Study Protocol and Analysis Plan

Study Official Title: A nurse-coordinated integrated care model to support decision-making and self-care in patients with atrial fibrillation: A randomized controlled trial

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Background of research

Health implications in patients with atrial fibrillation

Atrial fibrillation (AF) is a common abnormal cardiac rhythm characterized by an irregular and rapid heartbeat. In this condition, uncoordinated electrical activity causes ineffective atrial contractions and variable ventricular activation. Sluggish atrial blood flow increases the risk of blood clot formation, which itself independently increases the risk of cardio-embolic stroke by five-fold in AF patients, compared to people with a normal sinus rhythm.[1] In addition, AF is associated with tachycardia-induced cardiomyopathy in patients with a poorly controlled ventricular rate.[2] AF also predisposes patients to increased risks of myocardial infarction,[3, 4] heart failure,[5] dementia,[6] and death.[7] Indeed, the healthcare burden associated with AF-related hospitalization has largely surpassed that associated with heart failure.[8] Given these detrimental health consequences, international practice guidelines[9] have highlighted stroke prevention and arrhythmia control as the major focuses of AF management, whereas the management of modifiable risk factors is equally important to improving the their health outcomes of AF patients.[10, 11]

Challenges associated with stroke prevention

To minimize the AF-associated risk of stroke, international guidelines[9, 12] recommend providing oral anticoagulants (OACs), either vitamin K antagonist (VKA) or non-vitamin K antagonist oral anticoagulants (NOACs), to male patients with ≥ 1 and female patients with ≥ 2 of the following risk factors: congestive heart failure; hypertension; age ≥ 75 years; diabetes mellitus; prior stroke or transient ischemic stroke or thromboembolism; vascular disease; age 65 to 74 years and female sex (i.e., CHA_2DS_2-VASc score). Despite compelling evidence supporting the strong efficacy of OACs in preventing stroke in AF patients, the use of these agents is limited by three major factors: under-prescription, non-adherence, and a suboptimal therapeutic range for VKA treatment. A systematic review of 54 studies found that 50% of high-thromboembolic-risk AF patients did not receive appropriate OAC therapy.[13] Likewise, a recent study[14] of 9,727 patients with AF in Hong Kong reported that nearly 40% did not receive OAC therapy and another 40% received only conservative aspirin therapy, which has proven ineffective for AF-related stroke prevention. OAC under-prescription is mainly attributable to physicians' concerns regarding the side effect of an increased bleeding tendency,[15] as patients are more willing to bear this risk, given the benefit of preventing a stroke episode.[16] However, physicians inaccurately perceive that patients fear the risk of bleeding more than the risk of stroke.[17] The investigation team revealed similar findings in another local study,[18] where physicians reported the perception that patients were at a high risk of developing adverse events as the most common barrier to OAC prescription. The physicians reported moderately high levels of decisional conflict, as they did not fully understand patients' views regarding the risks and benefits of OAC use.[18] Such studies have shown that the inability of patients to effectively convey their values and preferences to physicians has contributed to the low OAC utilization rate among AF patients.

Even among patients receiving OAC therapy, the effectiveness is limited by poor adherence and suboptimal anticoagulation control quality. The efficacy of VKA depends strongly on the anticoagulation intensity, a parameter measured using the international normalized ratio (INR), for which the ideal therapeutic range lies between 2.0 and 3.0 for AF. Suboptimal anticoagulation control quality refers to a proportion of time in the therapeutic range of <70%.[9] Not only does the narrow therapeutic index of a traditional VKA increase the challenge of maintaining an optimal dose, but the requirements for frequent laboratory monitoring, dose adjustment, and strict lifestyle modifications to reduce drug–food interactions also reduce patient adherence. Although the newer NOACs provide improved anticoagulation predictability, which enables fixed dosing without requiring routine laboratory monitoring, the shorter plasma half-lives of these agents require perfect medication adherence to achieve the targeted therapeutic effects. Recent large-scale observational studies have reported that <50% of patients remain adherent to OAC therapy at 1- to 2-year follow-up time points,[19, 20] and up to 25–38% of patients fail to achieve optimal anticoagulation control.[21] The lack of knowledge surrounding AF, treatment options, and the consequences of non-adherence comprise the major determinants of non-adherence and suboptimal anticoagulation control.[22]

Challenges associated with arrhythmia and risk factor control

Both pharmacological and non-pharmacological strategies are equally important for arrhythmia control. Although pharmacological management is relatively less challenging than stroke prevention, non-pharmacological measures rely heavily on patients' self-care actions, including good adherence to therapeutic regimens, self-monitoring and management of signs and symptoms, management of crises related to disease deterioration and treatment complications, and lifestyle modifications.[9] Among these self-care actions, patients' efforts to accurately monitor their heart rates and detect irregularities comprise the most crucial factor informing treatment efficacy and, consequently, the need for treatment adjustment. This is especially true because symptom reporting does not truly reflect patients' responses to AF treatment.[23] Nevertheless, AF patients seldom perform self-monitoring in the form of pulse checks.[24] In addition, compelling evidence indicates that aggressive control of risk factors, such as hypertension, obesity, smoking, excessive alcohol intake, diabetes mellitus, and obstructive sleep apnea, is crucial to reducing the burden of AF and disease deterioration.[25] Moreover, risk factor control is pivotal to reducing the bleeding risk associated with OAC prescription.[9] The control of these risk factors relies considerably on the success of patients' behavioral modifications and treatment adherence. Yet, substantial evidence suggests poor self-care among AF patients in this regard,[26] as well as an association of suboptimal self-care with increases in AF-related hospitalizations and mortality.[9, 26]

The aforementioned complex challenges facing AF management suggest an imminent need to develop a model of care for optimizing OAC prescriptions and related therapeutic effects, improving arrhythmia and risk factor control, and enhancing patients' self-care regarding disease monitoring, maintenance, and crisis management. Therefore, a structured and multifaceted model of care is needed to meet all these challenges in this vulnerable group. Nurse-coordinated care with an emphasis on OAC optimization and self-care enhancement has emerged as a method for addressing these complicated care requirements of AF patients.

Empirical effects of nurse-coordinated care

The increasing recognition of the complicated care needs of AF patients has led more researchers to investigate the effects of nurse-coordinated care models. Gillis et al.[27] and Carter et al.[28] used a pre- and post-test study design to examine the effects of a nurse-led clinic for newly diagnosed AF patients referred by their family physicians or an emergency department. Patients underwent a stroke risk and symptom assessment conducted by the nurse, while the clinic physician developed an OAC and antiarrhythmic agent treatment plan based on the patients' risk and symptom profiles. This plan was then communicated to each patient's family physician to guide drug prescription. The nurse also provided a brief face-to-face group education session on AF management to patients. The preliminary study by Gillis et al. demonstrated reductions of 82% and 56% in AF-related emergency department visits and hospitalizations, respectively, among 68 patients,[27] whereas the study by Carter et al. reported a significant increase in OAC prescriptions but no significant differences in all-cause deaths, cardiovascular hospitalizations, and AF-related emergency visits at 12 months.[28]

Hendriks et al. adopted a more robust randomized controlled trial (RCT) design to examine the effects of an integrated nurse-led AF clinic in Europe (N = 712).[29-31] In that trial, the nurse determined the most appropriate treatment based on the patients' symptoms, AF type, and stroke risk with the support of guideline-based software. Following an endorsement by a cardiologist, the nurse communicated the treatment plans to the patients along with an education regarding AF, treatment, and symptom monitoring. Compared with the conventional care offered by cardiologists in the outpatient clinic, the nurse-led intervention significantly reduced cardiovascular-related deaths and hospitalizations,[29] and a cost-effectiveness analysis demonstrated that this intervention effectively reduced costs.[31] However, the nurse-led intervention failed to yield significant improvements in the patients' psychosocial outcomes, including the health-related quality of life (HRQoL), anxiety, and depression,[30] possibly because the included patients were relatively healthy and had low CHADS$_2$ scores. In addition, up to 25% of the patients had incomplete baseline data from the HRQoL analysis.

Whereas the above studies focused on stroke risk assessment and OAC optimization, Stewart et al. conducted an RCT to evaluate the effects of a home-based, nurse-led, transitional care intervention on patients admitted primarily because of AF.[32] This intervention focused mainly on optimizing patients' self-care. A pre-discharge assessment of self-care ability was conducted, and after discharge, a nurse provided clinical assessments and education about AF and its symptoms, reduced barriers to medical follow-up and optimum self-care, and made referrals to relevant health services according to patients' clinical statuses and needs through home visits. Despite the lack of a care component for optimizing OAC prescriptions, the nurse-led transitional care intervention significantly extended the number of non-hospitalized days and the survival duration, but did not reduce all-cause mortality or hospitalizations.[32] A comparison of these findings with the aforementioned study by Hendriks et al. suggests that an effective model of care should include components of self-care enhancement as well as OAC prescription optimization.

Even though previous studies demonstrated some positive effects of the nurse-coordinated care model for AF patients, they were strongly limited by the consideration of patients as passive care recipients. Indeed, this approach is contradictory to the philosophy of chronic disease management proposed by the World Health Organization

(WHO).[33] In response to the burgeoning population of patients affected by chronic diseases worldwide, the WHO proposed the Innovative Care for Chronic Conditions (ICCC) framework as a strategy for chronic disease management. The ICCC framework highlights the importance of empowering patients to become active care agents.[33] To address the complex needs of AF patients, the model of care must shift from a traditional paternalistic to a patient-participatory approach. Currently, the literature also lacks reports of a comprehensive model encompassing all important care components, including stroke risk-guided OAC prescription, self-care enhancement for arrhythmia optimization, and risk factor control. Despite the complexity of AF self-care, previous studies mainly used a didactic approach to self-care education. This method has been widely criticized as unable to internally motivate patients to make decisions and solve problems, and for ineffectively facilitating sustainable behavioral changes.[34] As patients with AF are their own major caregivers, successful management relies heavily on their efforts to engage in day-to-day self-care actions. For instance, decisions regarding OAC use require individuals to analyze the values of potential outcomes in a process requiring self-determination. In such cases, the active engagement of AF patients in various stages of disease management, from initial therapeutic planning to long-term self-care, is crucial to equipping and motivating patients to participate in self-care.

<u>Enhancing AF self-care through an empowerment-based approach</u>

Patient empowerment has recently emerged as an effective paradigm for improving health outcomes by promoting patient participation.[35] Empowerment is a philosophy of care in which interactive teaching strategies and experiential learning are used to develop patients' inherent capacities to gain control over the required behavioral changes and make decisions about their health problems.[36, 37] This patient-centered collaborative approach requires a goal-setting process to increase patients' motivation and autonomy,[36] and a subsequent process to assist patients with developing an action plan for goal attainment.[36] To the best of our knowledge, such an empowerment-based educational approach has not yet been used to promote self-care among AF patients. Nevertheless, extensive empirical evidence supports the beneficial effects of such an approach on the self-care of other chronic diseases, particularly diabetes and asthma.[34, 38, 39] Other studies have consistently reported that this approach effectively enhances patients' abilities to manage their chronic health conditions by fostering behavioral modifications and improving coping and problem-solving skills, as well as various disease-specific outcomes.[38, 40] Given the inadequacy of the current model of care to address the complex needs of AF patients, this project hypothesizes that a nurse-coordinated integrated care model featuring a patient-empowerment approach can improve the health outcomes of AF patients.

<u>Work done by us</u>

The proposed study will address the findings of research conducted by the investigation team. We previously investigated physicians' attitudes and beliefs regarding OAC prescription for AF patients and found that the physicians experienced moderately high levels of decisional conflict because they did not know their patients' views regarding the risks and benefits of OAC use.[18] In addition, an ongoing GRF project conducted by one of the Co-I (BY) has shown that the approach of using a single-lead ECG device for rapid AF screening is feasible, up to 1.7% of patients who attended medical outpatient clinics were newly diagnosed with AF. These patients are prone to developing disabling strokes if their conditions remain undetected and untreated. The preliminary data of this on-going GRF study also show that the use of didactic patient education is not effective in increasing OAC use in these patients. In this connection, this team of investigators, which has a strong track record in cardiac care, interventions to empower patients and caregivers, self-care enhancement using a patient empowerment model, and psychosocial interventions, intensify the model of care by adopting an evidence-based nurse-coordinated empowerment-based approach to improve the health outcomes of patients with AF.

**Research plan and methodology**

The proposed study will have two aims: i) to evaluate the effects of a nurse-coordinated integrated care model with a patient empowerment approach on the compatibility of patients' and physicians' decisions regarding OAC use, medication adherence, anxiety, depression, and HRQoL and ii) to explore how and why the intervention affects health outcomes from the patients' perspectives. The first aim is based on a research hypothesis in which AF patients exposed to the nurse-coordinated integrated care model will be more likely to report achieving compatible patient and physician decisions regarding OAC use, better changes in medication adherence, anxiety, depression, and HRQoL, compared to patients who receive conventional care.

<u>Study design</u>

This will be a sequential mixed-methods study with two phases. Phase 1 will comprise a prospective, single-blinded RCT to investigate the effects of the nurse-coordinated integrated care model on various health outcomes among patients with AF. Phase 2 will comprise an exploratory qualitative study to determine how and why the intervention works. Figure 1 outlines the Phase 1 study implementation protocol. After collecting baseline data, the research nurse (RA1) will randomly allocate patients into the intervention or control group. Block randomization (block size: 8, 10, or 12) will be used to ensure even participant distribution between the two groups. The block size

and respective study group allocation sequence will be determined using a computer-generated sequence. Chronologically recruited patients will be allocated to the study groups by RA1 according to this computer-generated sequence. Participants allocated to receive the nurse-coordinated integrated care model will be provided with an appointment 1–2 weeks before their next scheduled medical appointment to initiate the intervention. The participants allocated to the control group will continue to receive conventional care as arranged by the hospital. An independent research assistant (RA2) who is blinded to the study group allocations will collect post-intervention data through medical record reviews and telephone interviews upon completion of the intervention and 6 months thereafter.

Figure 1. Study implementation protocol
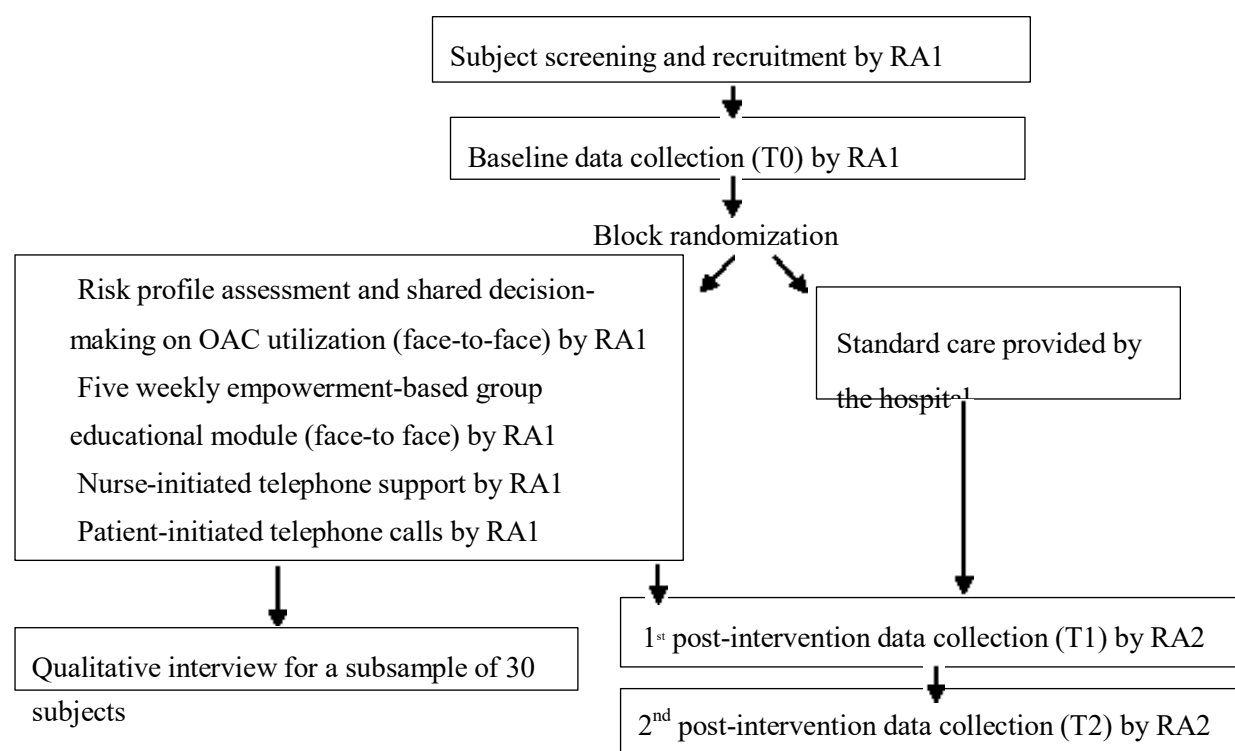
Study participants

The proposed study will be conducted at six medical out-patient clinics of the study hospital. We plan to use two approaches to recruit patients: 1) screening patients at the specialist out-patient clinics; and 2) identifying potential subjects from the Clinical Management System of the study hospital. All patients ≥65 years of age who attend the clinics will be invited to undergo rapid, single-lead ECG device-based screening for AF performed by trained student helpers. The study will arrange for patients with positive screening results to undergo a 12-lead ECG analysis onsite to confirm the diagnosis. The RA1 will check consecutive patients identified through this screening process against the following eligibility criteria for study participation: (1) age ≥65 years, (2) community-dwelling, (3) confirmed diagnosis of AF, (4) a CHA_2DS_2-VASc score of ≥1 in men and ≥2 in women, and (5) no use of OAC therapy. Patients with impaired communication or cognitive abilities (i.e., an Abbreviated Mental Test score ≤6) or severe co-existing medical conditions (e.g., terminal illness) that would hinder participation in research activities will be excluded. For the first approach, one of the co-investigators of this project (B Yan) had adopted the same approach, which indicated that the newly identified AF was found in 1.5% on a single time-point screening, and additional 1.2% was detected in those screened on multiple time-points.[41] As such, approximately 25,000 patients need to be screened to achieve the target sample size. To safeguard an adequate sample is recruited, a second approach to screen patients who have already established the diagnosis will be identified from the Clinical Management System (CMS). The RA1 will identify potential participants who are under the care of specialist out-patient clinics of the study hospital from the CMS. Patients with documented AF who met the aforementioned criteria and are not receiving appropriate OACs for stroke prevention will be approached for further screening according to the selection criteria. This approach is supported by a study [14] which indicated a serious gap between empirical evidence and practice in the local setting: among 9,727 patients with AF in Hong Kong: nearly 40% did not receive any OAC and another 40% were conservatively put on aspirin.

The proposed sample size was estimated based on the primary outcome of HRQoL. To our best knowledge, no previous study examined the effect of a nurse-coordinated empowerment-based care model on AF patients. However, we have identified a few similar interventional studies targeting patients with different diseases, including diabetes[42,

43] and hemodialysis recipients.[44] Of these studies, the effect sizes of the empowerment interventions on HRQoL ranged from 0.09 to 1.17, depending on the HRQoL domains. In general, an experimental design involving a larger sample size can enable researchers to detect a smaller effect size on an outcome at a specific statistical power and significance level. However, a small effect size may not be clinically important. Therefore, after considering both the clinical relevance and previous study findings, the sample size of this study was determined to yield adequate power for the detection of at least a small to medium effect size[45] on the primary outcome. Using power analysis software package PASS 13 (NCSS, Kaysville, USA), we estimated a sample size of 176 per study arm to yield 80% power at a 5% significance level for the detection of an effect size as small as 0.3 on our primary outcome when comparing the two study arms at the post-intervention time points. After allowing for a potential dropout rate of 10%, 392 participants (196 per arm) will be recruited.

For Phase 2 of the study, a purposive sample of 30 participants from the intervention group will be invited to participate in a qualitative interview. Participants with different treatment responses to the nurse-coordinated integrated AF care model will be recruited according to changes in their post-intervention HRQoL scores. Ten participants will be selected from each range of HRQoL changes: 0–34th percentile, 35th–68th percentile, and >68th percentile.

Study interventions
Intervention group: Nurse-coordinated integrated care model for AF
Participants in the intervention group will participate in a 13-week, nurse-coordinated integrated care model comprising the following care components intended to comprehensively address the needs of AF patients: 1) a risk profile assessment and shared decision-making regarding OAC use; 2) an empowerment-based educational module on AF self-care; 3) nurse-initiated telephone support; and 4) patient-initiated contact for professional advice. The details of each care component of the intervention (Figure 2) are described below.

Figure 2. Nurse-coordi
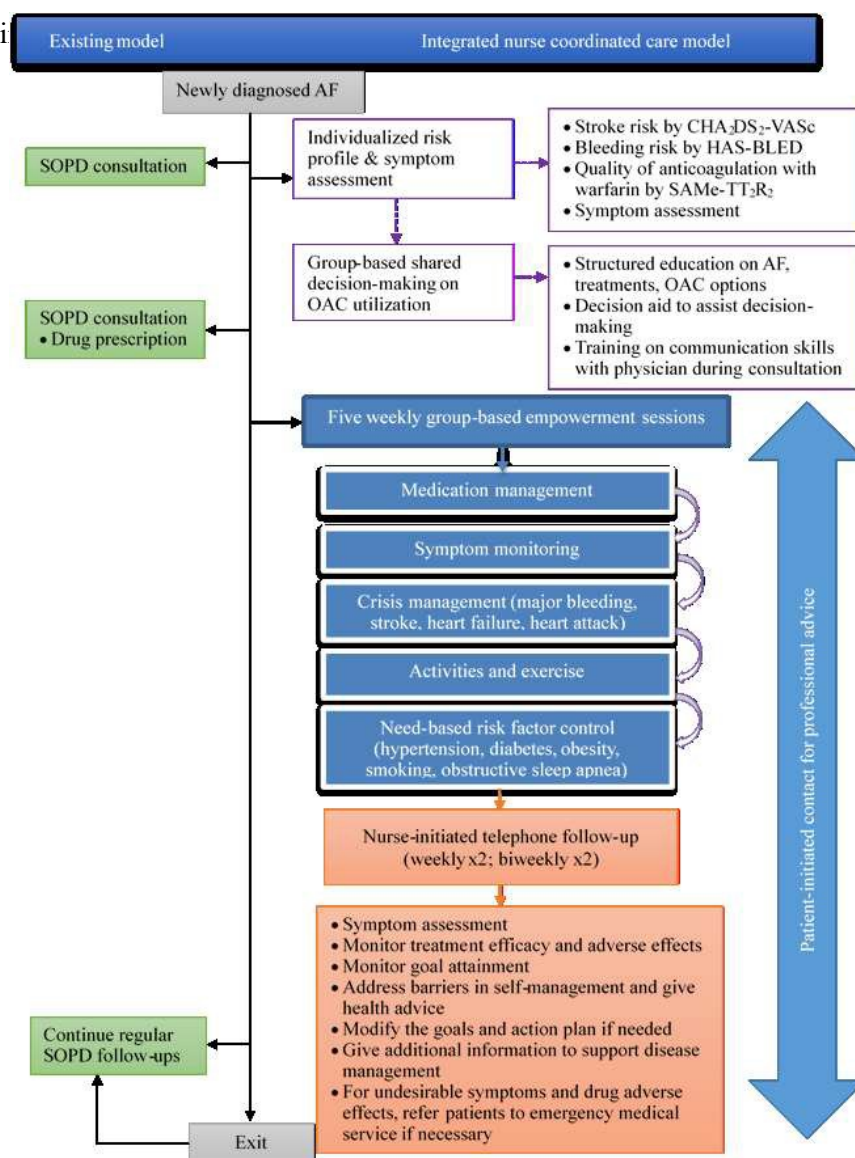
1.   Risk profile assessment and shared decision-making regarding OAC use

A pre-consultation session will be provided 1–2 weeks before the patient's next medical clinic consultation. This session will comprise two components: an individualized assessment and a group-based session to enhance patients' participation in shared decision-making. First, RA1 will conduct a comprehensive, individualized risk assessment of patients. The risk assessment will address multiple aspects, including i) the stroke risk based on the CHA_2DS_2-VASc score, ii) bleeding risk based on the HAS-BLED score, and iii) quality of VKA anticoagulation therapy based on the $SAMe$-TT_2R_2 score. Details of the CHA_2DS_2-VASc score were elaborated in a previous section of this proposal. The HAS-BLED score predicts the bleeding risk according to the following risk factors: hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, age >65 years, and concomitant drug/alcohol use. The $SAMe$-TT_2R_2 score assesses the likelihood of poor INR control among patients with AF on VKA therapy according to sex, age, medical history, treatment, tobacco use, and race. These risk stratification scores provide information crucial to determining the optimal treatment options for each patient.

After the risk assessment, the nurse will conduct a face-to-face session in a small-group (6–8 patients/group) format to empower patients regarding decision-making and communication with physicians. This face-to-face approach was selected in accordance with literature suggesting it to be more effective than a written format.[46] Additionally, group teaching can promote peer learning and modeling. The session will begin with a structured educational session on AF and its complications, with emphasis placed on understanding the link between AF and ischemic stroke and the deleterious effects of rapid ventricular rates on cardiac function. The currently available and suitable OAC options (warfarin and NOACs) and their pros and cons (including the self-financed nature of novel OAC) as well as the rationales for rate and rhythm control will also be discussed. To assist patients with decision-making regarding OAC use, a patient decision aid developed by the National Institute of Health and Care Excellence[47] will be used. This aid organizes treatment options in an Option Grids format, wherein 10 frequently asked questions are presented vertically downwards with the options presented horizontally across the table. This format facilitates comparison and clarifies the options. Numeric and graphic formats with pictograms will be used to help patients understand the absolute and relative risks of a stroke when not using OACs or a major bleeding episode while using OACs. Patients' individual risk profiles will be used to illustrate their stroke risks with and without OAC and their bleeding risk with OAC in a graphical format. The nurse will present the risk and benefit information in a fair and balanced manner.

Another care component will engage patients in shared decision-making regarding OAC use by empowering them to better communicate their decisions to physicians during upcoming medical consultations. This component will highlight the key points of assertive communication, including asking questions, expressing concerns, and stating opinions and preferences regarding OACs for stroke prevention. The patients will be encouraged to generate a list of questions and concerns to propose to their physicians. To enhance patients' confidence in their ability to maintain assertive communication in stressful situations, a series of scenario-based patient models in video format will be used to optimize the acquisition of skills for handling challenging encounters. A role-play-based rehearsal will be conducted to allow patients to practice their new skills and observe others' behavior. The nurse will debrief patients to discuss their performance and provide feedback. Throughout the session, the nurse will adopt a supportive and non-judgmental attitude.
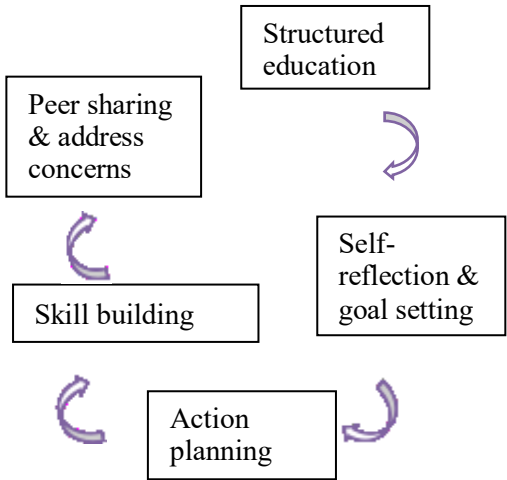
2.   Empowerment-based group educational module

The same group of patients will attend an empowerment-based educational module beginning 1 week after their medical appointments. The module will comprise five weekly educational sessions covering the following major topics related to AF self-care: i) medication management, ii) symptom monitoring, iii) crisis management, iv) activities and exercise, and v) risk factor management to reduce risks of stroke and bleeding. The educational content of each session will comply with the recommendations of major practice guidelines for AF managment.[9, 12]

During each session, the nurse will implement the empowerment process (Table 1) to enhance patients' knowledge, skill acquisition, and confidence in AF self-care. The empowerment approach emphasizes the use of interactive teaching strategies, experiential learning, and self-reflection during the educational process to optimize learning.[37] First, the nurse will deliver a structured educational session about the topic of the week. Emphasis will be placed on assisting patients with understanding the links between their self-care behaviors and health consequences to ensure that they appreciate the importance of their own efforts in managing AF. The nurse will encourage patients to share their current practices, and facilitate them to identify discrepancies between the suggested self-care and their current practices. The nurse will also highlight possible health consequences of these discrepancies and assist patients with setting self-directed goals related to those areas. After goal-setting, a subsequent interactive skill-building session will ensure that patients acquire the skills required to perform specific self-care behaviors. For example, to enhance patients' confidence regarding crisis management, a series of scenario-based patient models in video format will be used to optimize the acquisition of skills needed to handle challenging encounters related to possible crises, such as a major bleeding event or suspected stroke episode. A role-play-based rehearsal will be conducted, and the nurse will discuss the patients' performances and provide feedback. The nurse will make use of group dynamics by encouraging peer discussions of successful self-care actions, feelings, concerns, and perceived

barriers to goal achievement. The nurse will also work with the patients to mutually develop action plans for achieving goals set during each weekly educational session. Each subsequent session will begin with a discussion of progress in goal attainment. Challenges and barriers faced while implementing the action plans set during the previous week will also be discussed.

Table 1. The empowerment process.

5-step empowerment process	Intervener's counseling techniques for the empowerment process
	Be supportive to assist patients to identify their inadequacy in self-care Avoid judgmental attitudes Be patient-centered in identifying the barriers to self-care Use active listening to identify concerns, fears and beliefs that may hinder effective self-care Be collaborative with the patients to work through ambivalence to set patient-directed goals Use reflection and paraphrasing to validate patients' feelings and their capacities to solve problems Be respectful to the expertise of patients Genuinely believe in patients' ability to make the changes Acknowledge patients' right and responsibility to make self-care choices and to be the primary decision makers

3. Nurse-initiated telephone support

The nurse will provide continued support by telephone after the face-to-face sessions have been completed (two weekly and two bi-weekly calls). A telephone record containing patients' clinical profiles, AF-related treatments, self-management goals, and action plans will be used to facilitate the process. The nurse will monitor patients' adherence, symptom profiles, treatment efficacies, adverse effects, and goal attainment progress; identify barriers in the self-care process; and provide resolutions and continued support via the telephone. Health counseling and advice given will be documented to guide subsequent telephone correspondence.

4. Patient-initiated contact for professional advice

All participants from the intervention group will be provided with telephone access to the nurse for inquiries regarding disease management during office hours. The nurse will provide health advice and counseling accordingly. For severe undesirable symptoms and adverse reactions to medications, the nurse will attempt to advance patients' follow-up appointments or advise patients to seek emergency medical care if necessary. All correspondence and advice given will be documented in patients' profiles.

Control group: Conventional care

The control group will receive the conventional care provided by the study hospital.

Fidelity monitoring of the study intervention

Multiple methods will be used to monitor the fidelity of the study interventions. Assessment and record forms will be used to document the care activities provided to patients during the sessions, telephone calls, and patient-initiated contacts. The nurse will file these assessment records to facilitate care coordination. Care activities will be coded, tracked, and checked against the intervention protocol. A standardized manual will be developed to guide the delivery of each group-based education session. Moreover, the PI will randomly select five groups in the intervention arm for monitoring. Face-to-face sessions will be videotaped after obtaining the participants' consent. Two research

fellows will review the tapes and complete a performance checklist after a briefing session by the PI. In addition, the nurse will document reflective notes after each session and hold monthly discussions with the investigation team. Participants' attendance will be recorded. All these data will be submitted for interpretation.

Outcome measures

The following instruments will be administered at baseline, upon completion of the intervention, and 6 months thereafter.

Compatibility between patient and physician decisions

Patients will be asked to indicate whether a decision regarding the choice of OAC was made before the consultation and, if yes, details of the choice.[48] The physician's prescription of any OACs will be monitored after the consultation. The nurse will confirm prescriptions with the patients and trace prescription record information in the Hospital Authority's Clinical Management System. The patients' choices and physicians' prescription decisions will be examined to determine compatibility.

8-item Morisky Medication Adherence Scale (MMAS-8)

The MMAS-8 will be used to assess self-reported medication adherence.[49] Each item measures a specific medication-taking behavior using a dichotomous (yes/no) response (Items 1–7) or a 5-point Likert scale (Item 8). The scores range from 0 to 8, with higher scores indicating better adherence. The Chinese version yields acceptable internal consistency (Cronbach's α = 0.77), good test-retest reliability (r = 0.88), and construct validity.[49]

Atrial Fibrillation Effect on QualiTy-of-life (AFEQT) Questionnaire

The 20-item AFEQT[50] measures disease-specific HRQoL in AF patients using 4 subscales: symptoms, daily activities, treatment concerns, and treatment satisfaction. All subscales are rated on a 7-point Likert scale, with higher scores indicating a poorer HRQoL. The subscales' Cronbach's alphas ranged from 0.88 to 0.95, the test-retest reliability and construct validity are satisfactory, and the instrument is responsive to treatment.[50] This investigation team developed the Chinese version of the AFEQT, which is currently undergoing psychometric validation.

Hospital Anxiety and Depression Scale (HADS, Chinese-Cantonese version)

The 14-item Chinese-Cantonese version of the HADS[51] will be used to measure anxiety and depression. This instrument is rated on a 4-point Likert scale, with higher scores indicating more intense anxiety and depression. The HADS is reported to have good internal consistency (Cronbach's alpha = 0.86) and satisfactory factorial, concurrent, and criterion validity.[51]

Data analysis

The statistical analysis of the outcome comparisons will be performed based on the intention-to-treat principle. Variables with skewed data will be transformed appropriately prior to analysis. Baseline characteristics between the two study arms will be compared using the t-test or chi-square test where appropriate. A mixed-effects model will be used to compare differential changes in the outcome variables over time and between the two arms. The mixed-effects model can account for intra-correlated repeated-measures data and produce unbiased estimates even if some data are missing, as long as the data are missing at random. All statistical analyses will be performed using SAS version 9.4 (SAS Institute, Cary, NC). All statistical tests will be 2-sided, with a significance level of 0.05.

For the qualitative study, qualitative audiotape data will be transcribed verbatim, and the PI will ensure the accuracy of the transcripts. These data will be subjected to a content analysis, following an open coding session. The coded units will then be organized to create categories.[52] Particularly, the qualitative data will be analyzed to seek a better understanding of why and how the nurse-coordinated integrated care model affects the health outcomes of AF patients. The trustworthiness of the qualitative phase of the study will be enhanced by audiotaping all interviews, conducting an audit trail involving two investigators (PI and DY) who independently code the qualitative data, and comparing the coded data, with a discussion-based resolution of discrepancies. Themes emerging from the qualitative data will be used to explain the quantitative findings of the RCT study.

Ethical Consideration

This study followed the Declaration of Helsinki on medical protocol and ethics. Ethics approval will be obtained from both the Joint Clinical Research Ethics Committee of the Chinese University of Hong Kong and New Territory East Cluster. Patients are voluntary participants in the study. A written informed consent, which will include the research title, purpose, explanation of the research, and the procedures of the study, will be obtained from each eligible participant. Risks and benefits are also explained clearly to the participants. Participants have the right to withdraw from the study at any time. They will be protected from discomfort and harm during the study. Further, anonymity and confidentiality of the participants will be strictly protected. Their decision of participating in the study will not affect the quality of present or future care they receive in the hospital.

References:

1. Lip, G.Y., *Stroke and bleeding risk assessment in atrial fibrillation: when, how, and why?* European heart journal, 2013. **34**(14): p. 1041-1049.

2. Gupta, S. and V.M. Figueredo, *Tachycardia mediated cardiomyopathy: pathophysiology, mechanisms, clinical features and management.* International journal of cardiology, 2014. **172**(1): p. 40-46.

3. Soliman, E.Z., et al., *Atrial fibrillation and the risk of myocardial infarction.* JAMA internal medicine, 2014. **174**(1): p. 107-114.

4. Soliman, E.Z., et al., *Atrial fibrillation and risk of ST-segment elevation versus non-ST segment elevation myocardial infarction: the Atherosclerosis Risk in Communities (ARIC) Study.* Circulation, 2015: p. CIRCULATIONAHA. 114.014145.

5. Miyasaka, Y., et al., *Incidence and mortality risk of congestive heart failure in atrial fibrillation patients: a community-based study over two decades.* European heart journal, 2006. **27**(8): p. 936-941.

6. Kalantarian, S., et al., *Cognitive impairment associated with atrial fibrillation: a meta-analysis.* Annals of internal medicine, 2013. **158**(5_Part_1): p. 338-346.

7. Piccini, J.P., et al., *Incidence and prevalence of atrial fibrillation and associated mortality among Medicare beneficiaries, 1993–2007.* Circulation: Cardiovascular Quality and Outcomes, 2012: p. CIRCOUTCOMES. 111.962688.

8. Wong, C.X., et al., *The increasing burden of atrial fibrillation compared with heart failure and myocardial infarction: a 15-year study of all hospitalizations in Australia.* Archives of Internal Medicine, 2012. **172**(9): p. 739-741.

9. Kirchhof, P., et al., *2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS.* European Journal of Cardio-thoracic Surgery, 2016. **50**(5): p. e1-e88.

10. McCabe, P.J., *What patients want and need to know about atrial fibrillation.* J Multidiscip Healthc, 2011. **4**: p. 413-419.

11. Gallagher, C., et al., *Lifestyle management to prevent and treat atrial fibrillation.* Expert review of cardiovascular therapy, 2016. **14**(7): p. 799-809.

12. National Institute for Health and Care Excellence. *Atrial fibrillation: management*. 2014 18 June 2014; Available from: http://nice.org.uk/guidance/cg180

13. Ogilvie, I.M., et al., *Underuse of oral anticoagulants in atrial fibrillation: a systematic review.* The American journal of medicine, 2010. **123**(7): p. 638-645. e4.

14. Siu, C.-W., et al., *Risk of stroke and intracranial hemorrhage in 9727 Chinese with atrial fibrillation in Hong Kong.* Heart Rhythm, 2014. **11**(8): p. 1401-1408.

15. Devereaux, P., et al., *Differences between perspectives of physicians and patients on anticoagulation in patients with atrial fibrillation: observational studyCommentary: Varied preferences reflect the reality of clinical practice.* Bmj, 2001. **323**(7323): p. 1218.

16. Alonso-Coello, P., et al., *Values and preferences for oral antithrombotic therapy in patients with atrial fibrillation: physician and patient perspectives.* Health Expectations, 2015. **18**(6): p. 2318-2327.

17. Pugh, D., J. Pugh, and G.E. Mead, *Attitudes of physicians regarding anticoagulation for atrial fibrillation: a systematic review.* Age and ageing, 2011. **40**(6): p. 675-683.

18. Li, P.W.C. and D.S.F. Yu, *Under-utilization of oral anticoagulants for stroke prevention in patients with atrial fibrillation: What's the nurses' role in addressing this service gap?*, in *Sixth Pan-Pacific Nursing Conference and First Colloquium on Chronic Illness Care*. 2016: Hong Kong p. 60.

19. Yao, X., et al., *Effect of adherence to oral anticoagulants on risk of stroke and major bleeding among patients with atrial fibrillation.* Journal of the American Heart Association, 2016. **5**(2): p. e003074.

20. Coleman, C.I., M. Tangirala, and T. Evers, *Medication adherence to rivaroxaban and dabigatran for stroke prevention in patients with non-valvular atrial fibrillation in the United States.* International journal of cardiology, 2016. **212**: p. 171-173.

21. Andrade, J., et al., *The clinical profile and pathophysiology of atrial fibrillation.* Circulation research, 2014. **114**(9): p. 1453-1468.

22. Rivera-Caravaca, J.M., et al., *Non-vitamin K antagonist oral anticoagulants: impact of non-adherence and discontinuation.* Expert Opinion on Drug Safety, 2017: p. 1-12.

23. Mehall, J.R., et al., *Absence of correlation between symptoms and rhythm in "symptomatic" atrial fibrillation.* The Annals of thoracic surgery, 2007. **83**(6): p. 2118-2121.

24. McCabe, P.J., et al., *Knowledge and self-management behaviors of patients with recently detected atrial fibrillation.* Heart & Lung: The Journal of Acute and Critical Care, 2008. **37**(2): p. 79-90.

25. Menezes, A.R., et al., *Lifestyle modification in the prevention and treatment of atrial fibrillation.* Progress in cardiovascular diseases, 2015. **58**(2): p. 117-125.

26. Nasser, S., J. Mullan, and B. Bajorek, *Challenges of older patients' knowledge about warfarin therapy.* Journal of primary care & community health, 2012. **3**(1): p. 65-74.

27. Gillis, A.M., et al., *Treating the right patient at the right time: an innovative approach to the management of atrial fibrillation.* Canadian Journal of Cardiology, 2008. **24**(3): p. 195-198.

28. Carter, L., et al., *An integrated management approach to atrial fibrillation.* Journal of the American Heart Association, 2016. **5**(1): p. e002950.

29. Hendriks, J.M., et al., *Nurse-led care vs. usual care for patients with atrial fibrillation: results of a randomized trial of integrated chronic care vs. routine clinical care in ambulatory patients with atrial fibrillation.* European heart journal, 2012. **33**(21): p. 2692-2699.

30. Hendriks, J.M., et al., *The effect of a nurse-led integrated chronic care approach on quality of life in patients with atrial fibrillation.* Europace, 2014. **16**(4): p. 491-499.

31. Hendriks, J., et al., *Cost-effectiveness of a specialized atrial fibrillation clinic vs. usual care in patients with atrial fibrillation.* Europace, 2013. **15**(8): p. 1128-1135.

32. Stewart, S., et al., *Standard versus atrial fibrillation-specific management strategy (SAFETY) to reduce recurrent admission and prolong survival: pragmatic, multicentre, randomised controlled trial.* The Lancet, 2015. **385**(9970): p. 775-784.

33. Organization, W.H., *Innovative care for chronic conditions: building blocks for actions: global report.* 2002.

34. Newman, S., L. Steed, and K. Mulligan, *Self-management interventions for chronic illness.* The Lancet, 2004. **364**(9444): p. 1523-1537.

35. Anderson, R.M. and M.M. Funnell, *Patient empowerment: myths and misconceptions.* Patient education and counseling, 2010. **79**(3): p. 277-282.

36. Feste, C. and R.M. Anderson, *Empowerment: from philosophy to practice.* Patient education and counseling, 1995. **26**(1): p. 139-144.

37.   Aujoulat, I., W. d'Hoore, and A. Deccache, *Patient empowerment in theory and practice: polysemy or cacophony?* Patient education and counseling, 2007. **66**(1): p. 13-20.

38.   Bodenheimer, T., et al., *Patient self-management of chronic disease in primary care.* Jama, 2002. **288**(19): p. 2469-2475.

39.   Norris, S.L., et al., *Self-management education for adults with type 2 diabetes.* Diabetes care, 2002. **25**(7): p. 1159-1171.

40.   Anderson, R.M., et al., *Patient empowerment: results of a randomized controlled trial.* Diabetes care, 1995. **18**(7): p. 943-949.

41.   Freedman, B., et al., *Screening for Atrial Fibrillation: A Report of the AF-SCREEN International Collaboration.* Circulation, 2017. **135**(19): p. 1851-1867.

42.   Tang, T.S., et al., *Self-management support in "real-world" settings: an empowerment-based intervention.* Patient education and counseling, 2010. **79**(2): p. 178-184.

43.   Wu, S.F.V., et al., *A self-management intervention to improve quality of life and psychosocial impact for people with type 2 diabetes.* Journal of clinical nursing, 2011. **20**(17-18): p. 2655-2665.

44.   Moattari, M., et al., *The effect of empowerment on the self-efficacy, quality of life and clinical and laboratory indicators of patients treated with hemodialysis: a randomized controlled trial.* Health and Quality of life outcomes, 2012. **10**(1): p. 115.

45.   Cohen, J., *A power primer.* Psychological bulletin, 1992. **112**(1): p. 155.

46.   Harrington, J., L.M. Noble, and S.P. Newman, *Improving patients' communication with doctors: a systematic review of intervention studies.* Patient education and counseling, 2004. **52**(1): p. 7-16.

47.   National Institute for Health and Care Excellence. *Patient decision aid: Atrial fibrillation: medicines to help reduce your risk of a stroke – what are the options?* 2014; Available from: http://guidance.nice.org.uk/CG180/PatientDecisionAid/pdf/English.

48.   Man-Son-Hing, M., et al., *A patient decision aid regarding antithrombotic therapy for stroke prevention in atrial fibrillation: a randomized controlled trial.* Jama, 1999. **282**(8): p. 737-743.

49.   Yan, J., et al., *Translation and validation of a Chinese version of the 8-item Morisky medication adherence scale in myocardial infarction patients.* Journal of evaluation in clinical practice, 2014. **20**(4): p. 311-317.

50.   Spertus, J., et al., *Development and validation of the Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT) Questionnaire in patients with atrial fibrillation.* Circulation: Arrhythmia and Electrophysiology, 2010: p. CIRCEP. 110.958033.

51.   Leung, C., et al., *Validation of the Chinese-Cantonese version of the Hospital Anxiety and Depression Scale and comparison with the Hamilton Rating Scale of Depression.* Acta Psychiatrica Scandinavica, 1999. **100**(6): p. 456-461.

52.   Elo, S. and H. Kyngäs, *The qualitative content analysis process.* Journal of advanced nursing, 2008. **62**(1): p. 107-115.