Examining adherence to medication in patients with atrial fibrillation: The role of medication beliefs, attitudes and depression.

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Abstract

Background/Objectives: This study examined whether beliefs about medicines, drug attitudes, and depression independently predicted anticoagulant and antiarrhythmic adherence (focusing on the implementation phase of nonadherence) in patients with atrial fibrillation(AF).

Methods: This cross-sectional study was part of a larger longitudinal study. Patients with AF (*N* = 118) completed the Patient Health Questionnaire-8. The Beliefs about Medicines Questionnaire, Drug Attitude Inventory, and Morisky-Green-Levine Medication Adherence Scale (self-report adherence measure), related to anticoagulants and antiarrhythmics, were also completed. Correlation and logistic regression analyses were conducted.

Results: There were no significant differences in non-adherence to anticoagulants or antiarrhythmics. Greater concerns ($r = 0.23$, $P = .01$) were significantly, positively associated with anticoagulant nonadherence only. Depression and drug attitudes were not significantly associated with anticoagulant/antiarrhythmic adherence. Predictors reliably distinguished adherers and non-adherers to anticoagulant medication in the regression model, explaining 14% of the variance, but only concern beliefs (odds ratio, 1.20) made a significant independent contribution to prediction ($\chi 2 = 11.40$, $P = .02$, with df = 4). When entered independently into a regression model, concerns (odds ratio, 1.24) significantly explained 10.3% of the variance ($\chi 2 = 7.97$, $P = .01$, with df = 1). Regressions were not significant for antiarrhythmic medication ($P = .30$).

Conclusions: Specifying medication type is important when examining nonadherence in chronic conditions. Concerns about anticoagulants, rather than depression, were significantly associated with non-adherence to anticoagulants but not antiarrhythmics. Anticoagulant concerns should be targeted at AF clinics, with an aim to reduce nonadherence and potentially modifiable adverse outcomes such as stroke.

KEY WORDS: anticoagulants, antiarrhythmic agents, atrial fibrillation, attitudes, depression, health knowledge, medication adherence.

Introduction

The ABC Taxonomy defines adherence as the process by which patients take their prescribed medications.[1] Adherence consists of three processes including initiation (adherence to the first prescribed doses of medication), implementation (correspondence of the dosage with the prescribed regimen) and discontinuation (the end of therapy). Persistence of continuation with the recommended dosage refers to the time between initiation and discontinuation.[2] Non-adherence can lead to increased morbidity, mortality and increased healthcare costs.[3,4] Consequently, much literature focusses on understanding factors leading to non-adherence, aiming to enhance long-term adherence.

There has been little research conducted on understanding medication non-adherence in patients with atrial fibrillation (AF). AF is an irregular heart rhythm associated with a five-fold increased risk of stroke and invasive symptoms including dyspnoea and heart palpitations. [5,6] Antiarrhythmic medication is prescribed to alleviate symptoms, and anticoagulants (vitamin k-antagonists such as warfarin, or novel oral anticoagulants (NOACS) such as apixaban) prevent thromboembolism.

Taking anticoagulants correctly and achieving therapeutic International Normalised Ratio (INR) levels decreases stroke-risk by two-thirds and reduces stroke-related mortality and severity in patients taking warfarin. [7,8] Comparable effectiveness in reducing stroke is also achieved using NOACS.[9] Despite this, adherence to warfarin is low; as outlined by one study which measured adherence using the Medication Event Monitoring System (MEMS) which recorded time and date of pill bottle opening. This study measured non-adherence as a percentage of the number of days with no bottle openings when the patient was instructed to take medication, during the observed period. The study found that 36% of patients were non-adherent to warfarin 20% of the time.[10] Adherence data related to NOACS is limited due to their recent introduction, however a systematic review suggests adherence to NOACS

(measured using various methods, e.g. INR readings, questionnaires and MEMS) may be better than to warfarin, despite NOACs presenting additional challenges to adherence, such as adverse gastrointestinal issues. [11] Additionally, it is important to examine non-adherence to NOACS which have a shorter half-life to warfarin, so missed doses leave patients with greater stroke-risk.[12]

Unlike anticoagulants which prevent long term consequences of AF, antiarrhythmics treat AF symptoms. Antiarrhythmic adherence is high. For example, in a placebo-controlled trial of 665 patients, adherence to amiodarone was 98.1%.[13] Alleviation of 'concrete' symptoms may be viewed by patients as more necessary than reduction of a long-term threat (i.e. stroke). [14]

Factors related to general non-adherence, such as forgetting, may affect both anticoagulants and antiarrhythmics, however as the two AF medications are taken for different reasons, there may also be specific reasons for non-adherence. For antiarrhythmics, perceptions of symptom-severity may guide medication-taking, whilst beliefs about medications (i.e. concerns about side-effects) may link to anticoagulant non-adherence. A recent qualitative study suggested patients have negative perceptions about the potential harm of anticoagulants, but not antiarrhythmics. [15] Negative beliefs about anticoagulants may arise as vitamin-k antagonists, such as warfarin, require frequent INR monitoring to ensure patients are within therapeutic range (2.0-3.0), balancing bleeding complications with under-dosing and stroke-risk.[16] Dietary and drug interactions which affect INR, frequent INR-monitoring, and perceptions of warfarin as 'rat poison' add to greater perceived disease burden and may contribute to non-adherence. [15,17] These negative beliefs may not apply to NOACS which do not have dietary interactions or require frequent monitoring.[11] To our knowledge, no previous research has been conducted into beliefs about NOACS and quantitative research is needed to confirm the relationship between negative beliefs about anticoagulants and adherence.

The Common Sense Model (CSM) is a widely used as framework in quantitative research predicting non-adherence in long-term conditions (LTCs).[18] The extended CSM outlines that patients' beliefs about illness and treatment drive coping behaviours such as taking medication. Appraisal of coping behaviours as successful or unsuccessful in managing illness may then feedback to change cognitive representations of illness and treatment, thus outlining a dynamic self-regulatory process. Treatment beliefs include 1) necessity beliefs, relating to the perceived need for treatment and 2) concern beliefs, relating to side effects, dependence and tolerance to medication. [19,20] Treatment beliefs are a stronger predictor of adherence than clinical or demographic variables. [19] Two widely used self-report questionnaires, have been used to measure patients' beliefs about treatments. These include the Beliefs about Medicines Questionnaire (BMQ) and the Drug Attitude Inventory (DAI).[21,22]

The DAI examines attitudes towards medications, having been used in a range of LTCs including cardiovascular samples such as hypertension.[23-27] Similarly, the BMQ, which has two dimensions measuring general and specific medication beliefs has been used in cardiovascular populations, predicting adherence in hypertension and heart failure. [19,28,29]

To our knowledge no previous research has examined the DAI in AF patients. However, one study used both the BMQ-General and BMQ-Specific to examine medication beliefs in AF. The study found that specific concerns including poor understanding, and negative long-term effects of medication, predicted better physical health over 12 months.[30] This study argued that concerns prompted greater information seeking, which related to better adherence, and therefore better physical health.[30] However, this study did not measure adherence, did not specify medication-type, or examine beliefs about specific AF-medications.

In addition to medication beliefs, mood may also relate to medication non-adherence.

In particular, AF patients report higher levels of depression than the general population, with approximately one-third reporting elevated depression scores.[31,32] Depression has been found to independently predict adherence in LTCs including cardiovascular populations with similar co-morbidities and risk factors, to AF. [33,34,35,36] However, no previous studies have examined whether depression predicts adherence in AF.

The current study aimed to examine adherence to anticoagulant and antiarrhythmic medication in AF patients. Furthermore, the association between beliefs about medicines, drug attitudes, depression and adherence to anticoagulant and antiarrhythmic medication were explored. Specific hypotheses were: 1) Non-adherence will be significantly higher in warfarin than NOACs and higher in anticoagulants than antiarrhythmics. 2) Specific beliefs about medicines (lower perceived necessity and higher perceived concerns) and more negative attitudes to drugs will be significantly associated with greater non-adherence to anticoagulants than antiarrhythmic medications. 3) Symptomatic patients will be significantly more adherent to antiarrhythmics than asymptomatic patients. 4) Higher depression scores will be significantly associated with non-adherence to anticoagulant and antiarrhythmic medications. 5) Greater concerns and necessity-beliefs, and more negative attitudes to drugs will be significantly associated with depression. 6) Beliefs about medicines (higher concerns and lower necessity), negative attitudes to medication and depression will significantly independently predict non-adherence to anticoagulant medications.

Method

The study was approved by the National Health Service Research Ethics committee (London Bloomsbury REC: 14/LO/2148). This was a small baseline study embedded within a large longitudinal study. As part of a larger study, 386 participants were approached in clinic. Questionnaires were given to 246 eligible clinic patients (63%) who consented to participation, of whom 174 returned questionnaires (71%). Thirty-two Atrial Fibrillation

Association (AFA) patients responded to the online advert and 27 eligible patients (85%) who consented to participation, were sent the questionnaire, of whom 24 (84%) responded. In total, 73% of questionnaires were returned. For the current study, patients who were not taking anticoagulants or antiarrhythmics were excluded. The sample consisted of 166 clinic patients (88%) and 21 AFA patients (12%). Of these, 118 participants were included who were prescribed both anticoagulants and antiarrhythmic medication.

Participants

Participants over the age of 18 were recruited from cardiology pre-assessment clinics and online via the AFA website. Eligibility criteria included patients with a clinical diagnosis of persistent AF, prescribed anticoagulants and antiarrhythmics. Medication adherence was not an eligibility requirement. Patients with severe co-morbidities (active cancer, severe heart failure and recent diabetes-related hospitalisation) were excluded from the study.

Measures

Demographics were examined, including age, gender, ethnicity, and self-reported symptom status (asymptomatic/symptomatic). Questionnaires examining adherence, medication beliefs and drug attitudes were modified to relate to anticoagulant medication and antiarrhythmic medication.

The Beliefs about Medicines Questionnaire-Specific (BMQ) The BMQ-Specific is widely validated in LTCs and a more useful predictor of adherence than the BMQ-General, with better psychometric properties.[22,37-40] Therefore the current study used the BMQ-specific. The BMQ-specific has evidenced good internal consistency, test-retest reliability and discriminant validity.[22] The BMQ-specific consists of two components; concerns (5 items) and necessity (5 items), scored on a five-point Likert-type scale, from '*strongly disagree'* to '*strongly agree'.* The necessity-concerns differential is calculated by subtracting the total concerns score from the total necessity score, resulting in a range of +20 to -20

demonstrating generally stronger necessity and concerns beliefs respectively. The necessity-concerns differential consistently predicts non-adherence in a range of LTCs except cardiovascular disease. [40,41] This may be due to the wide range of medications prescribed for cardiovascular patients. Based on this evidence, and because the current study was specifically interested in individual factors associated with adherence, the focus of reporting was on the concerns and necessity components, rather than the combined differential. Good Cronbach's alpha was indicated for the BMQ specific related to antiarrhythmics (α= .77) and anticoagulants (α= .78) in the current sample.

The *Drug Attitude Inventory* (DAI) has evidenced good test-retest reliability and validity in the 30- and 10-item versions, however the DAI-10 is superior in clinical settings. [21,42] A shorter 6-item version of the DAI (DAI-6) was validated following suggestions of improving the DAI-10. [43] The DAI-6 was scored dichotomously (yes/no). Total score was rated on a continuum of 0-6. Higher scores (> 3) indicate more negative attitudes to medication and lower scores (≤ 3) indicate more positive attitudes to medications. Negative-attitude items related to perceived side-effects of medication, *('my anticoagulants make me feel tired and sluggish'*), whereas positive-attitudes related to perceived health benefits of taking medications, *('by staying on anticoagulants I can prevent myself from getting ill'*). Moderate and low Cronbach's alpha scores were found for the DAI related to anticoagulants (α= .46) antiarrhythmics (α= .29).

The *Morisky-Green-Levine Medication Adherence Scale* (MGLS) is a 4-item measure of adherence, scored dichotomously (yes/no), demonstrating concurrent and predictive validity and good reliability, having been used in a range of clinical trials, with cardiovascular patients and in AF patients prescribed anticoagulants.[44-48] Higher scores indicate greater non-adherence. Participants were classified as non-adherent (≥ 1) and adherent (0) in the regression analyses, as consistent with commonly used dichotomous

scoring for the MGLS, allowing for greater clinical relevance. [45,47-49] Cronbach's alpha indicated low-moderate reliability in antiarrhythmics (α= .45) and anticoagulants (α= .24) in the current sample.

The *Patient Health Questionnaire-8* (PHQ-8), measuring depression is scored on a 4-point Likert-type scale and items are summed for total depression score. A score of ≥ 10 can be used to detect clinically-relevant depression. The PHQ-8 has excellent construct validity, has been validated in cardiovascular populations, and in clinical settings. [50,51] Good reliability was evidenced for the PHQ-8 (α= .87)

Procedure

The direct care team approached patients in clinics, to ask if they were interested in participating in the research. If individuals were interested in participating, they were screened for eligibility by researchers. Eligible patients received an information sheet and consent form to read. Informed consent was given by patients who wished to take part. Patients were given both versions of the BMQ, DAI-6 and MGLS relating to antiarrhythmics and anticoagulants, and the PHQ-8. Patients returned completed questionnaires to researchers in the clinic, or by post. Patients identified through the AFA online advertisement were directed to an electronic version of the information sheet and consent form and screened for eligibility before eligible patients completed an electronic version of the questionnaire. All patients were thanked, debriefed and given the opportunity to contact researchers.

Statistical Analyses

Descriptive statistics were examined, including tests of normality in SPSS (V25). The 95% confidence level was used to indicate significance. Correlations (Pearson) between beliefs about medicines (concerns and necessity beliefs), drug attitudes, depression and adherence were conducted. Adherence was measured as a continuous variable when conducting correlations to provide a more realistic representation of adherence while retaining statistical

power.[52] When conducting regression analyses, adherence was measured as binary, to classify patients into more clinically relevant dichotomous groups (adherent and non-adherent), to be targeted for future interventions.[53] T-tests were conducted for symptomatic status and gender, which are risk factors for non-adherence in cardiovascular patients. [45,54]

Multiple logistic regression was used to examine adherence to anticoagulants and antiarrhythmics. The enter method was used and all predictor variables including drug attitudes, beliefs about medicines, and depression, but excluding the BMQ differential due to multicollinearity were entered at once, as although previous research has indicated that these factors may affect adherence, it makes no assumptions about the order the data is entered.[55,56]

Results

Table 1 summarises the demographic characteristics of the sample. Participants had a mean age of 63.52 (*SD* = 8.82). The majority were white, married and had GCSE qualifications or above. For anticoagulants, about half of patients were taking warfarin (53.4%) with the rest taking NOACs (rivaroxaban, 28.8%; apixaban, 11.9%; and other, 5.9%). For antiarrhythmics, approximately half were taking betablockers (50.8%), followed by amiodarone (20.2%), flecainide (8.8%) and other (21.1%).

[INSERT TABLE 1 ABOUT HERE]

Table 2 shows mean outcome scores. Mean PHQ-8 score for the whole sample was 5.40 (SD = 4.92) representing mild depressive symptoms. 17.8% showed clinically relevant depression scores (i.e. ≥ 10). Based on mean scores, patients had more positive than negative drug attitudes to both antiarrhythmics and anticoagulants, with lower scores (i.e. < 3) indicating more positive attitudes to medications). A paired samples t-test indicated significantly greater positive attitudes to anticoagulants (M= 1.64, SD= 0.98) compared to antiarrhythmics (M= 1.97, SD = 1.11) ($t(118) = 3.22$, p= .002). Mean BMQ scores were similar between anticoagulants and

antiarrhythmics. Paired samples t-tests indicated that necessity beliefs did not significantly differ between antiarrhythmics (M= 16.58, SD= 3.46) and anticoagulants (M= 16.30, SD= 3.46) (*t*(117) = -.88, p= 0.38). However, patients held significantly greater concerns about antiarrhythmic medication (M= 14.34, SD= 3.37) than anticoagulant medication (M=13.64, SD = 3.35) (*t*(117)= -2.43, p= .02.) Mean MGLS scores were similar in antiarrhythmics (79.3%) than anticoagulants (79.7%). A paired samples t-test indicated no significant differences between antiarrhythmic (M= .25, SD= .54) and anticoagulant adherence (M= .24, SD= .50) *t*(115)= 0.39, p= .67. A moderate significant correlation between adherence scores for antiarrhythmics and anticoagulants was evidenced (r= .59, p< .001). When examining anticoagulant sub-groups, adherence was higher in patients taking warfarin (82.5%) than NOACs (73.5%). However, an independent samples t-test revealed no significant differences between adherence in warfarin (M = .22, SD = .52) and NOACS (M = .25, SD = .48, t(116) -.35, p = .73).

In antiarrhythmics, adherence was highest for amiodarone and dronedarone (86.4%), followed by beta-blockers (84.7%) and flecainide (70%). When comparing adherence to beta-blockers (the most prescribed antiarrhythmic medication at 50.8%) with other antiarrhythmics (including amiodarone, flecainide, dronedarone), an independent samples *t*-test found no significant differences in adherence to beta-blockers (M = .18, SD = .47) and other antiarrhythmics (M = .33, SD = .60, t(108) 1.45, p = .15).

[INSERT TABLE 2 ABOUT HERE]

Antiarrhythmic medication

Correlations were conducted between the BMQ, DAI-6, PHQ-8 and the MGLS for patients taking antiarrhythmics. Depression was not significantly associated with antiarrhythmic non-adherence. No significant correlations were found between the BMQ, (concerns, necessity or the differential) and drug attitudes, with antiarrhythmic non-adherence (See Table 3).

However, greater concerns (r =.28, p = .002), and more negative drug attitudes (r = .20, p = .03) were associated with higher depression scores. More negative attitudes were also significantly associated with greater concerns as expected (r = .29, p = .001) and the necessity/concerns differential (r = -.25, p = .006). T-tests between symptomatic status (t(116) =-.53, p = .60) and gender; t(111) = -.03, p = .98) with antiarrhythmic adherence were non-significant and were therefore not included in subsequent analyses to reduce the number of parameters.

[INSERT TABLE 3 ABOUT HERE]

Multiple logistic regression was conducted, examining necessity and concern beliefs, drug attitudes and depression on adherence. In relation to antiarrhythmics, a test of the full model against the constant only model was not statistically significant, indicating depression, drug attitudes, concerns and necessity, did not reliably predict non-adherence *(Chi square* = 5.29, p = .26 with df = 4*).* See Supplementary Materials Table S1.

Anticoagulant medication

Table 4 presents the correlations between the BMQ, DAI-6, PHQ-8 and MGLS for anticoagulants. Depression was not significantly associated with anticoagulant non-adherence. Higher concerns were significantly positively correlated with greater non-adherence (r = .23, p= .01; see Table 4). More negative drug attitudes towards anticoagulants were significantly associated with greater concerns (r =.24, p =.01) and negatively associated with the BMQ differential (r = -.30, p = .001) but not depression (r =.11, p = .22) and necessity beliefs (r = -.11, p = .24). Concerns were not significantly associated with depression (r = .10, p = .31). T-tests between symptomatic status (t(116)= .51, p = .61) and gender (t(111) = -.30, p = .77), with anticoagulant non-adherence were not significant and therefore were not entered into the regression model.

Correlations examining anticoagulant-type, found that for warfarin (n = 63), concern (r = .03, p = .83) and necessity beliefs (r = .12, p = .36), the BMQ differential (r = .07, p = .58), drug attitudes (r = .07, p = .61) and depression (r = .02, p =.87) were not significantly associated with non-adherence. In NOACs (n =55) concern beliefs (r = .55 , p < .001) and the BMQ differential (r = -.38, p = .004) were significantly correlated with non-adherence, however necessity beliefs (r = .09, p = .53), drug attitudes (r = .23, p =.09) and depression (r = .13, p = .36) were not significantly associated with non-adherence.

[TABLE 4 ABOUT HERE]

In relation to anticoagulants, a test of the full model against the constant only model was statistically significant, indicating predictors reliably distinguished adherers and non-adherers to anticoagulant medication (*Chi square* = 11.40, p = .02 with df = 4) (Table 5). Results of the multiple logistic regression for anticoagulants showed R^2 of .145, indicating a weak relationship between prediction and non-adherence. Prediction success overall was 81.4% (98.9%. for adherent and 12.5% for non-adherent). The Wald criterion demonstrated that only concerns (OR= 1.20) independently made a significant contribution to prediction. To follow-up these results, a logistic regression was conducted with concerns and adherence only. Concerns (OR= 1.24) significantly distinguished adherers and non-adherers (*Chi square* = 7.97, p = 0.01 with df = 1). R^2 was .103 indicating a weak relationship, with concerns explaining 10.3% of the variance. This second analysis indicated that concerns accounted for the majority of the variance.

[INSERT TABLE 5 ABOUT HERE]

Discussion

To our knowledge, no previous research has examined whether depression, beliefs and attitudes to treatment, are associated with adherence in AF patients. We conducted analyses

separately for antiarrhythmic and anticoagulant medications. Although we predicted non-adherence would be higher in the latter, there were no significant differences in non-adherence to these medications (hypothesis one). This is consistent with a previous study which indicated no difference in adherence between patients taking vitamin K antagonists or NOACS using the MGLS.[45] In relation to the second hypothesis (that lower necessity-beliefs, higher concern-beliefs, and more negative attitudes to drugs would be associated with greater non-adherence) only greater concerns was associated with greater anticoagulant non-adherence. No significant correlations were found for antiarrhythmic non-adherence. These findings help explain the mixed findings for the relationship between treatment beliefs and non-adherence in cardiology patients. [41] Patients' beliefs about specific types of medication may differ, i.e. anticoagulants may be associated with greater concerns than other medications.

Depression was not correlated with non-adherence to anticoagulants or antiarrhythmics, but was correlated with concerns, necessity, and negative attitudes towards antiarrhythmics (supporting our fifth hypothesis, but not the fourth hypothesis). It is worth noting that beliefs may differ depending on anticoagulant medication sub-type. While previous research has indicated that non-adherence to warfarin may be greater than NOACs,[11] contrary to expectation (hypothesis one), no significant differences in adherence to NOACs and warfarin were found. Further sub-analyses showed that concerns were associated with adherence to NOACS but not with warfarin, although the sample size for this sub-analysis was small so these results should be treated with caution. Regular INR testing and clinic appointments required for warfarin, may help allay concerns and negative attitudes to warfarin, however further research is required to confirm this. Patients may also require further treatment-specific information when first prescribed NOACS. A recent qualitative study found that AF patients experienced anxiety about the side-effects of NOACs, poor

understanding of medication effects, and highlighted the need for support and information from health care professionals.[57]

The lack of relationship between BMQ necessity beliefs and adherence to anticoagulants, (hypothesis two) is in line with a systematic review which found no correlation between necessity beliefs and adherence in cardiovascular populations such as stroke and heart failure, and a much stronger relationship between concern beliefs and adherence.[41] As large numbers of medications are prescribed to cardiovascular patients, some patients may be unable to ascertain the therapeutic mechanisms of individual medications, and the necessity of each in improving health-related outcomes.[58] This is supported in AF patients by a qualitative study which reported AF patients' difficulty in identifying the benefits of individual treatments. [15]

Poor knowledge of the necessity for warfarin is well documented; One study found that a majority of patients were unable to name one risk or benefit of warfarin or the reason for taking it.[59] A previous intervention in AF patients, which focused on improving understanding of warfarin and reducing perceptions of harm, significantly improved adherence and time spent in the therapeutic range.[57] To further outline results relating to hypothesis two, our data suggest that targeting patients' concerns towards anticoagulants, is particularly important for non-adherence to anticoagulants. This may be because more generic attitudes towards medications, rather than specific concerns, are less likely to predict outcomes such as adherence. [40]

For antiarrhythmics, as predicted in hypothesis two, no significant correlations between medication beliefs and attitudes, with adherence, were found. While mean concern scores significantly differed between antiarrhythmics and anticoagulants, the effect of this was small (14.34 and 13.64). It may be that specific concerns differ between medications. For instance, more serious consequences are associated with non-adherence to anticoagulants (i.e.

stroke) than non-adherence to antiarrhythmics (i.e. palpitations), which may be associated with an increased likelihood of non-adherence. Negative lay beliefs about warfarin may also affect medication choice and adherence. In a randomised trial, patients were more likely to take warfarin if they were blinded to the medication-name. Once unblinded, 46% of patients switched to a different medication. [60]

Hypothesis three, that symptomatic patients would be more adherent to antiarrhythmics than asymptomatic patients, was not supported. Initially it was thought that the benefits of taking antiarrhythmics were more identifiable to patients as they led to symptomatic-relief, and therefore patients would be more adherent to this medication, in comparison to anticoagulants which do not reduce symptoms, but reduce the risk of stroke. A more robust measure of symptom severity could help to fully examine the effect of symptoms on antiarrhythmic non-adherence in AF patients. However, as discussed above, patients may not be able to identify the efficacy of individual prescribed medications.

The fourth hypothesis proposed that higher depression scores would be significantly associated with non-adherence to anticoagulant and antiarrhythmic medications, however this was not supported in the current study for either medication group. Contrary to research in other cardiovascular populations, depression was not associated with adherence to anticoagulants or antiarrhythmics. Comparable levels of depression in our sample, with other cardiovascular populations, which have found an association between adherence and depression, suggest that non-significant associations are not due to issues of power. However, in comparison to other AF samples, which found 32-38% of patients met the criteria for depression, levels of depression in the current study were much lower (18%).[32,61] It may be that depression is a secondary indicator of non-adherence, as it is associated with other factors related to non-adherence. One prospective study of 156 patients, which found no relationship between depression and warfarin adherence, suggested that non-adherence (as

measured by MEMS caps) was associated with factors related to depression, including social isolation and lack of receptivity to illness-related information from clinicians. [62]

In line with this, our results supported the fifth hypothesis that greater concerns and necessity-beliefs, and more negative attitudes to drugs were associated with greater depression in antiarrhythmics. However, this was not fully supported in anticoagulants, in which only greater concerns were associated with higher depression. While depression is not associated directly with adherence, depression may be a marker for non-adherence through an association with negative beliefs about medicines. However, it may be more accurate to profile for non-adherence on concerns about medications rather than mood. Additional research using mediation or path analysis could further examine the associations between depression, medication beliefs and adherence.

This was the first study to examine the association between attitudes, beliefs about medication, and depression in AF patients with adherence to antiarrhythmic and anticoagulant medication. However, it is important to recognise the limitations of the study. The sample size of our study (n =118), while comparable to other samples examining AF adherence,[63] was small. [48] In addition, we only examined patients with persistent AF and therefore our results may not be representative of other AF patients, or general patients taking anticoagulants. High reported adherence in our study may be a result of identifying participants through a hospital clinic and online website, who may have been more highly motivated. This may explain low levels of depression found in the study. Overestimation of adherence may also be due to using a self-report measure which is prone to bias and measurement errors. Similarly, two recent studies using the MGLS also evidenced comparably high levels of adherence. [47,48] The MGLS is a more indirect measure of adherence compared to pill counts, as it examines patients' attitudes to medication adherence. [47] Electronic methods could be used in conjunction with self-report measures to triangulate

results and improve the reliability of measuring adherence. [64] An additional limitation of the study is the low reliability reported for the DAI and MGLS. Low reliability may be due to small sample size, however future research could consider factor analysing these questionnaires in antiarrhythmic and anticoagulant populations. Modifying questionnaires to more specifically capture AF medication beliefs and behaviours would likely improve reliability. The sample consisted of patients taking both anticoagulants and antiarrhythmics, and did not aim to compare differences, rather it aimed to explore relationships and potential correlates of non-adherence, so caution is required when interpreting differences between medication groups. While statistically, patients prescribed only one type of medication could be compared, practically, polypharmacy is very common in AF patients, with the majority prescribed both anticoagulants and antiarrhythmics. Due to the cross-sectional nature of the research causation was not implied. Consequently, further longitudinal research could examine whether concern-beliefs predict adherence to anticoagulants.

In conclusion, our findings were partly consistent with the extended CSM. Concerns about anticoagulants explained a small percentage of the variance in anticoagulant non-adherence. No correlations were found with antiarrhythmic-adherence, indicating factors other than medication beliefs, drug attitudes, gender and symptomatic status, should be examined. When accounting for all variables, the most important factor associated with non-adherence was patients' anticoagulant concerns. Targeting anticoagulant-concerns at pre-assessment clinics, by delivering tailored advice and information, may help to reduce non-adherence. Additional longitudinal research should identify possible profiles of non-adherent AF patients to be targeted for future intervention.

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585 *Table 1*. Demographic characteristics and medication details of the sample.

Demographic variable (N=118)	Number (%)
Sex n (%)	
Male	90 (76.3)
Ethnicity n (%)	
White British/Irish/Any other white background	117 (99.2)
Other	1 (0.9)
Antiarrhythmic medication	
Betablockers	60 (50.8)
Amiodarone	23 (20.2)
Other	24 (21.1)
Flecainide	10 (8.8)
Anticoagulant medication	
Warfarin	63 (53.4)
NOACs	55 (46.6)
Rivaroxaban	34 (28.8)
Apixaban	12 (11.9)
Other	7 (5.9)
Relationship status	
Married/co-habiting	85 (72.0)
Education	
GCSE and above	100 (84.8)
Work status	
Retired	54 (45.8)
Employed (full or part-time)	46 (39.0)

586 *Note.* GCSE, General Certificate of Secondary Education; MGLS, Morisky Green Levine
587 Medication Adherence Scale.

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589 *Table 2.* Mean treatment beliefs (BMQ), drug attitudes (DAI-6), and adherence scores for
590 patients taking anticoagulants and antiarrhythmics.

	Antiarrhythmics N=118	Anticoagulants N=118
BMQ-necessity	16.58(SD=3.46)	16.30(SD=3.46)
BMQ-concerns	14.34 (SD=3.37)	13.64 (SD=3.35)
BMQ-differential	2.37 (SD=3.80)	2.66 (SD=4.04)
Drug attitudes (DAI-6)	1.97 (SD=1.11)	1.64 (SD=0.98)
Adherence to medication	0.25 (SD=0.54)	0.24 (SD=0.50)

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Table 3. Correlation matrix indicating relationships between adherence, beliefs about medicines, drug attitudes and depression for antiarrhythmic medication.

	Adherence	**Concerns**	**Necessity**	**Differential**	**Drug attitudes**	**Depression**
Adherence	1					
Concerns	0.17	1				
Necessity	0.03	0.29**	1			
Differential	-0.10	-0.57**	0.57**	1		
Drug attitudes	0.11	0.29**	0.001	-0.25**	1	
Depression	0.16	0.28**	0.16	-0.05	0.20*	1

Note. *p<0.05, **p< 0.01, ***, p< 0.001

Table 4. Correlation matrix indicating relationships between adherence, beliefs about medicines, drug attitudes and depression for anticoagulant medication.

	Adherence	**Concerns**	**Necessity**	**Differential**	**Drug attitudes**	**Depression**
Adherence	1					
Concerns	0.23**	1				
Necessity	0.10	0.27**	1			
Differential	-0.11	-0.61**	0.59**	1		
Drug attitudes	0.14	0.24**	-0.11	-0.30**	1	
Depression	0.08	0.10	0.09	0.002	0.11	1

Note. *p<0.05, **p< 0.01, ***, p< 0.001

622 *Table 5.* Multiple logistic regression examining adherence to anticoagulant medication.

Variable	B	Standard error	*P value*	*Odds ratio*	Lower CI	Upper CI
Depression (PHQ-8)	.04	.05	.36	1.04	.95	1.14
Drug Attitudes (DAI-6)	.34	.25	.17	1.41	.86	2.31
BMQ Concerns	.18	.09	.04	1.20	1.01.	1.42
BMQ Necessity	.06	.08	.57	1.06	.90	1.24
Nagelkerke R^2	.15					
X^2	11.40					

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