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Title: The relationship between knowledge, health literacy and adherence among patients taking oral anticoagulants for stroke thromboprophylaxis in atrial fibrillation

Concise title: Relationship between knowledge and adherence

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Abstract

Background

Patients' knowledge regarding their oral anticoagulant (OAC) treatment for stroke prevention in atrial fibrillation (AF), their level of medication adherence and health literacy are known to affect treatment outcomes. However, contemporary data regarding the relationships between these variables are lacking.

Objective

To investigate the relationships between anticoagulant knowledge, health literacy and self-reported adherence in patients taking warfarin and the directly acting oral anticoagulants.

Methods

A cross-sectional survey was conducted in 48 patients with AF identified from general practices. The Anticoagulation Knowledge Tool (AKT) was used to assess anticoagulation knowledge; the Short Test of Functional Health Literacy in Adults (s-TOHFLA) for health literacy; and the 8-item Morisky Medication Adherence Scale (MMAS) for medication adherence.

Results

Participants had mean scores of 61.6 ± 15.8, 7.2 ± 1.1 and 24.7 ± 9.5 for the AKT, MMAS-8 and s-TOHFLA, respectively. Significant correlations were observed between anticoagulation knowledge and health literacy with medication adherence (0.37, p <0.01 and 0.30, p < 0.05, respectively). Participants with inadequate health literacy had a significantly lower mean knowledge score than those with adequate health literacy (55.8 ± 15.9 vs 66.1 ± 14.4, p <0.05). Participants who self-reported adherence to their OAC had significantly higher knowledge scores than those who did not (67.5 ± 13.3 vs 56.1 ± 16.2, p < 0.05).

Conclusion

Significant correlations between health literacy, OAC knowledge and adherence were observed, and these relationships should to be considered by health professionals responsible for monitoring patients who are prescribed anticoagulants. We also observed serious gaps in OAC knowledge. Interventions designed to optimize the outcomes of anticoagulant treatment need to address these factors.

Introduction

Atrial fibrillation (AF) is associated with significant morbidity and mortality, and stroke resulting from AF presents a large and growing economic concern.[1] Anticoagulation therapy in at risk patients with AF can markedly reduce stroke risk and is therefore an important component of AF management. [1] Under-use of OACs in AF is often reported in terms of under-*prescribing* of treatment, but poor treatment outcomes in people with AF also commonly result from poor adherence or persistence with anticoagulant therapy even when it is prescribed, often with devastating consequences.[2]

Patients' oral anticoagulation knowledge, level of medication adherence and health literacy are known to affect treatment outcomes. However, contemporary data regarding the relationships between these variables are lacking.

Medication adherence in chronic disease is a worldwide problem. Up to 50% of patients are non-adherent to medications, including OACs.[3-5] Limited health literacy is associated with poor warfarin and AF knowledge.[6,7] In addition, poor warfarin knowledge and lack of education about warfarin have been associated with inadequate anticoagulant control and increased hemorrhagic events, and those at highest risk of stroke have been shown to have the poorest knowledge regarding their treatment. [6,8,9] It is unknown whether similar results will be seen in patients who take directly acting oral anticoagulants (DOACs).

The introduction of the DOACs has sought to address some of the pitfalls of warfarin therapy, however there are persisting challenges to overcome; adherence to the drug regimen being the most crucial. Due to their short half-lives, irregular or missed doses can increase the risk of stroke, as the patient will be inadequately anticoagulated during this time. [10,11]

The 2016 European Society of Cardiology (ESC) guidelines for the management of AF recommend an integrated approach to care with particular focus on the patient being central to effective management. Integral to patient centered care is patient education, which in turn empowers self-management and shared decision making. As a European Heart Rhythm Association, priority research area and acknowledged by the ESC guidelines, more research is needed to determine the best way to deliver an integrated approach.[1,12]

Given the interest in integrated AF care, and the lack of contemporary data investigating the relationships between health literacy, adherence behaviors and medication knowledge of patients taking OACs for stroke thromboprophylaxis in AF, the aim of this study was to investigate the relationships between these variables and to assess the strength of the relationship between knowledge and health literacy.

Methods

Recruitment

Participants were recruited to the study from participating general practices or outpatient cardiologist clinics in Tasmania, Australia. Invitation letters with a response form were sent to the practices requesting their participation in the study and asking that patients with AF in their practices be given the opportunity to participate in the study. To be eligible to participate, participants had to be over 18 years of age, have a diagnosis of non-valvular AF, be currently taking

warfarin or DOACs for stroke thromboprophylaxis and be able to provide informed consent. Participants were interviewed either at their regular GP surgery or in their home as these were considered familiar and comfortable surroundings. A $10 AUD shopping voucher was provided to all participants as recruitment incentive and as compensation for their time at the end of the interview.

Data Collection

The interview consisted of four validated questionnaires - the 8-item Morisky Medication Adherence Scale (MMAS-8), Anticoagulant Knowledge Tool (AKT), Short Test of Functional Health Literacy in Adults (s-TOFHLA) and the Atrial Fibrillation Effect on Quality of Life (AFEQT) questionnaire, presented to participants in this order. Participants were introduced to the study using a script and all questionnaires were undertaken in an interview style, with the exception of s-TOHFLA which participants completed by themselves within a seven-minute time limit. Each interview took between 20 and 45 minutes and all were completed in a single session.

Adherence

To assess self-reported adherence behavior, we used the MMAS-8 questionnaire, which asks seven dichotomous questions and one 5-point Likert scale question.[13-15] The validated MMAS-8 was chosen as it has been shown to be a reliable predictor of adherence in patients taking medications for chronic diseases, such as antihypertensives, and has been used to assess adherence in those taking OACs. [14,16,17] In assessing adherence using the MMAS-8, a score of 8 was considered adequate adherence, while a score of less than 8 was considered inadequate adherence.[16]

Knowledge

To assess the level of knowledge of OAC therapy and its role, including participant perceptions/understanding of the risks and benefits, we used the AKT, which was developed to assess the anticoagulant knowledge of patients taking either warfarin or DOACs. A score of '1' or '0' was given for correct and incorrect answers, respectively. Participants taking a DOAC were required to answer only section 'A' with a total maximum score of 25 and participants taking warfarin were required to answer sections 'A' and 'B' with a total maximum score of 35. Final scores were presented as percentages of correct answers for all participants.[18]

Health Literacy

To assess functional health literacy, we used the s-TOFHLA.[19] Dichotomous scoring of '1' for correct answers and '0' for incorrect answers was used and a maximum score of 36 could be achieved. In scoring the s-TOFHLA scale, a score of 23 and above was considered adequate health literacy, while a score of 22 and less was considered inadequate health literacy.[6,20]

Quality of Life

To assess AF specific health related quality of life we used the AFEQT. For AFEQT questions 1-20, responses were scored on a 1 to 7 Likert scale. An overall score of 0-100 could be achieved, corresponding to 'complete disability' to 'no disability', respectively. AFEQT was chosen as it combines the scores from four parameters: symptoms, daily activities, treatment concerns and satisfaction to a single measure with reliability, and has focused questions surrounding the use of anticoagulants.[21,22]

Statistical Analysis

Statistical analysis was performed using SPSS version 24 (IBM, Armonk, New York, US).

Means and standard deviations were used to summarize continuous variables, and independent sample t-tests were used for inferential statistics. s-TOFHLA and MMAS-8 scores were analyzed as both continuous and dichotomous variables. Correlations between AKT, s-TOFHLA and MMAS-8 scores were determined using the Spearman rank coefficient. Logistic regression analysis was used to estimate regression coefficients for AKT and s-TOFHLA against MMAS-8 adherence scores in both univariate and multivariate models. A p value of <0.05 was considered statistically significant for all analyses.

Sample size

Using a 5% margin of error and statistical power of 80%, we determined that a sample size of 40 participants would be sufficient to detect a moderate statistical correlation of 0.4 between the AKT score and s-TOFHLA score with the MMAS-8 adherence score.

Ethics

The Tasmanian Health and Medical Human Research Ethics Committee (reference number H0015395) approved this study. Informed consent was obtained from all individual participants included in the study.

Results

Demographic characteristics

Fifty participants were interviewed. The results of two participants were excluded because they had discontinued their OAC at the time of the interview, leaving data from 48 participants available for analysis. The average age of the participants was 76.4 ± 8.7 years and the majority (77.1%) were male (Table 1). Forty-two percent of participants had either high school education (Year 10 equivalent) or college (Year 12 equivalent) as the highest level of education completed. The majority of the participants were taking a DOAC (64.6%) at the time of the study, and had been taking an anticoagulant for greater than 2 years (75.0%).

Table 1. Demographic characteristics n (%)	
Parameter	**Overall Sample (n= 48)**
Male	37 (77.1)
Age in years (mean +/- SD)	76.4 ± 8.7
Highest education completed n (%)	
High school	14 (29.2)
College	6 (12.5)
Technical/ Vocational	13 (27.1)
Bachelor degree	11 (22.9)
Post graduate	4 (8.3)
Duration of anticoagulant therapy n (%)	
Less than 3 months	1 (2.1)
3-12 months	5 (10.4)
1-2 years	6 (12.5)
Greater than 2 years	36 (75.0)
Oral anticoagulant n (%)	
Warfarin	17 (35.4)
DOAC	31 (64.6)

Association between level of self-reported adherence and health literacy, knowledge and AF-related quality of life

Adequate adherence to the prescribed OAC was reported by 47.9% of participants and this group had a significantly higher total knowledge score than those who were non-adherent (67.5% vs 56.1%, p = 0.011) (Table 2). However, no association between the level of adherence with health literacy and AF-related quality of life was observed.

Table 2. Association between adherence level and study variables

Parameter	Overall Sample (n= 48)	Inadequate Adherence (MMAS-8 Score < 8) (n=25)	Adequate Adherence (MMAS-8 score = 8) (n=23)	p value
Total AKT score	61.6 ± 15.8	56.1 ± 16.2	67.5 ± 13.3	0.011*
s-TOFHLA	24.7 ± 9.5	22.9 ± 9.9	26.7 ± 8.8	0.171
Overall AFEQT	80.1 ± 15.8	81.3 ± 16.7	78.8 ± 14.9	0.593

*p<0.05

Level of health literacy and knowledge

As shown in Table 3, when participants were categorized based on their health literacy scores, those with inadequate health literacy had a significantly lower mean total anticoagulant knowledge score than those with adequate health literacy (55.8 ± 15.9 versus 66.1 ± 14.4, p = 0.02). Furthermore, participants with inadequate health literacy were less likely than those with adequate health literacy to know why they had been prescribed an OAC (57.1% versus 85.2%, p = 0.04), less likely to know how the medication worked (42.9% versus 88.9%, p = 0.001) and less likely to be able to describe one sign of side effects to watch out for whilst taking an anticoagulant (28.6% versus 70.4%, p = 0.03). In addition, only 16.7% of all participants could mention three signs of side effects to watch out for while taking an OAC (Table 3).

Table 3. Anticoagulation knowledge score according to health literacy level

Item	Overall Sample (n= 48) n (%)	Inadequate Health Literacy (n=21) n (%)	Adequate Health Literacy (n=27) n (%)	p value
What is the name of your anticoagulant medicine?	43 (89.6)	17 (81.0)	26 (96.3)	0.119
Why has your doctor prescribed you this medicine?	35 (72.9)	12 (57.1)	23 (85.2)	0.039*
How does this medicine work in your body?	33 (68.8)	9 (42.9)	24 (88.9)	0.001*
How many times a day do you need to take this medicine?	48 (100.0)	21 (100.0)	27 (100.0)	NA
For how long do you need to take this medicine (for example, 3 months, and 6 months, life-long)?	47 (97.9)	20 (95.2)	27 (100.0)	0.329
Why is it important to take this medicine exactly as your doctor has told you? (Stroke)	28 (58.3)	10 (47.6)	18 (66.7)	0.192
Why is it important to take this medicine exactly as your doctor has told you? (bleeding)	1 (2.1)	1(4.8)	0 (0.0)	0.329
Is it important to take this medicine at the same time each day?	42 (87.5)	18 (85.7)	24 (88.9)	0.748
Is it okay to double the next dose of this medicine if you miss a dose?	46 (95.8)	21 (100.0)	25 (92.6)	0.161
Is it possible that skipping one dose of this medicine could worsen your condition?	19 (39.6)	7 (33.3)	12 (44.4)	0.446
Is it appropriate to stop taking this medicine once you feel better?	44 (91.7)	18 (85.7)	26 (96.3)	0.231
Is it safe to take anti-inflammatory medicines like ibuprofen (Nurofen® or Advil®) while you are taking this medicine?	28 (58.3)	15 (71.4)	13 (48.2)	0.105

Is it safe to take vitamin supplements and herbal medicines with this medicine without consulting your doctor?	30 (62.5)	15 (71.4)	15 (55.6)	0.264
Is there any benefit in taking more of this medicine than your doctor has told you to take?	44 (91.7)	18 (85.7)	26 (96.3)	0.231
Will drinking too much alcohol increase the risk of side effects with this medicine?	18 (37.5)	9 (42.9)	9 (33.3)	0.513
Is it necessary to inform a surgeon, dentist or other health professional that you are taking this medicine before undergoing surgery or a procedure?	47 (97.9)	20 (95.2)	27 (100.0)	0.329
Is it important that all the health care practitioners you see know that you are taking this medicine?	47 (97.9)	20 (95.2)	27 (100.0)	0.329
What is the most important side effect of this medicine?	21 (43.8)	7 (33.3)	14 (51.9)	0.208
THREE signs of side effects that you should watch out for while taking this medicine are: (1/3)	25 (52.1)	6 (28.6)	19 (70.4)	0.003*
THREE signs of side effects that you should watch out for while taking this medicine are: (2/3)	15 (31.3)	5 (23.8)	10 (37.0)	0.337
THREE signs of side effects that you should watch out for while taking this medicine are: (3/3)	8 (16.7)	2 (9.5)	6 (22.2)	0.231
THREE things you can do to reduce your risk of side effects are: (1/3)	16 (33.3)	4 (19.1)	12 (44.4)	0.059
THREE things you can do to reduce your risk of side effects are: (2/3)	7 (14.6)	1 (4.8)	6 (22.2)	0.072
THREE things you can do to reduce your risk of side effects are: (3/3)	6 (12.5)	1 (4.8)	5 (18.5)	0.133
What is the best step to take if you accidentally take too much of this medicine?	34 (70.8)	16 (76.2)	18 (66.7)	0.482
Warfarin specific questions				
Item	**Overall Sample (n=17)**	**Inadequate Literacy (n=9)**	**Adequate Literacy (n=8)**	**p value**

	n %	n (%)	n (%)	
What is your target INR range?	11 (64.7)	5 (55.6)	6 (75.0)	0.431
What was your last INR reading?	16 (94.1)	8 (88.9)	8 (100.0)	0.347
Are routine INR tests necessary to know how well this medicine is working?	15 (88.2)	8 (88.9)	7 (87.5)	0.935
Is an INR value above your target range good for your general wellbeing?	13 (76.5)	6 (66.7)	7 (87.5)	0.334
Is it possible for INR values below your target range to be bad for your health?	12 (70.6)	5 (55.6)	7 (87.5)	0.161
Is it possible for what you eat to affect your warfarin therapy?	14 (82.4)	6 (66.7)	8 (100.0)	0.081
If you answered 'Yes' above, list THREE foods that can affect your anticoagulant therapy: (1/3)	12 (70.6)	5 (55.6)	7 (87.5)	0.161
If you answered 'Yes' above, list THREE foods that can affect your anticoagulant therapy: (2/3)	12 (70.6)	5 (55.6)	7 (87.5)	0.161
If you answered 'Yes' above, list THREE foods that can affect your anticoagulant therapy: (3/3)	11 (64.7)	4 (44.4)	7 (87.5)	0.066
List one vitamin that can significantly affect your anticoagulant therapy.	6 (35.3)	2 (22.2)	4 (50.0)	0.259
Total AKT score (%)	61.6 ± 15.8	55.8 ± 15.9	66.1 ± 14.4	0.022*

*p<0.05

Association between adherence, knowledge and health literacy

There were moderate positive correlations between the mean scores of self-reported adherence, anticoagulant knowledge and health literacy (Figure 1). Multivariate analysis showed that anticoagulation knowledge was significantly associated with MMAS-8 score even after adjusting for health literacy score (OR, 1.050; 95% CI, 1.003 – 1.100; p = 0.036), Table 4). There were no statistically significant relationships between total AF specific health related quality of life scores and other study variables.

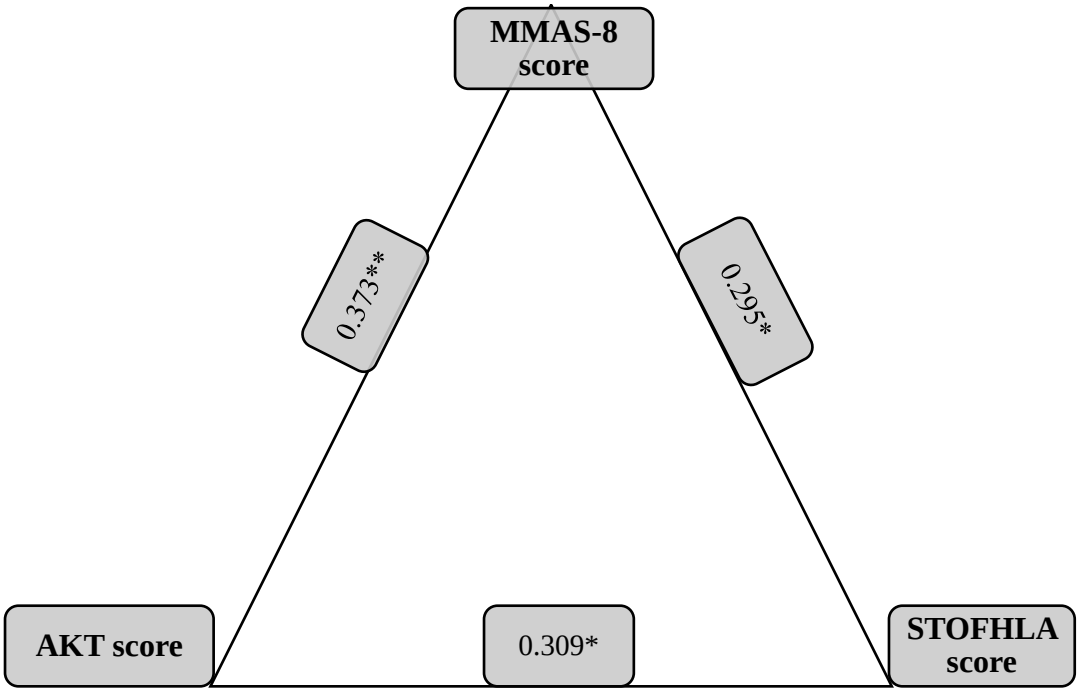

Figure 1 Correlations between study variables

*Correlation is significant at the 0.05 level (2-tailed)
** Correlation is significant at the 0.01 level (2-tailed)

Table 4. Association of knowledge and health literacy scores with MMAS-8 score (logistic regression)

Independent variables	Unadjusted model		Adjusted model	
	OR (95%CI)	p value	OR (95%CI)	p value
Knowledge Score	1.054 (1.009 – 1.101)	0.017*	1.050 (1.003 – 1.100)	0.036*
Health Literacy Score	1.045 (0.981 – 1.114)	0.171	1.018 (0.948 – 1.092)	0.631

Model statistics: *Nagelkerke* R^2 = 18.1%

CI, confidence interval; MMAS-8, 8-item Morisky medication adherence scale.

* $p<0.05$

Discussion

This study provides valuable data supporting relationships between adherence, OAC knowledge and health literacy. Participants who self-reported adherence to their OAC had significantly higher knowledge scores than those who did not. In addition, participants with adequate health literacy achieved significantly higher knowledge scores. Positive correlations between health literacy, knowledge and adherence scores were also observed, suggesting that these concepts are interlinked and should be considered when managing patients taking OACs for stroke thromboprophylaxis in AF. The Capability, Opportunity and Motivation (COM-B) model of Behavior to increase medication adherence provides a dynamic framework in order to identify appropriate interventions that address the modifiable factors influencing non-adherence. [23,24] Mapping the results from this study to the COM-B framework suggests each of the domains (COM) are involved and need to be addressed in order to increase OAC adherence (B).[23,24]

Poor adherence to OACs is frequently reported in the literature and has been associated with poor clinical outcomes. [2,4,5,25,26] In our study, 48% of participants reported adequate adherence to their prescribed OAC. This is similar to the study by Davis *et al.* in patients taking warfarin, in which only 50% of participants reported adequate adherence.[4] A recent review of adherence and persistence to

OACs in AF found that in the studies available, poor adherence is associated with poor treatment outcomes such as stroke and bleeding.[26] Yao *et al*. recently undertook a large retrospective cohort study in patients taking OACs for stroke prevention in AF and found that those with a high estimated stroke risk were at an increased risk of stroke when they were not taking anticoagulation for 6 months or more (hazard ratio 2.73, p <0.001), clearly indicating that better medication taking behavior leads to better outcomes.[2]

Taking into consideration the importance of adherence in ensuring a steady plasma concentration with DOACs and their lack of routine laboratory monitoring[11], our study suggests that patients taking DOACs may require routine follow up by health care practitioners (HCPs) to ensure that they adhere to their medication. This fit within the COM-B sub-category of Physical Opportunity, which suggests that HCP-patient communication and relationships can be improved through routine clinical follow up, in turn leading to increased adherence.[23,24]

We observed a total mean knowledge score of 62%. This is similar to the result of other studies in the literature, where a mean knowledge score of less than 70% has been reported in different populations.[18,27-29] From the results of our study, participants who were considered adherent had a significantly higher mean total knowledge score than those who were non- adherent, and knowledge remained significantly associated with adherence even after adjusting for the level of health literacy. Forty percent of all participants did not know that taking an OACs as the doctor had prescribed reduced the risk of stroke and 60% of all participants did not know that skipping a dose of their OAC could worsen their condition. In support of these findings, a recent study by Desteghe *et al*. found that 34% were unaware that AF could cause a stroke and 57% of the patients taking DOACs did not know what to do when they miss a dose.[29] Lane *et al*. found that only approximately 50% could name their condition and perceived it as a serious condition that could predispose them to a stroke.[30] Few studies have examined whether poor DOAC knowledge leads to poor clinical outcomes, however this has been demonstrated in those taking warfarin.[6,8,9] Our study reveals specific deficiencies in the knowledge of both warfarin and DOAC-taking participants. In addition, it provides a platform to inform the development of educational interventions and justifies the need for further research in this area.

Limited health literacy may be an indicator of deficits in warfarin knowledge.[6,7] Fang *et al* reported that 67% of patients taking warfarin for stroke prevention in AF had limited health literacy (s-TOFHLA score of 0-22) and this group had significantly inadequate disease and medication-related knowledge in comparison to those with adequate health literacy.[6] These results align well with our study, which found that those with inadequate health literacy had a significantly lower mean total anticoagulant knowledge score in comparison to those with adequate health literacy. Participants with inadequate health literacy were less likely than those with adequate health literacy to know why they had been prescribed an OAC, less likely to know how the medication works and less likely to be able to describe one sign of side effects to watch out for while taking an anticoagulant. Patients need to know what they have been prescribed and why, as well any possible side effects. Paucity in patients' knowledge can have a profound effect on the management of AF.[31]

Lack of knowledge and health literacy, comprehension of the disease and treatment, perception of illness and beliefs about treatment including concern of side effects and bleeding fits within the COM-B sub-categories of Psychological Capability and Reflective Motivation.[23,24] It has been

suggested that these categories can be addressed by HCPs giving information to patients to shape their knowledge, with the intention to enhance a patient's capability to understand and engage in their therapy.[23,24] With the goal of improving adherence through patient centered care, consideration of health literacy and its association with knowledge and adherence in patients taking OACs for stroke prevention in AF should therefore not be overlooked. Adherence may be improved through implementation of individually tailored educational interventions focusing on improving the disease and medication-related knowledge of the patient.

Limitations

There are a number of limitations to this study, including the cross-sectional methodology and small sample size. Furthermore, we did not collect information on the quality of education given to participants on their OACs upon initiation, nor did we determine if participants who were taking a DOAC at the time of the interview had previously been taking warfarin. The limitations of the tools used should also be considered. We anecdotally observed that many participants were unable to differentiate between the effect of AF and other co-morbidities such as heart failure or older age on quality of life. This made it difficult for participants to definitively say that AF was the condition causing their symptoms, such as shortness of breath or limiting their ability to exercise. Medication adherence was quantified by self-report; this approach can possibly overestimate the level of adherence observed.[32]

Implications for further research

Recent clinical guidelines have placed emphasis on integrating the patient and their preferences into AF management to improve outcomes.[1] The results of this study help to inform the implementation of patient centered integrated AF management and reinforce the need for additional research. Considering the demonstrated correlation between health literacy, knowledge and adherence, larger studies are required to determine if improving these patient centered aspects of OAC management in AF leads to improved treatment outcomes. Moreover, this study reveals gaps in the knowledge of participants taking OACs. A large prospective study assessing anticoagulant knowledge in this population will be useful in identifying specific areas of lacking knowledge to improve OAC education.

Conclusion

In conclusion, the results of this study demonstrate a significant relationship between health literacy, OAC knowledge and self-reported adherence behaviours. They also highlight inadequate medication adherence behavior and health literacy levels, and gaps in patient oral anticoagulation knowledge. To adopt a true patient centered approach to AF management, it is important for HCPs to consider these variables in patients taking OACs for stroke prevention in AF. Interventions designed to optimize the outcomes of anticoagulant treatment need to address these factors.

Conflict of interest

Luke Bereznicki and Leanne Chalmers have received consultancy funding from Aspen Pharmacare Australia for the development of education materials related to warfarin therapy. Luke Bereznicki has also received consultancy funding from Boehringer Ingelheim Pty Ltd for the development of educational materials for dabigatran/atrial fibrillation and provision of expert advice regarding the optimal use of anticoagulants in the prevention of stroke.

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