Consensus guideline on the holistic management of patients requiring anticoagulation

Guidelines

summarising clinical guidelines for primary care

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Consensus guideline on the holistic management of patients requiring anticoagulation

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Introduction

Anticoagulants are a group of drugs used in a variety of conditions to stop the formation of blood clots.[1] Conventionally, vitamin K antagonists such as warfarin[2] have been the most commonly prescribed oral anticoagulants, but they need frequent monitoring of international normalised ratio (INR) and dose adjustment to maintain therapeutic action and minimise bleeding risk.[3] Next-generation direct oral anticoagulants (DOACs) for the management of atrial fibrillation (AF) and venous thromboembolism (VTE)—apixaban, dabigatran, edoxaban▼, and rivaroxaban▼—[4–7] have become available with the advantage of providing consistent therapeutic anticoagulation with few pharmaceutical interactions. They do not require the regular INR monitoring needed by people taking vitamin K antagonists and can be readily prescribed in primary care by GPs without a dedicated monitoring service.[3]

Rationale for this guideline

Many guidelines exist on the management of patients with cardiovascular diseases. For example, NICE published a clinical knowledge summary on oral anticoagulation with management recommendations segmented by drug,[8] and other guidelines discuss anticoagulation for different patient cohorts, such as the British Thoracic Society guideline for the management of suspected acute pulmonary embolism (PE),[9] American Heart Association/American College of Cardiology/Heart Rhythm Society guideline for the management of patients with AF,[10] and the British Society for Haematology guideline on the peri-operative management of anticoagulation and antiplatelet therapy.[11] However, no specific UK guidance is available on the holistic management of patients requiring anticoagulation, with recommendations independent of the drug used and the patient cohort.

With two major pillars of the NHS long-term plan being around illness prevention and supporting the workforce,[12] it is increasingly important to ensure that the management of oral anticoagulants, with their highly effective risk reduction, is done well. This guideline supports members of the workforce of the practice and primary care networks to be involved in the management of patients to ensure effective and safe prescribing, and support our patients in caring for their own health.

Box 1: Initial assessment

- Patient profile
  - review patients discharged from hospital on anticoagulants
  - indication for anticoagulation
  - co-morbidities
  - bleeding risk
  - modifiable risk factors
  - metabolic assessment (FBC, LFTs)
  - weight
  - creatinine clearance (Cockcroft-Gault)
- Practical considerations
  - polypharmacy/drug interactions
  - frequency of other medications.

FBC=full blood count; LFT=liver function test.

Consensus guideline on the holistic management of patients requiring anticoagulation

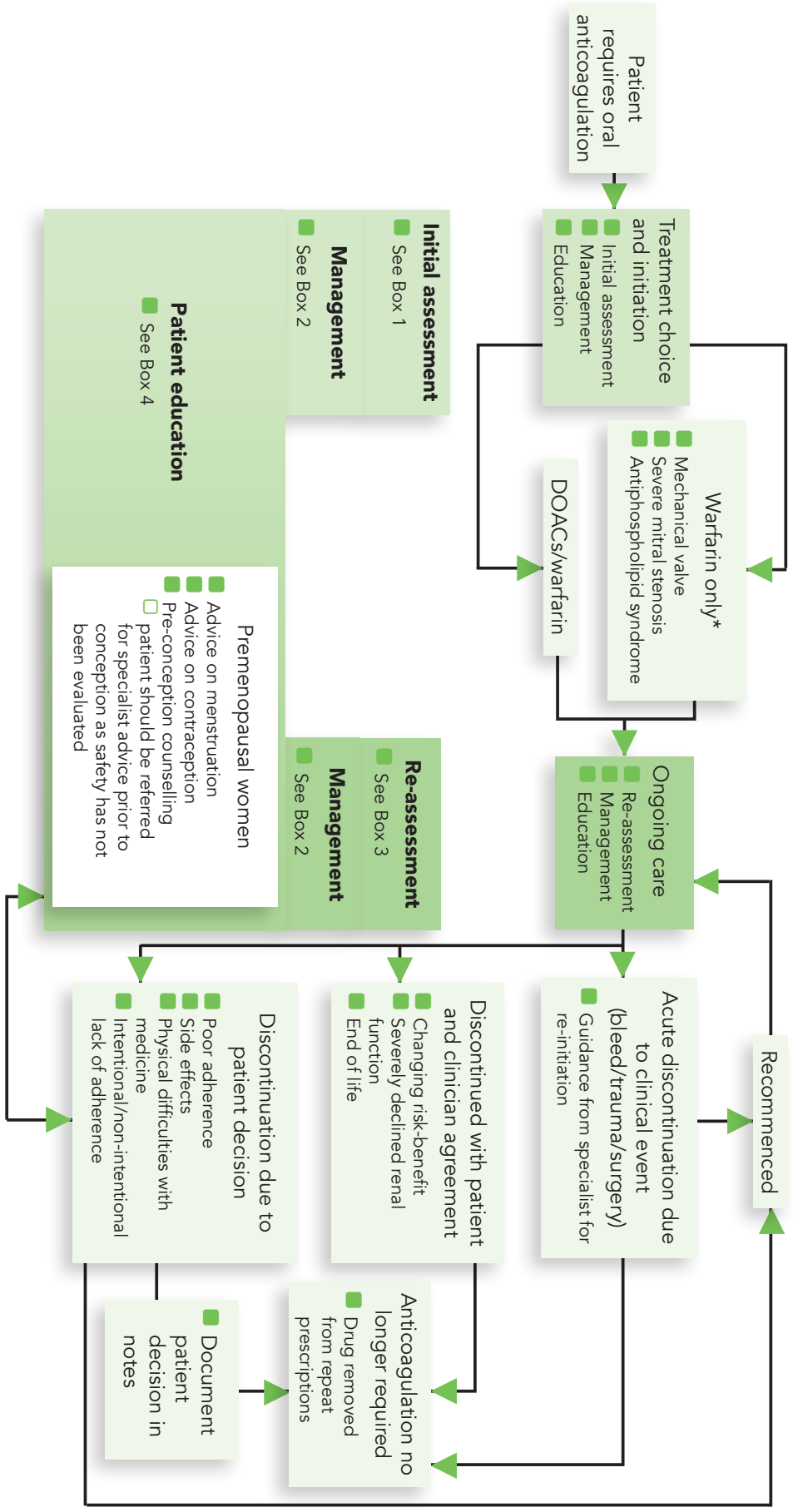
Figure 1 provides an algorithm summarising the working party group's consensus guideline for the holistic management of patients who have already been identified as requiring anticoagulation. This guideline is not intended to provide guidance on assessing whether patients need anticoagulation or advice on choice of specific anticoagulants, but offers a broader approach to the management of patients who have already been identified as needing anticoagulation.

Treatment choice and initiation

Initial assessment

- All patients who have been determined to require anticoagulation should undergo an initial assessment (see Box 1)
- Review the patient's profile
  - review patients discharged from hospital on anticoagulants 2–3 months after discharge
    - confirm the indication for anticoagulation, as different anticoagulants have different indications[2,4–7]

Figure 1: Treatment algorithm for the holistic management of patients requiring anticoagulation



*See the guidance on anticoagulation in the COVID-19 pandemic (Box 5).

DOACs=direct oral anticoagulants

Box 2: Management

- Drug choice and dose according to SmPC
- Discuss recommendations and patient preference with patient
- Follow up
  - frequency of assessment (CrCl÷10)
- Follow up in ongoing care, also assess:
  - adherence
  - adverse events (e.g. bleeding or side effects)
  - change in clinical status.

CrCl=creatinine clearance; SmPC=summary of product characteristics.

    - check whether the discharge drug is still appropriate and use this as an opportunity to change the drug, if required
    - check whether the discharge dose is still appropriate
      - the patient's clinical status may have changed since their admission—e.g. renal function or weight may have changed, therefore requiring re-calculation of creatinine clearance (CrCl)
    - check whether the frequency of dosing is acceptable to the patient—consider aligning the frequency of dosing with other medications such as statins and antihypertensives, as this may improve adherence; if missing doses, consider switching from twice daily to once daily
  - identify modifiable bleeding risk factors that can be corrected
  - obtain the patient's weight, which is important for correct dosing
  - calculate CrCl using the Cockcroft–Gault equation
    - renal function is important in choice of anticoagulant, and vital in determining the correct dosing
    - always use the same machine/app to calculate CrCl
    - note that some clinicians may use estimated glomerular filtration rate (eGFR) to estimate the dose—the summary of product characteristics (SmPCs) for all four DOACs state that dosing should be based on CrCl so there may be differences when it is calculated using the eGFR
  - order a metabolic assessment
    - full blood count (FBC)—to ensure there is no anaemia or persistent fall in haemoglobin while on a DOAC
    - liver function tests (LFTs)—to ensure that liver dysfunction, which may affect coagulation, is not developing
  - identify co-morbidities
  - determine the patient's bleeding risk
    - no HAS-BLED score is an absolute contraindication to anticoagulation (it only informs the overall bleeding risk)[13]
    - use the HAS-BLED score to identify any modifiable risk factors that can be adjusted to reduce the bleeding risk (e.g. controlling systolic blood pressure, stopping aspirin/nonsteroidal anti-inflammatory drugs)
- Assess practical considerations
  - identify patients with polypharmacy and potential drug interactions
    - many patients requiring anticoagulation will already be taking other medications
    - check SmPCs[2,4–7] or British National Formulary[14] for interactions
  - assess the frequency of current medications
    - patients are more likely to adhere when the regimen for a new drug coincides with a current regimen.

Management

- Drug choice and dosing (see Box 2)
  - remember that prescribers are responsible for problems even if they are continuing another clinician's initial prescription
    - incorrect dosing can lead to complications—underdosing increases the risk of stroke, while overdosing increases the risk of bleeding[15]
    - review patients regularly to ensure they are taking the correct dose at any given time
  - choose the anticoagulant and dose according to the SmPC[2,4–7] and prescriber guide[16–19]
  - consider all four available DOACs,[4–7] and decide on the most appropriate drug based on patient's individual circumstances
    - prescribe in line with the SmPC[4–7] and do not use lower doses than indicated
      - irrespective of which agent is prescribed, renal function is the most important consideration to ensure the patient is on the correct dose[4–7]
    - some cardiovascular conditions, including stroke, may dictate which DOAC is chosen (e.g. secondary prevention of cardiovascular disease in sinus rhythm where low dose rivaroxaban in conjunction with aspirin is the only therapy indicated)
    - in patients taking warfarin, consider switching to a DOAC if time in therapeutic range (TTR) is <65%[13]
  - warfarin may be required or preferred in some patients; use warfarin in patients with the following, in whom DOACs are not suitable:
    - mechanical heart valves
    - moderate-to-severe rheumatic mitral stenosis
    - antiphospholipid syndrome
    - poor renal function (dialysis and pre-dialysis patients)
  - do not start aspirin in AF, unless there are other indications to do so[13]
  - consider adding a proton pump inhibitor if the patient is at increased risk of gastric bleeding (e.g. with concomitant use of steroids, selective serotonin reuptake inhibitors, and bisphosphonates)[20]
- Discuss recommendations and patient preference with the patient
  - patients increasingly prefer to use DOACs
  - some patients prefer warfarin for personal and social reasons, including:
    - clinician and social contact at INR clinics

- Follow up (see Box 2)
  - follow up patients within one month of any change in drug or dose
  - frequency of follow up after initial review should be based on renal function
    - a useful rule of thumb is CrCl divided by 10—e.g. for a CrCl of 60 ml/min, follow up every 6 months
  - check CrCl at least annually
    - set up recall system
    - always use the same machine/app to calculate CrCl
    - patients whose renal function is showing trends to change rather than transitory fluctuations should be reviewed more frequently.

Patient education

- Educate patients to empower them and encourage them to take ownership of their condition and treatment
- Advise patient to familiarise themselves with the patient alert card of their prescribed DOAC, and to always carry the card with them[21–24]
- Lifestyle modifications
  - advise patients on:
    - usual lifestyle modifications for cardiovascular and stroke risk
    - diet and alcohol
      - maintain a good weight and body shape
      - alcohol may be a concern in patients taking warfarin
    - avoiding new physical activities that increase bleeding risk but maintaining any in which they are competent
      - for risky activities consider advising patients on DOACs to adjust the timing of dosing to minimise drug concentrations prior to the activity
  - use gloves while gardening
  - discuss additional risks with patients receiving anticoagulation for AF
- Medical support
  - provide patients with an INR booklet or national anticoagulation card, as appropriate
  - encourage patients to:
    - allow access to their shared summary care record
    - get a medic alert bracelet to identify them as a patient on anticoagulation
  - advise patients to visit their appropriate healthcare professional for monitoring, as recommended (at least every 12 months)
    - this is particularly important for DOACs, as lack of routine INR monitoring means that patients will not be seen in INR clinics for regular review
  - advise patients on action to take if bleeding occurs and situations that should prompt them to stop taking their anticoagulant
  - provide advice if patients require elective surgery or dental surgery
  - advise patients on how to use their community pharmacy for support, such as use of the new medicines service and when purchasing over-the-counter and off-the-shelf medicines, which may affect anticoagulants
- Patient responsibilities

Box 3: Re-assessment

- Patient profile
  - indication for anticoagulation
  - co-morbidities
  - bleeding risk
  - modifiable risk factors
  - metabolic assessment (FBC, LFTs)
  - weight
  - creatinine clearance (Cockcroft-Gault)
- Practical considerations
  - polypharmacy/drug interactions
  - frequency of other medications.

FBC=full blood count; LFT=liver function test.

  - encourage patients to take ownership of their treatment
  - emphasise why patients need anticoagulant therapy; reinforce the importance of adherence and discuss any concerns the patient may have
  - advise patients on the actions to take if they miss a dose, as recommended by the patient information leaflet for the chosen anticoagulant
- Premenopausal women
  - give premenopausal women specific advice on:
    - menstruation
      - patients taking combined oral contraceptives for menorrhagia should continue to do so, as DOACs will increase bleeding
      - there may be less menorrhagia with apixaban than rivaroxaban[25]
    - contraception
      - emphasise the importance of not falling pregnant while on anticoagulants, as DOACs have not been shown to be safe in pregnancy
    - preconception counselling
      - refer the patient for specialist advice prior to conception, as safety of DOACs has not been evaluated.

Ongoing care

- Patients taking anticoagulants should regularly undergo regular re-assessment and regular management review, and education should be reinforced at every opportunity
- Re-assess in line with the guidance for initial assessment (see Box 3)
- Manage in line with the guidance for initial management to regularly assess the need for and suitability of the anticoagulant (see Box 2)
- Additional management actions for ongoing care:
  - check adherence
  - ask whether patients have any adverse effects, e.g. bleeding or side effects
  - assess whether the patient's clinical status has changed over time—for example, development of new co-morbidities, renal function deterioration, or if they have increased bleeding risk—e.g. due to mucosal tumours

Box 4: Patient education

- Lifestyle
  - diet and alcohol
  - physical activities that increase bleeding risk
- Adherence
  - address need for therapy and any concerns
  - missed doses (as recommended by patient information leaflet)
  - understanding that this is a preventative therapy to reduce the risk of stroke
- Advice on action to take if bleeding
- Shared summary care record, Medalert bracelet, INR booklet, national anticoagulation card
- Advise to always carry the patient alert card of their prescribed DOAC with them
- Visit appropriate healthcare professional for monitoring as recommended (at least every 12 months)
- Advice for patients undergoing elective surgery/dental surgery
- Advice on how to use community pharmacy for support, such as use of NMS and over-the-counter and off-the-shelf medicines.

DOAC= direct oral anticoagulant; INR=international normalised ratio; NMS=new medicine service.

    - refer back to the clinician who initiated anticoagulation unless they can be confidently managed in general practice
    - if patients have bleeding issues, seek expert advice or another management option rather than switching to another DOAC, as bleeding is likely to be similar on all DOACs
      - as DOACs will worsen existing bleeding from other causes, rather than causing bleeding *de novo*,[26] investigate sources of bleeding—e.g. bladder and colon tumours may need to be excluded
    - if an acute event such as VTE occurs on long-term anticoagulation, check adherence
      - if adherence is good, consider another cause
    - no DOACs are licenced for a CrCl <15 ml/min; the need for a DOAC should be reviewed and the risks and benefits of intervention discussed[4–7]
      - review regularly, as renal function declines with increasing age
      - this switch is necessary, even if patients were previously switched from warfarin to DOACs due to poor TTR or patient preference
- Reinforce education in line with the guidance for initial education throughout treatment (see Box 4)
- Consider introducing a protocol to audit patients after DOACs have been initiated.

Discontinuation of anticoagulation

- Patients may need to discontinue anticoagulation for three main reasons
  - temporary discontinuation due to acute clinical event
  - discontinuation with patient and clinician agreement
  - discontinuation due to patient decision
- Temporary discontinuation due to acute clinical event, e.g. gastrointestinal bleed, intracranial haemorrhage, trauma, or surgery
  - check that anticoagulants have been stopped
    - for patients discontinuing prior to elective surgery, follow local hospital's policies
    - patients undergoing dental procedures should not stop anticoagulation completely, but those taking DOACs should not take it on the day of the procedure or should take it after the procedure if it is early in the day
  - limit the number of repeat prescriptions
  - seek guidance from a specialist for re-initiation
    - anticoagulation may no longer be required or appropriate
    - timeframe for restarting is usually dictated by a secondary care specialist
      - for intracranial bleeds, typically reassess after 8 weeks[27]
    - for patients who recommence anticoagulation, continue to provide ongoing care
    - be vigilant for future events, e.g. deep vein thrombosis
- Discontinuation with patient and clinician agreement due to:
  - changing risk–benefit
  - severely declined renal function
  - end of life
- Discontinuation due to patient decision, e.g. intentional or non-intentional poor adherence, side effects, or physical difficulties with the medicine
  - encourage patients to continue with anticoagulation, where still appropriate, reinforcing the need for the treatment
  - reinforce education in line with the guidance for education (see Box 4)
  - if patients decide not to continue treatment despite medical advice:
    - document this decision in the patient notes
    - send a letter to the patient explaining the need for treatment and confirming that they have chosen to stop despite medical advice
- If anticoagulation is no longer required according to any of these situations, remove the drug from the patient's repeat prescription.

Acknowledgements

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Box 5: Guidance on anticoagulation in the COVID-19 pandemic

- In the current COVID-19 pandemic, clinicians are increasingly switching patients from warfarin to a DOAC to avoid regular blood tests for INR monitoring
- The Royal Pharmaceutical Society has issued guidance for the safe switching of warfarin to DOACs for appropriate patients with AF and VTE (DVT/PE)[28]
- The British Society of Haematology, Haemostasis and Thrombosis Task Force released the following key points:[29]
  - INR is an essential component of safe anticoagulation that cannot be omitted due to social distancing
  - assess whether a DOAC can be used instead of warfarin
  - exclusions are:
    - mechanical heart valves
    - antiphospholipid syndrome
    - renal failure with creatinine clearance below 15 ml/min
    - patient requiring high range INR
    - concomitant use of medication that interacts with DOAC
  - if a DOAC is an option consider switching in line with patient's informed consent
  - if people have a high TTR then the interval between testing could be extended to 8–10 weeks
  - if people have to self isolate then the INR can be deferred until after self isolation
- The interval between INR tests may be extended and this should be considered when using Computer Aided Decision software
  - this may mean that the dosing system may require overriding to extend the testing interval.

AF= atrial fibrillation; DOAC=direct oral anticoagulant; DVT= deep vein thrombosis; INR=international normalised ratio; PE= pulmonary embolism; TTR=time in therapeutic range; VTE=venous thromboembolism.

Conflicts of interest

The group members have received an honorarium to develop this working party guideline. Some of the group members have also received consultancy fees from other pharmaceutical companies, which may include Mylan, for activities other than the development of this working party guideline.

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Useful resources

Resources for healthcare professionals

- National anticoagulation alert card: www.ahsn-nenc.org.uk/wp-content/uploads/2019/04/NOAC-Alert-Card-V3-order-specification.pdf
- European Heart and Rhythm Association (EHRA): www.escardio.org/Sub-specialty-communities/European-Heart-Rhythm-Association-(EHRA)

Resources for patients

- Atrial Fibrillation Association: www.heartrhythmalliance.org/afa/uk
- British Heart Foundation: www.bhf.org.uk
- Stroke Association: www.stroke.org.uk
- Anticoagulation UK: www.anticoagulationuk.org
- Thrombosis UK: www.thrombosisuk.org

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