Exploring emerging issues in anticoagulation therapy

Examining patient choice, education and adherence

Contributors

Nigel Breakwell

AF Association

Prof A John Camm - MD, FRCP, FMedSci

Professor of Clinical Cardiology, Honorary Consultant Cardiologist, Molecular and Clinical Sciences Research Institute, St George's University of London

Dr Matthew Fay - FRCP Edin

Clinical Chief Executive The Westcliffe Group, GP Principal The Willows Medical Practice, Honorary Clinical Lecturer Warwick Medical School

Prof Ahmet Fuat - PhD FRCGP FRCP (London) PGDiP Cardiology

Honorary Professor of Primary Care Cardiology, Durham University and Dr at Carmel Medical Practice, Darlington

Jo Jerrome

CEO Thrombosis UK

Trudie C A Lobban - MBE FRCP (Edin)

Founder and CEO, Arrhythmia Alliance, Founder and CEO AF Association

Sue Rhodes

VTE CNS and joint Anticoagulant Lead, Anticoagulant Service, Great Western Hospital, Swindon

Donna Sydenham

Anticoagulation Lead Nurse / Clinical Nurse Specialist, Modality Group, Bellevue Medical Centre, Birmingham

Advisors

Dr Mark Sullivan - MB ChB FRCGP

Medical Director, LumiraDx

Julie Varley

Registered General Nurse, Specialist Practitioner, and CPT Clinical Services Advocate, LumiraDx Care Solutions

Editor

Sherezade Garcia Rangel - PhD

Copy and Content Writer, LumiraDx Care Solutions

Introduction

Anticoagulation therapy is well established, yet as a long-term therapy optimal management of patients can be challenging. The impact of excellent anticoagulation services on population health and reduction of budget pressure is significant, but is there consensus on the best care pathway for patients on anticoagulants? How can patients be supported and optimally managed?

This collaborative discussion paper explores a series of questions in relation to optimal anticoagulation management for patients on direct oral anticoagulants (DOACs – also known as new/novel oral anticoagulants or NOACs).

The paper will examine:

- Patient choice in anticoagulation therapy
- DOACs in anticoagulation therapy today
- The official advice for excellent anticoagulation services
- Is there a consensus on a standardised process for DOACs?
- Adherence in DOACs anticoagulation therapy
- The importance of education in a patient-centred approach to long-term anticoagulation therapy
- Initiatives to support adherence for patients on DOACs

Under the guidance of the contributors, the paper gathers questions regarding the current and future issues of anticoagulation therapy, with particular focus on DOACs. It also explores what initiatives have been put in place to perfect anticoagulation management, including working with local pharmacies and nurse-led anticoagulation clinics in primary care.

This paper includes feedback and views from opinion leaders in anticoagulation to prompt a wider discussion on potential areas for development in anticoagulation management for patients on DOACs.

Editor's note

Being diagnosed with a long-term condition can be daunting – whether it is the result of a years-long search, an admission to hospital or a routine check-up. People are often at their most vulnerable when consulting their care team in search for an explanation, and even a solution, for something which already affects their lives. They want to feel listened to, consulted and supported. They want reassurance that any therapy or treatment takes into account their needs and adapts to the requirements of their lives whilst offering them the best available care.

We aim to start an informed debate on how this can be can achieved for patients in long-term anticoagulation therapy. Under the guidance of our advisors and with the expert insight of our contributors, this collaborative paper examines best practice and collates unanswered questions about the future of anticoagulation therapy.

Let us highlight some of the great efforts being made to support people on anticoagulation therapy and discuss what else can be done to achieve excellent management.

Contents

Introduction	2
Editor's note	3
Anticoagulation therapy today	5
Patient choice in anticoagulation therapy	5
DOACs in anticoagulation therapy today	7
Adherence in long-term therapies	9
Long-term therapies: a problem with adherence?	9
Excellent anticoagulation services	13
Recommendations for excellent anticoagulation services	13
What does excellence in anticoagulation services involve?	13
Shared decision making	14
Structured monitoring and follow-up	16
Best practice for DOACs	17
A standardised process for DOACs	17
Best practice and consensus	19
Adherence and DOACs	21
Is adherence an issue for patients on DOACs?	21
A dynamic process	24
Low-cost interventions	24
Case study: Involve pharmacists in the improvement of adherence – the Perfect pathway	25
The New Medicines Service and the Great Western Hospital	25
Case study: Excellent anticoagulation service in a nurse-led DOAC clinic in primary care	27
A patient-focused service	27
Comprehensive initial consultations	28
A clear pathway for structured follow-up	28
Supporting adherence	29
What can be done about adherence?	29
Comprehensive education and integrated technology	29
The future of anticoagulation therapy: findings and conclusion	31
Anticoagulation and an ageing population	31
The need for more data	32
Conclusion	34
Acknowledgements	34

Anticoagulation therapy today

Patient choice in anticoagulation therapy

The group of conditions requiring anticoagulation therapy include venous thromboembolism (VTE), stroke prevention for non-valvular atrial fibrillation and prosthetic heart valves. Usually started in secondary care or outreach clinics in primary care¹, anticoagulation therapy offers patients a choice between 5 usual medication types: warfarin, apixaban, dabigatran, edoxaban and rivaroxaban².

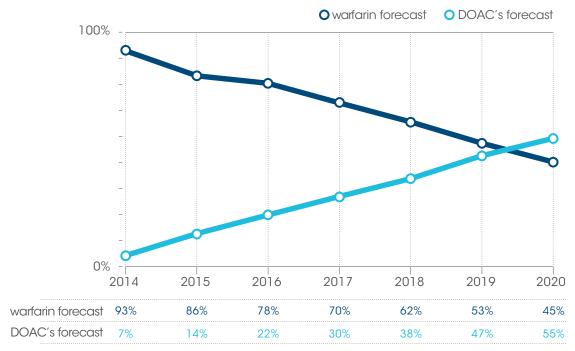
Warfarin is considered a cost-effective drug for anticoagulation therapy. However, although costs have been perceived as a barrier, the National Institute for Health and Care Excellence (NICE) has concluded that DOACs are also cost-effective when the medical, societal and personal savings from avoiding strokes are taken into account. These anticoagulants must then be available to patients within their licensed indications.^{3,4}

In the case of DOACs, NICE suggests that although there is no need for regular blood tests to check their international normalised ratio (INR), patients still require regular follow-up and monitoring⁵. As the anticoagulant effect of the DOACs decreases 12–24 hours after the last dose is taken, NICE also highlights the importance of adherence to reduce the risk of a thromboembolic event⁶.

For all anticoagulants it is recommended that patients are fully involved in the decision making about their treatment. Comprehensive education, decision support materials and an informed discussion of the benefits and side effects of each medication should be part of the initial consultation. An ongoing package of monitoring, reviews and support should also be agreed upon between patient and care team.⁷

"(...) although (unlike warfarin) there is no need to have regular blood tests to monitor the international normalized ratio (INR), they [patients on DOACs] will still require regular monitoring, blood tests, and review of their treatment."5

DOACs in anticoagulation therapy today



Public Health England, April 2016.8

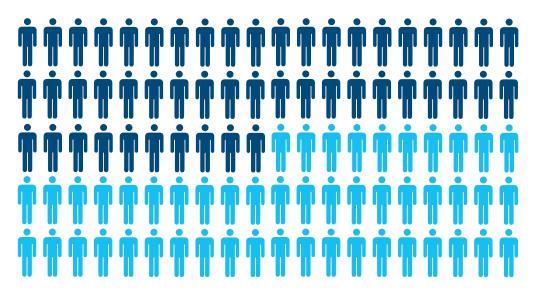
DOACs present potential advantages in fixed dosing, fewer drug interactions and fewer clinic appointments as compared to warfarin, which for years has been the standard of care for anticoagulation therapy. The prescribing trends for DOACs have shown an accelerated increase in the last couple of years⁸ and this is estimated to continue. Sue Rhodes, VTE CNS and joint Anticoagulant Lead at Great Western Hospital in Swindon, describes that the trend "continues to rise with the national average being a year-on-year increase of 10–11%."

However, some experts argue that the uptake has been lower and slower than expected. In England, the uptake of DOACs varies from 4.2% to 69.3% across CCGs° and in 2015, the average uptake was 16.5%, 3.5% lower than the 20% estimated for the first year°. Prof John Camm from St George's University Hospital, highlights that the perceived costs, the lack of monitoring and the choice between four different agents might be initial deterrents slowing the uptake. Nevertheless, the clear net clinical benefit of DOACs, he explains – as well as an improved quality of life for patients – should drive a faster increase in their use. Prof Camm also explains that long-term therapy is cost-effective and that "the costs of the DOACs are falling very quickly and this reduction will continue especially as the indications for lifelong therapy with these drugs increase".

NICE and the European Heart Rhythm Association (EHRA) provide recommendations for the use of DOACs in anticoagulation therapy. As an example, the EHRA suggests that treatment of patients on DOACs should be reviewed once every 3 months and that regular reviews must assess adherence, any event that might signal thromboembolism, adverse effects, co-medication and renal and hepatic function¹⁰. The implementation of advice around DOACs, however, is not optimal and consensus is still yet to be achieved about what would represent excellence in DOACs anticoagulation management, including adherence.

A report called 'One Year On: Why are patients still having unnecessary AF-related strokes?' reviews the implementation of the guideline from NICE (CG180) clinical guidance for Atrial Fibrillation (AF) management one year after guidance publication. This report determined that "around half of patients that should be treated with oral anticoagulation are not." NICE has estimated that implementing the CG180 for people with AF – the most common heart arrhythmia with an incidence expected to double in the next 50 years 14.15 – can result in 10,000 fewer strokes per year, reducing the risk of stroke by 31%14.

Optimal anticoagulation management can have an immeasurable impact on the lives of patients and their loved ones as well as a significant impact on the NHS with reductions in adverse events and improvement in cost-effective care. But how can excellent anticoagulation management be achieved?



"around half of patients that should be treated with oral anticoagulation are not." 13

Adherence in long-term therapies

Long-term therapies: a problem with adherence?

Compliance is defined as the "action or fact of complying to a wish or command" ¹⁶. Adherence, on the other hand, implies an agreement between the patient and the prescriber on the latter's recommendations and is defined by the degree to which a patient's actions follow this agreement ¹⁷. Understanding the patient as an active partner and striving for good communication between them and their care team is necessary for effective clinical practice ¹⁸.

Adherence in long-term conditions can be a challenge. It is estimated that between a third and a half of medicines prescribed for these conditions are not taken as recommended¹⁷. Studies have found that adherence to long-term therapy or treatment can average 50%^{19,20}.

Non-adherence represents a fundamental limitation in the delivery of healthcare which might result from a failure to fully agree with the patient on their treatment and to identify and provide the necessary support they will need later on¹⁷. Non-adherence can result in a lack of improvement or deterioration of health, as it limits the benefits of medicines generating an increased demand on the healthcare system from deteriorating population health¹⁷.

The causes of non-adherence have been described in two overlapping categories: intentional and unintentional¹⁷. These are their definitions:

 Unintentional non-adherence – "occurs when the patient wants to follow the agreed treatment but is prevented from doing so by barriers that are beyond their control." Examples include problems using the treatment, forgetting to take it and difficulty understanding the instructions. Adherence in long-term conditions can be a challenge. It is estimated that between a third and a half of medicines prescribed for these conditions are not taken as recommended 17. Studies have found that adherence to long-term conditions can average 50% 19,20.

• Intentional non-adherence – "occurs when the patient decides not to follow the treatment recommendations." ¹⁷ This can happen when the patient's beliefs and preferences don't align with the treatment, affecting their motivation to start and continue with it. ¹⁷ As an example, some patients are wary of becoming dependant on their medication, especially on long-term therapies²¹.

Adherence can also be affected by: 21

- The complexity of the treatment number of medicines and frequency of administration
- Social/economic factors including medication costs
- Condition-related factors such as the level of disability and the severity of the condition

In order to support adherence through the intrinsic complexities of long-term therapies, it is important that healthcare professionals find the most effective way of communicating with patients and also facilitate an environment of involvement and support¹⁷. This must start at diagnosis and initial prescriptions, but it ought to continue throughout treatment to minimise the effect of non-adherence as a fundamental limitation in the delivery of the healthcare system¹⁷.

Understanding the patient as an active partner, taking into account their preferences and enabling them to make informed decisions whilst striving for good communication with their care team is essential for effective clinical practice. An open, patient-centred approach that avoids focussing on blame and recognises non-adherence as a common issue, should encourage patients to be frank about their experience and to raise any doubts or concerns they have about treatment. Working with such an approach, care teams can identify specific, perceptual and practical adherence barriers for each individual on an ongoing basis²².

Jo Jerrome, CEO Thrombosis UK, explains the importance of a positive exchange between a healthcare professional and patient from the latter's perspective:

"Understanding your condition and treatment are key factors in helping to restore health and well-being. To be able to try to restore your life, you need to feel confident that you're in "safe hands" – that your care is monitored and responsive to you and your medical needs. This is especially critical when managing long-term conditions often requiring multiple healthcare providers. Nothing feels better than being able to leave a medical appointment reassured

of the care, sharing of information, treatment and planned monitoring that will keep you well and as safe as possible."

As highlighted in this quote, one of the pillars of excellent care is essential communication between healthcare professionals and patients. This creates a strong partnership supported by evidence-based information which takes into account the patient's needs and preferences for their treatment and care. ²³



Excellent anticoagulation services

Recommendations for excellent anticoagulation services

Effective anticoagulation therapy can reduce the risk of strokes, save lives and reduce costs related to long hospital stays, lower rates of discharge and severe stroke-related complications for the NHS.²⁴ Ensuring the best provision of care can have a significant impact on population health across the UK.

What does excellence in anticoagulation services involve?

The Interdisciplinary group for Stroke Prevention in Atrial Fibrillation (iSPAF) put forward a paper called 'Excellence in anticoagulation care: Defining the elements of an excellent anticoagulation service' from an in-depth review of best practice guidelines and examples as well as clinical evidence related to AF care. Consistent with most of the existing advice, and largely transferable to anticoagulation therapy for other conditions, the recommendations of this document describe that excellent anticoagulation services should include: 4.25

- Comprehensive patient education
- · Clear protocols of patient initiation, performance and reassessment
- Regular patient and medication reviews
- · Alternative treatment options where required
- Multidisciplinary expert care
- · A clear and simple electronic referral pathway
- Provision of regular and transparent performance data to commissioners and patients

High quality anticoagulation care will meet the patient's lifestyle needs, will integrate care across secondary and primary – especially for complex patients – and will be delivered accessibly and close to home.⁷

A one-stop anticoagulation service will include patient education, discussion and support as well as blood tests, dose changes and follow-up arrangements to help manage the patient's care.²⁶

Shared decision making

The factors that affect patients' decisions about medicines include their understanding of their condition, the view of their own need for the treatment, their concerns about the medicine and their awareness of the possible treatments²⁷. The active involvement of patients in anticoagulation therapy is highly important and should take place not only during initiation but throughout the management of their medication and the evolution of their condition. In order to enhance adherence, it is important to sustain the level of involvement of patients – especially those who have long-term conditions – to promote a continuous understanding of their anticoagulation medication and the importance and benefits of adherence.

Expert advice suggests that excellent anticoagulation services should be built around the needs of their patient populations and offer informed initial consultations on:²⁶

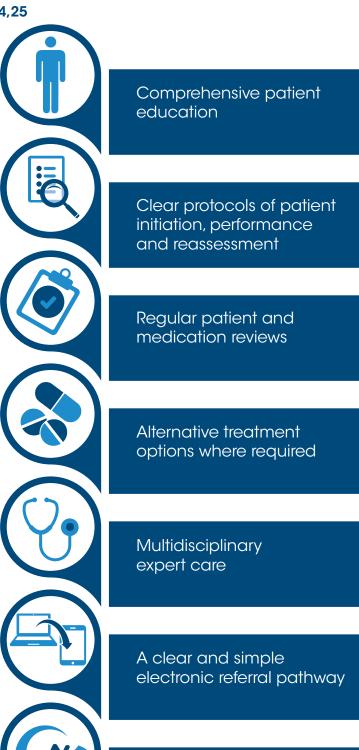
- The patient's condition
- The medical aims of anticoagulation therapy
- An overview of all the available anticoagulant options, how they will influence their conditions and what are their benefits and disadvantages

A working partnership between patient and clinician is then established which ideally clarifies what the patient hopes the treatment will achieve and avoids making assumptions about the patient's preferences.²⁷ Finally, through comprehensive education and decision support, they choose treatment and an ongoing package of monitoring, review, education and support.¹⁰

The process of informing and educating the patient is a continuous one. Their knowledge, understanding, views and concerns will change over time and that is why it is important to review them and offer repeat information whilst treating long-term conditions and multiple medicines. ²⁸ Effective treatment relationships rely on evidence-based explorations of the available therapeutic options, negotiations of the treatment, planned follow-up and informed discussions on adherence ¹⁷.

Excellent AC services

should include: 4,25



Regular and transparent performance data for

commissioners and patients

Structured monitoring and follow-up

Inconsistent anticoagulation therapy can lead to worse outcomes and, in the case of patients with AF, it might be associated with a higher risk of stroke-associated disability²¹. The AF Association, with a membership of over 30,000 patients, is an organisation with a designated help and support line for patients with AF and it promotes effective care following the 'Detect, Protect, Correct and Perfect'²⁹ care pathway brought together in the AF Toolkit. To ensure that the available, proven and recommended guidance is implemented at primary care level, the AF Association focuses on the 'Perfect the Patient Pathway' working in partnership with multiple stakeholders at regional and national level in England and the devolved nations to drive the uptake and implementation of best practice.³⁰

The AF Association explains that,

"It is critical that healthcare professionals work in partnership to manage patients with AF to ensure detection, appropriate anticoagulation therapy is prescribed, and specialist referral to appropriate treatment option for AF is given – however, without effective monitoring and follow-up this good work can still be tragically undone if patients do not adhere to anticoagulation therapy." ³¹

The monitoring of warfarin anticoagulation therapy is well established and structured. Reliant on the INR, patients and clinicians should work together to aim for the target INR and assess the time in therapeutic range (TTR) with a minimum NICE recommended TTR of 65%.³² Self-testing and self-management are as effective and safe as usual care for suitable patients and can improve the quality of oral anticoagulation for this group.³³

However, anticoagulation therapy is changing. DOACs with less drug interactions, fixed dosing, fewer visits to clinic and no need for routine coagulation monitoring, continue to rise in prescription numbers across England – sometimes quadrupling in a space of a few years such as the case of apixaban, edoxaban and rivaroxaban. But is there consensus on a standardised process for the management of patients on DOACs?

Best Practice for DOACs

A standardised process for DOACs

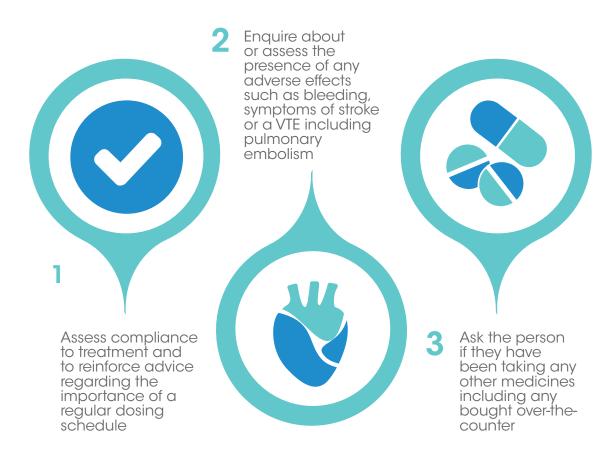
The 'EHRA Practical Guide on the Use of New Oral Anticoagulants (NOAC) in Patients with Non-Valvular Atrial Fibrillation' describes that structured follow-up is mandatory to ensure safe and effective drug intake. DOACs have a short half life and their therapeutic effect fades rapidly (12–24 hours after the last intake), compromising stroke/clot prevention. That is why all means to optimise anticoagulation therapy and medication adherence should be considered to support adequate protection. Alongside education, as for all anticoagulation therapy, the recommendation is that patient and care team agree on a clearly pre-specified follow-up schedule which might include expert care from different disciplines such as a general practitioner, cardiologist or electrophysiologist.¹⁰

NICE recommends patients on DOACs should be reviewed every 3 months to:34

- Assess compliance to treatment and reinforce advice regarding the importance of a regular dosing schedule
- Enquire about or assess the presence of any adverse effects such as bleeding, symptoms of stroke or a VTE including pulmonary embolism
- Ask the person if they have been taking any other medicines including any bought over-the-counter

NICE highlights that there is concern that the lack of monitoring will lead to poor adherence on DOACS – where due to the relatively short half-lives of these drugs adherence is important³⁵. NICE recommends that patients on DOACs still require regular monitoring, blood tests to determine kidney and liver function and review of their treatment³⁶. Additionally, NICE describes that patients should have access to ongoing education and support where "healthcare professionals ensure that patients understand why they are taking an anticoagulant and the expected benefits".³⁷

NICE recommends patients on DOACs should be reviewed every 3 months³⁴



Best practice and consensus

However, there are still questions about the implementation of the recommendations and whether there is consensus behind them. Our contributors raise some of them in this section.

Prof Camm explains,

"NICE guidelines are confusing because of the need to balance the books and the inability of NICE to see how therapy will inevitably develop. The EHRA guidance is less confusing but deals with the details of the use of NOACs which is far too much for the primary care physician – a less complicated version of this kind of document for GPs is needed."

Application of best practice and evidenced advice can vary across the UK and so does the access to life-saving treatment. A recent report by The Medical Technology Group called 'The North-South NHS Divide: How where you are not what you need dictates your care', found a vast range in admission rates for rapid treatment of stroke patients – which can make the difference between life and death: "from over eight out of ten patients being seen within this time [4 hours of arrival] (84.5 per cent) in Hillingdon to just a fifth (21 per cent) in Wyre Forest."³⁸

At St George's University Hospital, patients are receiving education from anticoagulation nurses and pharmacists. Prof Camm continues,

"The workload for DOACs is no greater than for vitamin K antagonist (VKA) therapy, but since the initiation and follow-up of this therapy takes place in different locations the funding for this follow-up must also follow the patients. At my hospital, we use anticoagulation nurses and pharmacists to educate patients and they are also responsible for the primary follow-up of the anticoagulant therapy in patients with AF. This is more difficult in general practice. There are some solutions such as use of community pharmacists or practice nurses, but much of this depends on the size of the group practice. Small practices cannot implement these solutions and should probably opt to have their patients followed in secondary care."

In a 2016 service audit, the Carmel Medical Practice, Darlington, identified a practice prevalence of AF of 2.7%³⁹. From a total patient population of 272, treatment of patients on DOACs was 57.9% from which 92.4% had their U+E/creatinine clearance level review in the past 12 months^{39,40}. Prof Ahmet Fuat from the Carmel Medical Practice, believes that EHRA's advice is the best

available and explained that his practice follows it:

"I think monitoring of DOACs is essential and we have a 6-monthly rolling audit of all our AF patients. We obviously need to monitor time in therapeutic range for warfarin every 6-months. All patients need full blood count, renal function and liver function tests at least once a year. If they are over 75 and/or frail, we check these once every 6 months (especially if dabigatran or edoxaban, which are more reliant on renal clearance). We should use creatinine clearance calculated using the Cockcroft-Gault criteria, as this is what all trials use and I do not agree with NICE guidance stating eGFR should be used. In otherwise reasonably fit patients under 75 with normal renal function assessment 12 monthly is enough."

At Great Western Hospital, the anticoagulation service is following up patients regularly. Sue Rhodes explains that follow-up is dependent on three elements: location, current service provision and system capacity to provide appropriate advice and carry out follow-up. She describes:

"Our service is predominantly secondary care led and we have incorporated the DOAC patients into our existing database so that we can follow them up at regular intervals and we are a point of contact for any queries. This is important to have especially for those patients who have switched from warfarin to a DOAC as the level of input from their healthcare professional is significantly reduced once they have been switched and this can be very unsettling for patients."

Adherence and DOACs

Is adherence an issue for patients on DOACs?

The EHRA and NICE provide advice which suggests that adherence, known to be ≤80% for most drugs in daily practice¹⁰, requires vigilance and optimisation. That is why all means to optimise compliance should be considered¹⁰.

According to Sue Rhodes,

"Adherence has always been an issue with any medication but the difference with the DOACs is that they are required to take every dose otherwise they are at risk of a stroke / further clot development. That is why it is imperative that full counselling is offered to patients commencing on these drugs in the same way that we would counsel regarding warfarin. Asking a patient to take a drug that may or may not prevent them from having a stroke is much more difficult than asking them to take the medication when they already have a condition (e.g. deep vein thrombosis/ pulmonary embolism) and the patient knows that it will get better [if they take the medication]. This has always been the case for warfarin, but we have the benefit of being able to check compliance with warfarin."

According to the AF Association, improvements have been made in the detection and protection of patients with AF, including medicines reviews. However, a gap remains of how to effectively communicate the value of anticoagulant therapy and its monitoring to patients. To ensure consistency in what is provided to patients on DOACs, the AF Association suggests a personalised package of care which includes:^{30,31}

- Stroke awareness and ways to prevent AF-related stroke
- Psychological support
- Contact details for further advice and support
- Comprehensive education

Adherence is known to be ≤80% for most drugs in daily practice¹⁰



Ensure consistency - the **AF Association suggests** a personalised package of care including:30,31 Stroke awareness and ways to prevent AF-related stroke Psychological support Comprehensive education Contact details for further advice and support

A dynamic process

Improving adherence requires a frank, open approach which accepts that non-adherence might be the norm and avoids blaming patients, encouraging them instead to communicate doubts and concerns about their treatment⁴¹.

Often healthcare professionals are unaware of how patients take their medicines and sometimes patients do not take their medicines as prescribed. For this reason, it is important to assess patients' readiness to follow treatments, provide advice on how to do it and take the opportunity to monitor their progress on every appointment 43.

Informed adherence should be one of the goals of a dynamic, multidisciplinary, patient-centred approach. This should include specific training for healthcare professionals on how to manage adherence and how to adapt interventions to different patient needs⁴³.

For anticoagulation therapy on DOACs, Prof Camm suggests that education is the best way forward. He also explains:

"Adherence and persistence are common problems, particularly with any therapy which prevents disease or complications when given for a condition which does not result in immediate improvement of symptoms. For most drugs it doesn't matter too much if occasional doses are missed, for example, statins or antihypertensive therapy. This is not the case with drugs which have relatively short half-lives and which are life- or irretrievable harm-saving therapies. Adherence is therefore crucial and in the absence of adequate monitoring is hard to assess."

Low-cost interventions

Low cost interventions on adherence can achieve significant cost-savings by focusing on the prevention of risk factors and adverse health outcomes⁴⁴. Adherence can be improved with tailored interventions that take into account the specific difficulties the patient is experiencing⁴⁵.

In the next section, we look at what some anticoagulation services are doing to provide an excellent service and take action on adherence.

Case study

Involve pharmacists in the improvement of adherence – the Perfect pathway

NICE describes that pharmacists can have a role in supporting adherence by reinforcing "the importance of treatment and the need to take every prescribed dose each time they dispense the patient's prescriptions"³⁷.

Anticoagulation care teams are already working in conjunction with pharmacists to conduct face-to-face medicine reviews and support adherence as part of an advance service called the new medicines service (NMS). This service aims to improve patient understanding of treatment and medicine concordance and it consists of structured interviews carried out by community pharmacist with patients during their first month of treatment with a new medicine.⁴⁶

At a multidisciplinary meeting in 2015, Sue Rhodes and Sarah Bond from Great Western Hospital expressed concerns about the reduced follow-up they could provide for DOAC patients. Fiona Castle from the local pharmaceutical committee (LPC) expressed concern about the community pharmacists' inability to identify patients early enough to provide follow-up through the NMS. As poor adherence for anticoagulants can result in potentially significant harm through ineffective treatment or side effects, these drugs are eligible for NMS. They agreed to work together to develop a referral scheme.⁴⁶

The New Medicines Service and Great Western Hospital

The anticoagulation team asked all new patients for details of their usual pharmacy and for permission to share information with them. Once they registered the information in PharmOutcomes, they began referring the patients to the NMS service, which emails the pharmacies and makes the information available in their system.⁴⁶

Sue Rhodes, from Great Western Hospital, describes:

"One of the things that we explored was to involve the community pharmacist by linking with PharmOutcomes. We ask the patient which pharmacy they collect their regular medications from and each week we upload the information to the community pharmacies via PharmOutcomes. This then prompts the pharmacist to either contact the patient by phone to go over their new medication, or they will ask the patient to attend the pharmacy for a face-to-face discussion to reiterate the counselling points. The patient is also checked each time their medication is collected and asked about any problems. We have found this service extremely useful."

Between October 2015 and January 2017, the anticoagulation service made 526 referrals at an average of 33 patients a month. Of these, 72.8% referrals were acknowledged by the pharmacy and 59.1% marked as completed on the system. Patients were followed up through the NMS system in the majority of cases – informal follow-up through telephone, post-discharge medicines use review and discussions when patients visited the pharmacy, also took place. Pharmacists reported 88% of the referrals useful and the system is now firmly embedded.⁴⁶

Sue Rhodes explains that,

"One hat does not fit all, but we need to work with existing services to enable them to carry out the relevant follow-up. It doesn't have to be complicated, but it needs to be owned so that someone has responsibility for these patients. The system that we use in our clinic could easily be replicated in primary care."

Case study

Excellent anticoagulation service in a nurse-led DOAC clinic in primary care

At a general practice surgery in Birmingham, a clinical nurse specialist (CNS)-led clinic was designed to manage patients receiving DOACs in primary care in a way which is safe, efficient and cost-effective⁴⁷.

The anticoagulation service at the GP surgery was already well-established and managing 125 patients on VKAs using INRstar, a clinical decision support software, but there was no formal management or follow-up for DOAC patients⁴⁷.

Donna Sydenham, CNS at the Bellevue Medical Centre in Birmingham, explained:

"I recognised there was no structured follow-up in primary care for patients that had been initiated on DOAC medications. Once they are initiated, they are then discharged back to the GP. This was a concern because: a) compliance was not being checked and b) renal function was not being monitored – these could potentially lead to serious adverse events. I decided to develop a system at our clinic that ensured excellent patient care and safety."

A list of patients taking DOACs was identified by the practice and added to INRstar for management and follow-up. All subsequent patients initiated on DOACs at the practice were also added to ensure appropriate management and support, and to facilitate the switching process from one anticoagulant to another⁴⁷.

A patient-focused service

One of the main aims of this clinic was to create a patient-focused, holistic approach to implement NICE guidance on DOACs and make the service safe, cost-effective and efficient⁴⁷. The initial consultation with the patient is an example of how this was achieved.

Comprehensive initial consultations

The appointment involves a detailed discussion of the indication and options for treatment, to include VKAs and DOACs, and the risks and benefits associated with each of the options in accordance with recommendations. The CNS took a holistic overview of the patient, taking into consideration lifestyle, comorbidities and other medications. The initial session also included a thorough discussion around the importance of adherence and a detailed overview of the way the patient currently takes their medications. This was important to ascertain if the patient is suitable for a DOAC.⁴⁷

A clear pathway for structured follow-up

Phone reviews were the first point of contact a month after DOAC initiation. The frequency of review after this is dependent on previous creatinine clearance results and includes at least an annual comprehensive review of liver and kidney function, weight, blood pressure and a full blood count.⁴⁷

The clinic says that the CNS-led clinic has been successful resulting in fewer admissions to hospital and fewer adverse events. They also said that feedback has been positive from staff and patients and concluded that appointing a clinical-lead or CNS for anticoagulation in each practice can provide many benefits, including improved outcomes, better continuity of care and a more positive experience for patients.⁴⁷

Supporting adherence

What can be done about adherence?

Studies have been shown that some patients started questioning the benefits of anticoagulation therapy soon after initiation. One study suggested that 1 in 3 patients become non-persistent within 6 months⁴⁸ whilst another study showed that during the first year, fewer than half of the patients took the medications consistently⁴⁹.

A multi-method approach that combines self-reporting and reasonable objective measures is the current state-of-the-art in the measurement of adherence¹⁷. Sue Rhodes suggests that one of the things that can be done is to "support practices in primary care who do currently provide a DOAC service by devising a way for them to accurately monitor these patients to ensure compliance, renal function and age are considered in order to maximise the appropriate dose for each patient."

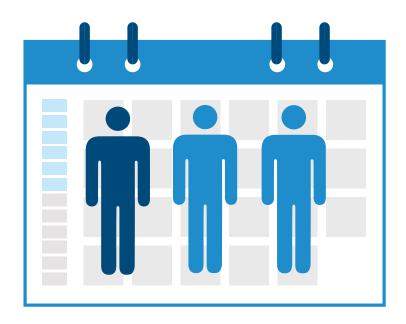
Comprehensive education and integrated technology

The AF Association recommends that the personalised package for patients on DOACs should include the latest, comprehensive education and information on:50

- cause
- effects and possible complications of AF
- management of rate and rhythm control
- anticoagulation (including practical advice to improve adherence)
- provision of self-monitoring and support networks such as AF Association and Arrhythmia Alliance

The AF Association also suggests that there needs to be a focus on how mobile technology can be used to help patients remain on therapy, by providing support and motivation, as well as connecting them to their clinician without the need for multiple GP appointments in already over-stretched services⁵⁰.

The AF Association explains that it has been at the forefront in working with new technologies to get them trialled by patients, producing data and pushing for the uptake of proven technologies. Their commitment continues: "we will do the same for technologies that enable patients to remain on therapy and connected to health reporting systems." ⁵⁰



1 in 3 patients become nonpersistent within 6 months⁴⁹

The future of anticoagulation therapy: findings and conclusion

Anticoagulation and an ageing population

Anticoagulants are one of the most frequently prescribed medications in elderly patients as the risk of thromboembolic complications that require anticoagulation therapy increases with age⁵¹. Dr Matthew Fay, Clinical Chief Executive The Westcliffe Group, explains that,

"The frail patient is at a tipping point in the benefits of anticoagulation for stroke risk reduction. Although we know that this is a group with a very high stroke risk, we can also see that the reduction of the number of stroke events balances with the number of bleeding events."

He raises questions about the care pathways when patients are not able to continue anticoagulation therapy with DOACs,

"We can return to the older VKA intervention. This will now be in an older, frailer patient who is warfarin naïve. They will require close monitoring as warfarin is a challenging medication in those with poor renal function. Should this switch be done before the absolute value of creatinine clearance necessitating a change occurs, thus giving time for stabilisation before true renal decline?

Should intervention be discontinued at this stage? If so who is to make this decision and how can we support the patient to make an informed choice? Should this be left to the individual clinician with their patient or can the discussion be widened to include other experts such as anticoagulation therapists, elderly care specialists or community matrons, cardiology-interested practitioners working in a multidisciplinary team (MDT) setting to ensure all the various facets of the decision are appropriately reviewed to assist the patient (and often their carer) make a fully informed decision?"

Sue Rhodes considered this and suggests,

"This is a dilemma, but I think adopting a MDT approach would work in some areas, perhaps a GP having a joint clinic with an anticoagulant specialist nurse to review the more elderly patients before a change is necessitated so that a discussion can begin with the patient outlining the options? In an area where anticoagulation may not be everyone's interest, this could be a mini-specialist clinic where patients from other practices were seen."

The need for more data

Dr Fay suggests research is necessary to discover safer ways to help patients through anticoagulation therapy well into old age and highlights the need of a secured system, "more work is required to research the best options for patients in this setting, but until clear evidence is available we need to ensure that both patients and their clinicians are in a safe and well-governed system."

Prof Fuat suggests the need for "independent data collection for patients in the real world. This could be done through a practice-based registry where all clinical outcomes for patients receiving DOACs could be collected." The AF Association is supporting efforts to use integrated mobile technology that can help patients remain on therapy and suggests that "apps that can educate and motivate patients, while connecting them to their doctor, and providing useful integrated feedback will be of significant benefit."

Sue Rhodes explains,

"We have managed to do this in Swindon and I see no reason why it could not be accomplished in primary care, it just needs ownership and the support of a specialist (this could be a secondary anticoagulant clinic where advice could be sought)." "(...)more work is required to research the best options for patients in this setting, but until clear evidence is available we need to ensure that both patients and their clinicians are in a safe and well-governed system."

Dr Matthew Fay, Clinical Chief Executive The Westcliffe Group

Conclusion

For patients taking long-term anticoagulation, the advent of the DOACs has opened the possibility of effective protection against stroke and VTE without many of the burdens of the treatment which the VKAs involved. For clinicians, the problems are changing from organising regular INR tests and adjusting warfarin doses, to ensuring that patients remain actively engaged, informed and adherent with their treatment.

The evidence presented in this paper strongly suggests that the tools we need to achieve this aim are based on genuine joint decision making and an ongoing relationship which involves continuous support, education and learning both for patients and clinicians.

Patients needing anticoagulation form a heterogeneous group in which no single solution is appropriate for everyone. For many people, treatment with DOACs will be the optimum choice and in these cases, anticoagulation care teams will need to develop robust ways of monitoring patients and maximise treatment adherence. For a significant number of patients – particularly the very elderly – warfarin will still play a role. Better ways of providing convenient, safe dosing advice and monitoring will need to be developed for these.

Broadening the delivery of anticoagulation care to include healthcare professionals other than the traditional hospital/GP/nurse model will help deliver the multidisciplinary comprehensive care that patients need. In line with the NHS' Five Year Forward View, another way forward will be to embrace the possibilities which technology⁵² can deliver for patients and their care teams.

Acknowledgements

We would like to thank all the key opinion leaders and associations involved in this collaborative discussion paper for their insight and support.

References

- ¹ National Institute for Heath and Care Excellence. 'Anticoagulation oral, Scenario: Warfarin.' Last revised: December 2016. Last accessed: 12 September 2017. Available at: https://cks.nice.org.uk/anticoagulation-oral#!scenario:4
- ² National Institute for Heath and Care Excellence. 'Anticoagulation oral: Summary.' Last revised: December 2016. Last accessed: 12 September 2017. Available at: https://cks.nice.org.uk/anticoagulation-oral#!topicsummary
- ³ National Health Service England (London Region), London Clinical Networks. Excellence in anticoagulant care: Defining the elements of an excellent anticoagulation service. August 2016, p. 5. Last accessed: 20 September 2017. Available at: http://thrombosisuk.org/downloads/stroke-af-anticoag-082016.pdf
- ⁴ National Health Service England (London Region), London Clinical Networks. 'Excellence in anticoagulant care: Defining the elements of an excellent anticoagulation service.' August 2016, p. 6. Last accessed: 20 September 2017. Available at: http://thrombosisuk.org/downloads/stroke-af-anticoag-082016.pdf
- ⁵ National Institute for Heath and Care Excellence. 'Anticoagulation oral: Summary.' Last revised: December 2016. Last accessed: 12 September 2017. Available at: https://cks.nice.org.uk/anticoagulation-oral#!scenario
- ⁶ National Institute for Heath and Care Excellence. `Anticoagulation oral: Summary.' Last revised: December 2016. Last accessed: 12 September 2017. Available at: https://cks.nice.org.uk/anticoagulation-oral#!scenariorecommendation:2
- ⁷ National Health Service England (London Region), London Clinical Networks. 'Excellence in anticoagulant care: Defining the elements of an excellent anticoagulation service.' August 2016, p. 4. Last accessed: 20 September 2017. Available at: http://thrombosisuk.org/downloads/stroke-af-anticoag-082016.pdf
- ⁸ Public Health England. 'Forecast of changes in prescribing of NOACs and warfarin 2014–2020.' Published date: April 2016.
- ⁹ Association of the British Pharmaceutical Industry, Stroke in Atrial Fibrillation Initiative. 'One year on Why are patients still having unnecessary AF-related strokes?' April 2016, p. 19. Last accessed: 12 September 2017. Available at: http://www.abpi.org.uk/Documents/Embargo9May_ABPI_OneYearOn_FINALREPORT.~pdf#search=One%2520year%2520on%2520why%2520are%2520 patients
- ¹⁰ European Society of Cardiology. 'European Heart Rhythm Association Practical Guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation'. Europace. 2013:15:625–651
- ¹¹ Association of the British Pharmaceutical Industry, Stroke in Atrial Fibrillation Initiative. 'One year on Why are patients still having unnecessary AF-related strokes?' April 2016. Last accessed: 12 September 2017. Available at: http://www.abpi.org.uk/Documents/Embargo9May_ABPl_OneYearOn_FINALREPORT.~pdf#search=One%2520year%2520on%2520why%2520are% 2520patients
- ¹² National Institute for Health and Care Excellence, 'Atrial fibrillation management, clinical guidance.' [NICE CG180]. Published date: 18 June 2014. Last update: August 2014. Last accessed: 20 September 2017. Available at: https://www.nice.org.uk/guidance/cg180/resources/atrial-fibrillation-management-pdf-35109805981381
- ¹³ Association of the British Pharmaceutical Industry, Stroke in Atrial Fibrillation Initiative. 'One year on Why are patients still having unnecessary AF-related strokes?' April 2016, p 7. Last accessed: 12 September 2017. Available at: http://www.abpi.org.uk/Documents/Embargo9May_ABPI_OneYearOn_FINALREPORT.~pdf#search=One%2520year%2520on%2520why%2520are%2520 patients

- ¹⁴ Association of the British Pharmaceutical Industry, Stroke in Atrial Fibrillation Initiative. 'One year on Why are patients still having unnecessary AF-related strokes?' April 2016, p. 4. Last accessed: 12 September 2017. Available at: http://www.abpi.org.uk/Documents/Embargo9May_ABPl_OneYearOn_FINALREPORT.~pdf#search=One%2520year%2520on%2520why%2520are% 2520patients
- Association of the British Pharmaceutical Industry, Stroke in Atrial Fibrillation Initiative. 'One year on Why are patients still having unnecessary AF-related strokes?' April 2016, p. 6. Last accessed:
 September 2017. Available at: http://www.abpi.org.uk/Documents/Embargo9May_ABPI_OneYearOn_FINALREPORT.~pdf#search=One%2520year%2520on%2520why%2520are%
 2520patients
- ¹⁶ Oxford English Dictionary. 'Compliance'. Last accessed: 12 Sept 2017. Available at: https://en.oxforddictionaries.com/definition/compliance
- ¹⁷ National Institute for Health and Care Excellence, 'Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence, clinical guide.' [NICE CG76]. 28 January 2009, p. 4. Last accessed: 12 September 2017. Available at: https://www.nice.org.uk/guidance/cg76/resources/medicines-adherence-involving-patients-in-decisions-about-prescribed-medicines-and-supporting-adherence-pdf-975631782085
- ¹⁸ World Health Organisation, 'Adherence to long-term therapies Evidence for action.' 2003, p. 4. Last accessed: 12 September 2017. Available at: http://apps.who.int/medicinedocs/pdf/s4883e/s4883e.pdf
- ¹⁹ Bloom BS. 'Daily regimen and compliance with treatment'. British Medical Journal, 2001, 323:647. doi.org/10.1136/bmj.323.7314.647
- ²⁰ Wahl C., Gregoire JP, Teo K. et. al. 'Concordance, Compliance and Adherence in Health Care: Closing Gaps and Improving Outcomes'. Healthc Q. 2005:8: 65–70. doi:10.12927/hcq..16941
- ²¹ Svetlana V. Garkina, Tatiana V. Vavilova, Dmitry S. Lebedev et al. 'Compliance and adherence to oral anticoagulation therapy in elderly patients with atrial fibrillation in the era of direct oral anticoagulants'. J Geriatr Cardiol. 2016:13:807–810. doi:10.11909/j.issn.1671-5411.2016.09.010
- National Institute for Health and Care Excellence, 'Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence, clinical guide.' [NICE CG76]. 28 January 2009, p. 5. Last accessed: 12 September 2017. Available at: https://www.nice.org.uk/guidance/cg76/resources/medicines-adherence-involving-patients-in-decisions-about-prescribed-medicines-and-supporting-adherence-pdf-975631782085
- ²³ National Institute for Health and Care Excellence, 'Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence, clinical guide.' [NICE CG76]. 28 January 2009, p. 6. Last accessed: 12 September 2017. Available at: https://www.nice.org. uk/guidance/cg76/resources/medicines-adherence-involving-patients-in-decisions-about-prescribed-medicines-and-supporting-adherence-pdf-975631782085
- ²⁴ Association of the British Pharmaceutical Industry, Stroke in Atrial Fibrillation Initiative. 'One year on Why are patients still having unnecessary AF-related strokes?' April 2016, p. 4. Last accessed: 12 September 2017. Available at: http://www.abpi.org.uk/Documents/Embargo9May_ABPI_OneYearOn_FINALREPORT.~pdf#search=One%2520year%2520on%2520why%2520are% 2520patients
- ²⁵ National Health Service England (London Region), London Clinical Networks. 'Excellence in anticoagulant care: Defining the elements of an excellent anticoagulation service.' August 2016, p. 3. Last accessed: 20 September 2017. Available at: http://thrombosisuk.org/downloads/stroke-af-anticoag-082016.pdf
- ²⁶ National Health Service England (London Region), London Clinical Networks. Excellence in anticoagulant care: Defining the elements of an excellent anticoagulation service.' August 2016, p. 7.

- ²⁷ National Institute for Health and Care Excellence, 'Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes.' [NICE NG5]. 4 March 2015, p. 10. Last accessed: 12 September 2017. Available at: https://www.nice.org.uk/guidance/ng5
- ²⁸ National Institute for Health and Care Excellence, 'Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence, clinical guide.' [NICE CG76], 28 January 2009, p. 7.
- ²⁹ National Health Service, London Clinical Networks. Atrial Fibrillation (AF) toolkit: 'Detect, Protect and Perfect working together across London to prevent AF related strokes.' 2017.
- ³⁰ Nigel Breakwell, Trudie Lobban. 'Comments and considerations for NOAC adherence white paper: AF Association position on improving the AF management pathway.' Unpublished. August 2017.
- ³¹ Nigel Breakwell, Trudie Lobban. 'Comments and considerations for NOAC adherence white paper: AF Association position on improving the AF management pathway.' Unpublished. August 2017, p. 1.
- ³² National Institute for Heath and Care Excellence. 'Anticoagulation oral, Scenario: Warfarin.' Last revised: December 2016. Last accessed: 12 September 2017. https://cks.nice.org.uk/anticoagulation-oral#!scenariorecommendation:47
- ³³ National Institute for Heath and Care Excellence. 'Anticoagulation oral, Scenario: Warfarin, Selftesting.' Last revised: December 2016. Last accessed: 12 September 2017. https://cks.nice.org.uk/anticoagulation-oral#!scenariorecommendation:50
- ³⁴ National Institute for Heath and Care Excellence. 'Anticoagulation oral, Scenario: Edoxaban.' Last revised: December 2016. Last accessed: 12 September 2017. https://cks.nice.org.uk/anticoagulation-oral#!scenario:2
- ³⁵ National Institute for Heath and Care Excellence, Implementation Collaborative. 'Consensus: Supporting local implementation of NICE guidance on the use of the novel (non-Vitamin K antagonist) oral anticoagulants in non-valvular atrial fibrillation.' Originally published: 2010. Update published: 2012, p. 2. Last accessed: 18 September 2017. Available at: https://www.nice.org.uk/guidance/cg180/resources/nic-consensus-statement-on-the-use-of-noacs-243733501
- ³⁶ National Institute for Heath and Care Excellence. 'Anticoagulation oral, Scenario: Apixaban.' Last revised: December 2016. Last accessed: 12 September 2017. Available at: https://cks.nice.org.uk/anticoagulation-oral#!scenario
- ³⁷ National Institute for Heath and Care Excellence, Implementation Collaborative. 'Consensus: Supporting local implementation of NICE guidance on the use of the novel (non-Vitamin K antagonist) oral anticoagulants in non-valvular atrial fibrillation.' Originally published: 2010. Update published: 2012, p. 7. Last accessed: 18 September 2017. Available at: https://www.nice.org.uk/guidance/cg180/resources/nic-consensus-statement-on-the-use-of-noacs-243733501
- ³⁸ The Medical Technology Group. 'The North-South NHS Divide: How where you are not what you need dictates your care.' 2017, p. 4. Last accessed: 18 September 2017. Available at: http://www.mtg.org.uk/wp-content/uploads/2017/08/The-North-South-NHS-divide-how-where-you-are-not-what-you-need-dictates-your-care-FINAL-low-res.pdf
- ³⁹ Professor Ahmet Fuat, Carmel Medical Practice. 'Audit of Oral Anticoagulation in Atrial Fibrillation (AF)'. Unpublished. December 2016, p. 2.
- ⁴⁰ Professor Ahmet Fuat, Carmel Medical Practice. 'Audit of Oral Anticoagulation in Atrial Fibrillation (AF).' Unpublished. December 2016, p. 3.
- ⁴¹ National Institute for Health and Care Excellence, 'Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence, clinical guide.' [NICE CG76]. 28 January 2009, p. 5. Last accessed: 12 September 2017. Available at: https://www.nice.org.uk/guidance/cg76/resources/medicines-adherence-involving-patients-in-decisions-about-prescribed-medicines-and-supporting-adherence-pdf-975631782085

- ⁴² National Institute for Health and Care Excellence, 'Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence, clinical guide.' [NICE CG76]. 28 January 2009, p. 13. Last accessed: 12 September 2017. Available at: https://www.nice.org.uk/guidance/cg76/resources/medicines-adherence-involving-patients-in-decisions-about-prescribed-medicines-and-supporting-adherence-pdf-975631782085
- ⁴³ World Health Organisation, 'Adherence to long-term therapies Evidence for action.' 2003, p. XIV. Last accessed: 12 September 2017. Available at: http://apps.who.int/medicinedocs/pdf/s4883e/s4883e.pdf
- ⁴⁴ World Health Organisation, 'Adherence to long-term therapies Evidence for action.' 2003, p. XIII. Last accessed: 12 September 2017. Available at: http://apps.who.int/medicinedocs/pdf/s4883e/s4883e.pdf
- ⁴⁵ National Institute for Health and Care Excellence, 'Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence, clinical guide.' [NICE CG76]. 28 January 2009, p. 7. Last accessed: 12 September 2017. Available at: https://www.nice.org. uk/guidance/cg76/resources/medicines-adherence-involving-patients-in-decisions-about-prescribed-medicines-and-supporting-adherence-pdf-975631782085
- ⁴⁶ Fiona Castle, Sarah Bond and Sue Rhodes. 'Referral scheme from secondary to primary care', Clinical Pharmacist. 22 June 2017;9:8. doi: 10.1211/CP.2017.20202983
- ⁴⁷ Donna Sydenham. 'A nurse-led direct oral anticoagulant clinic in primary care'. Thrombus. 2016:20(4):60-62.
- ⁴⁸ Jackevicius C.A., Tsadok M.A., Essebag V. et al. 'Early non-persistence with dabigatran and rivaroxaban in patients with atrial fibrillation'. Heart. 2017:103:1308–1309. Originally published: 07 Apr 2017. doi: 10.1136/heartjnl-2017-311305
- ⁴⁹ Xiaoxi Y., Neena S. Abraham, G. Caleb Alexander et al. 'Effect of Adherence to Oral Anticoagulants on Risk of Stroke and Major Bleeding Among Patients With Atrial Fibrillation'. J Am Heart Assoc. 2016:5:e003074. Originally published: 23 Feb 2016. doi: 10.1161/JAHA.115.003074
- ⁵⁰ Nigel Breakwell, Trudie Lobban. 'Comments and considerations for NOAC adherence white paper: AF Association position on improving the AF management pathway.' Unpublished. August 2017, p. 2.
- ⁵¹ Helia Robert-Ebadi, Grégoire Le Gal and Marc Righini. 'Use of anticoagulants in elderly patients: practical recommendations'. Clin Interv Aging, 2009:4:165–177. Published online: 14 May 2009. Last Accessed 21 September 2017. Available at: http://europepmc.org/articles/PMC2685237
- ⁵² National Health Service. 'Next Steps on the NHS Five Year Forward View'. Published: March 2017, p. 64. Last accessed: 21 September 2017. Available at: https://www.england.nhs.uk/wp-content/uploads/2017/03/NEXT-STEPS-ON-THE-NHS-FIVE-YEAR-FORWARD-VIEW.pdf

Learning and Communications Team LumiraDx Care Solutions UK Ltd 1 North Crofty Tolvaddon Energy Park Camborne United Kingdom TR14 0HX

hello@lumiradx.co.uk