Abstract

Background: In the treatment of atrial fibrillation (AF), anticoagulant medications such as warfarin and rivaroxaban are commonly prescribed to reduce the risk of ischaemic strokes, and other thromboembolic events. Research has highlighted advantages and disadvantages of each of these medications, but there remains an absence of qualitative evidence regarding the lived experiences of AF patients. The present study helps address this gap and obtain a greater understanding of the patient experience and beliefs surrounding their anticoagulant medication.

Method: Semi-structured qualitative interviews with a purposive sample of 20 participants (10 warfarin, 10 rivaroxaban). Interviews were transcribed verbatim and thematically analyzed.

Results: Data analysis led to the generation of three key themes: positive perceptions of medication, distrust of alternatives, and inconsistencies in support experiences.

Conclusions: Positive perceptions of one anticoagulant medication (ACM) and distrust of alternatives may influence patients' confidence in switching medications. This is potentially problematic where there is a lack of patient engagement in medication changes, as seen during the Covid pandemic. Gaps in patient understanding of anticoagulation, including lack of clarity around medications selection and misconceptions about treatment, were evident. By addressing these misconceptions, clinicians may be better positioned to support people with AF in self-management of their ACM.

Keywords: Atrial Fibrillation, Anticoagulants, Quality of life, Patient experience, DOACs.

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Accepted manuscript

Introduction

Atrial Fibrillation (AF) is a common sustained cardiac arrhythmia which significantly increases individual risk of stroke and heart failure. Public Health England suggest that AF currently affects around 1.5 million people in the UK, with a further half a million believed to be living undiagnosed with the condition (NHS England, 2017). Due to changing demographics and rises in the prevalence of risk factors such as hypertension and diabetes, this number is expected to double over the next 30 years (Jones et al., 2020).

To reduce the risk of serious illness patients with AF will commonly be prescribed an anticoagulant medication (ACM). ACMs work by preventing thromboembolic events and have been evidenced to greatly reduce the incidence of clots (Arnold et al., 1992). For 60 years warfarin was the dominant ACM treatment (Loo et al., 2017). Warfarin is highly efficacious in the treatment for AF and has been evidenced to reduce the risk of stroke by up to 62% (Nguyen et al., 2012). Nonetheless, the challenges and practicalities associated with taking warfarin are apparent. The prescribed dosage given to a patient is dependent on a multitude of factors such as age (Shepherd, 1977), weight and metabolism (Wadelius, et al., 2007), and other pre-existing medical conditions (Wittkowsky & Devine, 2004). Dosing schedules for the medication can be complex and subject to frequent change (Mazor et al., 2007). Furthermore, regular testing and monitoring check-ups are required to ensure international normalized ratios (INRs) remain within therapeutic range. For some, this process has been regarded as both time-consuming and inconvenient (Lamarche & Heale, 2007; Kauffman et al., 2015). The negative connotations associated with taking warfarin can cause reticence in both patients and health care professionals (Howitt & Armstrong, 1999).

Considering the limitations associated with warfarin, the introduction of pharmacological alternatives in 2008, in the form of direct acting oral anticoagulant (DOAC) medications, was well

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Accepted manuscript

received, with DOACs accounting for most first-time prescriptions since 2015 (Loo et al., 2017). DOACs, such as rivaroxaban, dabigatran and apixaban, are regarded as advantageous alternatives to warfarin due to not normally requiring dosage adjustments or blood test monitoring (Nguyen et al., 2012). Moreover, DOACs have been regarded as safer due to more predictable pharmacokinetics, fewer critical bleeding related side effects, and fewer adverse interactions with food, alcohol, prescribed medications and over the counter remedies (Carter et al., 2008; De Caterina et al., 2018). Collectively, these factors are believed to contribute to increased uptake and adherence to DOACs when compared to warfarin (Raparelli, et al., 2017). DOACs are not without limitations however. Most notably, until recently there has been a lack of established reversal agents for DOACs. Additionally, amongst older populations, the rapid offset and short half-life of DOACS can increase the risk of thromboembolic events if adherence is not optimal.

Whilst the emergence of DOACs has served as an important catalyst in the exploration of ACM efficacy, research which elucidates the lived experiences of AF populations on these medications remains largely equivocal and underreported as much research to date is focused on warfarin or concentrated around physician/patient decision-making (Borg Xuereb et al., 2012).Some research suggests that DOACs provide patients with greater health related quality of life than warfarin (Monz et al., 2013; Carvalho et al., 2013), but there is little to highlight how DOACs enable this to happen. Moreover, whilst there is some evidence that DOAC populations have increased ACM adherence compared to their warfarin counterparts (Schulman, et al. 2013; Savelieva & Camm, 2014), there is a scarcity of qualitative research which explores the underlying medicine related beliefs which may influence adherence behaviours.

A final issue relates to the question of ACM selection. Patient and clinician values (Andrade, et al., 2016), clinician familiarity with DOACs, (Schaefer et al., 2016), bleeding risk

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

factors (Lauffenburger, 2015), and cost (Harrington et al., 2013) are all pertinent considerations during the ACM selection process. But there is still a need for more detailed exploration of the patient perspective and the challenges and realities associated with long-term ACM use. Exploring this reality may not only prove advantageous in better informing initial ACM selection, but also aiding healthcare professionals and patients alike, in their decision to switch medications.

In acknowledgment of the need for more detailed exploration of the AF patient experience, this study will seek to explore challenges and realities faced by AF populations, who are currently prescribed warfarin or the DOAC drug rivaroxaban.

Method

The study was designed, undertaken, and reported to align with the Standards for Reporting Qualitative Research (SRQR) (O'Brien et al., 2014).

Participants

A total of 20 participants were selected for the present study (10 warfarin, 10 rivaroxaban). The average age of participants was 71.5 years old (warfarin Mean (M) M = 72.3, rivaroxaban M =70.9) with a range of 59-82 years, and the average time on their selected ACM was 8.7 years (warfarin M = 12.5 years, rivaroxaban M = 4.9 years) with a range of 1-36 years.

Ethics

The study was approved by the Health Research Authority (HRA) and the NHS Research Ethics Committee (REC). Research was conducted in accordance with BPS ethical guidelines and the World Medical Association Declaration of Helsinki.

Procedure

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Accepted manuscript

Participants were selected via a purposive sampling methodology. Inclusion criteria required participants to have been diagnosed with AF and be receiving either warfarin or rivaroxaban treatment. A list of potential participants was provided by the local National Health Service (NHS) Haemophilia and Thrombosis Centre. Potential participants were assigned a number before a random number generator was used to identify an initial pool of 60 participants (30 warfarin and 30 rivaroxaban). Letters containing a detailed overview of the study protocol, study information sheet and consent form were distributed from which the final sample of 20 participants (10 warfarin and 10 rivaroxaban) were recruited. Sample size was pragmatic based on access to participants within study time parameters, However, researchers (DS & LM) agreed no new participants perspectives were being raised within the data at the time data collection ceased.

Once written consent was received, participants completed a pre-interview questionnaire. In addition to demographic information, such as age, gender and time on medication, the pre-interview questionnaire included psychometric measures; the Beliefs about Medicines Questionnaire (BMQ; Horne et al., 1999), the Morisky Medication Adherence Scale (MMAS-4; Morisky et al.,1986) and the Patient Activation Measure (PAM-13; Hibbard et al., 2004). These measures were included to provide a descriptive context of the participants.

BMQ

The BMQ is an 18-item questionnaire which assesses beliefs about the necessity of prescribed medication (*Specific-Necessity*); concerns about prescribed medication (*Specific-Concern*); beliefs that medicines are harmful, addictive, or poisonous (*General-Harm*) and that medicines which *overused by doctors* (*General-Overuse*). Higher scores denoting stronger beliefs.

MMAS-4

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

The MMAS-4 is a medication-taking behavior scale consisting of four items used to determine levels of medication adherence. Each question is based on a scoring scheme of "Yes" = 0 and "No" = 1, with lower scores denoting higher levels of adherence.

PAM-13

The PAM-13 is a 13-item measure which assesses self-reported knowledge, skills, and confidence for self-management. Based on their responses, respondents receive a PAM score (between 0 and 100). The resultant scores relate to one of four levels of activation with higher levels denoting stronger levels of activation (Level 1 = 0-47.0; Level 2 = 47.1 – 55.1; Level 3 = 55.2 -72.5; Level 4 = 75.2 – 100).

Semi-Structured Interview

Having completed the questionnaire, participants took part in a semi-structured interview with the researcher (DS) (see supplementary materials for full-interview guide). A sole interviewer was used throughout to aid consistency in process, and experience, of data collection. The researcher had no prior relationship with participants and was not a member of the clinical team. Interviews were held in person or remotely based on participant preference. The interview sought to obtain an understanding of the patient experience in relation to the following areas: 1) Initial responses to ACMs; 2) Current issues, impacts and experiences related to ACMs; 3) Perceived pros and cons associated with current ACM; 4) Adherence and management experiences; 5) Perceptions of monitoring processes and alternative medications; 6) Advice and recommendations for AF patients and clinicians.

Data analysis

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

To identify salient themes from the data, an inductive thematic analysis was undertaken (Braun & Clarke, 2006). The researchers adopted a critical realist perspective whereby there is the assumption that findings generated, reflect the participant's reality as evident within the data. All interviews were transcribed verbatim, before repeated readings of each transcript were undertaken to search for initial meanings and patterns. Once familiar with the content of each transcript, initial codes were generated by DS across the data set, relating to features or segments of data that were of interest. Following initial coding, codes were grouped into an initial set of broader themes, attempting to avoid overlap between themes. Two researchers (DS and LM) identified themes which could be disregarded as either peripheral or ambiguous (e.g., if there are not enough data to support them). Finally, a map of salient themes was created, with researchers ensuring to define and refine themes to ensure each accurately encapsulated the 'essence' of what the data represented. A 3rd researcher (MH) oversaw coding discussions, application of meaning and generation of the final analysis to ensure credibility through verification of interpretation and grounding of the analysis in the data and research aims.

Results

Descriptive data

The data for the psychometric measures is included purely for descriptive purposes and to help situate this sample within a wider context. The non-significant results (see Table 1) are largely as expected due to the sample size but do provide an indication that the groups had similar attitudes towards treatment whereby both groups mean scores would be categorized as high adherence.

Suggest insert table 1 here.

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Key themes

The thematic analysis generated three prevailing themes (see Table 2). 1) Positive perceptions of current ACM; 2) Distrust of alternatives; and 3) Inconsistencies in support experiences.

Suggest insert table 2 here.

1. Positive Perceptions of current ACM

The first overarching theme highlights how, regardless of current treatment, participants expressed positive perceptions of their own medication.

Minimal side-effects

Both warfarin and rivaroxaban participants exhibited similarities in relation to their beliefs that the side effects associated with their treatment were minor and non-intrusive. For example, P4 (rivaroxaban) stated "the only real thing I've experienced since then is a slight (…) err (…) longer blood flow if cut myself. But that's not too long." Additional side-effects highlighted by both sets of participants included bruising, numbness in extremities, feelings of lethargy, tiredness and dizziness. However, it was difficult to determine the extent to which these side-effects could be attributed to their selected ACM or other factors:

> "I don't know how much (…) that-the-the medication contributes to tiredness or whether it is just the condition and an outcome of it is that I can feel lethargic at times …Um but I can't really say much beyond that I don't think." (P9, warfarin)

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Whilst episodes of excess bleeding when cutting themselves appeared a common symptom of the medication amongst both sets of participants, others seemed unaware of side-effects associated with their selected ACM, including an absence of any emotional or psychological effects: "I have to say, I haven't been aware of any side-effects whatsoever." (P17, rivaroxaban). This sentiment shared by P9 (warfarin) who suggested they were neither "depressed" nor "unduly worried" by the medication.

Reduced risk and reassurance

Common amongst both groups of participants was positive perceptions about their ACM medication reducing their risk of serious illness associated with AF. P2 (warfarin) stated "I get err a mental satisfaction I guess from knowing I'm reducing my risk of a clot." whilst P8 (rivaroxaban) claimed "I think it's a wonderful medicine. And I think what it prevents has made my life a lot happier." These assertions were further supported by most warfarin and rivaroxaban participants stating they felt they were "low-risk" for experiencing AF medical related issues whilst on their current medication.

For the warfarin participants, perceptions of reduced risk were further ameliorated by the monitoring process: "Well the positives are that folk are making sure that we're achieving the goal of getting an INR of between 2 and 3. Hopefully around 2.5 and err by regular monitoring that makes that fairly certain." (P11, warfarin). For many of the warfarin participants, regular monitoring was a positive aspect of treatment and a source of reassurance - not the inconvenience seen previously (Lamarche & Heale, 2007; Kauffman et al., 2015).

Lack of restrictions on daily functioning

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Both groups articulated that they felt largely unrestricted by their medication. P6 (warfarin) stated "I still carry on the same as I was doing. I like to be outdoors, that remains.". Similarly, "it's never stopped me doing anything." (P9, rivaroxaban). The analysis indicating that scope and quality of life remained largely unaffected by ACM type or usage. The only exception being regarding activities which could result in significant cuts and bleeding episodes, "I noticed um I had to be more careful doing things where I might knock myself um I could - I can bruise more easily." (P8, rivaroxaban). Further, some warfarin participants reported a need to attend to lifestyle factors, such as diet, alcohol and exercise which they believed to result in INR level fluctuations:

> **"**But when I stopped that contract and came back to sort of proper eating at home, my INR came down so yes I noticed the impact due to the lack of vegetables. So, my range is normal for my normal diet, when I step outside whatever my normal diet is um, I can - I can see the impact." (P9, warfarin).

This suggests there is an overall lifestyle behaviour benefit of regular monitoring for those receiving warfarin.

Ease of adherence

ACM adherence was largely perceived as easy and non-invasive: P3 (warfarin) stated "I just swallow the pill and that's it. Job done (…) And then I forget about it until the next evening." Similarly, P15 (rivaroxaban) suggested "I find it very easy really. I just take this little red tablet." These views also reflected in the MMAS-4 scores.

2. Distrust of alternatives

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Across the data was an evident distrust or reluctance to change medication. The theme can be understood through negative connotations associated with warfarin and inconvenience of the INR monitoring process referenced by rivaroxaban participants, and the lack of antidotes and monitoring for rivaroxaban highlighted by those receiving warfarin.

Amongst rivaroxaban participants, the reluctance toward warfarin primarily related to negative connotations associated with the medication's historic use as a rat poison (Ramachandran & Pitchai, 2018). "In my past I was in the drug squad for a couple of years. The warfarin was always used for the rat killers so (laughs) it must be a psychological thing. I just didn't want to trust it at all." (P4, rivaroxaban). These reservations something that warfarin participants had clearly overcome:

> "There was reluctance initially. I think of warfarin as rat poison. Um so there was a reluctance but um if it's going to avoid a stroke, well it's a no brainer." (P11, warfarin)

Two rivaroxaban participants stated their reluctance towards warfarin was, in part, attributed to negative experiences of family members:

> "I think he wanted to put me on warfarin, and I said I was really nervous about warfarin on account of my father flooding Minneapolis airport (laughs) with blood (laughs)." (P5, rivaroxaban)

> "My late husband - because he was - I had to drive him everywhere, he was in a wheelchair, I found taking him to have his blood tests done was quite a chore, not that I minded but it was hard for him to go out in his wheelchair and be tested regularly." (P8, rivaroxaban).

This highlighting the broader impact of long-term monitoring procedures on both patients and those in positions of care.

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

A reservation amongst warfarin participants was the absence of monitoring associated with rivaroxaban. This created a perception that rivaroxaban was less safe than warfarin. P2 (warfarin) suggested he had become accustomed after "30 odd years of having monitoring" and as such would be reluctant to change to a medication which did not provide the same level of support. P3 (warfarin) shared similar reservations: "It would be a little bit iffy if you suddenly decided that you're not having blood tests anymore." Further concerns were seen through the belief that rivaroxaban does not have a fast-acting antidote (unlike warfarin in the form of prothrombin complex concentrate), whereby warfarin participants felt they may be more at risk of bleeding on DOACs:

> "I didn't switch to the newer versions of anticoagulants because they didn't have an antidote. And whilst you don't plan to have an accident, you never know". (P10, Warfarin)
>
> "Well you could-you could switch to another drug …but there are some drawbacks in that um (…) if you-if you do have a bleed, if something goes wrong you know…there isn't going to be anything that we can do about it." (P14, warfarin)

The data clearly shows how beliefs about medications both influence patient perceptions during initial ACM selection, but also subsequent switching processes. This could be particularly problematic if these concerns are not considered as part of the current enforced changes to DOACs because of COVID-19.

3. Inconsistencies in support experiences

Inconsistencies in patient support experiences were highlighted within the data. Differences were apparent for participants in relation to the initial involvement in the ACM selection; initial support and education; and ongoing support.

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Data indicated there was a degree of disparity regarding the degree of autonomy participants were provided with regarding ACM selection. For most participants, it appeared there was either little discussion, or a clear preference, from clinicians regarding ACM choice: "No, there wasn't no (...) It just - it just yeah prescription (knocks on table) take that." (P1, rivaroxaban). Similarly, "I think the other one's were relatively new at the time (…) and that was why it - it was thought that I should be better off on warfarin." (P6, warfarin). For some warfarin participants, it could be that this perceived lack of autonomy regarding ACM selection may be because when first diagnosed with AF, alternative ACM selection were not an option. However, for rivaroxaban participants it would appear some clinicians favored the newer medication: "There was no discussion of any alternative medicine. He told me it was very safe drug and very new and extremely successful" (P8, rivaroxaban). These comments indicate discrepancies in clinicians' approaches to ACM selection, and certainly a lack of discussion, while highlighting the high level of trust patients place in clinicians during such processes.

A further area of disparity identified was in relation to perceived levels of education when first prescribed their selected ACM. Some participants (both warfarin and rivaroxaban) indicated that they were originally well-educated:

> "I was educated right from the very word go before I actually took the stuff. So, then it was up to me which-which way I would go, whether I would take the rivaroxaban or whether I would take the alternatives, and they explained how it would work." (P4, rivaroxaban)

> "Yeah the anticoag clinic here at the hospital are very good. They went through the process and ran through training and all the bits and pieces and err, then off I went. So, I was - I just carried on from there." (P13, warfarin).

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

In contrast, other participants (both warfarin and rivaroxaban) indicated an initial absence of support and education from clinicians:

> "I sense it was mostly a 'There you go, we've - we've diagnosed what-what you've got, you keep taking this' … I don't think I necessarily felt unsupported, but I don't think there was any proactive form of "Are you ok?" (P9, warfarin)

It seems apparent that some patients feel a lack of practical support following initial diagnosis, as both sets of participants alluded to feelings of "worry", "concern", and "uncertainty" when first being diagnosed with AF.

As mentioned previously, for warfarin participants it was evident that they perceived the INR monitoring process a positive avenue for additional support. Specifically, participants referred to the NHS anticoagulation support staff and the key role they play in providing reassurance and information regarding changes to dosing schedules:

> "The - the support I get from (…) the testing - the INR testing I thought was brilliant. I think the nurses are very good. Um there's been at least three since I started taking it and they-they've all you know err (…) pleased to see you erm chatting about holidays and things. Obviously to put your mind at ease whilst there sticking a needle in your arm, I've realised that." (P6, warfarin)

In contrast, rivaroxaban participants referred to a perceived absence of ongoing support. Participants felt being on the medication provided fewer support opportunities: **"**I've not had any reviews in terms of (…) blood itself (…) only the other medications I'm taking. So, I would - I would have expected that (…) but it didn't happen" (P4, rivaroxaban). Similarly, since making the

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

transition from warfarin to rivaroxaban P19 suggested *"*With this other tablet, rivaroxaban, there's no, there's no contact at all. There's no sort of like follow up at all." Once again, these findings present an issue of contention surrounding the monitoring process. Whilst the process may be perceived by some as time consuming and burdensome, it plays an important role as an additional source of ongoing support and reassurance. This is clearly something rivaroxaban participants suggest is currently lacking for them.

Discussion

The present study examines the comparative experiences of warfarin and rivaroxaban patients through the views of 20 ACM participants (10 warfarin and 10 rivaroxaban). From the data, three salient themes were identified in relation to positive perceptions of current ACM, distrust of alternatives, and inconsistencies in support experiences.

Regarding the first overarching theme, when asked to reflect their experiences relating to ACMs (including issues and issues related to ACM adherence) both warfarin and rivaroxaban participants' perceptions of their selected medication were largely positive. Previous research has alluded to several negative psychosocial ramifications associated with ACM adherence including reduced quality of life perceptions, poor emotional adjustment, and withdrawal from daily activities (Aliot et al., 2014; Dąbrowski, et al., 2010; Ekblad et al., 2013). Findings of the present study, however, appeared to indicate that both groups found their selected medication to be largely non-restrictive in relation to everyday functioning and perceived quality of life. Furthermore, despite suggestions that warfarin may cause issues such as bruising, bleeding, anxiety, and depression (De Caterina et al., 2018) there appeared to be little difference between the groups in

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

the presence, or absence, of reported physical and psychological symptomatology and ACM side effects.

Positive perceptions of selected ACMs further extended to beliefs surrounding adherence, whereby the consensus for both sets of participants reflected a predominant attitude that adherence was simply a case of "taking a pill". Difficulty with adherence has previously been evidenced as a reason why DOACs could be considered as superior (e.g., fixed dosing and no need for INR monitoring) to warfarin (Raparelli, et al., 2017). However, despite warfarin participants acknowledging that the monitoring process can at times be inconvenient, no barriers to adherence were articulated by either the warfarin or rivaroxaban participants. This also seen in participants' MMAS-4 scores (warfarin *M = 0.5; Rivaroxaban M =0.3*) indicating high levels of adherence.

Importantly, both groups of participants exhibited a reluctance to change medication. Rivaroxaban participants were vocal in their reluctance to pursue a medication which required regular monitoring. In contrast, warfarin participants stated that an absence of monitoring, as well as the lack of readily available antidotes, were barriers to switching. In recognition of the COVID-19 climate and the difficulties associated with attending regular INR monitoring sessions(which has led to enforced medication change for many) and the broader debate surrounding the potential merits and drawbacks of switching from warfarin to DOACS (Barnes et al., 2020; Kow et al, 2020), these findings highlight how enforced switching to DOACs may lead to increases in anxiety, as well reductions in patient satisfaction, adherence, and perceived quality of life, if patient concerns are not adequately addressed.

From a patient support and education perspective, some disparity was observed in relation to levels of autonomy regarding ACM selection, initial education, and ongoing support. Many participants reported their physicians either prescribed an ACM without discussion or exhibited a

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

clear medication preference. Whilst it should be noted some of the warfarin participants were prescribed their treatment prior to the widespread circulation of rivaroxaban, it was apparent that there were differences in the extent rivaroxaban participants felt a sense of choice over their medication. Physicians may choose to make decisions surrounding ACM selection based on what they are most comfortable and knowledgeable of (Steinberg et al., 2017), as opposed to enabling patients to play an active role. This may reflect a wider issue regarding possible clinician biases toward the adoption of a paternalistic decision-making approach, as opposed to acknowledging patient's preference towards shared decision making (Seaburg et al., 2014).

Initial education surrounding ACMs was a further issue of contention. Whilst some participants suggested that they were well educated regarding the realities associated with ACM adherence, others articulated a perceived absence of care and education when first being put on their medication. Previous research has indicated that addressing the balance of benefits, impacts and downsides of specific ACMs, are all pertinent topics for discussion following diagnosis (Dalmau et al., 2017). Nonetheless, in the present study, some participants articulated there was still a need for enhanced levels of support and education to mitigate initial concern, apprehension and uncertainty associated with starting new medication.

Importantly from an ongoing support perspective, findings reinforced existing assumptions that the monitoring process enables warfarin patients to feel reassured and supported. Conversely, whilst a majority of rivaroxaban participants were not overtly critical regarding the support they had received, they were less vocal in providing praise toward support provisions which had been provided and alluded to a lack of follow up support following diagnosis. To enhance support provisions for rivaroxaban participants, the possible introduction of monitoring processes (like the

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

warfarin INR process) has recently been discussed (e.g., Zhang et al., 2020) and should be considered.

Limitations

Although the study has been undertaken with an aim of ensuring methodological rigour and trustworthiness to ensure findings are of value to practice, there are some limitations that should be acknowledged. In considering the participant sample, whilst attempting to demonstrate sensitivity toward obtaining a sample which was representative of the AF wider population, all participants who consented to take part in the study were exclusively from a white British background. Statistics regarding the prevalence rates of AF can be challenged, however, there is research to suggest a higher prevalence of AF and uptake of ACMs from individuals of white backgrounds (when compared to those from black and Asian backgrounds; Bakhai et al., 2020). Nonetheless, obtaining the perspectives of individuals from underrepresented groups would enhance our understanding of the patient experience. Furthermore, it should be noted that whilst the study was designed to achieve comparable groups of patients on warfarin and rivaroxaban, it is likely that the sample demonstrated higher levels of activation around treatment because they volunteered for the study. The views of patients with mobility restrictions may not be fully reflected, and here, the perception of INR monitoring is probably very different. There was a difference between groups for length of time on anticoagulants, 12.5 years for warfarin and 4.9 years for rivaroxaban, which could mean the warfarin participants had strengthened perceptions towards their treatment and away from alternatives – although 4.9 years would still be viewed as habituated to treatment. Further, as all participants were required to have been on anticoagulants for at least 1 year, this study does not capture patient beliefs and experiences recently starting treatments.

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Clinical Implications

This study highlights several pertinent considerations for healthcare professionals. In choosing whether or not to have an ACM, the patient's interpretation of the relative importance of stroke and bleeding risks may well differ from that of the healthcare professional (Wilke et al, 2017). When initiating an ACM it is important to give factual and balanced explanations of the relative risks of different ACMs, including the role of different antidotes, as this information may affect long term attitudes and adherence to treatment.

It would be beneficial for clinicians to consider the study findings when discussing the possibility of switching from warfarin to DOACs. When switching ACMs, clinicians should be mindful that whilst patients may be open to a switch, they may also find this experience frightening due to previous knowledge and experience (Slavenburg et al., 2020). Patients who have been taking warfarin long term are likely to have beliefs about the importance of monitoring their ACM. Whilst clinicians may believe that monitoring for warfarin is inconvenient, their patient may be comfortable with blood tests or may use home fingerprick tests which they find convenient and reassuring (NHS England, 2014). Whilst clinicians are likely to believe that the lack of monitoring required for DOACs is an advantage, the patient may feel that monitoring keeps them safe. Reviewing the patient's knowledge and experience of ACMs and refreshing this with new information when changes are required, may help them feel more secure on a new treatment regime.

Conclusion

To further inform our understanding of ACM selection and switching processes, future research should seek to obtain a more detailed understanding of the practitioner perspective and the role of the patient in treatment selection processes. It is important to understand practitioner

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Accepted manuscript

414 and patient views regarding conversations pertaining to switching ACM medications. In
415 acknowledgment of the findings of the present study, it is important we remain cognisant of the
416 needs of patient populations currently prescribed on ACMs. It would be beneficial if clinicians can
417 attempt to mitigate fears and concerns through patient education and by addressing prevailing
418 misconceptions.

419

420

421 ***Funding:*** *The work was supported by funding from Bayer Plc. The funder had no active role in the research process*
422 *or article preparation.*

423 ***Declaration of Conflicting Interests:*** *The authors declare that there is no conflict of interest.*

424 ***Data Availability:*** *The data that support the findings of this study are available on request from the host site*
425 *author, Dr Tamara Everington. The data are not publicly available due to original ethical approval restrictions.*

426

427

428

Accepted manuscript

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

References

Aliot, E., Botto, G. L., Crijns, H. J., & Kirchhof, P. (2014). Quality of life in patients with atrial fibrillation: how to assess it and how to improve it. *Europace*, *16*(6), 787-796. https://doi.org/10.1016/j.cjco.2020.03.013

Andrade, J. G., Krahn, A. D., Skanes, A. C., Purdham, D., Ciaccia, A., & Connors, S. (2016). Values and preferences of physicians and patients with nonvalvular atrial fibrillation who receive oral anticoagulation therapy for stroke prevention. *Canadian Journal of Cardiology*, *32*(6), 747-753. https://doi.org/10.1016/j.cjca.2015.09.023

Arnold, A. Z., Mick, M. J., Mazurek, R. P., Loop, F. D., & Trohman, R. G. (1992). Role of prophylactic anticoagulation for direct current cardioversion in patients with atrial fibrillation or atrial flutter. *Journal of the American College of Cardiology*, *19*(4), 851-855. https://doi.org/doi:10.1016/S1525-2167(03)00075-1

Barnes, G.D. Burnett, A., Allen, A., Blumenstein, M., Clark, N.P., Cuker, A., Dager, W.E., Deitelzweig, S.B., Ellsworth, S., Garcia, D. and Kaatz, S., 2020. Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum. *Journal of Thrombosis and Thrombolysis*, 1. https://doi.org/10.1007/s11239-020-02138-z

Bakhai, A., Petri, H., Vahidnia, F., Wolf, C., Ding, Y., Foskett, N., & Sculpher, M. (2020). Real-world data on the incidence, mortality, and cost of ischaemic stroke and major bleeding events among non-valvular atrial fibrillation patients in England. *Journal of Evaluation in Clinical Practice*. https://doi.org/10.1111/jep.13400

Borg Xuereb, C., Shaw, R. L., & Lane, D. A. (2012). Patients' and health professionals' views and experiences of atrial fibrillation and oral-anticoagulant therapy: A qualitative meta-synthesis. *Patient Education and Counseling*, *88*(2), 330–337. https://doi.org/10.1016/j.pec.2012.05.011

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, *3*(2), 77-101. https/doi.org/10.1191/1478088706qp063oa

Carter, K., Streiff, M., Kraus, P., Ross, P., Thomas, M., Wellman, J., Stack, J., & Traill, T. (2011). Analysis of the projected utility of dabitagran, rivaroxaban and apixaban and their future impact on existing anticoagulation clinics at the John Hopkins Hospital in

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Proceedings of the 11th national conference on antigoagulation therapy; research Abstracts. *Journal of Thrombosis and Thrombolysis*, *31*, 367 – 400. https://doi.org/10.1007/s11239-012-0781-z

Carvalho, A.R., Ciol, M.A., Tiu, F., Rossi, L.A., Dantas, R.A. (2013). Oral Anticoagulation: the impact of the therapy in health-related quality of life at six-month follow-up. *Revista Latino-Americana de Enfermagem*, 21, 105-12. https://doi.org/10.1590/S010411692013000700014

Dąbrowski, R., Smolis-Bąk, E., Kowalik, I., Kazimierska, B., Wójcicka, M., & Szwed, H. (2010). Quality of life and depression in patients with different patterns of atrial fibrillation. *Kardiologia Polska (Polish Heart Journal)*, *68*(10), 1133-1139. https://doi.org/10.1093/europace/euv233

Dalmau, G. M., Arderiu, E. S., Montes, M. B. E., Solà, I., Saco, S. P., & Coello, P. A. (2017). Patients' and physicians' perceptions and attitudes about oral anticoagulation and atrial fibrillation: a qualitative systematic review. *BMC Family Practice*, *18*(1), 3. https://doi.org/10.1186/s12875-016-0574-0

De Caterina, R., Brueggenjuergen, B., Darius, H., Koehler, S., Lucerna, M., Pecen, L., & Le Heuzey, J. Y. (2018). Quality of life and patient satisfaction in patients with atrial fibrillation on stable vitamin K antagonist treatment or switched to a non-vitamin K antagonist oral anticoagulant during a 1-year follow-up: A PREFER in AF Registry substudy. *Archives of Cardiovascular Diseases*, *111*(2), 74-84. https://doi.org/10.1016/j.acvd.2017.04.007

Ekblad, H., Rönning, H., Fridlund, B., & Malm, D. (2013). Patients' well-being: experience and actions in their preventing and handling of atrial fibrillation. *European Journal of Cardiovascular Nursing*, *12*(2), 132-139. https://doi.org/10.1177/1474515112457132

Harrington, A. R., Armstrong, E. P., Nolan Jr, P. E., & Malone, D. C. (2013). Cost-effectiveness of apixaban, dabigatran, rivaroxaban, and warfarin for stroke prevention in atrial fibrillation. *Stroke*, *44*(6), 1676-1681. https://doi.org/10.1161/strokeaha.111.000402

Hibbard, J. H., Stockard, J., Mahoney, E. R., & Tusler, M. (2004). Development of the Patient Activation Measure (PAM): conceptualizing and measuring activation in patients and consumers. *Health Services Research*, *39*(4p1), 1005-1026. https://doi.org/10.1111/j.1475-6773.2004.00269.x

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Horne R, Weinman J, & Hankins M. (1999). The Beliefs about Medicines Questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology & Health*, *14*,1–24 https://doi.org/10.1080/08870449908407311

Howitt, A., & Armstrong, D. (1999). Implementing evidence based medicine in general practice: Audit and qualitative study of antithrombotic treatment for atrial fibrillation. *British Medical Journal*, *318*(7194), 1324–1327. https://doi.org/10.1136/bmj.318.7194.1324

Jones, N. R., Taylor, C. J., Hobbs, F. R., Bowman, L., & Casadei, B. (2020). Screening for atrial fibrillation: a call for evidence. *European heart journal*, *41*(10), 1075-1085. https://doi.org/10.1093/eurheartj/ehz834

Kauffman, Y. S., Schroeder, A. E., & Witt, D. M. (2015). Patient specific factors influencing adherence to INR monitoring. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, *35*(8), 740-747. https://doi.org/10.1002/phar.1616

Kow, C. S., Sunter, W., Bain, A., Zaidi, S. T. R., & Hasan, S. S. (2020). Management of Outpatient Warfarin Therapy amid COVID-19 Pandemic: A Practical Guide. *American Journal of Cardiovascular Drugs*, 1. hhttps://doi.org/ 10.1007%2Fs40256-020-00415-z

Lamarche, K., & Heale, R. (2007). Communicating the safety essentials of oral anticoagulant therapy. *Home Healthcare Now*, *25*(7), 448-458. https://doi.org/ 10.1097/01.NHH.0000281612.50929.1a

Loo, S. Y., Dell'Aniello, S., Huiart, L., & Renoux, C. (2017). Trends in the prescription of novel oral anticoagulants in UK primary care. *British Journal of Clinical Pharmacology*, *83*(9), 2096–2106. https://doi.org/10.1111/bcp.13299

Mazor, K. M., Baril, J., Dugan, E., Spencer, F., Burgwinkle, P., & Gurwitz, J. H. (2007). Patient education about anticoagulant medication: Is narrative evidence or statistical evidence more effective? *Patient Education and Counseling*, *69(1-3), 145–157.* https://doi.org/10.1016/j.pec.2007.08.010

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Monz, B. U., Connolly, S. J., Korhonen, M., Noack, H., & Pooley, J. (2013). Assessing the impact of dabigatran and warfarin on health-related quality of life: results from an RE-LY sub-study. *International journal of cardiology*, *168*(3), 2540-2547. https://doi.org/10.1016/j.ijcard.2013.03.059

Morisky D. E., Green L. W., & Levine D. M. (1986) Concurrent and predictive validity of a self-reported measure of medication adherence. *Medical Carem 24*(1), 67–74. http://www.jstor.org/stable/3764638

Nguyen, T., Yacoub, M., Chan, T. I., & Quach, K. (2012). Atrial fibrillation: Focus on anticoagulant pharmacotherapy. *The Journal for Nurse Practitioners*, *8*(7), 560-565. https://doi.org/10.1016/j.nurpra.2012.05.020

NHS England. (2014). TECS CASE STUDY 001: Health Call International Normalisation Ratio (INR) Monitoring, Patient Self-Testing for patients on warfarin Location and commissioners: County Durham and Darlington FT Provider: Inhealthcare using Roche CoaguChek XS Ambition level: 1. Available at: https://www.england.nhs.uk/wp-content/uploads/2014/12/tecs-durham.pdf

NHS England. (2017). NHS launches new drive to save thousands of people from heart attacks and strokes. Available at: https://www.england.nhs.uk/2017/09/nhs-launches-new-drive-to-save-thousands-of-people-from-heart-attacks-and-strokes/

O'Brien, B. C., Harris, I. B., Beckman, T. J., Reed, D. A., & Cook, D. A. (2014). Standards for reporting qualitative research: A synthesis of recommendations. *Academic Medicine*, *89*(9), 1245–1251. https://doi.org/10.1097/ACM.0000000000000388

Ramachandran, S., & Pitchai, S. (2018). Story of warfarin: From rat poison to lifesaving drug. *Indian Journal of Vascular and Endovascular Surgery*, *5*(3), 174. https://doi.org/ 10.4103/ijves.ijves_49_18

Raparelli, V., Proietti, M., Cangemi, R., Lip, G. Y., Lane, D. A., & Basili, S. (2017). Adherence to oral anticoagulant therapy in patients with atrial fibrillation. *Thrombosis and Haemostasis*, *117*(02), 209-218. https://doi.org/10.1160/TH17-10-0710

Savelieva I, Camm AJ. (2014). Practical considerations for using novel oral anticoagulants in patients with atrial fibrillation. *Clinical Cardiology*, 37(1):32–47.

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

https://doi.org/10.1002/clc.22204

Schaefer, J. K., McBane, R. D., & Wysokinski, W. E. (2016). How to choose appropriate direct oral anticoagulant for patient with nonvalvular atrial fibrillation. *Annals of Hematology*, *95*(3), 437-449. hhtps://doi.org/10.1007/s00277-015-2566-x

Schulman, S., Shortt, B., Robinson, M., & Eikelboom, J. W. (2013). Adherence to anticoagulant treatment with dabigatran in a real-world setting. *Journal of Thrombosis and Haemostasis*, *11*(7), 1295-1299.

Seaburg, L., Hess, E. P., Coylewright, M., Ting, H. H., McLeod, C. J., & Montori, V. M. (2014). Shared decision making in atrial fibrillation: where we are and where we should be going. *Circulation*, *129*(6), 704-710. https://doi.org/10.1161/CIRCULATIONAHA.113.004498

Shepherd, A. M., Hewick, D. S., Moreland, T. A., & Stevenson, I. H. (1977). Age as a determinant of sensitivity to warfarin. *British Journal of Clinical Pharmacology*, *4*(3), 315-320. https://doi.org/10.1111/j.1365-2125.1977.tb00719.x

Slavenburg, M., van den Bent, J. H., Barten, T., Reijs-Scheijgrond, M., & de Koning, C. (2020). Perceptions and Experiences of Atrial Fibrillation Patients on Their Condition and Oral Anticoagulant Treatment. *Cardiology and Therapy*. 9(2),409–420. hhtps://doi.org/10.1007/s40119-020-00173-8

Steinberg, B. A., Gao, H., Shrader, P., Pieper, K., Thomas, L., Camm, A. J., & Haas, S. (2017). International trends in clinical characteristics and oral anticoagulation treatment for patients with atrial fibrillation: results from the GARFIELD-AF, ORBIT-AF I, and ORBIT-AF II registries. *American Heart Journal*, *194*, 132-140. https://doi.org/10.1016/j.ahj.2017.08.011

Wadelius, M., Chen, L.Y., Eriksson, N., Bumpstead, S., Ghori, J., Wadelius, C., Bentley, D., McGinnis, R. and Deloukas, P., 2007. Association of warfarin dose with genes involved in its action and metabolism. *Human Genetics*, *121*(1), pp.23-34. hhtps://doi.org 10.1007/s00439-006-0260-8

Wilke, T., Bauer, S., Mueller, S., Kohlmann, T., & Bauersachs, R. (2017). Patient preferences for oral anticoagulation therapy in atrial fibrillation: a systematic literature review. *The Patient-Patient-Centered Outcomes Research*, *10*(1), 17-37.

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

hhttps://doi.org/10.1007/s40271-016-0185-9

Wittkowsky, A. K., & Devine, E. B. (2004). Frequency and causes of overanticoagulation and underanticoagulation in patients treated with warfarin. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, *24*(10), 1311-1316. https://doi.org/10.1592/phco.24.14.1311.43144

Zhang, J., Toupin, D., Lebel, M. C., & Blostein, M. (2020). Development of an INR for rivaroxaban monitoring using plasma samples from patients. *Thrombosis Research*, *187*, 122-124. hhttps://10.1016/j.thromres.2020.01.009

Table 1

Descriptive Statistics of Psychometric Measures by Treatment Group

Measure	Warfarin Mean (SD)	Rivaroxaban Mean (SD)	MW-U test Z
MMAS-4	0.5 (0.67)	0.3 (0.46)	0.45
BMQ- Specific Necessity	16.9 (3.75)	17.5 (2.91)	0.49
BMQ- Specific Concern	13.4 (4.36)	10.8 (1.66)	-1.5
BMQ- General Overuse	10.1 (3.11)	12 (2.4)	1.28
BMQ- General Harm	8.4 (2.50)	9.8 (2.63)	0.87
PAM-13	62.4 (10.0)	63.6 (10.1)	0.04

Note: Morisky Medication Adherence Scale (MMAS); Beliefs about Medicines Questionnaire (BMQ); Patient Activation Measure (PAM). None of the differences are statistically significant.

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.

Accepted manuscript

Table 2

Final Thematic Table of Main & Sub-themes

Theme	Sub-Themes
Positive perceptions of current treatments	• Minimal side-effects. • Reduce clot risk and reassurance. • Lack of restrictions on everyday functioning. • Ease of adherence
Distrust of alternatives	• Warfarin has negative connotations. • INR monitoring is an inconvenience. • Rivaroxaban has no monitoring or antidote.
Inconsistencies in support experiences	• Patient choice in ACM selection • Initial support and education • Ongoing support

Accepted manuscript

This is an accepted manuscript of an article published by Wiley in Journal of Evaluation in Clinical Practice, available online at https://onlinelibrary.wiley.com/doi/10.1111/jep.13628. It is not the copy of record. Copyright © 2021, Wiley.