are sort of limits within which these things are being introduced and It's like when you're filling in that new form you are not doing something else and whatever that may be."

Discussion

This was an exploratory study that sought to understand mental healthcare professionals experience in the prevention of AF-related stroke and their perspective on the potential impact of an eCDSS in improving that experience. Clinicians reported many challenges related to stroke prevention in MHOA wards, including difficulty identifying patient pertinent medical history, perceived lack of knowledge and expertise in the management of physical conditions, fragmented medical care, and patient psychotic beliefs. To improve clinical practice, they suggested reminding clinicians of the latest guidelines through alerts on patient electronic records, having clear policies at the system level, and providing clinicians with training sessions on AF-related stroke management. Clinicians reported many potential benefits for the eCDSS including improving clinical effectiveness, better identification of patients at risk, safer and more comprehensive care, consistency in decision making and saving time. However, they noted that the digital tool could have potential risks such as rigidity in decision making, overreliance, reduced critical thinking, false positive recommendations, annoyance, and increased workload.

Physical comorbidities among people with mental illness present complex clinical scenarios that require a specialised and holistic approach to care. Fragmentation between primary and secondary health services could contribute to uncertainty regarding which provider is responsible for the management of physical conditions among people with mental illness (23). This could result in missed opportunities for the identification of physical conditions which may be hampered by often poor(er) documentation in mental health services (23). Additionally, inadequate training and lack of physical care skills may reduce mental healthcare professionals' confidence in managing physical conditions (24). Continuous training, access to resources and specialist support are all factors that may influence the level of confidence in dealing with acute conditions considered out of their specialty (24). Another common scenario that prevents or delays the management of physical conditions among people with mental illness is diagnostic overshadowing which refers to the misattribution of physical symptoms to mental illness (25). Features of the mental illness itself may also create major challenges as people experiencing cognitive impairment, hallucinations or delusions may not recognise or have difficulty communicating symptoms, may resist medication or struggle with medication adherence (25).

The impact of eCDSSs on AF knowledge, oral anticoagulation prescription, adherence to guidelines, and patient outcomes has been investigated in general healthcare settings (12-21), with mixed findings on their effectiveness (12-21). Research aiming to understand clinician perception of how an eCDSS can be supportive and useful is scarce although this could serve as a basis for creating digital health tools that are impactful and aligned with their needs. In a study conducted in China to evaluate the acceptance of an eCDSS that automatically assesses the risks of stroke and bleeding and suggests treatments accordingly, general practitioners showed positive attitudes towards the digital tool, reporting that it would be helpful and would strengthen their confidence and capabilities in managing patients with AF (26). This is consistent with results of our study where clinicians expressed lack of confidence in managing stroke-risk related to AF and their need to refer to guidelines or to seek advice from specialists even if they already knew about current recommendations. Thus, implementing an eCDSS providing the latest guidelines, tools required to complete clinical assessments for stroke and bleeding risks, and guidance on how to interpret these scores would decrease dependence on specialist inputs and increase clinical efficiency. Our findings are also in line with those of a recent systematic review aiming to identify barriers and facilitators of using CDSSs by primary care professionals (27). In this review, the reported benefits of the digital tools were improving quality of care, saving time, facilitating decision making, improving professional self-confidence, and updating knowledge (27). The main barriers were resistance or reluctance, alert fatigue, information overload, disruption of workflow, negative attitude, lack of motivation to use, lack of computer skills, and validity concerns (27).

This study has potential limitations. First, some healthcare professionals might have been reluctant to express their lack of knowledge and confidence in assessing physical health conditions which could have potentially resulted in reporting bias. However, this was minimised by explicitly informing clinicians that data generated from interviews will be de-identified and that the purpose of the study was to understand their experiences in managing AF related stroke risk and accordingly implement an eCDSS in as helpful a way as possible. Second, participants included in the study were restricted to psychiatrists and pharmacists, since they are the ones who usually deal with clinical assessments such as stroke and bleeding risks. Including other healthcare professionals with various degrees of clinical experiences could also have influenced our findings. Finally, the sample size was relatively small, however, its effect was mitigated by the fact that data collection continued until saturation was achieved. This approach allowed for a comprehensive

exploration of the research questions and ensured that key themes and patterns were sufficiently captured.

Conclusion

The study findings indicate that adoption of an eCDSS for stroke risk screening in a psychiatric health service has the potential to be a valuable tool. However, healthcare organisations and clinicians need to be mindful of the challenges associated with increased workload and the potential overreliance on the system's recommendations. To maximise the clinical benefits while minimising the drawbacks, a balanced approach to eCDSS integration is essential. This might involve ongoing training, customisation of the system to local practice, and clear guidelines on how to use eCDSS recommendations in conjunction with clinical judgment to provide patient-centered care.

List of abbreviations

AF: atrial fibrillation
eCDSS: electronic clinical decision support systems
EHR: electronic health records
MHOA: mental health of older adult
NICE: National Institute for Health and Care Excellence
SLaM: South London and NHS Foundation Trust
GP: general practitioners

Declarations

Ethics approval and consent to participate

Ethical approval was granted by the King's College London Research Ethics Committee, SLaM Capacity and Capability (Trust R&D Reference: R&D2023/004) and NHS Health Research Authority (22/HRA/5452).The study was conducted in accordance with the principles of the Declaration of Helsinki (1996) and all applicable regulatory requirements including but not limited to the UK policy framework for health and social care research, Trust and Research Office policies and procedures and any subsequent amendments. Information gathered in this study were kept confidential and managed based on the Data Protection Act, NHS Caldicott Guardian, The Research Governance Framework for Health and Social Care and HRA Approval.

A written informed consent for partaking in the study and publishing data gathered during interviews was obtained from all participants.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Funding

DF is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust and by the KCL funded Centre for Doctoral Training (CDT) in Data-Driven Health.

MA is in part funded by the Guy's and St Thomas' Charity and the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

JO and FG are in part supported by the National Institute for Health Research's (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. In addition, FG is supported by the Maudsley Charity and by the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust.

Authors' contributions

FG and MA supervised the study.

FG, MA, and DF designed the study.

DF collected data.

DF and HC analysed and interpreted data.

JO, FG and MA revised data analysis and interpretation.

DF wrote the first manuscript draft.

All authors commented on the first draft.

All authors read and approved the final manuscript.

Acknowledgments

The successful completion of this study was made possible through the gracious cooperation and invaluable contributions of numerous individuals. We would like to express our deepest gratitude to the ward managers who facilitated access to clinicians on their respective wards. We would like to thank all the clinicians who participated in this study. Their willingness to share their insights and experiences played a pivotal role in shaping the findings and outcomes of our research. We

are truly grateful for their time, openness, and collaboration.

DF, FG and MA are supported by the National Institute for Health and Care Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust. JO and FG are in part supported by the National Institute for Health Research's (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London, the Maudsley Charity. The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

References

1- Kawamoto K, Houlihan CA, Balas EA, Lobach DF. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. Bmj. 2005 Mar 31;330(7494):765.

2- Sutton RT, Pincock D, Baumgart DC, Sadowski DC, Fedorak RN, Kroeker KI. An overview of clinical decision support systems: benefits, risks, and strategies for success. NPJ digital medicine. 2020 Feb 6;3(1):17.

3- Muhiyaddin R, Abd-Alrazaq AA, Househ M, Alam T, Shah Z. The impact of clinical decision support systems (CDSS) on physicians: a scoping review. The Importance of Health Informatics in Public Health during a Pandemic. 2020:470-3.

4- Moja L, Kwag KH, Lytras T, Bertizzolo L, Brandt L, Pecoraro V, Rigon G, Vaona A, Ruggiero F, Mangia M, Iorio A. Effectiveness of computerized decision support systems linked to electronic health records: a systematic review and meta-analysis. American journal of public health. 2014 Dec;104(12):e12-22.

5- Alasiri SF, Douiri A, Altukistani S, Porat T, Mousa O. The Role of Clinical Decision Support Systems in Preventing Stroke in Primary Care: A Systematic Review. Perspectives in Health Information Management. 2023;20(2).

6- Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Kardiologia Polska (Polish Heart Journal). 2016;74(12):1359-469.

7- O'Brien EC, Simon DN, Thomas LE, Hylek EM, Gersh BJ, Ansell JE, Kowey PR, Mahaffey KW, Chang P, Fonarow GC, Pencina MJ. The ORBIT bleeding score: a simple bedside score to assess bleeding risk in atrial fibrillation. European Heart Journal. 2015 Dec 7;36(46):3258-64.

8- Perry M, Betty SK, Downes N, Andrews N, Mackenzie S. Atrial fibrillation: diagnosis and management—summary of NICE guidance. BMJ. 2021 May 21;373.

9- MDcalc. ORBIT bleeding risk score for atrial fibrillation [Internet]. Available from: https://www.mdcalc.com/calc/10227/orbit-bleeding-risk-score-atrial-fibrillation [cited 2024 May 1].

10- Ahn HJ, Lee SR, Choi EK, Bae NY, Ahn HJ, Kwon S, Lee SW, Han KD, Oh S, Lip GY. Increased risk of incident atrial fibrillation in young adults with mental disorders: A nationwide population-based study. Heart Rhythm. 2023 Mar 1;20(3):365-73.

11- Farran D, Feely O, Ashworth M, Gaughran F. Anticoagulation therapy and outcomes in patients with atrial fibrillation and serious mental illness: A systematic review and meta-analysis. Journal of Psychiatric Research. 2022 Nov 16.

12- Wess ML, Schauer DP, Johnston JA, Moomaw CJ, Brewer DE, Cook EF, Eckman MH. Application of a decision support tool for anticoagulation in patients with non-valvular atrial fibrillation. Journal of general internal medicine. 2008 Apr;23:411-7.

13- Cook DA, Enders F, Caraballo PJ, Nishimura RA, Lloyd FJ. An automated clinical alert system for newly-diagnosed atrial fibrillation. PLoS One. 2015 Apr 7;10(4):e0122153.

14- Robson J, Dostal I, Mathur R, Sohanpal R, Hull S, Antoniou S, MacCallum P, Schilling R, Ayerbe L, Boomla K. Improving anticoagulation in atrial fibrillation: observational study in three primary care trusts. British Journal of General Practice. 2014 May 1;64(622):e275-81.

15- Arts DL, Abu-Hanna A, Medlock SK, van Weert HC. Effectiveness and usage of a decision support system to improve stroke prevention in general practice: a cluster randomized controlled trial. PloS one. 2017 Feb 28;12(2):e0170974.

16- Karlsson LO, Nilsson S, Bång M, Nilsson L, Charitakis E, Janzon M. A clinical decision support tool for improving adherence to guidelines on anticoagulant therapy in patients with atrial fibrillation at risk of stroke: a cluster-randomized trial in a Swedish primary care setting (the CDS-AF study). PLoS medicine. 2018 Mar 13;15(3):e1002528.

17- Thomson RG, Eccles MP, Steen IN, Greenaway J, Stobbart L, Murtagh MJ, May CR. A patient decision aid to support shared decision-making on anti-thrombotic treatment of patients with atrial fibrillation: randomised controlled trial. BMJ Quality & Safety. 2007 Jun 1;16(3):216-23.

18- Fraenkel L, Street Jr RL, Towle V, O'Leary JR, Iannone L, Van Ness PH, Fried TR. A pilot randomized controlled trial of a decision support tool to improve the quality of communication and decision-making in individuals with atrial fibrillation. Journal of the American Geriatrics Society. 2012 Aug;60(8):1434-41.

19- Guo Y, Chen Y, Lane DA, Liu L, Wang Y, Lip GY. Mobile health technology for atrial fibrillation management integrating decision support, education, and patient involvement: mAF app trial. The American journal of medicine. 2017 Dec 1;130(12):1388-96.
20- Sheibani R, Sheibani M, Heidari-Bakavoli A, Abu-Hanna A, Eslami S. The effect of a clinical decision support system on improving adherence to guideline in the treatment of atrial fibrillation: an interrupted time series study. Journal of medical systems. 2018 Feb;42:1-7.
21- Simmons BJ, Jenner KM, Delate T, Clark NP, Kurz D, Witt DM. Pilot Study of a Novel Patient Self-Management Program for Warfarin Therapy Using Venipuncture-Acquired International Normalized Ratio Monitoring. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2012 Dec;32(12):1078-84.
22- Braun V, Clarke V. Thematic analysis. American Psychological Association; 2012.
23- Stange KC. The problem of fragmentation and the need for integrative solutions. The Annals of Family Medicine. 2009 Mar 1;7(2):100-3.
24- Terry J, Cutter J. Does education improve mental health practitioners' confidence in meeting the physical health needs of mental health service users? A mixed methods pilot study. Issues in Mental Health Nursing. 2013 Apr 1;34(4):249-55.
25- Nash M. Diagnostic overshadowing: a potential barrier to physical health care for mental health service users. Mental Health Practice. 2013 Dec 1;17(4).
26- Ru X, Wang T, Zhu L, Ma Y, Qian L, Sun H, Pan Z. Using a Clinical Decision Support System to Improve Anticoagulation in Patients with Nonvalve Atrial Fibrillation in China's Primary Care Settings: A Feasibility Study. International Journal of Clinical Practice. 2023 Jan 18;2023.
27- Meunier PY, Raynaud C, Guimaraes E, Gueyffier F, Letrilliart L. Barriers and facilitators to the use of clinical decision support systems in primary care: A mixed-methods systematic review. The Annals of Family Medicine. 2023 Jan 1;21(1):57-69.

CHAPTER 8- CLINICIANS' EXPERIENCE WITH AN ELECTRONIC CLINICAL DECISION SUPPORT SYSTEM TO SCREEN FOR STROKE RISK IN A MENTAL HEALTHCARE SETTING -Paper 5

Dina Farran[1], Juliana Onwumere[2,3,4], Nicola Funnell[3], Delia Bishara[3], Trevor Tiedt[3], Damian Larkin[3], Barbara Arroyo[3], Mark Ashworth[5], Fiona Gaughran[1,3, 4, 6]

1-Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
2-Department of Psychology, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
3-South London and Maudsley NHS Foundation Trust, London, UK
4-NIHR Biomedical Research Centre for Mental Health South London and Maudsley NHS, London, UK
5-School of Life Course and Population Sciences, King's College London, London, UK
6-NIHR Applied Research Collaboration South London, UK

Corresponding author

Dina Farran
Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
16 De Crespigny Park, London SE5 8AB, UK
+447402011448/ +96170163721
dina.1.farran@kcl.ac.uk

Abstract

Background

Obtaining feedback from clinicians regarding digital tools such as electronic Clinical Decision Support Systems (eCDSS) plays a fundamental role in refinement and optimization. This study aims to explore clinician experience with a novel eCDSS that screens for stroke risk among patients with Atrial Fibrillation (AF) in a mental health setting.

Methods

An eCDSS for prevention of AF related stroke was developed for use in a mental health trust in London, UK. A mixed-method study incorporating a questionnaire and semi-structured interviews was conducted to evaluate its feasibility and acceptability. Thematic analysis using an inductive approach was conducted for the qualitative aspect.

Results

The sample comprised 9 clinicians. All considered the eCDSS helpful in improving stroke and bleeding risk assessment, however, 88% reported that the tool hindered their workflow. Three overarching themes were identified: clinician feedback on the eCDSS itself, barriers to its use, and suggestions to improve user experience. Clinicians perceived the digital tool as simple, comprehensive and well designed. They discussed its potential impact on saving time, prompting them towards guidelines, boosting clinician confidence, and identifying patients at risk. Perceived barriers included the low admission rate of patients with AF, lack of awareness of the tool, low alert visibility, and potential impact of the eCDSS on workload. Clinicians suggested reinforcing awareness of the tool through training and reminders as well as changing the digital location and making it unavoidable.

Conclusion

Positive feedback from clinicians was received regarding the tool, however barriers to use were reported. To ensure effectiveness, ongoing evaluation should be done by continuously monitoring

performance, gathering feedback from healthcare professionals, and accordingly making any adjustments.

Keywords: atrial fibrillation, mental illness, stroke risk, clinical decision support systems, digital health alerts.

Introduction

Informatics has the potential to impact on many aspects of healthcare from diagnostics to treatment, fostering unprecedented improvements in patient care (1). Among such innovations are electronic Clinical Decision Support Systems (eCDSSs), tools designed to help healthcare professionals with decision making by providing evidence-based guidelines and patient specific recommendations through alerts or reminders (2). These tools utilise medical knowledge databases, electronic health records (EHRs) and algorithms to provide real time support for compliance with guidelines, personalised care, diagnostics, identification of patients at risk, earlier intervention, improved patient safety and outcomes, improved efficiency, resource optimisation and enhanced communication and collaboration with healthcare teams (3,4,5).

Atrial fibrillation (AF) is a common arrythmia affecting more than 1.5 million people in the United Kingdom (6). It is one of the main risk factors for ischaemic stroke (7). Strokes associated with AF tend to be more serious, resulting in brain damage and worse long-term outcomes (7). Risk stratification and early initiation of preventive therapy significantly reduces the risk of stroke associated with AF (8). Prevention relies mainly on oral anticoagulation (OAC). To identify those with AF who would benefit from OAC, a clinical assessment for stroke and bleeding risks using the CHA_2DS_2-VASc and ORBIT tools respectively should be performed (8).

ECDSSs for the management of multiple physical health conditions, including AF-related stroke have been implemented in various hospital settings (9). Despite the acknowledged significance of these digital tools, there is considerable evidence of low adoption by clinicians (10). Many factors could contribute to the underutilisation or resistance to adoption of eCDSSs in clinical practice including limited customisation, unfamiliarity with the clinical system, and difficulty navigating through it (11). Alert fatigue has been also reported, especially now that eCDSSs are becoming integral components of healthcare and the number of alerts generated is increasing (11,12). Additionally, alerts tend to be ignored if their integration in the system is not seamless or if they disrupt the workflow (12). Further, digital tools may impact workload as introducing a new system may add to the responsibilities of clinicians who are already under significant time pressures (12).

Previous research has assessed clinician acceptability of eCDSSs within general hospital settings, but a notable gap in knowledge still exists particularly in mental healthcare settings. We set out to (i) develop an eCDSS to identify inpatients with AF and deliver guideline-based prompts to assess for stroke and bleeding risks in a UK mental health hospital Trust; (ii) explore clinician feedback on the eCDSS; and (iii) gain insights on clinician experience with the digital tool, including both successful aspects and any challenges encountered.

Methods

Intervention

A digital alerting system to improve screening for stroke risk among people with AF and co-morbid mental illnesses was implemented in CogStack, an information retrieval and extraction platform for electronic Health Records (EHRs). The system was made of three parts. The first part was a patient data pipeline that routinely searches for documented AF in clinical notes in near real time. The second part was a technical implementation of a clinical algorithm to screen for AF-related stroke in adult patients admitted to the Trust. The algorithm, approved by the Trust, was developed based on National Institute for Health and Care Excellence (NICE) guidelines and input from multi-disciplinary healthcare professionals (including general practitioners, psychiatrists, and pharmacists). The third part was a technical implementation and piloting of an automated alerting system. After consultation with the Trust, the alerts for this study were positioned in the Trust ePHR, alongside the Trust's electronic prescribing system (ePMA). Noteworthy, EHR is accessed through the main electronic patient notes system, called the electronic Patient Journey System (ePJS).

Clinicians were prompted to confirm the presence of AF and to conduct in accordance with NICE guidelines, a clinical assessment for stroke and bleeding risks using the CHA_2DS_2VASc and ORBIT scales respectively (Tables 1&2). Clinicians were then asked to record the scores on ePJS and to refer those identified to be at risk of stroke to the relevant oral anticoagulation clinic, details of which were provided. The alert included a link to all the training material required to perform this task (also made available on an intranet page) including NICE guidelines for management of

stroke related to AF, links to the CHA_2DS_2VASc and ORBIT score calculators and step by step guidance on where to find the alert, where to record the scores, and how to refer patients at risk. The study was introduced to the clinical team by a research member (DF). Additionally, an email was sent bi-weekly to clinicians on board reminding them of the digital tool and providing them with links to all the training materials.

Research Design

This is a cross-sectional study employing a mixed-methods approach. It incorporates both quantitative and qualitative aspects by using a short survey to gather structured data and semi-structured interviews to explore healthcare professionals' perspectives in greater depth.

Study setting and ethical considerations

The eCDSS was implemented in three mental health of older adult (MHOA) inpatient wards in London in August 2023. The survey and interviews were administered to healthcare professionals on wards participating in the study between December 2023 and January 2024. The study was granted ethical approval by the King's College London Research Ethics Committee, Trust Capacity and Capability (Trust R&D Reference: R&D2023/004) and NHS Health Research Authority (22/HRA/5452).

Recruitment

Purposive sampling was employed to recruit participants targeting all pharmacists and psychiatrists on the three wards. Potential participants were approached with an information leaflet detailing the study aims and were given an opportunity to inquire about any aspects of the research project. Upon expressing agreement to participate, they were asked to sign a consent form. Notably, the number of participants was not pre-defined and was contingent upon achieving theme saturation in the qualitative part of the project.

Data collection

Data was collected from a short online survey and semi-structured online interviews four months following the implementation of the digital tool. The survey comprised two sections. The first section asked about age, gender, professional background, and years of clinical experience, defined

as years a healthcare professional spent in clinical practice since professional qualification. The second section asked healthcare professionals to rate their level of agreement with specific statements related to their awareness of the guidelines, confidence in identifying, managing, and referring AF patients at risk of stroke, relevance of the eCDSS, its integration in the workflow, effect on workload, clarity, and accessibility. Example statements for consideration included:

- "Having access to an eCDSS would help me to better assess stroke and bleeding risks in patients with AF."
- "The content of alerts provides trustworthy evidence-based information."
- "The decision support provided is clinically relevant."
- "The system hinders my existing workflow."
- "Alerts from the eCDSS are not accessible at the right time."

The interview topic guide was informed by field experts including general practitioners and psychiatrists. Interviews were semi-structured and aimed to capture clinician feedback on the eCDSS (including the alerts and training material) and their experience with the system. Interviews lasted for around 20 minutes and were conducted via Microsoft Teams by the same researcher (DF). All interviews were audio recorded, transcribed verbatim and de-identified before analysis.

Data analysis

For a detailed exploration of the qualitative data, a thematic analysis using an inductive approach was conducted (13). This consisted of data familiarisation where the researcher (DF) gained a comprehensive understanding of the content of the interview transcripts. Subsequently, codes were generated based on key concepts and patterns within the data. These codes were organised into potential themes which were then refined and assigned labels based on rigorous discussions with other researchers on board.

Reflexivity played a key role in shaping the interpretation of findings in this study by enhancing transparency and trustworthiness. The researcher working on data collection and analysis (DF) consistently reflected on potential impact, biases, and preconceptions throughout the study. Discussions were held between team members to explore potential subjectivity in any aspect of the research.

Results

The sample included 9 participants of whom 4 identified themselves as females and 5 as males. Age of participants ranged between 25 and 47 with a mean of 33.3. In terms of professional background, 5 were psychiatrists and 4 were pharmacists. The mean years of clinical experience was 7.3.

Findings of the survey showed that all participants considered that the eCDSS is clinically relevant, that there is a clear positive benefit gained from using the digital tool, and that having access to it would help them to better assess stroke and bleeding risks among AF patients. Around 75% of participants believed that the alerts generated from the eCDSS provided clear recommended actions for clinicians to act on, and that the content of the alerts provided trustworthy evidence-based information. However, 88% reported that the system hindered their workflow and 25% thought that the system was difficult to use. Most participants (n=8) reported that they would continue to make use of the eCDSS if it remains available on the ward.

Thematic analysis of the interviews identified three overarching themes: **(1)** clinician feedback on the eCDSS, **(2)** barriers to the use of the digital tool, and **(3)** suggestions to improve clinician experience with the eCDSS (fig1).

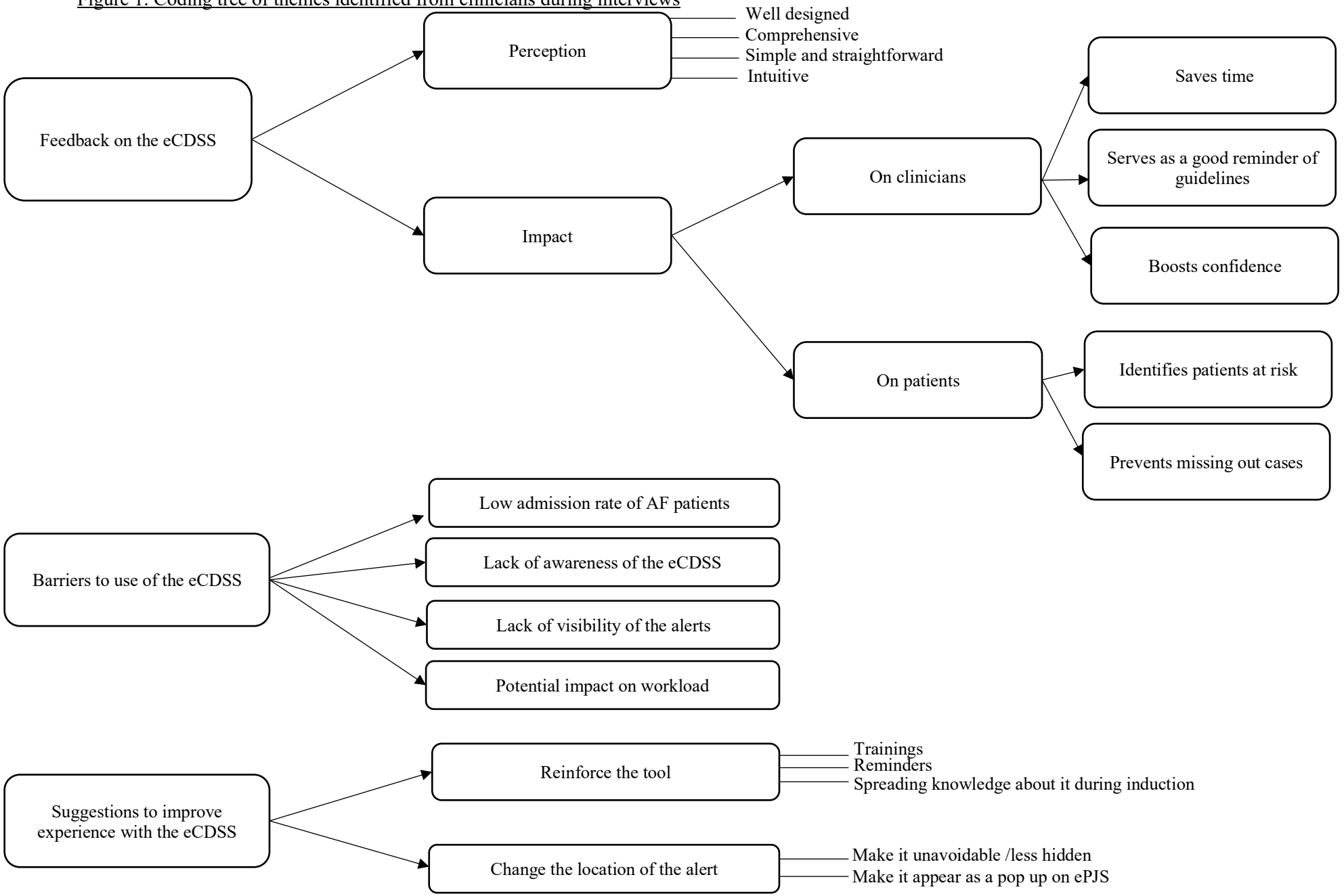
Table 1. CHA_2DS_2-VASc Scale for Atrial Fibrillation Stroke Risk

Age	<65 **0**	65-74 **+1**	≥75 **+2**
Sex	Male **0**	Female **+1**	
Congestive heart failure history	No **0**	Yes **+1**	
Hypertension history	No **0**	Yes **+1**	
Stroke/ transient ischemic attack (TIA)/thromboembolism history	No **0**	Yes **+1**	
Vascular disease history prior myocardial infarction, peripheral artery disease or aortic plaque	No **0**	Yes **+1**	
Diabetes history	No **0**	Yes **+1**	

Table 2. ORBIT Bleeding Risk Scale for Atrial Fibrillation

Sex	Male	Female
Anaemia Haemoglobin <13g/dl and haematocrit <40% for males or haemoglobin <12g/dl and haematocrit <36% for females	No **0**	Yes **+2**
Age >74 years	No **0**	Yes **+1**
Bleeding history Any history of gastrointestinal bleeding, intracranial bleeding, or haemorrhagic stroke	No **0**	Yes **+2**
Glomerular filtration rate <60mL/min/1.73 m^2	No **0**	Yes **+1**
Treatment with antiplatelet agents	No **0**	Yes **+1**

Figure 1. Coding tree of themes identified from clinicians during interviews



Theme 1: Clinician feedback on the eCDSS

Feedback on the eCDSS was grouped into two sub-themes: perception and impact. Healthcare professionals perceived the digital tool as simple, straightforward, and intuitive. The training material was perceived as comprehensive and well-designed, containing all the required information to clinically assess for stroke and bleeding risks, refer patients and document scores in clinical notes.

- "I went through your algorithm, it looks really good, looks very intuitive. I mean the flow diagram that you had is very simple. The training material looks very good. I really like the table you had on the referral clinics, I mean the contact details, because I didn't have that information on hand whether there's anticoagulation clinic in different boroughs" (P1).
- "To be fair, the flow chart I think was quite nice. It was nicely set out. Nice to have a bit of color. It was easy to read and follow. There's not too much information on it. It's not information overload. UM, it's also nice to have the scores on there and kind of guiding you, you know, not what you have to do, but what the scores might mean. I appreciated the links to MD Calc as well because that was useful. Really nice to have the steps and the screenshots of how to record the scores on the ePJS. I liked at the bottom of one of the links you had a table with where to refer to with an email and a phone number based on where you are, because that is probably like one of the most nightmarish things for us. If this person has this condition, who do I call? Who do I refer to? How do I refer to clinic? So that's really, really good"(P2).

Healthcare professionals also discussed the impact of the digital tool on themselves and their patients. At a clinician level, some participants reported that the eCDSS saves time by providing all the information needed to complete the clinical task thus eliminating the need to search guidelines or consult specialists for advice. They also noted that the digital tool serves as a good reminder of the guidelines particularly in a mental healthcare setting where assessment of physical conditions such as stroke associated with AF may not be something done regularly. Additionally, knowing that they are not missing on anything and that they are adhering to guidelines boosts their confidence and make them feel more comfortable. At a patient care level, healthcare professionals

reported that the eCDSS help in identifying patients at risk and prevent missing out cases (fig 1, table 3).

- "It might save us a bit of time because it's all already there. So then I don't have to go in research it all myself, or ask a senior or get some advice from somewhere else. It's a nice one, any kind of alert like that is useful. So, I don't necessarily need to go digging around for that information" (P2).
- "It reminded me that there is an assessment for people with AF because I feel like when you work in a mental hospital you forget about doing these assessments, so it reminded me about it early on throughout my time in the hospital" (P5).
- "I was more confident in advising the doctors on what should be done next. It just gave me confidence that we are doing that and we're not missing anything" (P3)
- "But you know in terms of lighting up the potentially risky patients and their referring, I think the intervention is very useful and particularly in our cohort where we've got people with more physical health care morbidities" (P4).
- "It alerts us to the fact that someone might need treatment, and it alerts us to the fact that someone might have AF and that we might have missed that on" (P5).

Theme 2: Barriers to clinician use of the eCDSS

Healthcare professionals discussed many barriers to the use of the eCDSS in MHOA wards. Many participants observed that the number of AF patients admitted to their ward is low, making the tool one that is not frequently used. Another barrier hindering uptake was a lack of awareness of the digital tool among clinicians (n=2). This was felt to be due to the rotation of junior doctors and pharmacists across various wards every few months resulting in a lack of familiarity of the incoming staff with the digital tool particularly since it was not available in all other wards. Additionally, many participants reported that the lack of electronic visibility of the alerts generated may deter them from engaging with the system regularly, thus impeding its integration in routine clinical practice. Finally, the additional workload that the eCDSS may impose on healthcare professionals may also discourage them from consistently using it (fig 1, table 3).

- “I don't think anyone has been admitted to the ward with AF for the last few months, so I haven't had the opportunity to use it” (P7).
- “I don't think it's widely known about, basically It's not a tab that doctors commonly use, so it's one of those tabs that most doctors don't even know about. The only thing this particular tab is used for is the AF alert, otherwise it's not routinely used. So I guess that really limits its value because unless you know about this study, for example, then you wouldn't go on that tab” (P5).
- “It doesn't sort of jump at you. There's nothing sort of, you know, you have to actually decide to use it and then go use it. It's not sort of like in your face the whole time where you can say “click”. We have such short attention spans so if it's not all there in your face, you're not gonna use it that much” (P6).
- “It requires too many clicks, even though it's not many clicks it's probably one or two clicks, too many for it to be routinely looked at. The fact that you know it's an extra thing that we need to look at and it's in a different place, it's likely to slow things down, likely to not be completed consistently. Particularly there are already lots of different investigations and assessments and lots of forms on ePJS that we're doing so it's hard enough to ensure that all of these forms are consistently completed” (P4).

Theme 3: Suggestions to improve clinician experience with the eCDSS

To improve their experience and enhance the effectiveness of the eCDSS, healthcare professionals suggested reinforcing the tool in a number of ways. They suggested giving additional training to clinicians familiarising them with the tool, showing them where to find the alerts, and how to use them. They also mentioned that the training material could be circulated to healthcare professionals joining the wards during induction. Others suggested enhancing the alerts by sending emails to clinicians notifying them that they need to do a clinical assessment alongside the notification on the ePHR.

Another suggestion was to change the location of the alert, as most participants considered it a little hidden. They proposed making it appear as a pop up on the main page of the ePJS (rather than ePHR) in a way that cannot be avoided or disregarded (fig 1, table 3).

- “I think the only thing is maybe training, showing people what they need to do, maybe familiarizing themselves with the scales or through the tools if they're not familiar with them. Umm, initially you know, to train everyone. But I think it is a good idea to do it in the induction. So train your doctors and pharmacists when they kind of get a handover. When they swap wards this should be part of the handover for pharmacist for sure” (P8).
- “I think for it to be really used, it would need to come up on ePJS as a prompt or it needs to be unavoidable in some way rather than people having to make a few clicks through to look in a particular area” (P4).

Table 3. Illustrative quotations for the identified sub-themes

Sub-themes	Examples
Perception of the tool	• "That page you have made on the Intranet was really helpful because it has all the links of the different anticoagulation clinic" (P5). • "All of the resources sound perfect. They would all be appropriate and helpful to us when managing these scenarios" (P4). • "I went through your algorithm, it looks really good, looks very intuitive. I mean the flow diagram that you had is very simple. The training material looks very good. I really like the table you had on the referral clinics, I mean the contact details, because I didn't have that information on hand whether there's anticoagulation clinic in different boroughs" (P1). • "To be fair, the flow chart I think was quite nice. It was nicely set out. Nice to have a bit of color. It was easy to read and follow. There's not too much information on it. It's not information overload. UM, it's also nice to have the scores on there and kind of guiding you, you know, not what you have to do, but what the scores might mean. I appreciated the links to MD Calc as well because that was useful. Really nice to have the steps and the screenshots of how to record the scores on the ePJS. I liked at the bottom of one of the links you had a table with where to refer to with an email and a phone number based on where you are, because that is probably like one of the most nightmarish things for us. If this person has this condition, who do I call? Who do I refer to? How do I refer to clinic? So that's really, really good"(P2). • "It was quite straightforward. It's quite intuitive" (P6). • "Junior doctors don't feel confident in knowing what drugs to start or they never knew where to refer, so I think it's really good that all that information is now within the system and you know it's an easy referral process. So I think it would be it really useful definitely" (P8).
Impact of the tool on clinicians: Saves time	• "It might save us a bit of time because it's all already there. So then I don't have to go in research it all myself, or ask a senior or get some advice from somewhere else. It's a nice one, any kind of alert like that is useful. So, I don't necessarily need to go digging around for that information" (P2). • "You know, it actually helped me out because if not, I would have had to look at different resources or go to NICE to see what to do but typically everything being there really helped me. It saved me a lot of time and helped me in clinical decisions as well. Probably it would have taken me a little longer without the eCDSS" (P3).

Impact of the tool on clinicians: Serves as good reminder of guidelines	• "It just keeps in the back of your mind that this is something you need to do and refer to an anticoagulation clinic. We do ECG on admission for every patient anyways so if there's AF it gets picked up but just to then refer it is one step further, so it is something that's correct on there" (P1). • "Uh, actually, it's also good whenever you have these kind of NICE guidelines, flow diagrams or whatever, it's actually good kind of learning, a good refresher for us" (P2). • "It reminded me that there is an assessment for people with AF because I feel like when you work in a mental hospital you forget about doing these assessments so It reminded me about it early on throughout my time in the hospital" (P5). • "That sort of reminders is really helpful because it could prompt when you're on someone's chart to actually think oh, I need to check this and have a look at it this" (P9).
Impact of the tool on clinicians: Boosts confidence	• "I was more confident in advising the doctors on what should be done next. It just gave me confidence that we are doing that and we're not missing anything" (P3) • "Uh, confidence adhering to clinical guidelines, it would probably help in that, because all the guidelines are provided and there is step by step instructions as to how to respond to the alerts" (P4). • "I think it would definitely add to confidence and obviously I'm a psychiatrist I'm not a cardiologist. So, so you know, I would probably speak to a geriatrician before starting any anticoagulant, mainly because we're at old age mental Health ward, where we don't really have monitoring for things. But it would give me confidence to speak quite confidently to geriatricians across the road" (P6). • "I think it will help with confidence of knowing where to refer when you need to refer" (P8). • "I'll definitely feel a lot more comfortable that we've carried out all the necessary sort of screening for a patient with AF" (P9).
Impact of the tool on patients: identifies patients at risk	• "It is very useful, it just points out patients at risk" (P3). • "But you know in terms of lighting up the potentially risky patients and their referring, I think the intervention is very useful and particularly in our cohort where we've got people with more physical health care morbidities" (P4). • "The eCDSS would improve the ability to recognize when a patient is at high risk of stroke" (P2). • "You know, because there's a lot of things happening, so it directs our attention to the main sort of thing that needs actioning upon. It gives the orbits cut off point and the CHADVASc cut off point that needs actioning, a quick referral to anticoagulation clinic, so that you know the stroke risk minimised and yeah so in terms of you know quick action on any stroke risk" (P1). • "It will impact patient care positively because we could be helping reduce patient have a risk of stroke by implementing the system" (P7).

	• "I think this is really good for, you know, automatically anyone with AF will have this consistently assessed to make sure that they're not extra risk factors" (P8).
Impact of the tool on patients: prevents missing out cases	• "So it was easier to, uh, to pick up anything I would have missed otherwise" (P3). • "It alerts us to the fact that someone might need treatment, and it alerts us to the fact that someone might have AF and that we might have missed that on" (P5). • "It means more patients will have AF perhaps picked up and the ones who do have it picked up will have, you know, follow up on it and have plan put in place" (P2). • "There must be so many patients that are missed, you know, doing these assessments and using the tools, will definitely improve safety basically" (P8). • "I think it would definitely help because at the point, particularly during admission, a lot of the times things might be missed. I think it'll make it more likely that they get screened properly and then it gets reviewed regularly and I think it'll be done in a more standardized way which I think is really important" (P9).
Low admission rate of AF patients	• "I have not seen the alerts yet, but we haven't had many AF cases. I can only think of one case, but he wasn't in AF at the time of presentation, so AF was in the past history" (P1). • "I think in my patient group, none of them had atrial fibrillation. So It felt really nice knowing that I could sort of screen for stroke risk. It just that I didn't get any result from it mainly because there was no new diagnosis of atrial fibrillation in my patient group" (P6). • "I don't think anyone has been admitted to the ward with AF for the last few months, so I haven't had the opportunity to use it" (P7).
Lack of awareness of the eCDSS	• "I don't think it's widely known about, basically It's not a tab that doctors commonly use, so it's one of those tabs that most doctors don't even know about. The only thing this particular tab is used for is the AF alert, otherwise it's not routinely used. So I guess that really limits its value because unless you know about this study, for example, then you wouldn't go on that tab" (P5). • "I never used it. I just wasn't aware, didn't know it existed" (P2). • "The junior doctors are changing, you know, some of them every four months. So the new junior doctors would come in and they wouldn't necessarily know to check there because it's not something that they would usually be expected to do" (P4). • "I think other people who don't know about the tool being there will not know" (P7).

Lack of visibility of the alerts	• "The position where the alerts come up is not very obvious and a bit more hidden so when we click there, it's either to look at ePMA or the London care record. I think everything else are kind of excluded from our vision" (P4). • "I mean it's very rarely that I go and look for alerts in ePHR" (P1). • "I think the place where it is, is a little hidden and it's not very obvious. For clinicians to go into ePHR and then look at the alerts tab for every patient for the possibility that they might have AF risk, I don't think that would be practically manageable. I don't think they would do that just for the possibility that somebody's gotten AF risk. There's no other alerts that that we check in that area and so it's not a place that we routinely would go to" (P4). • "It doesn't sort of jump at you.There's nothing sort of, you know, you have to actually decide to use it and then go use it. It's not sort of like in your face the whole time where you can say "click". We have such short attention spans so if it's not all there in your face, you're not gonna use it that much" (P6). • "I'm not really accustomed to it myself because it's not something that pharmacists use, and I only really go there if I'm looking for physical health medications" (P7).
Potential impact on workload	• "When I was having a look at how to input the data it did seem a bit tedious having to click into that and then click into that" (P7). • "The factor that would hinder use is workload of the ward, so you're not sort of thinking about these things" (P1). • "It requires too many clicks, even though it's not many clicks it's probably one or two clicks, too many for it to be routinely looked at. The fact that you know it's an extra thing that we need to look at and it's in a different place, it's likely to slow things down, likely to not be completed consistently. Particularly there are already lots of different investigations and assessments and lots of forms on ePJS that we're doing so it's hard enough to ensure that all of these forms are consistently completed" (P4). • "I think you have to understand that a doctor's clinical and mental load is actually already a lot so making them click on five different tabs and do five different things, It's just not gonna happen. It's in the alerts tab which is not commonly used, but then it also tells you which patient has AF, but then you have to use the chadvasc score from a different website and then you have to input the information on ePJS so it's a lot of additional websites. It's not seamline and then you have to email the team in the hospital. I guess it's also not something that a lot of people would probably do" (P5).
Re-inforce the tool	• "I think that table on referral clinics, if you just maybe circulate it during an induction to us, so everybody has access to it. It just takes a lot of time to figure out where the right anticoagulation clinic is and the right contact for that" (P1).

	• "Every four months when doctors are changing, then having some either, whether a call or an email with pictures, screenshots and things like that for doctors as they come through. So for junior doctors to be able to keep it in their head, it probably needs to be printed and laminated on a board in front of their head. It needs to be kind of reinforcement that we are regularly using it" (P4). • "So it might need to be promoted a bit as well" (P7). • "I think the only thing is maybe training, showing people what they need to do, maybe familiarizing themselves with the scales or through the tools if they're not familiar with them. Umm, initially you know, to train everyone. But I think it is a good idea to do it in the induction. So train your doctors and pharmacists when they kind of get a handover. When they swap wards this should be part of the handover for pharmacist for sure" (P8). • "Emailing clinicians if somebody's flagged up would be helpful, you know automatically emailing the ward doctors to say this person has been flagged up, please check the alerts tab or something" (P4).
Change the location of the alert	• "I guess I would modify the location of that, I think the odds of it being seen will be a lot more. When you click on someone, if it shows on ePJS, or if it's a pop up in the ePMA or in where you are prescribing, I think that would be more helpful"(P5). • "If there's a way to sort of makes it automatically appear in ePJS. That would, yeah, would actually speed up things" (P1). • "I think for it to be really used, it would need to come up on ePJS as a prompt or it needs to be unavoidable in some way rather than people having to make a few clicks through to look in a particular area" (P4). • "Making it more visible, I think that makes a huge difference" (P6). • "Maybe it would be better if it was separate on the assessment, so it wasn't within the physical health section, so if it was just separate by itself and you could just fill it in and you could easily access the scores that were calculated" (P7). • "If it does pop up automatically when they go into the patients notes. If the alert could pop up automatically to say this person has AF, can you do the following screening with the tools? rather than having to click somewhere else. So, if there's an automatic alert that comes up when they're looking into the patient's notes, as soon as they go in" (P8). • "You could link to the Chadvasc and the orbit calculators on MDCalc. That would make it very quick. Or if you can sort of somehow code for it so it becomes inbuilt in your system then that would be faster as well" (P1).

*AF: atrial fibrillation; eCDSS: electronic clinical decision support system; ePMA:e-prescribing and medicines administration; ePJS: electronic patient journey system; NICE: national institute for health and care excellence; ECG: electrocardiogram.

Discussion

This study sought to explore healthcare professionals experience with an eCDSS to screen for stroke risk among people with AF admitted to a mental health service. Clinicians perceived the digital tool as simple, straightforward, comprehensive, and well designed. They discussed its potential impact in saving time, reminding clinicians of the guidelines, boosting clinician confidence, and identifying patients at risk. However, healthcare professionals reported some barriers to the use of the digital tool in clinical practice. These barriers included low admission rate of AF patients to the mental health service, lack of awareness of the digital tool, low visibility of the alerts, and a potential impact of the eCDSS on workload. To improve their experience with the system, they suggested reinforcing the tool through training and reminders as well as changing the location of the alert by making it appear in an unavoidable way on the main electronic health record page.

In healthcare settings where eCDSSs are implemented, adoption rates are lower than expected, with more than 49% of recommendations or alerts being ignored or overridden for multiple reasons (10). The healthcare setting is characterised by interconnected factors at system, clinician, and organisational levels that may influence successful integration of such tools (14). Given this complexity, an improvement at one level does not necessarily guarantee effectiveness (14). Additionally, eCDSSs are not like other traditional information technology tools (15). They integrate an evidence-based approach into clinical practice which can sometimes challenge beliefs about professional autonomy and hierarchical structures in the clinical setting resulting in scepticism regarding its use (16).
Previous studies reported that the lack of uptake could be also attributed to the poor alignment of the digital tools with the workflow mainly due to the interruptive notifications (15,17). Inadequate consideration of human factors such as the additional steps required to act on the alerts, lack of specificity, and failure to adequately capture nuances of care or co-morbidities are other limitations that have been identified in the adoption of eCDSSs (18). In this study, healthcare professionals emphasized on the effectiveness of the implemented eCDSS in saving resources and facilitating clinical practice. They underscored how the system streamlines the process by providing instant access to necessary guidelines and information, sparing doctors the time and effort otherwise spent seeking out such resources. However, other clinicians stressed on the importance of considering the workload imposed on healthcare professionals. Despite the convenience of the eCDSS, they noted that the additional tasks it demands could exacerbate an already heavy workload.

Greenhalgh et al.'s framework on Non-Adoption, Abandonment, Scale-up, Spread and Sustainability (NASSS) suggests that only when the digital tool tackles a "simple" condition, needs little troubleshooting or training, has excellent usability, and generates value for patients and clinicians would be used in clinical practice (19). Several studies also highlight the importance of an eCDSS being intuitive, i.e. how easily healthcare professionals can interact and navigate with the system, in enhancing overall clinician comfort and experience (20). This is in line with our findings as most healthcare professionals noted that the system is user-friendly and straightforward underscoring its use in clinical practice.
Ease of digital access has also been found crucial as alerts prominently displayed are more likely to capture the attention of healthcare professionals whereas those blended in the background of the EHR interface may be difficult to locate and thus may be overridden (21). In this study, visibility

and accessibility of alerts were considered barriers to their utilisation. A key factor contributing to this lack of visibility was the integration of alerts within ePHR rather than ePJS. This setup allowed clinicians to open and input notes into the ePJS without necessarily accessing the ePHR, leading to instances where alerts remained unnoticed.
To improve their operational skills and enhance their understanding of how to make full use of it, previous research has stressed the significance of healthcare professionals receiving tailored trainings which was highlighted by healthcare professionals in our study (22).

This study has potential limitations. Some of the interviewed healthcare professionals had never used the digital tool and answered questions of the survey and interview based on their perspective rather than practical experience with the eCDSS. This was mainly attributed to the low admission rate of AF cases. However, awareness of the digital tool was maximised by regularly sending emails to clinicians on board informing them of the digital tool and providing them with links to all the training material required to do the clinical task. Another limitation is that participation in this pilot study was restricted to pharmacists and psychiatrists. Including other healthcare professionals with various levels of clinical experiences could have affected the results. We conducted the intervention for a duration of four months before starting the interview process; extending the intervention period could have allowed for more AF admissions thus increasing familiarity and experience with the eCDSS. Although the sample size (n=9) may appear small, the number is deemed acceptable in relation to the targeted population (N=15). It is also important to note that data collection continued until saturation was reached to ensure that key themes were captured.

Conclusion

Positive feedback from healthcare professionals was received regarding the implementation of an eCDSS for stroke risk screening in a mental health service. However, clinicians also reported barriers to the use of the digital tool, most notably digital placement, and provided suggestions for improvement. eCDSSs could be key in promoting evidence-based practice and decision making, but for these tools to be effective, ongoing evaluation is needed to continuously monitor the performance and usage of the digital tool, gathering feedback from healthcare professionals, and accordingly making the necessary adjustments. The evaluation process should be comprehensive and should include clinician satisfaction, integration in workflow, and clinical effectiveness.

Declarations

Ethics approval and consent to participate

Ethical approval was granted by the King's College London Research Ethics Committee, SLaM Capacity and Capability (Trust R&D Reference: R&D2023/004) and NHS Health Research Authority (22/HRA/5452).The study was conducted in accordance with the principles of the Declaration of Helsinki (1996) and all applicable regulatory requirements including but not limited to the UK policy framework for health and social care research, Trust and Research Office policies and procedures and any subsequent amendments. Information gathered in this study were kept confidential and managed based on the Data Protection Act, NHS Caldicott Guardian, The Research Governance Framework for Health and Social Care and HRA Approval.

A written informed consent for partaking in the study and publishing data gathered during interviews was obtained from all participants.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Funding

DF is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust and by the KCL funded Centre for Doctoral Training (CDT) in Data-Driven Health.

MA is in part funded by the Guy's and St Thomas' Charity and the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

JO and FG are in part supported by the National Institute for Health Research's (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. In addition, FG is supported by the Maudsley Charity and by the National Institute for Health Research (NIHR) Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust.

References

28- Chen, Zhao, et al. "Harnessing the power of clinical decision support systems: challenges and opportunities." *Open Heart*10.2 (2023): e002432.

29- Kawamoto K, Houlihan CA, Balas EA, Lobach DF. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. Bmj. 2005 Mar 31;330(7494):765.

30- Sutton RT, Pincock D, Baumgart DC, Sadowski DC, Fedorak RN, Kroeker KI. An overview of clinical decision support systems: benefits, risks, and strategies for success. NPJ digital medicine. 2020 Feb 6;3(1):17.

31- Muhiyaddin R, Abd-Alrazaq AA, Househ M, Alam T, Shah Z. The impact of clinical decision support systems (CDSS) on physicians: a scoping review. The Importance of Health Informatics in Public Health during a Pandemic. 2020:470-3.

32- Moja L, Kwag KH, Lytras T, Bertizzolo L, Brandt L, Pecoraro V, Rigon G, Vaona A, Ruggiero F, Mangia M, Iorio A. Effectiveness of computerized decision support systems linked to electronic health records: a systematic review and meta-analysis. American journal of public health. 2014 Dec;104(12):e12-22.

33- Factsheet UK. British Heart Foundation. London, UK. 2024. https://www.bhf.org.uk/-/media/files/for-professionals/research/heart-statistics/bhf-cvd-statistics-uk-factsheet.pdf.

34- Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Kardiologia Polska (Polish Heart Journal). 2016;74(12):1359-469.

35- Jones C, Pollit V, Fitzmaurice D, Cowan C. The management of atrial fibrillation: summary of updated NICE guidance. Bmj. 2014 Jun 19;348.

36- Alasiri SF, Douiri A, Altukistani S, Porat T, Mousa O. The Role of Clinical Decision Support Systems in Preventing Stroke in Primary Care: A Systematic Review. Perspectives in Health Information Management. 2023;20(2).

37- Wasylewicz AT, Scheepers-Hoeks AM. Clinical decision support systems. Fundamentals of clinical data science. 2019:153-69.

38- Meunier PY, Raynaud C, Guimaraes E, Gueyffier F, Letrilliart L. Barriers and facilitators to the use of clinical decision support systems in primary care: A mixed-methods systematic review. The Annals of Family Medicine. 2023 Jan 1;21(1):57-69.

39- Ancker JS, Edwards A, Nosal S, Hauser D, Mauer E, Kaushal R, With the HITEC Investigators. Effects of workload, work complexity, and repeated alerts on alert fatigue in a clinical decision support system. BMC medical informatics and decision making. 2017 Dec;17:1-9.

40- Braun V, Clarke V. Thematic analysis. American Psychological Association; 2012.

41- Yusof MM, Kuljis J, Papazafeiropoulou A, Stergioulas LK. An evaluation framework for Health Information Systems: human, organization and technology-fit factors (HOT-fit). International journal of medical informatics. 2008 Jun 1;77(6):386-98.

42- Sutton RT, Pincock D, Baumgart DC, Sadowski DC, Fedorak RN, Kroeker KI. An overview of clinical decision support systems: benefits, risks, and strategies for success. NPJ digital medicine. 2020 Feb 6;3(1):17.

43- Liberati EG, Ruggiero F, Galuppo L, Gorli M, González-Lorenzo M, Maraldi M, Ruggieri P, Polo Friz H, Scaratti G, Kwag KH, Vespignani R. What hinders the uptake of

computerized decision support systems in hospitals? A qualitative study and framework for implementation. Implementation Science. 2017 Dec;12(1):1-3.
44- Greenes RA, Bates DW, Kawamoto K, Middleton B, Osheroff J, Shahar Y. Clinical decision support models and frameworks: seeking to address research issues underlying implementation successes and failures. Journal of biomedical informatics. 2018 Feb 1;78:134-43.
45- Devaraj S, Sharma SK, Fausto DJ, Viernes S, Kharrazi H. Barriers and facilitators to clinical decision support systems adoption: a systematic review. Journal of Business Administration Research. 2014 Jul 24;3(2):36.
46- Greenhalgh T, Wherton J, Papoutsi C, Lynch J, Hughes G, Hinder S, Fahy N, Procter R, Shaw S. Beyond adoption: a new framework for theorizing and evaluating nonadoption, abandonment, and challenges to the scale-up, spread, and sustainability of health and care technologies. Journal of medical Internet research. 2017 Nov 1;19(11):e8775.
47- Saputra GA, Ali H. Factors Affecting Decision Support System: Knowledge, Training, Ease of Use. Dinasti International Journal of Digital Business Management. 2023 Oct 31;4(6):1053-8.
48- Robertson J, Moxey AJ, Newby DA, Gillies MB, Williamson M, Pearson SA. Electronic information and clinical decision support for prescribing: state of play in Australian general practice. Family practice. 2011 Feb 1;28(1):93-101.
49- Moxey A, Robertson J, Newby D, Hains I, Williamson M, Pearson SA. Computerized clinical decision support for prescribing: provision does not guarantee uptake. Journal of the American Medical Informatics Association. 2010 Jan 1;17(1):25-33.

PART 4- GENERAL DISCUSSION

CHAPTER 9- DISCUSSION

9.1 Summary of findings

The aim of this thesis was to examine stroke prevention in patients with AF and co-morbid physical and mental health problems. This was done by systematically reviewing the literature to gain insights on the prevalence, management, and outcomes of AF among people with mental illness and by conducting two observational studies to explore any disparity in anticoagulation therapy between SMI and non-SMI patients in a general hospital setting and the factors influencing anticoagulation for AF-related stroke risk in a mental health Trust in London. This thesis further details the development, feasibility, and acceptability of an eCDSS which mainly aims to enhance safety of AF patients at high risk of stroke in SLaM. This chapter provides a summary of the findings followed by a discussion of the research implications, and a review of the methodological strengths and limitations related to this thesis.

The systematic review (paper 1) demonstrated a low age-adjusted prevalence of AF among people with bipolar disorder and schizophrenia compared to the general population. The study also showed that despite evidence of the substantial net benefit from OACs in the general population, people with AF and co-morbid SMI were less likely to receive the therapy even after adjusting for age. Among people receiving warfarin, those with SMI, particularly bipolar disorder, although not schizophrenia, experienced poor anticoagulation control as measured by time in INR therapeutic range. A key finding was the result of the meta-analysis showing no significant association between SMI and ischaemic stroke or major bleeding after controlling for risk factors.

In paper 2, CogStack@KCH was used to identify a cohort of AF patients who had an admission to KCH between 2011 and 2020. This observational study showed that among admitted AF patients, those with co-morbid SMI had significantly higher stroke and bleeding risk scores. People with AF and co-morbid SMI were less likely than those without SMI to be prescribed any OAC, particularly warfarin. However, there was no evidence of a significant difference between the two groups since 2019. Noteworthy, DOAC prescribing rate has shown a substantial increase over time whereas warfarin use has decreased in both groups.

Another observational study (paper 3) was conducted using data extracted from CRIS on active AF patients in SLaM between 2011 and 2019. Adjusting for age, sex, CHA2DS2VASc and ORBIT scores, patients with AF and co-morbid SMI were less likely to be prescribed any OAC compared to those with dementia, substance use disorders or common mental disorders. A key finding of the study was that among AF patients at increased risk of stroke, only 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, leaving many unprotected. Among the full cohort of AF patients, warfarin was also less likely to be prescribed to those having ADL impairment and alcohol or substance dependency, whereas among the subgroup of AF patients with co-morbid SMI, it was less likely to be prescribed to those having a history of serious self-injury, hallucinations or delusions, alcohol or substance dependency, and ADL impairment. Self-injury, cognitive problems and other mental illnesses were associated with lower likelihood of warfarin prescription among people with AF and co-morbid substance use disorder.

Based on the findings of the systematic review and the two observational studies, an eCDSS to improve screening for patients with AF at high risk of stroke was developed and piloted in a mental health service in London (chapter 6). To inform its integration into daily clinical practice, a cross-sectional study (paper 4) employing mixed methods research design was conducted between March and May 2023. Clinicians reported many challenges related to stroke prevention in MHOA wards, including difficulty identifying patient pertinent medical history, perceived lack of knowledge and expertise in the management of physical conditions, fragmented medical care, and patient psychotic beliefs. To improve clinical practice, they suggested that reminding clinicians of the latest guidelines through alerts on patient electronic records, having clear policies at the system level, and providing clinicians with training sessions on AF-related stroke management would have benefit. The reported potential benefits for the eCDSS included improving clinical effectiveness, better identification of patients at risk, safer and more comprehensive care, consistency in decision making and saving time. However, clinicians also noted that the digital tool could have potential risks such as rigidity in decision making, overreliance, reduced critical thinking, false positive recommendations, annoyance, and increased workload.

After implementation of the eCDSS, another cross-sectional study (paper 5) employing a questionnaire and semi-structured interviews was conducted to explore healthcare professionals'

experience with the implemented eCDSS. Clinicians perceived the digital tool as simple, straightforward, comprehensive, and well designed. They argued that it might be helpful in saving time, reminding clinicians of the guidelines, boosting clinician confidence, and identifying patients at risk. However, many barriers to the use of the digital tool in clinical practice were reported including low admission rate of AF patients to the mental health wards, insufficient clinician awareness of the digital tool, low visibility of the alerts, and noted the potential impact of the eCDSS on workload. For a better experience, they suggested reinforcing the tool through training and reminders as well as making the alert appear in an unavoidable way on the ePJS.

9.2 Implications and future directions

9.2.1 Research implications

To better understand the implications of AF, one of the main aims of the systematic review was to investigate AF prevalence among people with SMI. First, it was noted that research addressing this prevalence is very scarce with studies reporting a low prevalence of AF in people with schizophrenia and bipolar disorder compared to the general population (88,89,90). One explanation for this finding could be the under-diagnosis of AF in people with SMI, potentially due to less frequent healthcare visits, diagnostic overshadowing, or a lack of screening for AF in this population. No previous studies compared AF screening among people with SMI and those with no SMI. Conducting such a study would be highly informative, as it could help determine whether the lower prevalence of AF observed in people with SMI is a true reflection of disease incidence or primarily a result of under-detection. Additionally, given that people with SMI, compared to the general population, have disproportionately higher cardiovascular risk factors including AF, the low reported prevalence of AF raises questions about potential underreporting in clinical practice (91,92). Further research should prioritise addressing these gaps using comprehensive healthcare databases or population-based studies. Only through investigation of the true prevalence of AF in this population will a comprehensive understanding of the magnitude of the health issue be obtained and an assessment of who might be at increased risk can derived. Second, the need for further research is underscored by the fact that existing research on the

prevalence of AF in people with SMI were limited to Taiwan and the UK which may not be representative of the worldwide population (88-90). Further research across different geographical settings and diverse populations with various socioeconomic, cultural, and healthcare system contexts should be conducted to yield generalisable findings. Overall, understanding the prevalence of AF in people with SMI is key for improving outcomes, implementing tailored screening, prevention, and management strategies.

In addition to the discrepancy in AF identification, there is also a notable disparity in OAC prescription among people with SMI versus the general population. To date few studies have investigated OAC prescription in people with SMI with those focusing on whether the use of DOACs has reduced OAC gap between SMI and non-SMI patients being limited so far (61, 93,94,95,96). Fenger-Grøn et al. reported an increase in OAC initiation and prevalence among people with schizophrenia and bipolar disorder after the introduction of DOACs although a significant anticoagulation treatment deficit remained for those with schizophrenia (93). Another Danish study also found that initiation of OAC was substantially lower among patients with AF and schizophrenia compared to matched AF peers despite the increase in OAC use noted among people with schizophrenia following the introduction of DOACs (94). This is in line with findings of our study conducted at King's College Hospital, where we reported an increasing trend of DOAC use among AF patients with co-morbid SMI between 2011 and 2020. A significant difference in OAC prescription between SMI and non-SMI patients was noted until 2019, after that there was no evidence of a significant difference (61). The absence of difference between the two groups after 2019 could be due to an improvement in OAC prescription, particularly DOAC, but could be also due to lack of comprehensive data after that date (61). None of the above-mentioned studies included data after 2020. Continued monitoring of OAC prescription trend is necessary to assess whether the disparity between SMI and non-SMI persists over time. Longitudinal studies could be also helpful in understanding the consequences of this disparity on stroke incidence, morbidity, and mortality among people with mental illness.

The OAC treatment gap may stem from various factors including active features of mental illness (53). Our observational study conducted in SLaM was the first to investigate association between mental illness severity and functional impairment with OAC prescription in eligible patients (62).

Further research is needed to validate the findings and confirm generalisability in other mental healthcare settings. Qualitative studies could also delve into patient preferences, and the systemic barriers influencing treatment decisions. Elucidating the underlying reasons for OAC treatment gap could serve as the basis for developing strategies to improve provision of therapy in specific subgroups such as people with hallucinations and delusions, activity of daily living impairment, or alcohol or substance dependence.

Based on the findings of the systematic review and the observational studies conducted in general and mental healthcare settings, an eCDSS to screen for stroke risk among patients with AF and co-morbid mental illness was developed (84). Although many eCDSSs have been developed for the same purpose, ours marks a significant milestone as it is the first to screen for AF-related stroke risk in a mental healthcare setting (70-79). The fragmented nature of the healthcare system may inadvertently lead to gaps in identification of risk factors; therefore, such integration promotes a holistic approach to healthcare delivery, particularly for people with complex health needs. Future research should explore the scalability of the digital tool across various mental healthcare settings to evaluate its effectiveness in improving stroke risk assessment and OAC clinic referral practices. Additionally, research comparing standard care versus use of eCDSSs in stroke risk screening can provide valuable insights into the effect of the digital tool on clinical outcomes and healthcare delivery.

To ensure successful implementation and utilisation of the eCDSS in SLaM, interviews aiming to understand clinician perception and experience with the digital tool were conducted. The qualitative research allowed us to identify barriers, facilitators, and nuances that could not otherwise have been captured through quantitative data alone. Insights gained from these studies were essential to identify areas that needed refinement or improvement for the digital tool to better align with the preferences and needs of clinicians. This iterative approach of feedback and adoption was considered key for enhancing the overall experience and fostering a sense of engagement among clinicians. Similar research should be conducted in other mental healthcare services having different organisational structures, healthcare providers, and patient demographics to allow for generalisation of findings beyond a single context. Highlighting factors that consistently hinder or facilitate implementation as well as other contextual factors affecting outcomes would inform

development of guidelines and best practices for the implementation of such digital tools across various settings.

9.2.2 Clinical and service implications

The reduced life expectancy of people with mental illness compared to the general population is a major public health concern (12-14). Cardiovascular diseases are the leading cause of death with the risk being up to 5-fold higher in people with SMI compared to the general population across both sexes and all ages and ethnic groups (37). Efforts to reduce cardiovascular mortality including advancements in interventions, increased adherence to guidelines and improvements in lifestyle behaviour have not been mirrored in people with SMI compared to non-SMI (97). Consequently, a disparity persists between the two groups (97).

People with AF are at increased risk of stroke and most require OAC treatment (37). A disparity in AF identification and OAC prescription has multifaceted clinical implications. AF is a type of arrhythmia that increases the risk of stroke by elevating the chances of blood clot formation (37). Thus, failure to mitigate this risk through appropriate treatment measure could result in devastating health outcomes affecting patient quality of life, especially that strokes associated with AF tend to be more severe compared to those without AF resulting in emotional distress, significant disability (such as cognitive deficit, speech impairment, and paralysis) and sometimes death (80). Strokes do not only impact patients, but also impose serious burden on their families and caregivers who may as a result face physical and emotional issues impacting their well-being (98). Additionally, prolonged hospitalisations, increased healthcare costs, greater demands on resources for long term care and stroke rehabilitation impose a significant economic burden, emphasising the need for adherence to evidence-based guidelines to reduce morbidity and mortality associated with unmanaged AF related stroke risk, particularly because strokes related to AF are often preventable (99). The disparity in OAC therapy could also convey significant repercussions in terms of health inequity. Failure to provide appropriate therapy to this vulnerable population may worsen existing disparities in health outcomes.

Implementing an eCDSS for stroke risk screening in a mental healthcare setting have many clinical implications. First, such a digital tool would enhance the detection of a history of AF itself, which, because AF can be intermittent, may be missed on re-presentation, along with quantification of risk factors, mainly components of the CHA_2DS_2VASc and ORBIT scales, among people with mental illness. This is considered crucial especially that physical health conditions are not always prioritised in mental healthcare settings often leading to under-recognition and under-treatment (65,100). Second, the digital tool allows healthcare providers to systematically identify people at high risk of stroke related to AF and accordingly make referrals to OAC clinics, potentially reducing the number of missed cases and ensuring those at risk are receiving appropriate treatment (70,73). Third, the digital tool can support a holistic approach to healthcare delivery. Guiding mental health clinicians by providing them with evidence-based guidelines and decision support tools allows them to address all relevant aspects of patient health, promoting a patient-centred approach to care (65). At the service level, the eCDSS has substantial implications such as enhancing quality of care, improving efficiency, promoting evidence-based practice, interdisciplinary collaboration, and optimisation of resource utilisation (65). While the eCDSS developed in this study was tested in an inpatient setting, expanding its use to outpatient settings and GP practices may have significant advantages. In these settings, the number of people with AF could be higher, which means that screening for associated stroke risk could identify more individuals at high risk. This would allow for early prevention in a greater number of patients, timely interventions, and potential reduction in the stroke incidence. Outpatient and GP settings also offer more opportunities for direct patient engagement and education, empowering patients to understand and manage their stroke risk more effectively.

Qualitatively assessing end-user perception of the eCDSS can provide valuable insight into its potential impact on clinical decision-making processes including decision support, clinical reasoning, quality of care and adherence to guidelines. A positive perception can facilitate the integration of the tool into routine practice, whereas a negative one may suggest challenges highlighting potential areas for improvement and refinement. Additionally, understanding clinician perception of an eCDSS, such as the one implemented in this project, reveals the extent to which digital tools for the management of physical health conditions could be successfully integrated in a mental healthcare setting. Understanding the challenges and barriers to adoption

encountered in real-world clinical settings is crucial for optimising the design and functionality of the system so that it becomes more aligned with healthcare provider preferences and workflow, eventually boosting satisfaction and usability. Moreover, healthcare provider perception is fundamental to understand the accuracy, relevance, user-friendliness, the effect of the digital tool on workload and workflow efficiency, and on patient safety and outcomes. All these insights can inform customisation strategies and quality improvement initiatives aiming at maximising the benefits of the digital tool and enhancing healthcare delivery.

9.3 Strengths and limitations

Strengths and limitations of each study included in this thesis have been listed in chapters 2 to 7. Further discussion surrounding strengths and limitation are provided in this chapter.

9.3.1 Strengths

Paper 1 had many strengths (60). It provided a comprehensive overview of existing evidence on the topic, helped identify gaps in knowledge, and accordingly directed the subsequent investigations in the project (60). The risk of bias was reduced by pre-registering the protocol on PROSPERO, assigning a researcher to independently replicate data retrieval and extraction processes, utilising PRISMA guidance for reporting, searching multiple databases using a variety of keywords, and assessing the risk of bias for each included study using the NOS (60). In the meta-analysis, the risk estimates included were all adjusted for OAC use and stroke and bleeding risk factors which led to more robust findings (60).

The main strength of paper 2 is that it evaluated OAC prescription rates over a period of 10 years (2011-2020) in a large inner-city hospital (61). The study was based on data extracted using a NLP tool, an approach that has several advantages (61). Compared to manual extraction methods, NLP tools allow for efficient extraction of patient data from large volumes of unstructured text including clinical notes and EHRs (101). This approach allows researchers to capture a wide range of information (including demographics, symptoms, diagnoses, laboratory results, treatments, and medication) providing a comprehensive overview of patient health status (102). Accordingly, researchers can conduct studies at a larger scale with minimum time and effort (102). In paper 3,

the association between mental illness severity and functional impairment with the prescription of OAC therapy among people with AF was investigated for the first time (62). NLP tools were similarly used to detect the presence of physical comorbidities in EHRs of patients over a 9-year period between 2011 and 2019 (62).

The strength of the eCDSS implemented in SLaM lies in its emphasis on patient safety. The digital tool's main function was to support clinicians in identifying AF patients at high risk of stroke so that they can be referred to OAC clinics. This approach would prevent missing out cases and guarantee that clinicians retain the decision to prescribe anticoagulants mitigating potential risks associated with inappropriate OAC prescription. Another strength lies in the clinical risk assessment plan that was thoroughly developed whereby all potential hazards were identified and attempts were made to reduce them to as low as reasonably practical.

Papers 4 and 5 shared similar strengths. First, they both incorporated quantitative and qualitative data collection and analysis methods providing a comprehensive understanding of the topic of interest and a holistic assessment of the intervention. While the quantitative methods provided numerical data, the qualitative one offered a deeper exploration of clinician perception and experience with the digital tool. Second, both studies were conducted in three wards in London enhancing the robustness, applicability, and impact of the research findings. Third, data collection continued until saturation was achieved to ensure that a wide range of perspectives and experiences was captured, and bias was minimised. Fourth, reflexivity was practiced throughout the research process to ensure objectivity and credibility of the studies. This was done by frequently questioning preconceptions and recording assumptions and personal biases. Finally, in paper 4 two researchers independently worked on data extraction and analysis which enhanced the rigor and transparency of the research process, validated results, increased reliability of findings, and reduced researcher bias.

9.3.2 Limitations

Despite the strength of the methodologies employed to synthesise evidence in each study, it is important to acknowledge several limitations.

In paper 1, studies investigating the prevalence, management, and outcomes of AF in people with SMI were limited, affecting generalisability of findings to broader populations or settings (60). Among studies included in the review, eleven were rated as of good quality, three as fair, and two as of poor-quality using Newcastle-Ottawa Scale. Low quality studies may have introduced bias influencing findings. Moreover, studies investigating OAC prescription rate in AF patients with co-morbid SMI mainly focused on warfarin, whereas research on DOAC use was limited, although DOACs are increasingly preferred in practice (103). Findings of these studies were not pooled because data presented were not directly comparable. The small number of studies (n=4) included in the meta-analysis may have resulted in limited statistical power to detect an effect for SMI on stroke and bleeding risks and could have made the study more susceptible to publication bias. Additionally, the variability in SMI definition, populations, study designs, and outcome measures among studies included in the meta-analysis resulted in increased heterogeneity.

In papers 2 and 3, data were extracted from EHRs using NLP tools. Despite the benefits associated with this approach, it has some limitations (61,62). NLP tools may struggle to extract information from poorly structured data fields and free-text notes mainly due to the lack of standardised terminologies, coding schemes and data formats as well as misinterpretation of abbreviations, acronyms, and clinical jargon resulting in errors in the data extracted. In paper 2, the study population was limited to patients admitted to the hospital which could have resulted in findings being of limited generalisability. Hospitalised patients may systematically differ from outpatients in terms of demographics, illness severity, and comorbidities. By only including hospitalised patients, those with mild or moderate conditions could have been underrepresented. Additionally, co-morbidities captured in this study were restricted to the CHA2DS2-VASc and HAS-BLED components. Other risk factors associated with increased risk of poor outcomes in AF patients with co-morbid mental illness may have been overlooked. In paper 3, data were extracted from mental health records where physical health conditions and associated treatments could be poorly recorded (62). The low prescription rate of OAC may not always reflect under-recording or undertreatment but could also be related to active clinical decision making not to treat with OAC involving other non-modifiable factors. Finally, associations presented in this study between mental illness severity and OAC prescription do not necessarily imply causality.

In papers 4 and 5, the sample size was small which could have introduced some bias as the perspectives and experiences of few healthcare providers might have disproportionately influenced the findings. However, it is important to note that the sample size in both studies was considered acceptable in relation to the targeted population and that data collection continued until saturation was achieved. Another limitation is that participants included in both studies were restricted to psychiatrists and pharmacists. Including other healthcare professionals with various degrees of clinical experiences could have broadened the findings. In paper 4, some healthcare professionals might have been reluctant to express their lack of knowledge and confidence in assessing physical health conditions which could have potentially resulted in reporting bias. In paper 5, few of the interviewed healthcare professionals had ever used the digital tool and instead, answered questions in the survey and interview based on their perspective rather than practical experience with the eCDSS. Noteworthy, the interview process started four months after the implementation of the digital tool. Extending the intervention period could have allowed for more AF admissions, thus increasing familiarity and experience of healthcare professionals with the eCDSS. Finally, due to time limitations, data extraction and analysis were not replicated by a second independent researcher in paper 5.

9.4 Conclusions

In this thesis, I presented findings of five studies aiming to investigate prevention of AF-related stroke in people with mental illness at multiple levels.

In paper 1, I conducted a systematic review to examine prevalence, management, and outcomes of AF in people with SMI versus the general population (60). I suggested that low reported rates of AF among people with SMI could be due to under-recognition or recording gaps (60). I also showed that people with AF and SMI were less likely to receive OAC therapy compared to the general population (60). When receiving warfarin, those with bipolar disorder experienced poor anticoagulation control as measured by time in INR therapeutic range (60). The meta-analysis showed that in AF patients, SMI was not significantly associated with an increased risk of stroke or major bleeding when adjusted for underlying stroke and bleeding risks using the CHA2DS2VASc and HASBLED scales respectively (60).

In papers 2 and 3, I investigated OAC prescription rates among people with AF and SMI in primary and tertiary mental healthcare services (61,62). In both studies, I proposed that among people with AF, those with co-morbid SMI are less likely to be prescribed OAC therapy to reduce their risk of stroke (61,62). In paper 2, I showed an increasing trend of DOAC use and decreasing trend of warfarin use between 2011 and 2020 in all AF patients regardless of their mental health status (61). In paper 3, I demonstrated that a total of 62% of SMI patients at risk of AF- related stroke were not prescribed an OAC (62). Among this population, warfarin was less likely to be prescribed to people with self-injury, hallucinations or delusions, ADL impairment, or alcohol or substance dependence (62).

To improve screening for stroke related to AF in people with mental illness, I developed an eCDSS that consisted of a visual prompt on patient ePHR (84). The tool was implemented in three MHOA wards in SLAM. Healthcare professionals were prompted to confirm the presence of AF, complete clinical assessment of stroke and bleeding risks using the CHA_2DS_2VASc and ORBIT scales, and record scores on ePJS. If patients were found to be at high risk of stroke, clinicians were prompted to refer them to oral anticoagulation clinics.

Pre-implementation of the digital alerting system, I explored mental health clinician experience in screening for stroke risk among patients with AF and their perception of the potential impact of an eCDSS in improving care quality. I established that challenges encountered by mental health professionals included difficulty identifying relevant medical history of patients, clinician perceived lack of expertise, fragmented medical care, and patients' mental health symptoms. Suggestions to improve clinical practice included clinicians receiving alerts containing latest guidelines and policies on stroke management, and bespoke training sessions designed to advance the knowledge, competencies, and confidence of clinicians. Healthcare professionals perceived eCDSSs as potentially beneficial in enhancing clinical effectiveness, saving time, and improving health outcomes. Reported perceived risks were rigidity in decision making, annoyance, and increased workload.

After implementation of the eCDSS, I investigated healthcare professionals' perception and experience with the digital tool. The tool was perceived as simple, comprehensive, and well designed. Clinicians discussed its impact on saving time, prompting them towards guidelines, boosting their confidence, and identifying patients at risk. Barriers to using the tool included low admission rate of patients with AF, insufficient awareness of the tool, low alert visibility, and

impact of the eCDSS on workload. Clinicians suggested reinforcing awareness of the tool through training and reminders as well as changing the digital location and making it unavoidable.

Overall, in this body of work I demonstrated that there is a disparity in OAC prescription among people with AF and co-morbid SMI compared to non-SMI. Implementing a digital alerting system to improve stroke risk screening among people with AF admitted to a mental healthcare service is feasible and acceptable by clinicians. To ensure effectiveness of the tool, ongoing evaluation should be done by continuously monitoring performance, gathering feedback, and adjusting the system accordingly.

REFERENCES

1- Ruggeri M, Leese M, Thornicroft G, Bisoffi G, Tansella M. Definition and prevalence of severe and persistent mental illness. The British Journal of Psychiatry. 2000 Aug;177(2):149-55.

2- Velthorst E, Fett AK, Reichenberg A, Perlman G, van Os J, Bromet EJ, Kotov R. The 20-year longitudinal trajectories of social functioning in individuals with psychotic disorders. American Journal of Psychiatry. 2017 Nov 1;174(11):1075-85.

3- World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. World Health Organization; 1992.

4- Grande I, Berk M, Birmaher B, Vieta E. Bipolar disorder. The Lancet. 2016 Apr 9;387(10027):1561-72.

5- Benazzi F. Bipolar II disorder: epidemiology, diagnosis and management. CNS drugs. 2007 Sep;21(9):727-40.

6- American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders (5th Edition), American Journal of Psychiatry. https://doi.org/10.1176/appi.books.9780890425596.744053

7- Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, Rush AJ, Walters EE, Wang PS. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). Jama. 2003 Jun 18;289(23):3095-105.

8- Otte C, Gold SM, Penninx BW, Pariante CM, Etkin A, Fava M, Mohr DC, Schatzberg AF. Major depressive disorder. Nature reviews Disease primers. 2016 Sep 15;2(1):1-20.

9- U.S. Department of Health and Human Services. What is dementia? Symptoms, types, and diagnosis [Internet]. Bethesda (MD): National Institute on Aging; [cited 2024 May 1]. Available from: https://www.nia.nih.gov/health/what-is-dementia

10- Wing JK, Curtis RH, Beevor AS. Health of the Nation Outcome Scales (HoNOS): glossary for HoNOS score sheet. The British Journal of Psychiatry. 1999 May;174(5):432-4.

11- Lovaglio PG, Monzani E. Validation aspects of the health of the nation outcome scales. International Journal of Mental Health Systems. 2011 Dec;5:1-1.

12- Chang CK, Hayes RD, Perera G, Broadbent MT, Fernandes AC, Lee WE, Hotopf M, Stewart R. Life expectancy at birth for people with serious mental illness and other major disorders from a secondary mental health care case register in London. PloS one. 2011 May 18;6(5):e19590.

13- Lawrence D, Hancock KJ, Kisely S. The gap in life expectancy from preventable physical illness in psychiatric patients in Western Australia: retrospective analysis of population based registers. Bmj. 2013 May 21;346.

14- Brodaty H, Seeher K, Gibson L. Dementia time to death: a systematic literature review on survival time and years of life lost in people with dementia. International psychogeriatrics. 2012 Jul;24(7):1034-45.

15- Popovic D, Benabarre A, Crespo JM, Goikolea JM, González-Pinto A, Gutiérrez-Rojas L, Montes JM, Vieta E. Risk factors for suicide in schizophrenia: systematic review and clinical recommendations. Acta Psychiatrica Scandinavica. 2014 Dec;130(6):418-26.

16- Hoang U, Goldacre MJ, Stewart R. Avoidable mortality in people with schizophrenia or bipolar disorder in E ngland. Acta Psychiatrica Scandinavica. 2013 Mar;127(3):195-201.

17- Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. JAMA psychiatry. 2015 Apr 1;72(4):334-41.

18- Correll CU, Solmi M, Veronese N, Bortolato B, Rosson S, Santonastaso P, Thapa-Chhetri N, Fornaro M, Gallicchio D, Collantoni E, Pigato G. Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: a large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls. World Psychiatry. 2017 Jun;16(2):163-80.

19- Wolters FJ, Segufa RA, Darweesh SK, Bos D, Ikram MA, Sabayan B, Hofman A, Sedaghat S. Coronary heart disease, heart failure, and the risk of dementia: a systematic review and meta-analysis. Alzheimer's & Dementia. 2018 Nov 1;14(11):1493-504.

20- Deckers K, Schievink SH, Rodriquez MM, van Oostenbrugge RJ, van Boxtel MP, Verhey FR, Köhler S. Coronary heart disease and risk for cognitive impairment or dementia: Systematic review and meta-analysis. PloS one. 2017 Sep 8;12(9):e0184244.

21- Brain J, Greene L, Tang EY, Louise J, Salter A, Beach S, Turnbull D, Siervo M, Stephan B, Tully PJ. Cardiovascular disease, associated risk factors, and risk of dementia: An umbrella review of meta-analyses. Frontiers in Epidemiology. 2023 Feb 9;3:1095236.

22- Zhang F, Xian D, Feng J, Ning L, Jiang T, Xu W, Liu Y, Zhao Q, Peng M. Causal relationship between Alzheimer's disease and cardiovascular disease: a bidirectional Mendelian randomization analysis. Aging (Albany NY). 2023 Sep 9;15(17):9022.

23- Ringen PA, Faerden A, Antonsen B, Falk RS, Mamen A, Rognli EB, Solberg DK, Andreassen OA, Martinsen EW. Cardiometabolic risk factors, physical activity and psychiatric status in patients in long-term psychiatric inpatient departments. Nordic journal of psychiatry. 2018 May 19;72(4):296-302.

24- Vancampfort D, Firth J, Schuch FB, Rosenbaum S, Mugisha J, Hallgren M, Probst M, Ward PB, Gaughran F, De Hert M, Carvalho AF. Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: a global systematic review and meta-analysis. World Psychiatry. 2017 Oct;16(3):308-15.

25- Firth J, Solmi M, Wootton RE, Vancampfort D, Schuch FB, Hoare E, Gilbody S, Torous J, Teasdale SB, Jackson SE, Smith L. A meta-review of "lifestyle psychiatry": the role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders. World psychiatry. 2020 Oct;19(3):360-80.

26- Hartman YA, Karssemeijer EG, van Diepen LA, Olde Rikkert MG, Thijssen DH. Dementia patients are more sedentary and less physically active than age-and sex-matched cognitively healthy older adults. Dementia and geriatric cognitive disorders. 2018 Aug 24;46(1-2):81-9.

27- Osborn DP, Wright CA, Levy G, King MB, Deo R, Nazareth I. Relative risk of diabetes, dyslipidaemia, hypertension and the metabolic syndrome in people with severe mental illnesses: systematic review and metaanalysis. BMC psychiatry. 2008 Dec;8(1):1-4.

28- Yen FS, Wei JC, Yip HT, Hwu CM, Hsu CC. Diabetes, hypertension, and the risk of dementia. Journal of Alzheimer's Disease. 2022 Aug 30(Preprint):1-1.

29- Goldfarb M, De Hert M, Detraux J, Di Palo K, Munir H, Music S, Piña I, Ringen PA. Severe mental illness and cardiovascular disease: JACC state-of-the-art review. Journal of the American College of Cardiology. 2022 Aug 30;80(9):918-33.

30- De Hert M, Detraux J, Van Winkel R, Yu W, Correll CU. Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. Nature Reviews Endocrinology. 2012 Feb;8(2):114-26.

31- Lawrence D, Kisely S. Inequalities in healthcare provision for people with severe mental illness. Journal of psychopharmacology. 2010 Nov;24(4_suppl):61-8.

32- Guo J, Lv X, Liu Y, Kong L, Qu H, Yue W. Influencing factors of medication adherence in schizophrenic patients: a meta-analysis. Schizophrenia. 2023 May 15;9(1):31.

33- Kilbourne AM, Rofey DL, McCarthy JF, Post EP, Welsh D, Blow FC. Nutrition and exercise behavior among patients with bipolar disorder 1. Bipolar disorders. 2007 Aug;9(5):443-52.

34- Pérez-Piñar M, Mathur R, Foguet Q, Ayis S, Robson J, Ayerbe LJ. Cardiovascular risk factors among patients with schizophrenia, bipolar, depressive, anxiety, and personality disorders. European Psychiatry. 2016 May;35:8-15.

35- Centers for Disease Control and Prevention. Atrial fibrillation [Internet]. Available from: https://www.cdc.gov/heartdisease/atrial_fibrillation.htm [cited 2024 May 1].

36- NHS. Atrial fibrillation [Internet]. Available from: https://www.nhs.uk/conditions/atrial-fibrillation/ [cited 2024 May 1].

37- Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Kardiologia Polska (Polish Heart Journal). 2016;74(12):1359-469.

38- Potpara TS, Lip GY. Oral anticoagulant therapy in atrial fibrillation patients at high stroke and bleeding risk. Progress in cardiovascular diseases. 2015 Sep 1;58(2):177-94.

39- Shikdar S, Vashisht R, Bhattacharya PT. International normalized ratio (INR) [Internet]. Available from: https://pubmed.ncbi.nlm.nih.gov/29939529/ [cited 2024 May 1]

40- Ruddox V, Sandven I, Munkhaugen J, Skattebu J, Edvardsen T, Otterstad JE. Atrial fibrillation and the risk for myocardial infarction, all-cause mortality and heart failure: a systematic review and meta-analysis. European journal of preventive cardiology. 2017 Sep 1;24(14):1555-66.

41- Violi F, Soliman EZ, Pignatelli P, Pastori D. Atrial fibrillation and myocardial infarction: a systematic review and appraisal of pathophysiologic mechanisms. Journal of the American Heart Association. 2016 May 20;5(5):e003347.

42- Grajek S, Kałużna-Oleksy M, Siller-Matula JM, Grajek M, Michalak M. Non-vitamin K antagonist oral anticoagulants and risk of myocardial infarction in patients with atrial fibrillation with or without percutaneous coronary interventions: a meta-analysis. Journal of Personalized Medicine. 2021 Oct 9;11(10):1013.

43- Patel S, Singh R, Preuss CV, Patel N. Warfarin [Internet]. 2017 [cited 2024 Sep 5]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470313/

44- British Heart Foundation. Direct oral anticoagulants (DOACs) [Internet]. Available from: https://www.bhf.org.uk/informationsupport/heart-matters-magazine/medical/drug-cabinet/doac [cited 2024 May 1].

45- Clinical Excellence Commission. Direct Oral Anticoagulant (DOAC) Guidelines [Internet]. 2023 [cited 2024 Sep 5]. Available from: https://www.cec.health.nsw.gov.au/keep-patients-safe/medication-safety/high-risk-medicines/anticoagulants

46- Julia S, James U. Direct oral anticoagulants: a quick guide. European Cardiology Review. 2017 Aug;12(1):40.

47- Perry M, Betty SK, Downes N, Andrews N, Mackenzie S. Atrial fibrillation: diagnosis and management—summary of NICE guidance. bmj. 2021 May 21;373.

48- MDcalc. CHA_2DS_2-VASc score for atrial fibrillation stroke risk [Internet]. Available from: https://www.mdcalc.com/calc/801/cha2ds2-vasc-score-atrial-fibrillation-stroke-risk [cited 2024 May 1].

49- MDcalc. HAS-BLED score for major bleeding risk [Internet]. Available from: https://www.mdcalc.com/calc/807/has-bled-score-major-bleeding-risk [cited 2024 May 1].

50- MDcalc. ORBIT bleeding risk score for atrial fibrillation [Internet]. Available from: https://www.mdcalc.com/calc/10227/orbit-bleeding-risk-score-atrial-fibrillation [cited 2024 May 1].

51- García S, Martinez-Cengotitabengoa M, Lopez-Zurbano S, Zorrilla I, Lopez P, Vieta E, Gonzalez-Pinto A. Adherence to antipsychotic medication in bipolar disorder and

schizophrenic patients: a systematic review. Journal of clinical psychopharmacology. 2016 Aug;36(4):355.

52- Semahegn A, Torpey K, Manu A, Assefa N, Tesfaye G, Ankomah A. Psychotropic medication non-adherence and its associated factors among patients with major psychiatric disorders: a systematic review and meta-analysis. Systematic reviews. 2020 Dec;9(1):1-8.

53- Patierno C, Fava GA, Carrozzino D. Illness Denial in Medical Disorders: A Systematic Review. Psychotherapy and Psychosomatics. 2023 Jul 10:1-6.

54- Gray M, Gills JL, Glenn JM, Vincenzo JL, Walter CS, Madero EN, Hall A, Fuseya N, Bott NT. Cognitive decline negatively impacts physical function. Experimental gerontology. 2021 Jan 1;143:111164.

55- McMaughan DJ, Oloruntoba O, Smith ML. Socioeconomic status and access to healthcare: interrelated drivers for healthy aging. Frontiers in public health. 2020 Jun 18;8:231.

56- Coombs NC, Meriwether WE, Caringi J, Newcomer SR. Barriers to healthcare access among US adults with mental health challenges: A population-based study. SSM-population health. 2021 Sep 1;15:100847.

57- Joo JY. Fragmented care and chronic illness patient outcomes: A systematic review. Nursing Open. 2023 Jan 9.

58- Knaak S, Mantler E, Szeto A. Mental illness-related stigma in healthcare: Barriers to access and care and evidence-based solutions. InHealthcare management forum 2017 Mar (Vol. 30, No. 2, pp. 111-116). Sage CA: Los Angeles, CA: SAGE Publications.

59- Hallyburton A. Diagnostic overshadowing: An evolutionary concept analysis on the misattribution of physical symptoms to pre-existing psychological illnesses. International Journal of Mental Health Nursing. 2022 Dec;31(6):1360-72.

60- Farran D, Feely O, Ashworth M, Gaughran F. Anticoagulation therapy and outcomes in patients with atrial fibrillation and serious mental illness: A systematic review and meta-analysis. Journal of Psychiatric Research. 2022 Nov 16.

61- Farran D, Bean D, Wang T, Msosa Y, Casetta C, Dobson R, Teo JT, Scott P, Gaughran F. Anticoagulation for atrial fibrillation in people with serious mental illness in the general hospital setting. Journal of Psychiatric Research. 2022 Sep 1;153:167-73.

62- Farran D, Broadbent M, Dima A, Ashworth M, Gaughran F. Factors Associated With Oral Anticoagulant Use in Patients With Atrial Fibrillation and Mental Disorders. The Journal of clinical psychiatry. 2024 Jan 3;85(1):50936.

63- Kawamoto K, Houlihan CA, Balas EA, Lobach DF. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. Bmj. 2005 Mar 31;330(7494):765.

64- Berner ES. Clinical decision support systems. New York: Springer Science+ Business Media, LLC; 2007.

65- Sutton RT, Pincock D, Baumgart DC, Sadowski DC, Fedorak RN, Kroeker KI. An overview of clinical decision support systems: benefits, risks, and strategies for success. NPJ digital medicine. 2020 Feb 6;3(1):17.

66- Moja L, Kwag KH, Lytras T, Bertizzolo L, Brandt L, Pecoraro V, Rigon G, Vaona A, Ruggiero F, Mangia M, Iorio A. Effectiveness of computerized decision support systems linked to electronic health records: a systematic review and meta-analysis. American journal of public health. 2014 Dec;104(12):e12-22.

67- Muhiyaddin R, Abd-Alrazaq AA, Househ M, Alam T, Shah Z. The impact of clinical decision support systems (CDSS) on physicians: a scoping review. The Importance of Health Informatics in Public Health during a Pandemic. 2020:470-3.

68- Bright TJ, Wong A, Dhurjati R, Bristow E, Bastian L, Coeytaux RR, Samsa G, Hasselblad V, Williams JW, Musty MD, Wing L. Effect of clinical decision-support systems: a systematic review. Annals of internal medicine. 2012 Jul 3;157(1):29-43.

69- Njie GJ, Proia KK, Thota AB, Finnie RK, Hopkins DP, Banks SM, Callahan DB, Pronk NP, Rask KJ, Lackland DT, Kottke TE. Clinical decision support systems and prevention: a community guide cardiovascular disease systematic review. American journal of preventive medicine. 2015 Nov 1;49(5):784-95.

70- Wess ML, Schauer DP, Johnston JA, Moomaw CJ, Brewer DE, Cook EF, Eckman MH. Application of a decision support tool for anticoagulation in patients with non-valvular atrial fibrillation. Journal of general internal medicine. 2008 Apr;23:411-7.

71- Cook DA, Enders F, Caraballo PJ, Nishimura RA, Lloyd FJ. An automated clinical alert system for newly-diagnosed atrial fibrillation. PLoS One. 2015 Apr 7;10(4):e0122153.

72- Robson J, Dostal I, Mathur R, Sohanpal R, Hull S, Antoniou S, MacCallum P, Schilling R, Ayerbe L, Boomla K. Improving anticoagulation in atrial fibrillation: observational study in three primary care trusts. British Journal of General Practice. 2014 May 1;64(622):e275-81.

73- Arts DL, Abu-Hanna A, Medlock SK, van Weert HC. Effectiveness and usage of a decision support system to improve stroke prevention in general practice: a cluster randomized controlled trial. PloS one. 2017 Feb 28;12(2):e0170974.

74- Karlsson LO, Nilsson S, Bång M, Nilsson L, Charitakis E, Janzon M. A clinical decision support tool for improving adherence to guidelines on anticoagulant therapy in patients with atrial fibrillation at risk of stroke: a cluster-randomized trial in a Swedish primary care setting (the CDS-AF study). PLoS medicine. 2018 Mar 13;15(3):e1002528.

75- Thomson RG, Eccles MP, Steen IN, Greenaway J, Stobbart L, Murtagh MJ, May CR. A patient decision aid to support shared decision-making on anti-thrombotic treatment of patients with atrial fibrillation: randomised controlled trial. BMJ Quality & Safety. 2007 Jun 1;16(3):216-23.

76- Fraenkel L, Street Jr RL, Towle V, O'Leary JR, Iannone L, Van Ness PH, Fried TR. A pilot randomized controlled trial of a decision support tool to improve the quality of communication and decision-making in individuals with atrial fibrillation. Journal of the American Geriatrics Society. 2012 Aug;60(8):1434-41.

77- Guo Y, Chen Y, Lane DA, Liu L, Wang Y, Lip GY. Mobile health technology for atrial fibrillation management integrating decision support, education, and patient involvement: mAF app trial. The American journal of medicine. 2017 Dec 1;130(12):1388-96.

78- Sheibani R, Sheibani M, Heidari-Bakavoli A, Abu-Hanna A, Eslami S. The effect of a clinical decision support system on improving adherence to guideline in the treatment of atrial fibrillation: an interrupted time series study. Journal of medical systems. 2018 Feb;42:1-7.

79- Simmons BJ, Jenner KM, Delate T, Clark NP, Kurz D, Witt DM. Pilot Study of a Novel Patient Self-Management Program for Warfarin Therapy Using Venipuncture-Acquired International Normalized Ratio Monitoring. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2012 Dec;32(12):1078-84.

80- Vinding NE, Kristensen SL, Rørth R, Butt JH, Østergaard L, Olesen JB, Torp-Pedersen C, Gislason GH, Køber L, Kruuse C, Johnsen SP. Ischemic stroke severity and mortality in patients with and without atrial fibrillation. Journal of the American Heart Association. 2022 Feb 15;11(4):e022638.

81- Bártlová S, Šedová L, Havierniková L, Hudáčková A, Dolák F, Sadílek P. Quality of life of post-stroke patients. Slovenian Journal of Public Health. 2022 Mar 21;61(2):101-8.

82- Jackson R, Kartoglu I, Stringer C, Gorrell G, Roberts A, Song X, Wu H, Agrawal A, Lui K, Groza T, Lewsley D. CogStack-experiences of deploying integrated information retrieval and extraction services in a large National Health Service Foundation Trust hospital. BMC medical informatics and decision making. 2018 Dec;18(1):1-3.

83- Kraljevic Z, Searle T, Shek A, Roguski L, Noor K, Bean D, Mascio A, Zhu L, Folarin AA, Roberts A, Bendayan R. Multi-domain clinical natural language processing with medcat: the medical concept annotation toolkit. Artificial intelligence in medicine. 2021 Jul 1;117:102083.

84- Electronic Clinical Decision Support System (eCDSS) for Prevention of Atrial Fibrillation-related Stroke (eCDSS). ClinicalTrials.gov. Available from: https://clinicaltrials.gov/study/NCT06014268?cond=electronic+clinical+decision+support+system+for+atrial+fibrillation&rank=1

85- Aronson JK, Heneghan C, Ferner RE. Medical devices: definition, classification, and regulatory implications. Drug safety. 2020 Feb;43(2):83-93.

86- Card AJ, Ward JR, Clarkson PJ. Beyond FMEA: The structured what-if technique (SWIFT). Journal of Healthcare Risk Management. 2012;31(4):23-9.

87- NHS Digital. DCB0160: Clinical risk management: its application in the deployment and use of health IT systems [Internet]. Available from: https://digital.nhs.uk/data-and-information/information-standards/information-standards-and-data-collections-including-extractions/publications-and-notifications/standards-and-collections/dcb0160-clinical-risk-management-its-application-in-the-deployment-and-use-of-health-it-systems [cited 2024 May 1].

88- Smith DJ, Martin D, McLean G, Langan J, Guthrie B, Mercer SW. Multimorbidity in bipolar disorder and undertreatment of cardiovascular disease: a cross sectional study. BMC medicine. 2013 Dec;11:1-1.

89- Smith DJ, Langan J, McLean G, Guthrie B, Mercer SW. Schizophrenia is associated with excess multiple physical-health comorbidities but low levels of recorded cardiovascular disease in primary care: cross-sectional study. BMJ open. 2013 Jan 1;3(4):e002808.

90- Yang HY, Huang JH, Lin YK, Hsu CY, Chen SA, Chen YJ. Bipolar disorder and schizophrenia present different risks of atrial fibrillation: a nationwide population-based analysis. Acta Cardiologica Sinica. 2014 Jan;30(1):46.

91- De Hert M, Cohen DA, Bobes J, Cetkovich-Bakmas M, Leucht S, Ndetei DM, Newcomer JW, Uwakwe R, Asai I, Moeller HJ, Gautam S. Physical illness in patients with severe mental disorders. II. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level. World psychiatry. 2011 Jun;10(2):138.

92- Nash M. Diagnostic overshadowing: a potential barrier to physical health care for mental health service users. Mental Health Practice. 2013 Dec 1;17(4).

93- Fenger-Grøn M, Vestergaard CH, Ribe AR, Johnsen SP, Frost L, Sandbæk A, Davydow DS. Association between bipolar disorder or schizophrenia and oral anticoagulation use in Danish adults with incident or prevalent atrial fibrillation. JAMA network open. 2021 May 3;4(5):e2110096-.

94- Højen AA, Nielsen PB, Riahi S, Jensen M, Lip GY, Larsen TB, Søgaard M. Disparities in oral anticoagulation initiation in patients with schizophrenia and atrial fibrillation: A nationwide cohort study. British journal of clinical pharmacology. 2022 Aug;88(8):3847-55.

95- Jaakkola J, Teppo K, Biancari F, Halminen O, Putaala J, Mustonen P, Haukka J, Linna M, Kinnunen J, Tiili P, Aro AL. The effect of mental health conditions on the use of oral anticoagulation therapy in patients with atrial fibrillation: the FinACAF study. European Heart Journal-Quality of Care and Clinical Outcomes. 2022 May;8(3):269-76.

96- Schmitt SK, Turakhia MP, Phibbs CS, Moos RH, Berlowitz D, Heidenreich P, Chiu VY, Go AS, Friedman SA, Than CT, Frayne SM. Anticoagulation in atrial fibrillation: impact of mental illness. Am J Manag Care. 2015 Nov 1;21(11):e609-17.

97- Polcwiartek C, O'Gallagher K, Friedman DJ, Correll CU, Solmi M, Jensen SE, Nielsen RE. Severe mental illness: cardiovascular risk assessment and management. European Heart Journal. 2024 Feb 21:ehae054.

98- Haley WE, Roth DL, Hovater M, Clay OJ. Long-term impact of stroke on family caregiver well-being: a population-based case-control study. Neurology. 2015 Mar 31;84(13):1323-9.

99- Strilciuc S, Grad DA, Radu C, Chira D, Stan A, Ungureanu M, Gheorghe A, Muresanu FD. The economic burden of stroke: a systematic review of cost of illness studies. Journal of medicine and life. 2021 Sep;14(5):606.

100- Lerbæk B, Jørgensen R, McCloughen A. "It's Not Important"—The Social Constructing of Poor Physical Health as 'Normal'among People with Schizophrenia: Integrated Findings from an Ethnographic Study. International Journal of Environmental Research and Public Health. 2023 Jun 15;20(12):6133.

101- Kumar A, Gond A. NATURAL LANGUAGE PROCESSING: HEALTHCARE ACHIEVING BENEFITS VIA NLP. ScienceOpen Preprints. 2023 Aug 2.

102- Hisan UK, Chaaben AB, Adeleye AO, Kaushik A. Impact of Natural Language Processing on Healthcare Quality: A Review of Clinical and Public Health Applications. Journal of Advanced Analytics in Healthcare Management. 2022 Jan 20;6(1):19-42.

103- Zeng S, Zheng Y, Jiang J, Ma J, Zhu W, Cai X. Effectiveness and safety of DOACs vs. warfarin in patients with atrial fibrillation and frailty: a systematic review and meta-analysis. Frontiers in Cardiovascular Medicine. 2022 Jun 24;9:907197.

APPENDICES

Appendix A

Search Strategy

1. MEDLINE (PubMed) Search String:

#1 "atrial fibrillation"[MeSH Terms] OR "atrial fibrillation"[All Fields]
#2 ("serious mental illness"[All Fields] OR "severe mental illness"[All Fields] OR "schizophrenia"[MeSH Terms] OR "schizophrenia"[All Fields] OR "bipolar affective disorder"[MeSH Terms] OR "bipolar affective disorder"[All Fields] OR "schizoaffective disorder"[MeSH Terms] OR "schizoaffective disorder"[All Fields] OR "non-organic psychosis"[All Fields])
#3 ("oral anticoagulants"[All Fields] OR "non-vitamin K antagonist oral anticoagulants"[All Fields] OR "Direct Oral Anticoagulant"[All Fields] OR "DOAC"[All Fields] OR "Novel Oral Anticoagulant"[All Fields] OR "NOAC"[All Fields] OR "dabigatran"[All Fields] OR "rivaroxaban"[All Fields] OR "apixaban"[All Fields] OR "edoxaban"[All Fields] OR "vitamin K antagonist"[All Fields] OR "warfarin"[MeSH Terms] OR "warfarin"[All Fields])
#4 ("Therapeutic range"[All Fields] OR "International Normalized Ratio"[All Fields] OR "International Normalised Ratio"[All Fields] OR "INR"[All Fields] OR "prothrombin time"[MeSH Terms] OR "prothrombin time"[All Fields])
#5 ("cerebrovascular accident"[MeSH Terms] OR "cerebrovascular accident"[All Fields] OR "cerebral thrombosis"[All Fields] OR "haemorrhage"[All Fields] OR "hemorrhage"[All Fields] OR "cerebral infarct"[All Fields] OR "cerebral infarction"[All Fields] OR "bleeding"[All Fields] OR "stroke"[MeSH Terms] OR "stroke"[All Fields] OR "mortality"[MeSH Terms] OR "mortality"[All Fields] OR "death"[All Fields])
#6 #1 AND #2
#7 #6 AND #3 OR #4 OR #5
#8 Filters: English[lang] AND ("2004/01/01"[PDat] : "2022/12/31"[PDat])

2. EMBASE Search String:

#1 'exp atrial fibrillation/ OR atrial fibrillation.mp.'
#2 ('serious mental illness' OR 'severe mental illness' OR 'schizophrenia'/exp OR schizophrenia.mp. OR 'bipolar affective disorder'/exp OR 'bipolar affective disorder'.mp. OR 'schizoaffective disorder'/exp OR 'schizoaffective disorder'.mp. OR 'non-organic psychosis').mp.

#3 ('oral anticoagulants' OR 'non-vitamin K antagonist oral anticoagulants' OR 'Direct Oral Anticoagulant' OR 'DOAC' OR 'Novel Oral Anticoagulant' OR 'NOAC' OR 'dabigatran' OR 'rivaroxaban' OR 'apixaban' OR 'edoxaban' OR 'vitamin K antagonist' OR 'warfarin'/exp OR warfarin.mp.).mp.
#4 ('Therapeutic range' OR 'International Normalized Ratio' OR 'International Normalised Ratio' OR 'INR' OR 'prothrombin time'/exp OR 'prothrombin time'.mp.).mp.
#5 ('cerebrovascular accident'/exp OR 'cerebrovascular accident'.mp. OR 'cerebral thrombosis' OR 'haemorrhage' OR 'hemorrhage' OR 'cerebral infarct' OR 'cerebral infarction' OR 'bleeding' OR 'stroke'/exp OR 'stroke'.mp. OR 'mortality'/exp OR 'mortality'.mp. OR 'death').mp.
#6 #1 AND #2
#7 #6 AND #3 OR #4 OR #5
#8 Filters: limit to (English language and yr="2004 - 2022")

3. PsycINFO Search String:

#1 'atrial fibrillation'.mp.
#2 ('serious mental illness' OR 'severe mental illness' OR 'schizophrenia' OR 'bipolar affective disorder' OR 'schizoaffective disorder' OR 'non-organic psychosis').mp.
#3 ('oral anticoagulants' OR 'non-vitamin K antagonist oral anticoagulants' OR 'Direct Oral Anticoagulant' OR 'DOAC' OR 'Novel Oral Anticoagulant' OR 'NOAC' OR 'dabigatran' OR 'rivaroxaban' OR 'apixaban' OR 'edoxaban' OR 'vitamin K antagonist' OR 'warfarin').mp.
#4 ('Therapeutic range' OR 'International Normalized Ratio' OR 'International Normalised Ratio' OR 'INR' OR 'prothrombin time').mp.
#5 ('cerebrovascular accident' OR 'cerebral thrombosis' OR 'haemorrhage' OR 'hemorrhage' OR 'cerebral infarct' OR 'cerebral infarction' OR 'bleeding' OR 'stroke' OR 'mortality' OR 'death').mp.
#6 #1 AND #2
#7 #6 AND #3 OR #4 OR #5
#8 Filters: English language, Publication Year from 2004 to 2022

Eligibility Criteria for Retrieved Articles

Inclusion Criteria:

1. **Must Include Both Conditions**: The article must explicitly include both atrial fibrillation (AF) and serious mental illness (SMI) in the study population.

2. **Additional Considerations**:
    - **Oral Anticoagulants (OACs)**: Articles that include information on the use of oral anticoagulants (e.g., DOACs, warfarin) for managing AF in individuals with SMI.
    - **Anticoagulation Control**: Articles discussing aspects of anticoagulation control such as therapeutic range, INR, or prothrombin time.
    - **Outcomes**: Articles reporting on outcomes related to stroke, bleeding, or mortality.

Exclusion Criteria:

1. **Lacking Both Conditions**: Articles that do not explicitly include both AF and SMI.
2. **Irrelevant Conditions**: Articles that focus solely on arrhythmias or cardiovascular diseases in general without specifically addressing AF.
3. **Not Relevant to OAC or Outcomes**: Articles that do not discuss oral anticoagulants, anticoagulation control, or relevant outcomes.
4. **Non-Research Publications**: Reviews, commentaries, case reports, and conference abstracts.

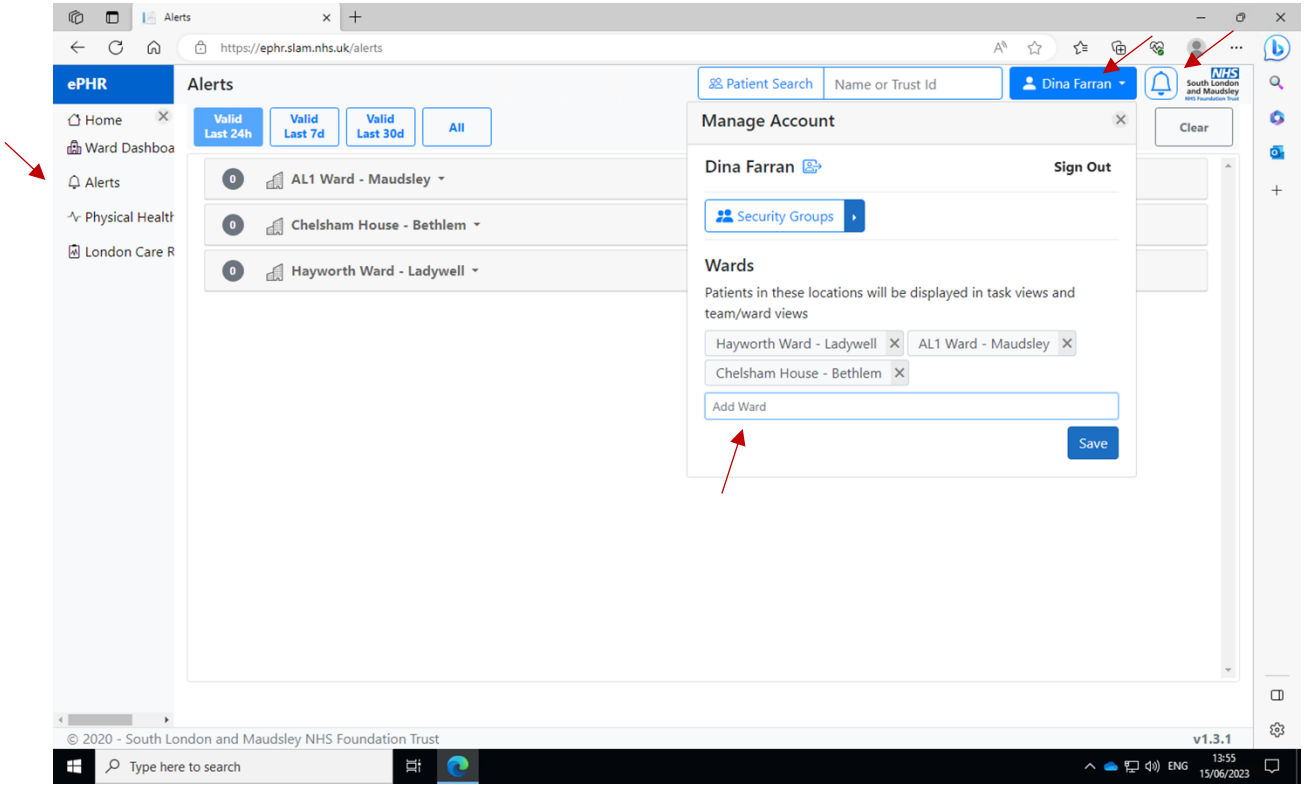
Additional Information:

- **Screening for Additional Articles**: Additional articles were identified by screening the reference lists of the retrieved studies.
- **Publication Date Restriction**: The search was restricted to articles written in English and published between 2004 and 2022. This is because, after 2004, aspirin was no longer considered an effective treatment for AF-related stroke (Van Walraven et al., 2002).

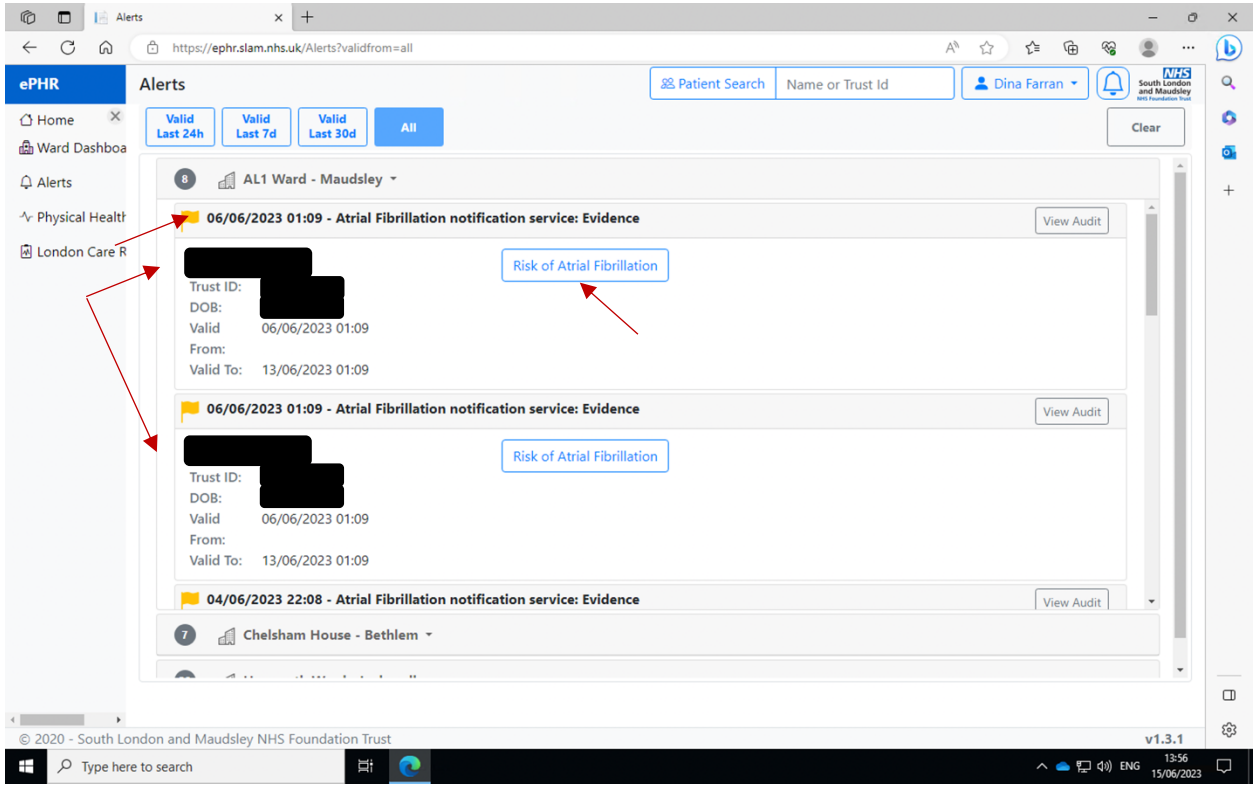
Appendix B

Guidance on where to find the AF alerts in ePHR

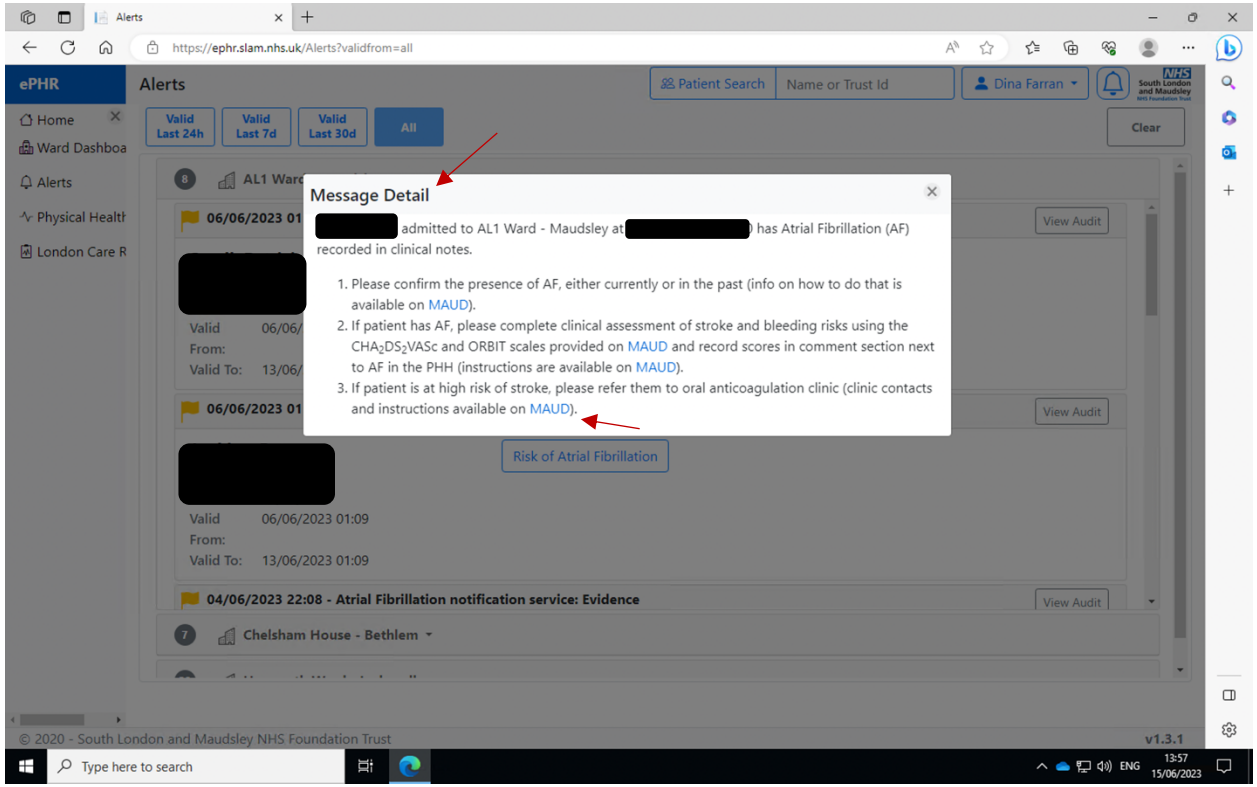
- Login to SLaM electronic patient health record portal.
- Go to Alerts.
- At the top right corner, click on your name to manage your account.
- Add the wards for which you would like to receive notifications.
- Notifications will appear on the bell sign at the top right corner.

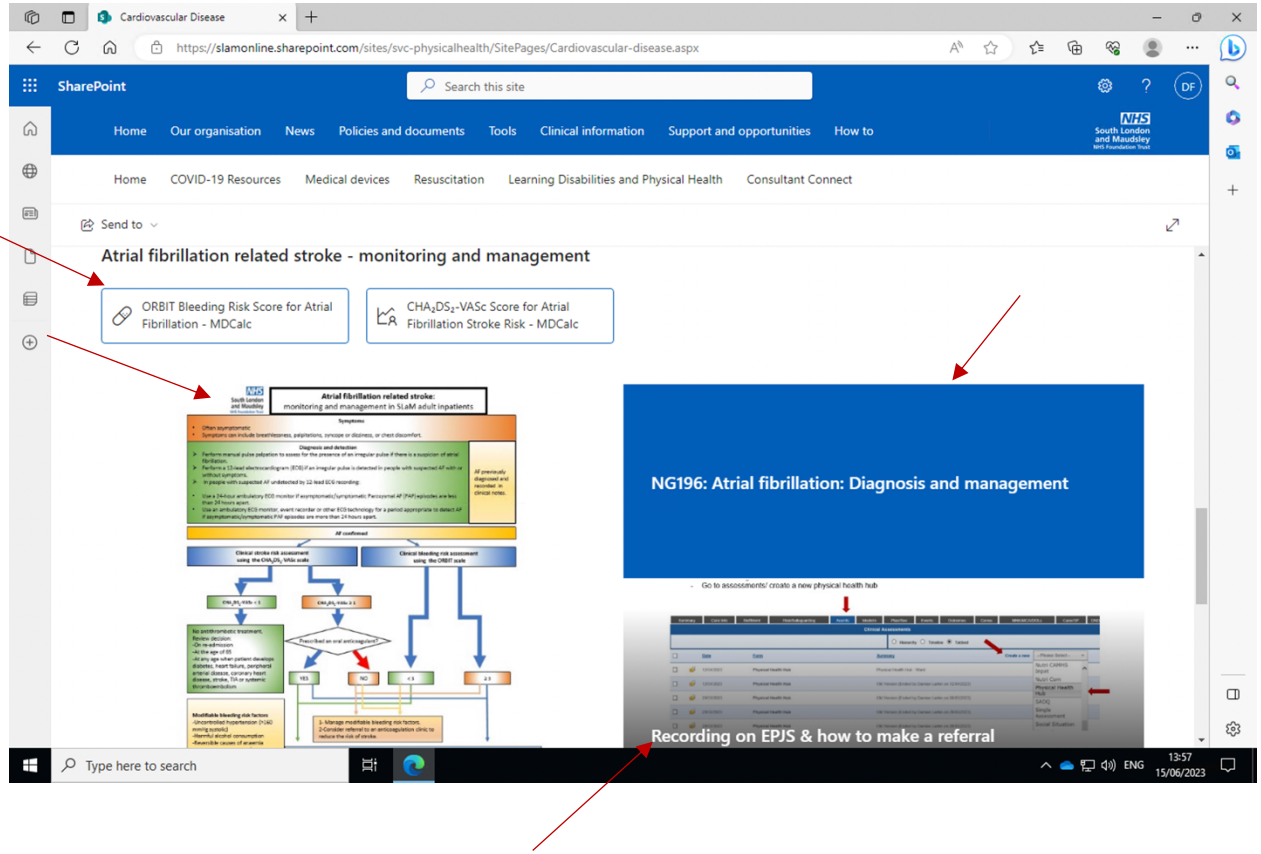


- By clicking on the ward, you will have the option to view all the alerts, the ones generated the past 30 days, past 7 days or past 24h. For example, the screenshot below shows a total of 8 alerts in AL1.
- A list of patients (name, trust ID, date of birth) with AF admitted to the ward will appear.
- Click on the risk of atrial fibrillation.



- A message will appear (please see screenshot below).
- Click on the hyperlink “MAUD” to be redirected to the MAUD (intranet) page where you can find instructions on how to monitor and manage AF-related stroke in SLAM adult inpatients, links to the CHAD2DS2VASc and ORBIT calculators, NICE guidelines on the diagnosis and management of AF related stroke and step by step guidance on how to record the stroke and bleeding risks in ePJS and how to make a referral to an oral anticoagulation clinic.


Alerts
https://ephr.slam.nhs.uk/Alerts?validfrom=all
ePHR
Alerts
Patient Search
Name or Trust Id
Dina Farran
Home
Ward Dashboa
Alerts
Physical Health
London Care R
Valid Last 24h
Valid Last 7d
Valid Last 30d
All
Clear
Message Detail
[redacted] admitted to AL1 Ward - Maudsley at [redacted] has Atrial Fibrillation (AF) recorded in clinical notes.
1. Please confirm the presence of AF, either currently or in the past (info on how to do that is available on MAUD).
2. If patient has AF, please complete clinical assessment of stroke and bleeding risks using the CHA_2DS_2VASc and ORBIT scales provided on MAUD and record scores in comment section next to AF in the PHH (instructions are available on MAUD).
3. If patient is at high risk of stroke, please refer them to oral anticoagulation clinic (clinic contacts and instructions available on MAUD).
06/06/2023 01
View Audit
Valid From:
Valid To:
Risk of Atrial Fibrillation
Valid From: 06/06/2023 01:09
Valid To: 13/06/2023 01:09
04/06/2023 22:08 - Atrial Fibrillation notification service: Evidence
Chelsham House - Bethlem
© 2020 - South London and Maudsley NHS Foundation Trust
v1.3.1
Type here to search
ENG
13:57
15/06/2023

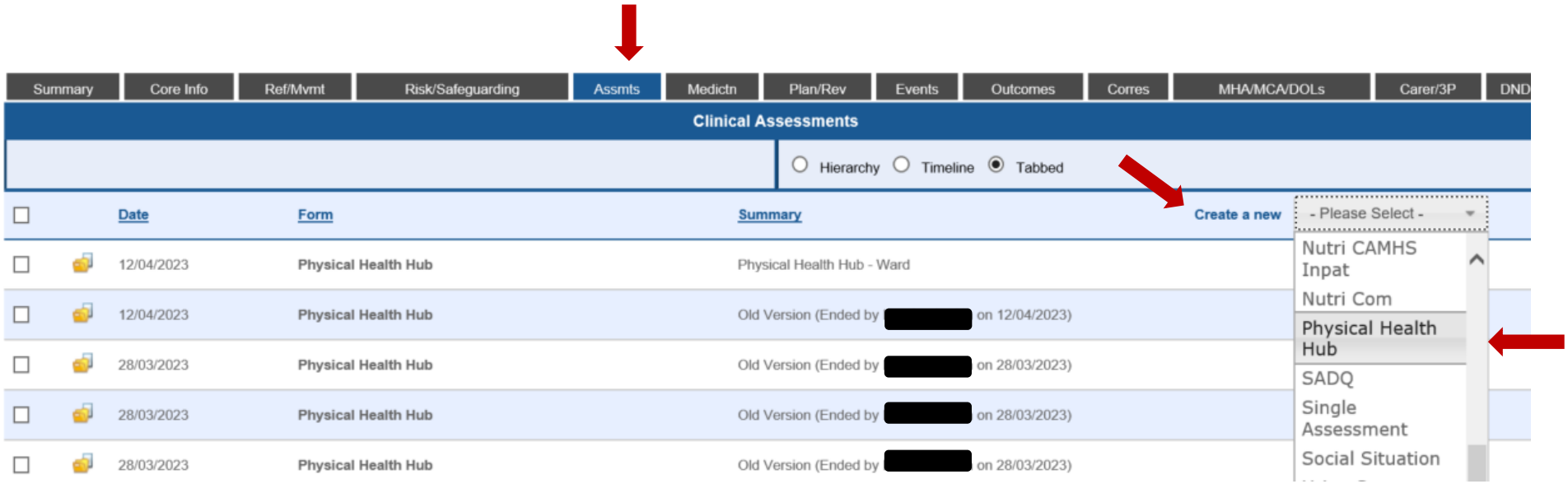

Cardiovascular Disease
https://slamonline.sharepoint.com/sites/svc-physicalhealth/SitePages/Cardiovascular-disease.aspx
SharePoint
Search this site
Home
Our organisation
News
Policies and documents
Tools
Clinical information
Support and opportunities
How to
Home
COVID-19 Resources
Medical devices
Resuscitation
Learning Disabilities and Physical Health
Consultant Connect
Send to
Atrial fibrillation related stroke - monitoring and management
ORBIT Bleeding Risk Score for Atrial Fibrillation - MDCalc
CHA2DS2-VASc Score for Atrial Fibrillation Stroke Risk - MDCalc
Atrial fibrillation related stroke:
monitoring and management in SLaM adult inpatients
NG196: Atrial fibrillation: Diagnosis and management
Recording on EPJS & how to make a referral
Type here to search
ENG
13:57
15/06/2023

Appendix C

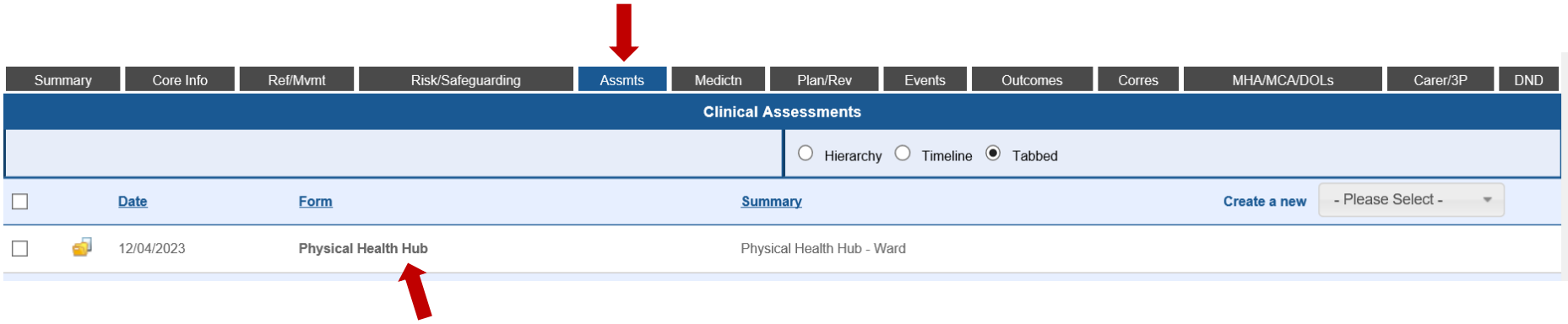
Guidance on where to record the CHA2DS2VASc and ORBIT scores in the Physical health hub and how to make a referral

→ Where to record the CHA2DS2VASc and ORBIT scores in the Physical Health (PH) Hub?

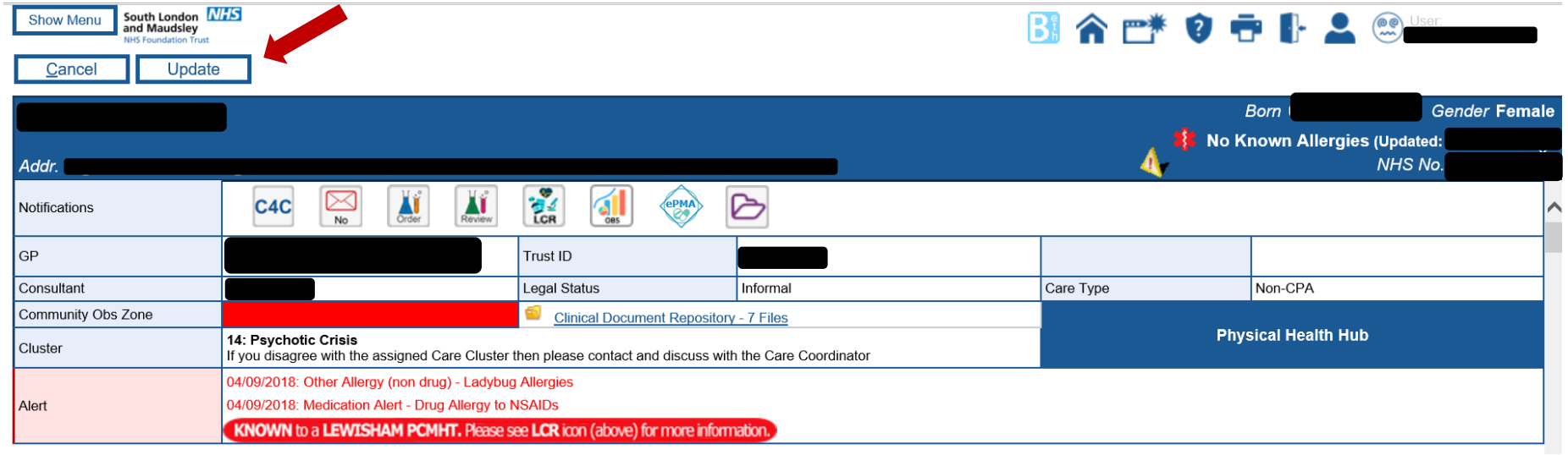
- First time creating PH Hub:
  - Go to assessments/ create a new physical health hub



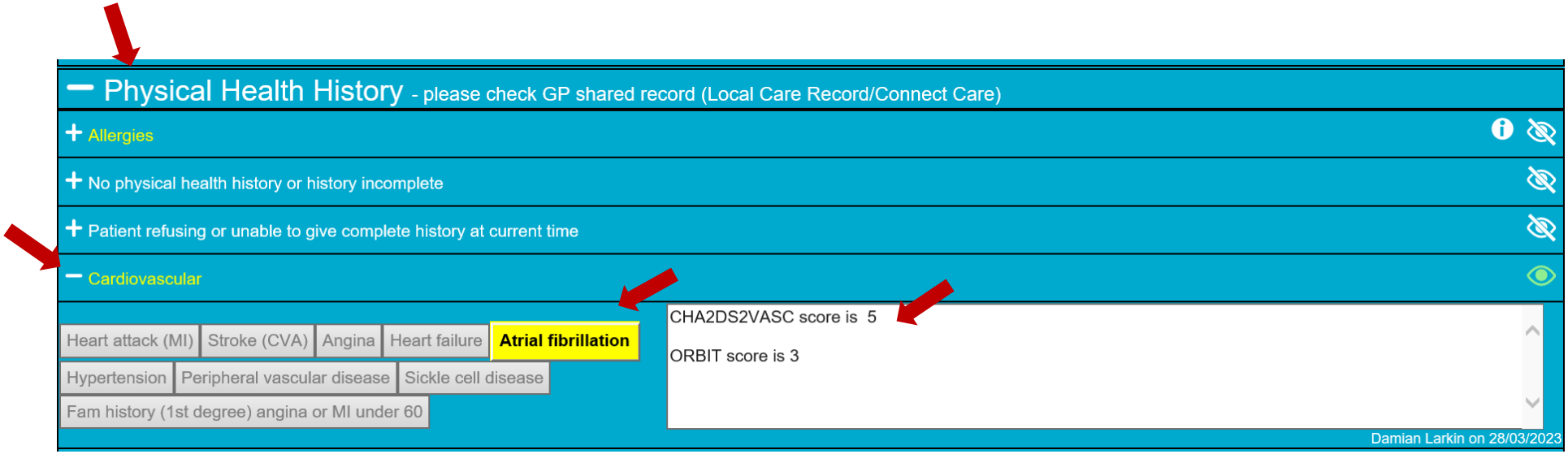
- Existing PH Hub:
  - Go to assessments/ click on existing physical health hub



- Updating medical records:
  - Click on update to edit the medical record



- Recording Atrial Fibrillation, CHA2DS2VASc and ORBIT scores
  - Go to the physical health history, then to cardiovascular
  - Click on atrial fibrillation
  - Add the CHA2DS2VASc and ORBIT scores (links to corresponding calculators are available on MAUD) in the comment section as shown below



- Saving medical records:
  - click save

→ How to print the PH hub:

- At the top right corner of the screen click on the print icon. It will print the entire Summary and will also display other important demographic information such as the patients name (as it is recorded on ePJS).
- Save print output as a pdf on your PC.

Cancel Print

User: [redacted]

STAFF NOTE

To print this document you may need to adjust your page setup.
1. Right click and select Print preview.
2. Click the 'Cog' icon (Page setup).
3. Change the Margins to 10mm.
4. Enable the Print Background Colors and Images option.
5. Select -Empty- for all the Header and Footer options.

Document created by [redacted] on 08/12/2020 **Document updated by** [redacted] on 26/04/2023

Name:Ms [redacted]
Gender:Female
Age:41
GP:ROAD WEST SURGERY Old
NHS No: [redacted]
Trust ID: [redacted]

Summary

Patient's current view	
	I would like to be more active
COVID-19	No Summary
Flu vaccination	
Flu vaccination (this flu season)	
Flu vaccination at SLaM	Had Flucelvax Tetra jab at SLaM
Flu risk assessment and consent	

→ How to make a referral?

- Refer patients at high risk of stroke to one of the following oral anticoagulation clinics based on their GP address.
- In the referral email, mention that the patient has been diagnosed with atrial fibrillation and that the stroke and bleeding risks have been assessed using the CHA2DS2VASc and ORBIT scales.
- Include the PH summary as an attachment in the referral email.
- List of OAC clinics:

UHL	[redacted]	[redacted]
QEH	[redacted]	[redacted]
PRUH	[redacted]	[redacted]
KCH	[redacted]	[redacted]
GSST	[redacted]	[redacted]
Croydon	[redacted]	[redacted]
Bexley (Community)	[redacted]	
Bromley (Community)	[redacted]	

Appendix D

Risk Classification and Matrix

Likelihood Category	Interpretation
Very high	Certain or almost certain; highly likely to occur
High	Not certain but very possible; reasonably expected to occur in the majority of cases
Medium	Possible
Low	Could occur but in the great majority of occasions will not
Very low	Negligible or nearly negligible possibility of occurring

Hazard likelihood definitions

Severity Classification	Interpretation	Number of Patients Affected
Catastrophic	Death	Multiple
	Permanent life-changing incapacity and any condition for which the prognosis is death or permanent life-changing incapacity; severe injury or severe incapacity from which recovery is not expected in the short term	Multiple
Major	Death	Single
	Permanent life-changing incapacity and any condition for which the prognosis is death or permanent life-changing incapacity; severe injury or severe incapacity from which recovery is not expected in the short term	Single
	Severe injury or severe incapacity from which recovery is expected in the short term	Multiple
	Severe psychological trauma	Multiple
Considerable	Severe injury or severe incapacity from which recovery is expected in the short term	Single
	Severe psychological trauma	Single

Severity Classification	Interpretation	Number of Patients Affected
	Minor injury or injuries from which recovery is not expected in the short term.	Multiple
	Significant psychological trauma.	Multiple
Significant	Minor injury or injuries from which recovery is not expected in the short term.	Single
	Significant psychological trauma	Single
	Minor injury from which recovery is expected in the short term	Multiple
	Minor psychological upset; inconvenience	Multiple
Minor	Minor injury from which recovery is expected in the short term; minor psychological upset; inconvenience; any negligible severity	Single

Appendix E

INFORMATION SHEET FOR PARTICIPANTS
YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of project

Implementation of an electronic clinical decision support system (eCDSS) for prevention of atrial fibrillation-related stroke in a mental healthcare setting: a feasibility study

Invitation Paragraph

We would like to invite you to participate in this PhD research project conducted at KCL. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask the research team if there is anything that is not clear or if you would like more information.

What is the purpose of the project?

The purpose of the study is to assess the feasibility and acceptability to staff of an electronic clinical decision support system (eCDSS) (run on Cogstack@Maudsley) for the prevention of atrial fibrillation-related stroke in Mental Health of Older Adults inpatient wards.

Why have I been invited to take part?

You are being invited to participate in this project because you work clinically on a Mental Health of Older Adult (MHOA) inpatient ward at South London and Maudsley NHS Foundation Trust (SLaM) where this research is taking place and because your ward manager has expressed an interest in partaking in the study.

What will happen if I take part?

If you choose to take part in the project you will be asked to complete a short survey and an individual interview asking about the views and experiences of clinicians in managing atrial fibrillation in people with mental illness, and the views of clinicians on the use of digital technologies to assist in clinician led management (perceived appropriateness, potential barriers or facilitators, desired frequency, along with the optimal clinical information to include in the alert). Surveys will be completed online (www.onlinesurveys.ac.uk) and interviews (lasting for 30 minutes) will be conducted remotely via Teams and will be audio recorded with your consent.

The eCDSS will consist of an email sent to the NHS Trust email account addresses of clinicians on the participating ward and a visual prompt (accessed by the clinician) on a patient's electronic Personal Health Record (ePHR). The emails will ask clinicians to clinically assess and record the risk of stroke (using CHAD2AD2-VASc tool) and the risk of bleeding (using ORBIT tool) for their patient having AF on ePJS. Prompts appearing on the ePHR will direct

the clinician to a CHAD2AD2-VASc and ORBIT calculator. Once the components of the tools are filled, stroke and bleeding risk scores will be automatically generated. A note will appear below the scores with corresponding recommendations. Components, scores, and recommendations will be automatically saved on ePJS and discharge summaries. Recommendations include reviewing the stroke and bleeding scores annually, referral to an anticoagulation clinic to reduce AF-related stroke risk (a referral template and emails/ telephone of the OAC clinics will be provided) and managing modifiable bleeding risk factors. A thank you message with a link to NICE guidelines will appear before the alert window closes. The alert will appear on the screen of all clinicians taking care of the admitted patient. Once any of the healthcare providers act on it, the alert will be marked as addressed and will disappear. If not acted upon, a reminder will be sent. Completing the clinical assessment is highly appreciated as it would help the research team conduct the research, however it is not mandatory.

At the end of the study period (4 months later), you will be asked to complete another short survey and an individual remote interview (for 30 minutes) asking about your views and experiences of the implementation of eCDSS on your ward (what worked well, what could be improved and any potential adverse effects for the use of the eCDSS).

Participants will be made aware during consenting that in the event information is disclosed during the interview which indicates that the participant, or another individual is potentially at significant risk of harm either to themselves or others, a further detailed discussion will be had with them at the end of the interview and dependent on the circumstances, information may be passed onto their line manager.

Do I have to take part?

Participation is completely voluntary. You should only take part if you want to and choosing not to take part will not disadvantage you in anyway. Once you have read the information sheet, please contact the research team if you have any questions that will help you make a decision about taking part. If you decide to take part you will be asked to sign a consent form and you will be given a copy of this consent form to keep.

What are the possible risks of taking part?

There are no expected risks from participating in the study. If you find any of the questions uncomfortable, you can choose to terminate the interview or the survey at any time point.

What are the possible benefits of taking part?

There are no personal benefits from taking part in the research. It is hoped that the research will ensure a safe and effective prescribing of anticoagulation therapy among patients with atrial fibrillation admitted to SLaM.

How will we use information about you?

We will need to use information from you for this research project. This information (requested in the surveys) will include your age, gender, professional background and number of years of clinical experience. People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to SLaM (InformationGovernance@slam.nhs.uk) or KCL (Olenka Cogias, info-compliance@kcl.ac.uk),
- by ringing to Professor Fiona Gaughran on 07860880144.

What will happen to the results of the project?

Findings of this study will be formally written, submitted for publication in peer reviewed journals and presented in national medical conferences. Participants will be invited to provide a contact telephone number so that the results of the study can be fed back to them once data has been analysed, at their request. Results will be also disseminated within South London and Maudsley NHS Foundation Trust and shared in their communications.

What if I have further questions, or if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions.

If you remain unhappy and wish to complain formally, you can contact Tanya Shlovogt (Director of Research Quality, Joint R&D Office of SLaM and IoPPN): tanya.shlovogt@kcl.ac.uk. In the event that something does go wrong, and you are harmed during the research, you may have grounds for legal action for compensation against King's College London and/or SLaM NHS Foundation Trust, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Thank you for reading this information sheet and for considering taking part in this research.

Appendix F

Please put your initials in the boxes below after you have read the Information Sheet and/or listened to an explanation about the research.

Title of Study: Implementation of an electronic clinical decision support system (eCDSS) for prevention of atrial fibrillation-related stroke in a mental healthcare setting: a feasibility study

Thank you for considering taking part in this research. If you have any questions related to the project, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form.

1. I confirm that I have read and understood the participant information sheet version 1.1 dated 11/01/2023 for the study. I have had the opportunity to consider the information and ask questions which have been answered to my satisfaction. ☐
2. I consent voluntarily to be a participant in this study and understand that I can refuse to answer questions and that I can withdraw from the study at any time. ☐
3. I understand that my personal information will be processed for the purposes explained to me in the participant information sheet. I understand that such information will be handled in accordance with the terms of the General Data Protection Regulation. ☐
4. I understand that my information may be subject to review by responsible individuals from the King's College London and/or from the sponsor for monitoring and audit purposes. ☐
5. I understand that confidentiality and anonymity will be maintained, and it will not be possible to identify me in any research outputs. ☐
6. I consent to the interviews being audio recorded. ☐
7. I understand that members of KCL having access to my data. ☐

_____	_____	_____
Name of Participant	**Date**	**Signature**
_____	_____	_____
Name of Researcher	**Date**	**Signature**

One copy to be kept by participant, one copy to be retained by researcher

Appendix G

Implementation of an electronic clinical decision support system (eCDSS) for prevention of atrial fibrillation-related stroke in a mental healthcare setting: a feasibility study

Clinician Survey

Pre-intervention

Age:
Gender:
Professional background:
Number of years of clinical experience:

Please rate the degree to which you agree or disagree with each of the following:

	Question	Strongly disagree	Disagree	Somewhat Disagree	Not sure	Somewhat Agree	Agree	Strongly Agree
1	I am aware of guidelines relating to atrial fibrillation-related stroke prevention							
2	I am confident in identifying atrial fibrillation patients eligible for oral anticoagulation therapy							
3	I am confident in managing atrial fibrillation-related stroke risk in mental healthcare settings							
4	I am confident in making referrals to oral anticoagulation clinics							
5	I am confident in assessing the stroke risk using the CHA_2DS_2VASc tool							
6	I am confident in assessing the bleeding risk using the ORBIT tool							
7	I am confident in managing bleeding risk factors							

8	Having access to an electronic clinical decision support tool (eCDSS)* would help me to better assess stroke and bleeding risks in patients with atrial fibrillation.							
9	Atrial fibrillation-related stroke prevention on the ward I work on is currently optimal							

**An eCDSS is a health information technology system designed to assist clinicians and other health care professionals in clinical decision-making. In this project, the eCDSS will provide automated CHA_2DS_2VASc and ORBIT scores.*

After intervention

Age:
Gender:
Professional background:
Number of years of clinical experience:

Please rate the degree to which you agree or disagree with each of the following:

	Question	**Strongly disagree**	**Disagree**	**Somewhat Disagree**	**Undecided**	**Somewhat Agree**	**Agree**	**Strongly Agree**
1	I am aware of guidelines relating to atrial fibrillation-related stroke prevention							
2	I am confident in identifying atrial fibrillation patients eligible for oral anticoagulation therapy							
3	I am confident in managing atrial fibrillation-related stroke risk in mental healthcare settings							
4	I am confident in making referrals to oral anticoagulation clinics							
5	I am confident in assessing the stroke risk using the CHA_2DS_2VASc tool							
6	I am confident in assessing the bleeding risk using the ORBIT tool							
7	I am confident in managing bleeding risk factors							

8	Having access to an electronic clinical decision support tool (eCDSS)* would help me to better assess stroke and bleeding risks in patients with atrial fibrillation.							
9	Atrial fibrillation-related stroke prevention on the ward I work on is currently optimal							
10	There is a clear positive benefit to be gained from using the eCDSS							
11	Alerts from the eCDSS are easily integrated into my existing workload							
12	Alerts from the eCDSS are easily integrated into existing hospital IT systems							
13	The content of alerts provides trustworthy evidence-based information							
14	The decision support provided is clinically relevant							
15	Alerts from the eCDSS provide clear recommended actions for clinicians to act on							
16	The total number of alerts from the eCDSS is acceptable							
17	The system is difficult to use							
18	The system hinders my existing workflow							
19	Alerts from the eCDSS are delivered in an appropriate manner							
20	Alerts from the eCDSS are not accessible at the right time							
21	I would continue to make use of the eCDSS if it remained available on my ward							

**An eCDSS is a health information technology system designed to assist clinicians and other health care professionals in clinical decision-making. In this project, the eCDSS will provide automated CHA_2DS_2VASc and ORBIT scores.*

Appendix H

Implementation of an electronic clinical decision support system (eCDSS) for prevention of atrial fibrillation-related stroke in a mental healthcare setting: a feasibility study

Semi structured interview topic guide
(Pre- intervention)

- Exploration of clinician perspectives on atrial fibrillation-related stroke prevention in secondary mental healthcare.
What challenges do you experience in the prevention of atrial fibrillation-related stroke in this setting? What goes well and what goes less well?

- Exploration of clinician knowledge of atrial fibrillation-related stroke prevention in secondary mental healthcare.
How knowledgeable do you consider yourself to be in the prevention of atrial fibrillation-related stroke in this setting?
Where do you seek additional guidance when unsure?
How knowledgeable do you consider yourself to be when assessing the stroke and bleeding risks in atrial fibrillation patients? Are you aware of any tools for these assessments?

- Exploration of clinician perspectives of barriers and facilitators to adhering to clinical care guidelines (such as NICE), relating to atrial fibrillation-related stroke prevention.
Are you aware of any guidelines relating to atrial fibrillation-related stroke prevention? If so, which ones?
What do you consider to be the key obstacles to adhering to guidelines for atrial fibrillation-related stroke prevention?
What might make it easier for you to adhere to guidelines for atrial fibrillation-related stroke prevention?

- Exploring clinician perspectives on what might improve atrial fibrillation-related stroke prevention at an individual and wider system level.
What do you think might help improve atrial fibrillation-related stroke prevention at:
1. *Individual clinician level*
2. *Wider system level (eg ward or hospital level or Trust level?)*

- Exploring clinician perspectives on use and impact of electronic clinical decision support systems (eCDSSs) in improving clinician led care.
Do you know what electronic clinical decision support systems are and what they do?
Have you ever used an eCDSS? If yes, was it helpful?
What potential impact might greater adoption of eCDSSs by clinicians have on patient care?
What are the potential benefits and harms of using an eCDSS?

What information would be useful to include in an eCDSS for prevention of atrial fibrillation stroke?

(After intervention)

- Experiences of using the eCDSS

How did you experience the electronic clinical decision support system? What was useful? What was not so useful?
Can you describe any factors that you think made it easy to use the eCDSS?
Can you describe any factors that you think made it difficult to use the eCDSS?
What would you like to change or modify to improve your experience of using the eCDSS?
Did it impact on your workflow (facilitate or hinder)? If so how?

- Views regarding impacts of the eCDSS on clinicians and patients

What impact did the eCDSS have on you professionally? (workload, time, care processes, confidence adhering to clinical guidelines for atrial fibrillation-related stroke prevention)
How did the eCDSS impact patient care?
Were there any problems or issues that arose?
Were there any adverse events? Were there any unintended consequences for you, other ward staff, the ward as a whole, or patients?

- Perspectives on using the eCDSS within the context of atrial fibrillation-related stroke prevention.

Was information included in the alerts relevant? Was it concise? Was it accurate?
Thinking of managing patients with atrial fibrillation diagnosis: do you think the eCDSS improved your ability to recognise when a patient is at high risk of stroke (make a referral to an oral anticoagulation clinic) or high risk of bleeding (manage bleeding risk factors)?
Can you think of other ways in which eCDSS might be useful in secondary mental healthcare settings?
Would you continue to make use of the eCDSS if it remained available on the ward? Would you recommend it to colleagues?
Any other points of discussion regarding the electronic clinical decision support system?