NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline

Venous thromboembolic diseases: diagnosis, management and thrombophilia testing

Draft for consultation, November 2019

This guideline covers diagnosing and managing venous thromboembolic diseases in adults. It aims to support quick diagnosis and effective treatment for people who develop deep vein thrombosis (DVT) or pulmonary embolism (PE). It also covers testing for conditions that can make a DVT or PE more likely, such as thrombophilia (a blood clotting disorder) and cancer.

Who is it for?

- Commissioners and providers of venous thromboembolism services
- Healthcare professionals in primary, secondary and tertiary care
- Adults (18 and over) with suspected or confirmed DVT or PE, their families and carers
- First-degree relatives of people with inherited thrombophilia or other venous thromboembolic diseases

This guideline will update NICE guideline CG144 (published June 2012, updated November 2015).

We have reviewed the evidence on D-dimer testing, pulmonary embolism rule-out criteria (PERC), outpatient treatment for low-risk PE, anticoagulation treatment for both suspected and confirmed DVT or PE, inferior vena caval filters and investigations for cancer in people with confirmed DVT or PE.

You are invited to comment on the new and updated recommendations. These are marked as **[2020]**.

We have not reviewed the evidence for the recommendations shaded in grey, and cannot accept comments on them. Yellow shading in these recommendations indicates changes made to the wording. In some cases, we have made minor wording changes that are not shaded in yellow. All changes made to recommendations shaded in grey are explained in update information.

This draft guideline contains:

- the draft recommendations
- recommendations for research
- rationale and impact sections that explain why the committee made the 2020 recommendations and how they might affect practice
- the guideline context.

Information about how the guideline was developed is on the guideline's page on the NICE website. This includes the evidence reviews, the scope, and details of the committee and any declarations of interest.

Full details of the evidence and the committee's discussion on the 2020 recommendations are in the evidence reviews. Evidence for the 2012 recommendations is in the full version of the 2012 guideline. Evidence for the 2015 update is in the November 2015 addendum.

Contents

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Diagnosis and initial management

Signs or symptoms of deep vein thrombosis

1.1.1 For people who present with signs or symptoms of DVT, such as a swollen or painful leg, assess their general medical history and do a physical examination to exclude other causes. **[2012]**

1.1.2 If DVT is suspected, use the 2-level DVT Wells score (table 1) to estimate the clinical probability of DVT. **[2012]**

Table 1 Two-level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more, or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is a least as likely as DVT	−2
Clinical probability simplified score	
DVT likely	**2 points or more**
DVT unlikely	**1 point or less**
* Adapted with permission from Wells PS et al. (2003) Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis.	

DVT likely (Wells score 2 points or more)

1.1.3 Offer people with a **likely** DVT Wells score (2 points or more):

- a proximal leg vein ultrasound scan, with the result available within 4 hours if possible (if the scan result cannot be obtained within 4 hours follow recommendation 1.1.4)
- a D-dimer test if the scan result is negative. **[2012]**

1.1.4 If a proximal leg vein ultrasound scan result cannot be obtained within 4 hours, offer people with a DVT Wells score of 2 points or more:

- interim therapeutic anticoagulation (see interim therapeutic anticoagulation for suspected DVT or PE)
- a D-dimer test

- a proximal leg vein ultrasound scan with the result available within 24 hours. **[2012, amended 2020]**

1.1.5 For people with a positive proximal leg vein ultrasound scan:

- offer or continue anticoagulation treatment (see anticoagulation treatment for confirmed DVT or PE) **or**
- if anticoagulation treatment is contraindicated, offer a mechanical intervention (see mechanical interventions).

For people with symptomatic iliofemoral DVT see thrombolytic therapy. **[2012]**

1.1.6 For people with a negative proximal leg vein ultrasound scan and a positive D-dimer test result:

- stop interim therapeutic anticoagulation
- offer a repeat proximal leg vein ultrasound scan 6 to 8 days later **and**
  - if the repeat scan result is positive, follow the actions in recommendation 1.1.5
  - if the repeat scan result is negative, follow the actions in recommendation 1.1.7. **[2012, amended 2020]**

1.1.7 For people with a negative proximal leg vein ultrasound scan and a negative D-dimer test result:

- stop interim therapeutic anticoagulation
- think about alternative diagnoses
- tell the person that it is not likely they have DVT. Discuss with them the signs and symptoms of DVT and when and where to seek further medical help. **[2012, amended 2020]**

DVT unlikely (Wells score 1 point or less)

1.1.8 Offer people with an **unlikely** DVT Wells score (1 point or less):

- a D-dimer test with the result available within 4 hours (see D-dimer testing) **or**

- if the D-dimer test result cannot be obtained within 4 hours, offer interim therapeutic anticoagulation while awaiting the result (see interim therapeutic anticoagulation for suspected DVT or PE). **[2012, amended 2020]**

1.1.9 If the D-dimer test result is negative, follow the actions in recommendation 1.1.7. **[2012]**

1.1.10 If the D-dimer test result is positive, offer:

- a proximal leg vein ultrasound scan, with the result available within 4 hours if possible **or**
- interim therapeutic anticoagulation (see interim therapeutic anticoagulation for suspected DVT or PE) and a proximal leg vein ultrasound scan with the result available within 24 hours. **[2012, amended 2020]**

1.1.11 If the proximal leg vein ultrasound scan is:

- positive, follow the actions in recommendation 1.1.5
- negative, follow the actions in recommendation 1.1.7. **[2012]**

D-dimer testing

1.1.12 When offering D-dimer testing for suspected DVT or PE, consider a point-of-care test if laboratory facilities are not immediately available. **[2020]**

1.1.13 If using a point-of-care D-dimer test, choose a fully quantitative test. **[2020]**

1.1.14 When using a point-of-care or laboratory D-dimer test, consider an age-adjusted D-dimer test threshold for people aged over 50. **[2020]**

For a short explanation of why the committee made the 2020 recommendations on D-dimer testing and how they might affect practice, see rationale and impact.

Full details of the evidence and the committee's discussion are in evidence review A: D-dimer testing in the diagnosis of deep vein thrombosis and pulmonary embolism.

Signs or symptoms of pulmonary embolism

1.1.15 For people who present with signs or symptoms of pulmonary embolism (PE), such as chest pain, shortness of breath or coughing up blood, assess their general medical history, do a physical examination and offer a chest X-ray to exclude other causes. **[2012]**

Pulmonary embolism rule-out criteria (the PERC rule)

1.1.16 If clinical suspicion of PE is low[1], consider using the pulmonary embolism rule-out criteria (PERC) to help determine whether any further investigations for PE are needed. **[2020]**

For a short explanation of why the committee made the 2020 recommendation on the PERC rule and how it might affect practice, see rationale and impact.

Full details of the evidence and the committee's discussion are in evidence review B: the use of the pulmonary embolism rule-out criteria for diagnosis of pulmonary embolism.

1.1.17 If PE is suspected, use the 2-level PE Wells score (table 2) to estimate the clinical probability of PE. **[2012]**

[1] The clinician estimates the likelihood of PE to be less than 15% based on the overall clinical impression and other diagnoses are feasible.

Table 2 Two-level PE Wells score*

Clinical feature	Points
Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3
An alternative diagnosis is less likely than PE	3
Heart rate more than 100 beats per minute	1.5
Immobilisation for more than 3 days or surgery in the previous 4 weeks	1.5
Previous DVT/PE	1.5
Haemoptysis	1
Malignancy (on treatment, treated in the last 6 months, or palliative)	1
Clinical probability simplified scores	
PE likely	**More than 4 points**
PE unlikely	**4 points or less**

* Adapted with permission from Wells PS et al. (2000) Derivation of a simple clinical model to categorize patients' probability of pulmonary embolism: increasing the model's utility with the SimpliRED D-dimer.

PE likely (Wells score more than 4 points)

1.1.18 For people with a **likely** PE Wells score (more than 4 points):

- offer a computed tomography pulmonary angiogram (CTPA) immediately if possible **or**
- for people with an allergy to contrast media, severe renal impairment (estimated creatinine clearance[2] less than 30 ml/min) or a high risk from irradiation, assess the suitability of a ventilation/perfusion single photon emission computed tomography (V/Q SPECT) scan or, if a V/Q SPECT scan is not available, a V/Q planar scan, as an alternative to CTPA.

If a CTPA, V/Q SPECT or V/Q planar scan cannot be done immediately, offer interim therapeutic anticoagulation (see interim therapeutic anticoagulation for suspected DVT or PE). **[2012, amended 2020]**

[2] Estimated creatinine clearance calculated using the Cockcroft and Gault formula described in the BNF.

1.1.19 If PE is identified by CTPA, V/Q SPECT or V/Q planar scan:

- offer or continue anticoagulation treatment (see anticoagulation treatment for confirmed DVT or PE) **or**
- if anticoagulation treatment is contraindicated, consider a mechanical intervention (see mechanical interventions).

For people with PE and haemodynamic instability see thrombolytic therapy. **[2012, amended 2020]**

1.1.20 If PE is not identified by CTPA, V/Q SPECT or V/Q planar scan:

- consider a proximal leg vein ultrasound scan if DVT is suspected
- if DVT is not suspected:
  - stop interim therapeutic anticoagulation
  - think about alternative diagnoses
  - tell the person that it is not likely they have PE. Discuss with them the signs and symptoms of PE and when and where to seek further medical help. **[2012, amended 2020]**

PE unlikely (Wells score 4 points or less)

1.1.21 Offer people with an **unlikely** PE Wells score (4 points or less):

- a D-dimer test with the result available within 4 hours if possible (see D-dimer testing) **or**
- if the D-dimer test result cannot be obtained within 4 hours, offer interim therapeutic anticoagulation while awaiting the result (see interim therapeutic anticoagulation for suspected DVT or PE).

If the D-dimer test result is:

- positive, follow the actions in recommendations 1.1.18 and 1.1.19
- negative, follow the actions in recommendation 1.1.20. **[2012, amended 2020]**

Signs or symptoms of both deep vein thrombosis and pulmonary embolism

1.1.22 For people who present with signs or symptoms of both DVT and PE, carry out initial diagnostic investigations for either DVT or PE, basing the choice of diagnostic investigations on clinical judgement. **[2012]**

1.2 Outpatient treatment for low-risk pulmonary embolism

1.2.1 Consider outpatient treatment for suspected or confirmed low-risk pulmonary embolism (PE), using a validated risk stratification tool to determine risk. **[2020]**

1.2.2 When offering outpatient treatment to people with suspected PE, follow recommendations 1.1.15 to 1.1.21 on diagnosis and initial management. **[2020]**

1.2.3 When offering outpatient treatment to people with confirmed PE, follow recommendations 1.3.4 to 1.3.14 on anticoagulation treatment. **[2020]**

1.2.4 Agree a plan for monitoring and follow-up with people having outpatient treatment for suspected or confirmed low-risk PE. Give them:

- written information on symptoms and signs to look out for, including the potential complications of thrombosis and of treatment
- direct contact details of a healthcare professional or team with expertise in thrombosis who can discuss any new symptoms or signs, or other concerns
- information about out-of-hours services they can contact when their healthcare team is not available. **[2020]**

For a short explanation of why the committee made the 2020 recommendations on outpatient treatment for low-risk pulmonary embolism and how they might affect practice, see rationale and impact.

Full details of the evidence and the committee's discussion are in evidence review E: outpatient treatment of low-risk VTE.

1.3 Anticoagulation treatment for suspected or confirmed deep vein thrombosis or pulmonary embolism

For other NICE guidance on anticoagulation treatment for suspected or confirmed deep vein thrombosis (DVT) or pulmonary embolism (PE) see:

- Apixaban for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism
- Dabigatran etexilate for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism
- Edoxaban for treating and for preventing deep vein thrombosis and pulmonary embolism
- Rivaroxaban for treating pulmonary embolism and preventing recurrent venous thromboembolism
- Rivaroxaban for the treatment of deep vein thrombosis and prevention of recurrent deep vein thrombosis and pulmonary embolism.

1.3.1 Follow the recommendations on involving patients in decisions about prescribed medicines and supporting adherence in the NICE guideline on medicines adherence and the NICE guideline on medicines optimisation. **[2020]**

Interim therapeutic anticoagulation for suspected DVT or PE

1.3.2 Follow the recommendations on when to offer interim therapeutic anticoagulation for suspected proximal DVT or PE in diagnosis and initial management. **[2020]**

1.3.3 When using interim therapeutic anticoagulation for suspected proximal DVT or PE:

- offer one of:
  - apixaban[3, 4]

[3] In June 2019 the Medicines and Healthcare Products Regulatory Agency (MHRA) published a drug safety update on direct-acting oral anticoagulants (DOACs): increased risk of recurrent thrombotic events in patients with antiphospholipid syndrome.

[4] At the time of consultation (November 2019) apixaban did not have a UK marketing authorisation for the treatment of suspected DVT or PE. The prescriber should follow relevant professional guidance,

  - rivaroxaban[3, 5]
  - low molecular weight heparin (LMWH)[6].

- carry out baseline blood tests including full blood count and clotting profile, and tests of renal and hepatic function.

Do not wait for the results of baseline blood tests before starting anticoagulation treatment, but ensure these tests have been reviewed (and acted upon if necessary) within 24 hours of starting treatment. **[2020]**

Anticoagulation treatment for confirmed DVT or PE

1.3.4 For people with confirmed proximal DVT or PE:

- offer anticoagulation treatment for at least 3 months
- if not already done, carry out baseline blood tests including full blood count and clotting profile, and tests of renal and hepatic function.

Do not wait for the results of baseline blood tests before starting anticoagulation treatment, but ensure these tests have been reviewed (and acted upon if necessary) within 24 hours of starting treatment. **[2020]**

1.3.5 When offering anticoagulation treatment for confirmed proximal DVT or PE, take into account comorbidities, contraindications and the person's preferences.

Follow the recommendations on anticoagulation treatment for:

- PE with haemodynamic instability

taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[5] At the time of consultation (November 2019) rivaroxaban did not have a UK marketing authorisation for the treatment of suspected DVT or PE. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[6] At the time of consultation (November 2019) some low molecular weight heparins did not have a UK marketing authorisation for the treatment of suspected DVT or PE. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

- DVT or PE with renal impairment or established renal failure
- DVT or PE with a BMI of 40 kg/m^2 or more
- DVT or PE with cancer. **[2020]**

1.3.6 Offer either apixaban[3] or rivaroxaban[3] to people with confirmed proximal DVT or PE unless they have one of the comorbidities listed in recommendation 1.3.5. If neither apixaban nor rivaroxaban is suitable offer:

- low molecular weight heparin (LMWH) for 5 days followed by dabigatran[3] or edoxaban[3] **or**
- LMWH concurrently with a vitamin K antagonist (VKA) for at least 5 days, or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own. **[2020]**

1.3.7 Do not routinely offer unfractionated heparin (UFH) with a VKA to treat confirmed proximal DVT or PE unless the person has established renal failure (estimated creatinine clearance[2] less than 15 ml/min, see recommendation 1.3.10) or an increased risk of bleeding. **[2020]**

1.3.8 Do not routinely offer self-management or self-monitoring of INR to people who have had DVT or PE and are having treatment with a VKA. **[2012]**

Anticoagulation treatment for PE with haemodynamic instability

1.3.9 For people with PE and haemodynamic instability, offer continuous UFH infusion and consider thrombolytic therapy (see thrombolytic therapy). **[2020]**

Anticoagulation treatment for DVT or PE with renal impairment or established renal failure

1.3.10 Offer anticoagulation treatment to people with confirmed proximal DVT or PE and renal impairment or established renal failure as follows:

- For people with renal impairment (estimated creatinine clearance[2] between 15 and 50 ml/min) offer one of:
  - apixaban[3]

- rivaroxaban[3]
- LMWH[7] for 5 days followed by:
  - ◊ either edoxaban[3] or dabigatran[3] if estimated creatinine clearance is between 30 and 50 ml/min **or**
  - ◊ edoxaban[3] if estimated creatinine clearance is between 15 and 29 ml/min
- either LMWH[7] or UFH, given concurrently with a vitamin K antagonist (VKA) for at least 5 days or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own.

- For people with established renal failure (estimated creatinine clearance[2] less than 15 ml/min) offer either UFH or LMWH[7].

When giving anticoagulation treatment to people with renal impairment or established renal failure, note the cautions and requirements for dose adjustment and monitoring in the medicine's summary of product characteristics, and follow locally agreed protocols or advice from a specialist or multidisciplinary team. **[2020]**

Anticoagulation treatment for DVT or PE with a BMI of 40 kg/m^2 or more

1.3.11 For people with a BMI of 40 kg/m^2 or more and suspected or confirmed proximal DVT or PE, consider a VKA with INR monitoring to ensure effective anticoagulation treatment. **[2020]**

Anticoagulation treatment for DVT or PE with cancer

1.3.12 Offer people with active cancer and confirmed proximal DVT or PE anticoagulation treatment for 6 months[8], then review the treatment. **[2020]**

[7] At the time of consultation (November 2019) some low molecular weight heparins did not have a UK marketing authorisation for the treatment of DVT or PE in people with severe renal impairment (estimated creatinine clearance 15 to 30 ml/min) or established renal failure (estimated creatinine clearance less than 15 ml/min). The prescriber should consult the medicine's summary of product characteristics for details, and follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[8] Although this use is common in UK clinical practice, at the time of consultation (November 2019) most anticoagulants did not have a UK marketing authorisation for the treatment of DVT or PE beyond 6 months in people with cancer. The prescriber should consult the summary of product characteristics for the specific anticoagulant and follow relevant professional guidance, taking full

1.3.13 When choosing anticoagulation treatment for people with active cancer and confirmed proximal DVT or PE, take into account the tumour site and the person's bleeding risk. Consider:

- a direct-acting oral anticoagulant[3, 9] **or**
- LMWH with a VKA if a direct-acting oral anticoagulant is not suitable and the person prefers an oral medication.

Consider LMWH[10] on its own **only if** the person finds oral medicine difficult to tolerate or a VKA is contraindicated. **[2020]**

1.3.14 For people with cancer that is in remission and confirmed DVT or PE, follow the recommendations in anticoagulation treatment for confirmed DVT or PE. **[2020]**

For a short explanation of why the committee made the 2020 recommendations on anticoagulation treatment for confirmed DVT or PE and how they might affect practice, see rationale and impact.

Full details of the evidence and the committee's discussion are in evidence review D: pharmacological treatment in people with suspected or confirmed deep vein thrombosis and/or pulmonary embolism.

responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[9] At the time of consultation (November 2019) direct-acting oral anticoagulants did not have a UK marketing authorisation for the treatment of DVT or PE in people with active cancer. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[10] At the time of consultation (November 2019) some low molecular weight heparins did not have a UK marketing authorisation for 6 months of treatment of DVT or PE in people with cancer. The prescriber should consult the summary of product characteristics for the specific LMWH and make adjustments for people with cancer. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

1.4 Reviewing anticoagulation treatment

1.4.1 Assess and discuss the benefits and risks of continuing, stopping or changing the anticoagulant with people who have had 3 months of anticoagulation treatment after a proximal DVT or pulmonary embolism (PE). Follow the recommendations on medication review in NICE's guideline on medicines optimisation. **[2020]**

1.4.2 For people who had a provoked DVT or PE, consider stopping anticoagulation treatment after 3 months if the clinical course has been uncomplicated. If anticoagulation treatment is stopped, advise them about the risk of recurrence and give them:

- written information on symptoms and signs to look out for
- direct contact details of a healthcare professional or team with expertise in thrombosis who can discuss any new symptoms or signs, or other concerns
- information about out-of-hours services they can contact when their healthcare team is not available. **[2020]**

1.4.3 For people who had an unprovoked DVT or PE, consider continuing anticoagulation treatment after 3 months. Base the decision on the balance between the person's risk of VTE recurrence and their risk of bleeding. Discuss the risks and benefits with the person, and take their preferences into account. **[2020]**

1.4.4 Explain to people with unprovoked DVT or PE and a low bleeding risk that the benefits of continuing anticoagulation treatment are likely to outweigh the risks. **[2020]**

1.4.5 Do not rely solely on predictive risk tools to assess the need for long-term anticoagulation treatment. **[2020]**

1.4.6 Consider using the DASH prediction score for recurrent VTE to assess and inform discussions about the risk of recurrence with people aged 65 and under who have had an unprovoked DVT or PE and are thinking of stopping anticoagulation treatment. **[2020]**

1.4.7 Consider using the HAS-BLED score to assess the risk of major bleeding in people having anticoagulation treatment for unprovoked proximal DVT or PE. Discuss stopping anticoagulation if the HAS-BLED score is 4 or more and cannot be modified. **[2020]**

1.4.8 For people who are continuing anticoagulation treatment beyond 3 months and do not have any of the comorbidities listed in recommendation 1.4.9:

- carry on with the current treatment **or**
- if the current treatment is a direct-acting oral anticoagulant other than apixaban, consider changing to apixaban[3].

Take into account the person's preferences and their clinical situation. **[2020]**

1.4.9 Consider carrying on with the current treatment for people who have any of the following comorbidities and who are continuing anticoagulation treatment beyond 3 months:

- renal impairment (estimated creatinine clearance[2] less than 50 ml/min)
- BMI 40 kg/m^2 or more
- cancer.

Take into account the person's preferences and their clinical situation. **[2020]**

1.4.10 For people who decline continued anticoagulation treatment, consider aspirin (75 or 150 mg daily)[11]. **[2020]**

[11] At the time of consultation (November 2019) aspirin did not have a UK marketing authorisation for the secondary prevention of DVT or PE. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

1.4.11 Review general health, risk of VTE recurrence, bleeding risk and treatment preferences at least once a year for people having long-term anticoagulation treatment. **[2020]**

For a short explanation of why the committee made the 2020 recommendations on reviewing anticoagulation treatment and how they might affect practice, see rationale and impact.

Full details of the evidence and the committee's discussion are in:

- evidence review D: pharmacological treatment in people with suspected or confirmed deep vein thrombosis and/or pulmonary embolism
- evidence review F: what factors determine the optimum duration of pharmacological treatment for DVT or PE in people with a VTE?

1.5 Information and support for people having anticoagulation treatment

1.5.1 Give people having anticoagulation treatment verbal and written information about:

- how to use anticoagulants
- how long to take anticoagulants
- possible side effects of anticoagulants and what to do if these occur
- how other medications, foods and alcohol can affect oral anticoagulation treatment
- any monitoring needed for their anticoagulant treatment
- how anticoagulants may affect their dental treatment
- taking anticoagulants if they are planning pregnancy or become pregnant
- how anticoagulants may affect activities such as sports and travel
- when and how to seek medical help. **[2012]**

1.5.2 Give people who are having anticoagulation treatment information and an 'anticoagulant alert card' that is specific to their treatment. Advise them to carry the 'anticoagulant alert card' at all times. **[2012]**

1.5.3 Be aware that heparins are of animal origin and that apixaban and rivaroxaban contain lactose from cow's milk. For people who have concerns about using animal products, see giving information and planning for discharge in the NICE guideline on venous thromboembolism in over 16s. **[2012, amended 2020]**

1.6 Thrombolytic therapy

For other NICE guidance on thrombolytic therapy for deep vein thrombosis (DVT) or pulmonary embolism (PE) see:

- Ultrasound-enhanced, catheter-directed thrombolysis for deep vein thrombosis
- Ultrasound-enhanced, catheter-directed thrombolysis for pulmonary embolism.

Deep vein thrombosis

1.6.1 Consider catheter-directed thrombolytic therapy for people with symptomatic iliofemoral DVT who have:

- symptoms lasting less than 14 days **and**
- good functional status **and**
- a life expectancy of 1 year or more **and**
- a low risk of bleeding. **[2012]**

Pulmonary embolism

1.6.2 Consider pharmacological systemic thrombolytic therapy for people with PE and haemodynamic instability (see also anticoagulation treatment for PE with haemodynamic instability). **[2012]**

1.6.3 Do not offer pharmacological systemic thrombolytic therapy to people with PE and haemodynamic stability with or without right ventricular dysfunction (see also anticoagulation treatment for confirmed DVT or PE). If the person develops haemodynamic instability, refer to recommendation 1.6.2. **[2015]**

1.7 Mechanical interventions

For other NICE guidance on mechanical interventions for deep vein thrombosis (DVT) see Percutaneous mechanical thrombectomy for acute deep vein thrombosis of the leg.

Inferior vena caval filters

1.7.1 Do not offer an inferior vena caval (IVC) filter to people with proximal DVT or pulmonary embolism (PE) unless:

- it is part of a prospective clinical study **or**
- anticoagulation is contraindicated or a PE has occurred during anticoagulation treatment (see recommendations 1.7.2 and 1.7.3). **[2020]**

1.7.2 Consider a temporary IVC filter for people with proximal DVT or PE when anticoagulation treatment is contraindicated. Remove the IVC filter when anticoagulation treatment is no longer contraindicated and has been established. **[2020]**

1.7.3 Consider an IVC filter for people with proximal DVT or PE who have a PE while taking anticoagulation treatment only after:

- checking adherence to anticoagulation treatment
- increasing the dose of anticoagulant or changing to an anticoagulant with a different mode of action
- eliminating other sources of hypercoagulability. **[2020]**

1.7.4 Before fitting an IVC filter, ensure that there is a strategy in place for it to be removed at the earliest possible opportunity. Document the strategy and review it if the clinical situation changes. **[2020]**

For a short explanation of why the committee made the 2020 recommendations on inferior vena caval filters and how they might affect practice, see rationale and impact.

Full details of the evidence and the committee's discussion are in evidence review H: inferior vena caval filters for people with venous thromboembolism (VTE).

Elastic graduated compression stockings

1.7.5 Do not offer elastic graduated compression stockings to prevent post-thrombotic syndrome or VTE recurrence after a DVT. This recommendation does not cover the use of elastic stockings for the management of leg symptoms after DVT. **[2015]**

1.7.6 If offering elastic graduated compression stockings to manage leg symptoms after DVT, explain how to apply and use them, how long they should be worn and when they should be replaced. **[2012]**

1.8 Investigations for cancer

1.8.1 For people with unprovoked DVT or PE who are not known to have cancer, review their history (including imaging results), baseline blood test results including full blood count and clotting profile, and renal and hepatic function test results, and offer a physical examination (including urinalysis). **[2020]**

1.8.2 Do not offer further investigations for cancer to people with unprovoked DVT or PE unless the person has relevant clinical symptoms or signs (for further information see NICE's guideline on suspected cancer). **[2020]**

For a short explanation of why the committee made the 2020 recommendations on investigations for cancer and how they might affect practice, see rationale and impact.

Full details of the evidence and the committee's discussion are in evidence review C: investigations for cancer in people with unprovoked venous thromboembolism.

1.9 Thrombophilia testing

1.9.1 Do not offer testing for hereditary thrombophilia to people who are continuing anticoagulation treatment. **[2012, amended 2020]**

1.9.2 Do not offer thrombophilia testing to people who have had provoked DVT or PE. **[2012]**

1.9.3 Consider testing for antiphospholipid antibodies in people who have had unprovoked DVT or PE if it is planned to stop anticoagulation treatment, but be aware that these tests are affected by anticoagulants and specialist advice may be needed. **[2012, amended 2020]**

1.9.4 Consider testing for hereditary thrombophilia in people who have had unprovoked DVT or PE and who have a first-degree relative who has had DVT or PE if it is planned to stop anticoagulation treatment, but be aware that these tests are affected by anticoagulants and specialist advice may be needed. **[2012, amended 2020]**

1.9.5 Do not routinely offer thrombophilia testing to first-degree relatives of people with a history of DVT or PE and thrombophilia. **[2012]**

Terms used in this guideline

Provoked DVT or PE

Deep vein thrombosis or pulmonary embolism in a person with a recent (within 3 months) and transient major clinical risk factor for VTE, such as surgery, trauma, significant immobility (bedbound, unable to walk unaided or likely to spend a substantial proportion of the day in bed or in a chair), pregnancy or puerperium – or in a person who is having hormonal therapy (oral contraceptive or hormone replacement therapy).

Proximal DVT

Deep vein thrombosis at or above the level of the popliteal trifurcation area.

Unprovoked DVT or PE

Deep vein thrombosis or pulmonary embolism in a person with no recent major clinical risk factor for VTE (see provoked DVT or PE) who is not having hormonal therapy (oral contraceptive or hormone replacement therapy).

Wells score

Clinical prediction rule for estimating the probability of deep vein thrombosis or pulmonary embolism. There are a number of versions of Wells scores available. This guideline recommends the 2-level DVT Wells score and the 2-level PE Wells score.

Recommendations for research

The guideline committee has made the following recommendations for research.

Key recommendations for research

1 Clinical and cost effectiveness of inferior vena caval filters in people with VTE

What is the short- and long-term clinical and cost effectiveness of inferior vena caval filters in people with VTE? **[2020]**

To find out why the committee made this research recommendation see rationale and impact.

2 Clinical and cost effectiveness of direct-acting oral anticoagulants based on individual patient data

What is the clinical and cost effectiveness of direct-acting oral anticoagulants compared with each other, with LMWH + VKA, with LMWH alone, placebo or aspirin for the initial and long-term treatment of DVT or PE based on individual patient data from existing trials? **[2020]**

To find out why the committee made this research recommendation see rationale and impact.

3 Prediction tools compared with clinical judgement

What is the prognostic accuracy of a tool to predict both VTE recurrence and major bleeding compared with clinical judgement in people with unprovoked proximal DVT or PE? **[2020]**

To find out why the committee made this research recommendation see rationale and impact.

4 Lower-dose thrombolysis for people with acute PE and right ventricular dysfunction

Does lower-dose thrombolysis reduce the risk of major bleeding and improve outcomes for people with acute PE and right ventricular dysfunction? **[2015]**

5 Diagnosis of DVT

What is the clinical and cost effectiveness of a whole-leg ultrasound scan compared with a proximal leg vein ultrasound scan in the diagnosis of acute DVT? **[2012]**

Other recommendations for research

Treatment strategy for people who use intravenous drugs

What is the optimal pharmacological treatment strategy for DVT or PE in people who use intravenous drugs? **[2020]**

Predicting VTE recurrence and major bleeding

What is the prognostic accuracy of a tool to predict both VTE recurrence and major bleeding after 3 months of initial anticoagulation treatment and in the long term? **[2020]**

Thrombolytic therapy for DVT

What is the clinical and cost effectiveness of clot removal using catheter-directed thrombolytic therapy or pharmacomechanical thrombolysis compared with standard anticoagulation therapy for the treatment of acute proximal DVT? **[2012]**

Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice. They link to details of the evidence and a full description of the committee's discussion.

D-dimer testing

Recommendations 1.1.12 to 1.1.14

Why the committee made the recommendations

Point-of-care D-dimer testing

The committee agreed that, if both laboratory-based and point-of-care D-dimer testing are immediately available, laboratory testing is preferable because it provides more rigorous quality assurance and greater certainty of diagnostic accuracy. However, if laboratory-based testing is not immediately available, the committee were in agreement that offering immediate point-of-care testing is more beneficial for patients than delaying diagnosis by waiting for laboratory testing. Although point-of-care tests are more expensive than laboratory tests, the additional cost may be offset by faster results that will reduce the need for additional GP time and unnecessary interim anticoagulation.

Evidence on fully quantitative point-of-care D-dimer tests for DVT suggested that they are as accurate as laboratory tests and more accurate than qualitative or semi-quantitative tests. There is little evidence on these tests for PE but the committee agreed that the evidence on DVT is applicable to PE because it is very unlikely that there is a biological reason that the accuracy of the tests would differ between these groups. The committee were aware that quantitative tests are more commonly used than qualitative or semi-quantitative tests. However, because the latter types of tests are still used in some services, they specified that point-of-care tests should be fully quantitative.

Age-adjusted D-dimer test thresholds

In people aged over 50, there was limited prospective evidence available for DVT and only retrospective evidence available for PE. This evidence suggested that

adjusting D-dimer test thresholds for age improves the usefulness of these tests for ruling out VTE in this age group. The evidence also suggested that age adjustment does not reduce the accuracy of the tests in identifying VTE. The committee noted that adjusting test thresholds for age could be beneficial in reducing anxiety and unnecessary imaging for people with suspected DVT or PE. Although the evidence was not plentiful, the committee agreed that, taken together with the potential benefits, it was sufficient to support a recommendation suggesting age adjustment in D-dimer test thresholds for people aged over 50.

How the recommendations might affect practice

Services that do not currently provide quantitative point-of-care D-dimer tests may need to acquire new equipment and provide training on how to conduct and interpret the tests. It is uncertain what impact this would have on practice, because it is unclear what proportion of primary care centres already use point-of-care testing. Facilities for point-of-care testing are only needed if rapid laboratory testing is not available.

The number of D-dimer tests that are adjusted for age is likely to increase, leading to a reduction in the number of additional investigations for VTE.

Return to recommendations

Pulmonary embolism rule-out criteria (the PERC rule)

Recommendation 1.1.16

Why the committee made the recommendations

In people with signs or symptoms of a PE, but in whom clinical suspicion of PE is low (the clinician estimates the likelihood of PE to be less than 15% based on the overall clinical impression and other diagnoses are feasible), there was some evidence showing that the PERC rule can accurately eliminate PE as a possible diagnosis. The committee agreed that using the PERC rule can reduce anxiety and avoid unnecessary D-dimer testing, imaging and interim anticoagulation treatment for people with a low probability of PE and none of the PERC criteria for PE. However, the evidence was limited so the committee agreed to recommend that the PERC rule be considered as part of initial assessment.

How the recommendation might affect practice

The PERC rule is not widely used in current practice. This recommendation is expected to increase its use within a subgroup of people in whom clinical suspicion of PE is low and for whom discharge is being considered. Increased use of PERC can be expected to reduce the need for D-dimer testing and imaging for people with none of the PERC criteria for PE, leading to some reductions in waiting times in primary care and emergency departments. It will also help to avoid unnecessary anticoagulation treatment. However, the overall impact of this recommendation is not expected to be substantial because of the limited population it affects.

Return to recommendation

Outpatient treatment for low-risk pulmonary embolism

Recommendations 1.2.1 to 1.2.4

Why the committee made the recommendations

The committee noted that outpatient treatment for people with PE who have a low risk of poor outcomes is increasingly being used in settings such as ambulatory care units. There was limited evidence comparing outpatient with inpatient treatment for PE so the committee were unable to reach firm conclusions about the overall benefits and risks of outpatient treatment. However, no evidence showed that outpatient treatment is less effective or less safe than inpatient treatment for people with low-risk PE. The committee agreed that outpatient care offers substantial benefits for people with PE and for hospital services and should be considered for those with suspected or confirmed low-risk PE.

The committee emphasised the importance of clear arrangements for monitoring and follow-up to ensure that outpatients receive the same quality of care as inpatients.

How the recommendations might affect practice

Outpatient treatment for PE is common practice in many services with ambulatory care units. These recommendations might lead to the establishment of ambulatory care units in services that do not currently have them, and this will reduce hospital stays in those services.

Return to recommendations

Anticoagulation treatment for suspected or confirmed deep vein thrombosis or pulmonary embolism

Recommendations 1.3.2 to 1.3.14

Why the committee made the recommendations

Interim therapeutic anticoagulation for suspected DVT or PE

There was no evidence specifically on interim anticoagulation treatment for suspected DVT or PE. However, the committee agreed that it is vital to start treatment if DVT or PE is suspected and diagnostic test results are delayed by more than 4 hours. They reasoned that anticoagulation treatments that are effective for confirmed DVT or PE are likely to be equally effective when used as interim treatment while awaiting a confirmed diagnosis. They noted the benefit of being able to continue treatment with apixaban or rivaroxaban, or to use LMWH before starting treatment with edoxaban or dabigatran, if diagnosis is confirmed. They also noted that apixaban, rivaroxaban and LMWH produce an immediate anticoagulant effect, which is essential for people with suspected VTE if their test results are delayed.

Anticoagulation treatment for confirmed DVT or PE

Evidence suggested that treatment with a direct-acting oral anticoagulant (DOAC) is less likely to result in bleeding complications than treatment with LMWH and VKA. Additionally, people taking a DOAC benefit by being able to have an oral treatment and avoid the frequent monitoring that is necessary with other types of anticoagulation treatment.

Within the DOACs, there was evidence showing that apixaban is the most cost-effective option because it results in the fewest bleeds. Rivaroxaban was the second most cost-effective option and only slightly less cost effective than apixaban. However, the committee had reservations about this evidence because the inclusion criteria setting out which patients took part in the studies were not the same in each study. In particular, the apixaban study did not include patients with provoked VTE unless it was caused by a persistent risk factor, so a larger proportion of patients in the apixaban study had unprovoked VTE compared with the rivaroxaban studies.

This made it difficult to compare the results of the studies. Because of this, the committee were not confident that apixaban should be the only option for a DOAC and recommended a choice of apixaban or rivaroxaban. They also made a recommendation for research on DOACs compared with each other and with other anticoagulants.

The committee recognised that apixaban or rivaroxaban might not be suitable for everyone, so they included options for treatment with LMWH followed by dabigatran or edoxaban, or LMWH with VKA.

The evidence did not support a recommendation for fondaparinux. It showed that fondaparinux is more likely to result in bleeding and is less cost effective than other treatments. However, the committee decided not to make a recommendation precluding its use because they were aware that it may be needed in rare circumstances.

UFH was associated with increased bleeding complications, greater recurrence rates of VTE and higher mortality rates than other treatments so the committee did not think it should be offered routinely. They recognised that it may be a suitable option for some people with VTE.

Anticoagulation treatment for PE with haemodynamic instability

The committee agreed that intravenous UFH should be offered to people with PE and haemodynamic instability because the anticoagulant effect needs to be carefully controlled for these people. People with haemodynamic instability have poor peripheral circulation and because UFH is administered intravenously it allows for a more certain therapeutic effect. Additionally, the anticoagulant effect of UFH wears off relatively quickly if treatment needs to be stopped.

The committee did not review the evidence on thrombolytic therapy and the 2012 recommendation that it be considered for this population is unchanged.

Anticoagulation treatment for DVT or PE with renal impairment or established renal failure

Renal impairment increases the risk of anticoagulants accumulating in the body, which can increase bleeding risk. There was very limited evidence on anticoagulant treatment for VTE in people with renal impairment.

Based on their expertise and the summary of product characteristics (SPC) for each treatment, the committee agreed that LMWH, UFH or direct-acting oral anticoagulants (DOACs) are suitable options to treat VTE in people with renal impairment. However, dabigatran is not an option for people with more severe renal impairment (estimated creatinine clearance 15 to 29 ml/min) based on its SPC. For people with estimated creatinine clearance less than 15 ml/min, UFH or LMWH are the only options. The committee emphasised the importance of following the SPCs and locally agreed protocols, and seeking advice from specialist colleagues or a multidisciplinary team to ensure correct dosing and monitoring.

Anticoagulation treatment for DVT or PE with a BMI of 40 kg/m^2 or more

Based on their knowledge and experience, the committee agreed that the pharmacokinetics (including absorption, distribution and elimination) of anticoagulants could potentially be altered at extremes of weight. Although the evidence for effectiveness of any specific anticoagulant for people with a BMI of 40 kg/m^2 or more is limited, they agreed that a VKA with INR monitoring would be likely to ensure adequate and reliable anticoagulation.

Anticoagulation treatment for DVT or PE with cancer

There was very little evidence available on the duration of anticoagulation treatment for people with DVT or PE and cancer. The committee agreed, based on the evidence and their experience, that anticoagulation treatment should continue for 6 months and then be reviewed.

The effectiveness of direct-acting oral anticoagulants (DOACs) compared with other anticoagulation treatments in people with active cancer has not been studied sufficiently to enable firm conclusions to be made. Evidence from studies in people without cancer may not be applicable because cancer could affect the action of these drugs. In studies that recruited only people with cancer and VTE, rivaroxaban,

edoxaban and LMWH were found to be similarly effective, although bleeding complications were more frequent with edoxaban. These studies did not look at apixaban or dabigatran. In studies that looked at apixaban and dabigatran and in which a small number of people within the study population had active cancer, the effects of apixaban and dabigatran were similar in people with and without cancer. Economic evidence from these studies showed apixaban to be the most cost-effective option, although the evidence for apixaban was based on a relatively small number of people.

The committee agreed that, if suitable, a DOAC should be considered to treat VTE in people with cancer but, because of the lack of evidence, they could not be more specific about the choice of DOAC.

The committee acknowledged that a DOAC might not be suitable for everyone with cancer and included LMWH with a VKA as an alternative. However, although LMWH with a VKA is more cost effective than LMWH alone, it might not be practical for people with cancer because of difficulties with INR monitoring and maintaining INR within the therapeutic range.

LMWH on its own is commonly used in practice and is the only licensed option for people with VTE and cancer. It is expensive and not cost effective, and the committee agreed that reducing its use would be beneficial in conserving NHS resources. However, they recognised that there are circumstances in which no other option is suitable so agreed that it could be considered when this is the case.

How the recommendations might affect practice

The recommendations are expected to lead to increased use of DOACs, particularly apixaban and rivaroxaban, to treat suspected and confirmed VTE. This should reduce the need for resources to monitor INR, manage bleeding complications and administer parenteral anticoagulation. The recommendation to start anticoagulation treatment before blood test results are available may increase community prescribing of anticoagulation treatment. However, more use of DOACs may also increase the need for expensive reversal agents.

For people with haemodynamically unstable PE, the recommendations can be expected to increase the use of UFH, potentially reducing the need for thrombolysis.

More people with renal impairment are likely to be offered a DOAC or LMWH, reducing the use of UFH. This can be expected to produce cost savings by increasing the number of people with renal impairment who can have outpatient care for VTE. Current VTE management for people with a BMI of 40 kg/m^2 or more is not expected to change substantially, although the use of DOACs might be reduced.

For people with cancer, it is expected that there will be an increase in the use of DOACs and a concomitant decrease in the use of more expensive treatments such as LMWH alone. This will also reduce the amount of district nursing support needed to provide assistance with parenteral therapies.

Return to recommendations

Reviewing anticoagulation treatment

Recommendations 1.4.1 to 1.4.11

Why the committee made the recommendations

The committee agreed that the benefits of anticoagulation treatment become less certain over time. After 3 months, the aim changes from treatment to reducing the risk of recurrence. For this reason the committee chose 3 months as the point at which treatment should be reviewed and discussed with the person with VTE.

Predicting VTE recurrence and assessing bleeding risk after provoked or unprovoked DVT or PE

The committee noted that continuing anticoagulation treatment after 3 months is less beneficial for people who have had a provoked DVT or PE because of the lower rate of recurrence compared with unprovoked DVT or PE.

For people with unprovoked DVT or PE, the benefits and risks of continuing anticoagulation treatment are less certain and the committee agreed that they need to be carefully balanced. However, for most people with a low bleeding risk, the committee agreed that the benefits of continuing anticoagulation treatment outweigh the risks.

The committee agreed that the tools currently available to predict the risk of recurrence of VTE or the risk of bleeding are not sufficiently accurate or validated to

be used as the sole basis for a decision, and that using them in such a manner might result in incorrect predictions and subsequent harm to the patient. However, they also agreed that, in certain circumstances, a clinical prediction tool can be a useful adjunct to discussion with people offered long-term anticoagulation treatment. In the committee's experience, a significant proportion of people with VTE decline long-term treatment. For those aged 65 or under who decline long-term treatment, the committee agreed that the DASH tool can help to guide the discussion about stopping or continuing anticoagulation treatment because evidence showed that this tool has good accuracy for predicting recurrent VTE in people aged 65 or under. This level of prognostic accuracy is not maintained in people aged over 65. Evidence on the HAS-BLED score showed that it can identify people with unprovoked proximal DVT or PE who are at particularly high risk of major bleeding and might benefit from stopping anticoagulation.

Because of the uncertainty in predicting VTE recurrence and the risk of major bleeding, the committee made recommendations for research to develop a new prediction tool and to compare this tool with clinical judgement.

Continuing or changing current treatment

The committee agreed that there are risks involved in switching anticoagulant treatment, particularly if there have been no adverse events with the current treatment. They also expressed concerns about convenience for people who are asked to switch from a direct-acting oral anticoagulant (DOAC) with no monitoring to a VKA regimen with frequent monitoring, or problems with adherence if switching from a VKA to a DOAC. Based on these concerns and their clinical experience, the committee agreed that if treatment is continued beyond 3 months, the first option for most people should be to continue the current treatment.

Some evidence indicated that there are fewer major bleeds with apixaban than with rivaroxaban, dabigatran or a VKA. However, the committee were not entirely convinced by this evidence because the study of apixaban had stricter inclusion criteria, setting out which patients took part, than the other studies. Additionally, the studies recorded a very low number of major bleeds, leading to uncertainty about the effects of the different anticoagulation treatments on the likelihood of major bleeding. Apixaban was shown by the economic evidence to be the most cost-effective long-

term treatment so the committee agreed that switching to apixaban should be considered as an option for people currently taking a DOAC other than apixaban.

There was a lack of evidence on longer-term treatment for people with renal impairment, BMI 40 kg/m^2 or more, or cancer. Based on their clinical experience, the committee agreed that continuing the current treatment for people in these groups should be considered, taking into account their preferences and clinical situation.

For people who do not continue anticoagulation treatment, evidence showed that aspirin is better than no treatment at reducing DVT or PE recurrence for up to 2 years, although there was no difference in DVT or PE recurrence between aspirin and no treatment at 4 years. On balance, the committee agreed that aspirin can be considered as an option for people who wish to stop anticoagulation treatment, using a prophylactic dose based on current UK practice (75 or 150 mg daily).

To ensure that treatment is guided by the person's changing balance of benefits and risks, and changes in their preferences over time, the committee agreed that people taking long-term anticoagulation treatment should have their risk of VTE recurrence, bleeding risk and general health reviewed at least once a year.

How the recommendations might affect practice

The recommendations to review anticoagulation treatment at 3 months, and annually thereafter, reflect most current practice but may increase the number of appointments and clinician time needed in services that do not currently provide these reviews. Giving patients who stop anticoagulation treatment information on signs and symptoms and a point of contact should ensure that a comprehensive safety net is in place.

Discussions about the benefits and risks of stopping or continuing anticoagulation treatment may increase the time needed for consultations, particularly if a prediction tool is used as part of the decision-making process. Using HAS-BLED can be expected to reduce long-term anticoagulation treatment in people with a high risk of major bleeding.

For people without renal impairment, BMI 40 kg/m^2 or more, or cancer, increased use of DOACs, particularly apixaban, for long-term therapy can be expected to lower

costs by reducing the need for clinical visits, INR monitoring and managing bleeding events. For people with these comorbidities, the recommendations are not expected to change current practice. The use of aspirin may increase for people who decline long-term anticoagulation. This may decrease the incidence of recurrent VTE in people who would otherwise not receive treatment.

Return to recommendations

Inferior vena caval filters

Recommendations 1.7.1 to 1.7.4

Why the committee made the recommendations

There was little good evidence on inferior vena caval (IVC) filters. The evidence in a number of populations, including people about to have surgery, people with cancer, people with a high risk of having a subsequent PE and people with a high risk of a poor outcome from a subsequent PE, did not show a benefit from IVC filters. The committee therefore agreed that the use of IVC filters should be restricted to prospective clinical studies (including but not limited to prospective cohort studies and randomised controlled trials) unless anticoagulation is contraindicated or a PE has occurred during anticoagulation treatment. They made a recommendation for research to further investigate the effectiveness of IVC filters.

For people with proximal DVT or PE and a contraindication to anticoagulation treatment, a small amount of new evidence has become available since the 2012 guideline was published. This evidence did not show a clear difference in outcomes such as mortality and VTE recurrence between people who were given IVC filters and those who were not. One study found evidence of an increase in DVT recurrence at 1 year in the group given IVC filters. However, based on their experience and knowledge of IVC filters, the committee agreed that they can help to reduce the risk of PE when therapeutic anticoagulation cannot be given. The committee also had concerns about the inherent risks involved in using IVC filters, including the invasive nature of the procedure for placing them and the potential for complications such as migration or fracture of the filter. In light of this, the committee agreed that the evidence was not sufficient to retain the 2012 recommendation to offer temporary IVC filters to people who cannot have anticoagulation treatment.

However, they recognised that these people have a high risk of recurrent VTE and a limited number of alternative treatments, so agreed that a recommendation to consider an IVC filter for them is justified. They also agreed to retain the 2012 advice to remove the IVC filter when anticoagulation is no longer contraindicated, adding that anticoagulation treatment should be established before the IVC filter is removed.

There was very limited evidence on the use of IVC filters for people who have a PE while taking anticoagulation treatment for an initial proximal DVT or PE. The evidence suggested a reduction in short-term mortality from all causes in people in this group who had an IVC filter fitted. Because of the limited amount of evidence, the committee agreed that IVC filters could be considered for people in this group only after problems with adherence or other causes of hypercoagulability have been excluded, and different anticoagulation treatments or treatment regimens have been explored. The committee reasoned that, in many cases, optimising anticoagulation treatment will obviate the need for an IVC filter.

The committee agreed there should be a plan to ensure that IVC filters are removed as soon as they are no longer needed.

How the recommendations might affect practice

It is expected that the overall impact of the recommendations will be to reduce the use of IVC filters. For people with VTE at acute risk of thrombosis, clinicians may fit an IVC filter as part of a clinical trial.

Return to recommendations

Investigations for cancer

Recommendations 1.8.1 and 1.8.2

Why the committee made the recommendations

Unprovoked VTE is associated with an increased risk of cancer, which may be undiagnosed when the VTE occurs. The committee agreed that a physical examination and review of medical history and investigations (including imaging) performed to date are worthwhile precautions for people who have had an

apparently unprovoked DVT or PE. However, the evidence did not show any benefit from further investigations for cancer for people who have no signs or symptoms. Moreover, these investigations can be costly, time consuming, potentially invasive or pose a radiation risk, and cause anxiety. The committee therefore agreed that further investigations for cancer should not be offered to people without relevant signs or symptoms.

How the recommendations might affect practice

A physical examination and a review of medical history and the results of recent investigations results is current practice for people with unprovoked DVT or PE. The recommendations can be expected to reduce costs by reducing further investigations for cancer in people without symptoms or signs.

Return to recommendations

Context

In venous thromboembolism (VTE), a blood clot forms in a vein, usually in the deep veins of the legs or pelvis. This is known as deep vein thrombosis, or DVT. The blood clot can dislodge and travel in the blood, particularly to the pulmonary arteries. This is known as pulmonary embolism, or PE. The term 'VTE' includes both DVT and PE.

Failure to diagnose and treat VTE correctly can result in fatal PE, in which the blood clot blocks the blood supply to the lungs. However, diagnosis of VTE is not always straightforward. This guideline includes advice on the Wells score, D-dimer measurement, ultrasound and radiological imaging. It also offers guidance on treating VTE, investigations for cancer in people with VTE and thrombophilia testing. The guideline covers adults with suspected or confirmed DVT or PE. It does not cover children or young people aged under 18, or women who are pregnant.

Since publication of the original guideline in 2012, new evidence has emerged and practice has changed in relation to the use of direct oral anticoagulants, prognostic tools, diagnosis of VTE using age-adjusted and point-of-care D-dimer testing, pulmonary embolism rule-out criteria, outpatient treatment for PE, inferior vena caval

filters and investigations for cancer in people with unprovoked VTE. This 2020 update includes new and updated recommendations in these areas.

Finding more information and resources

To find out what NICE has said on topics related to this guideline, see our web page on cardiovascular conditions.

Update information

March 2020

This guideline is an update of NICE guideline CG144 (published June 2012, updated November 2015) and will replace it.

We have reviewed evidence on D-dimer testing, the PERC rule for pulmonary embolism, outpatient management of low-risk PE, anticoagulation treatment for suspected and confirmed DVT or PE, inferior vena caval filters and investigations for cancer for people with suspected or confirmed DVT or PE.

Recommendations are marked **[2020]** if the evidence has been reviewed.

Recommendations that have been deleted or changed without an evidence review

In recommendations shaded in grey and ending **[2012, amended 2020],** we have made changes that could affect the intent without reviewing the evidence. Yellow shading is used to highlight these changes, and reasons for the changes are given in table 3.

In recommendations shaded in grey and ending **[2012]** or **[2015]**, we have not reviewed the evidence. In some cases minor changes have been made – for example, to update links, or bring the language and style up to date – without changing the intent of the recommendation. Yellow shading has not been applied to these changes. They are listed in table 4.

See also the previous NICE guideline and supporting documents.

Table 3 Amended recommendation wording (change to intent) without an evidence review

Recommendation in 2012 (updated 2015) guideline	Recommendation in current guideline	Comment
All recommendations in section 1.1 on diagnosis that refer to an 'interim 24-hour dose of a parenteral anticoagulant'	Recommendations 1.1.4, 1.1.8 and 1.1.10, 1.1.18, and 1.1.21	'Interim 24-hour dose of a parenteral anticoagulant' has been changed to 'interim therapeutic anticoagulation' in these recommendations to reflect the inclusion of direct oral anticoagulants in the 2020 update.
Recommendations in section 1.1 on diagnosis	Recommendations 1.1.6 and 1.1.7, and 1.1.20	The 2012 guideline stipulated that interim anticoagulation treatment should be a '24-hour dose'. Because this stipulation has been removed in the 2020 update, 'stop interim therapeutic anticoagulation' has been added to these recommendations to ensure that interim anticoagulation is discontinued when no longer needed.
Recommendations on D-dimer testing for people with 'unlikely' DVT or PE Wells scores in section 1.1 on diagnosis	Recommendations 1.1.8 and 1.1.21	A limit of 4 hours on D-dimer test results has been added to correspond with the limit of 4 hours recommended for proximal leg vein ultrasound scan results.
1.1.12 Diagnose PE and treat (see the recommendations on treatment in section 1.2) patients with a positive CTPA or in whom PE is identified with a V/Q SPECT or planar scan. **[2012]**	1.1.19 If PE is identified by CTPA, V/Q SPECT or V/Q planar scan: • offer or continue anticoagulation treatment (see anticoagulation treatment for confirmed DVT or PE) or • if anticoagulation treatment is contraindicated, consider a mechanical intervention (see mechanical interventions). For people with PE and haemodynamic instability see thrombolytic therapy. **[2012, amended 2020]**	'Offer' a mechanical intervention has been changed to 'consider' to align with the updated recommendations on mechanical interventions in the 2020 guideline.

1.3.3 Be aware that heparins are of animal origin and this may be of concern to some patients (see Religion or belief: a practical guide for the NHS). For patients who have concerns about using animal products, consider offering synthetic alternatives based on clinical judgement after discussing their suitability, advantages and disadvantages with the patient. (This recommendation is from Venous thromboembolism: reducing the risk [NICE guideline CG92]). **[2012]**	1.5.3 Be aware that heparins are of animal origin and that apixaban and rivaroxaban contain lactose from cow's milk. For people who have concerns about using animal products, see giving information and planning for discharge in the NICE guideline on venous thromboembolism in over 16s. **[2012, amended 2020]**	Information about apixaban and rivaroxaban has been added because these medicines are recommended in the 2020 guideline. The NICE guideline on venous thromboembolism: reducing the risk (CG92, 2010) was fully updated in 2018 and the reference to it has been amended to link to the 2018 guideline.

1.1.11 For patients who have an allergy to contrast media, or who have renal impairment*, or whose risk from irradiation is high: • Assess the suitability of a ventilation/perfusion single photon emission computed tomography (V/Q SPECT) scan or, if a V/Q SPECT scan is not available, a V/Q planar scan, as an alternative to CTPA. • If offering a V/Q SPECT or planar scan that will not be available immediately, offer immediate interim parenteral anticoagulant therapy. **[2012]** *Reduced renal function that may be acute or chronic. An estimated glomerular filtration rate of less than 90 ml/min/1.73 m^2 indicates a degree of renal impairment in chronic kidney disease. (For NICE guidance on the classification of chronic kidney disease see chronic kidney disease [NICE guideline CG182])	1.1.18 For people with a likely PE Wells score (more than 4 points): • offer a computed tomography pulmonary angiogram (CTPA) immediately if possible **or** • for people with an allergy to contrast media, severe renal impairment (estimated creatinine clearance less than 30 ml/min) or a high risk from irradiation, assess the suitability of a ventilation/perfusion single photon emission computed tomography (V/Q SPECT) scan or, if a V/Q SPECT scan is not available, a V/Q planar scan, as an alternative to CTPA. If a CTPA, V/Q SPECT or V/Q planar scan cannot be done immediately, offer interim therapeutic anticoagulation (see interim therapeutic anticoagulation for suspected DVT or PE). **[2012, amended 2020]**	Renal impairment has been defined as severe (estimated creatinine clearance less than 30 ml/min) to clarify that CTPA is not excluded for all renal impairment but that people with severe renal impairment may be best served by a discussion about alternative imaging modalities.

Do not offer thrombophilia testing to patients who are continuing anticoagulation treatment. **[2012]** [1.6.1]	1.9.1 Do not offer testing for hereditary thrombophilia to people who are continuing anticoagulation treatment. **[2012, amended 2020]**	This change has been made to differentiate between hereditary thrombophilia and antiphospholipid syndrome, which is an acquired form of thrombophilia. In light of the Medicines and Healthcare products Regulatory Agency June 2019 drug safety update on direct-acting oral anticoagulants (DOACs): increased risk of recurrent thrombotic events in patients with antiphospholipid syndrome, it is now possible that people taking the direct oral anticoagulants recommended in the 2020 guideline may need to be offered testing for antiphospholipid syndrome.
Consider testing for antiphospholipid antibodies I people who have had unprovoked DVT or PE if it is planned to stop anticoagulation treatment. **[2012]** [1.6.2]	1.9.3 Consider testing for antiphospholipid antibodies in people who have had unprovoked DVT or PE if it is planned to stop anticoagulation treatment, but be aware that these tests are affected by anticoagulants and specialist advice may be needed. **[2012, amended 2020]**	Wording has been added to ensure clinicians are aware that anticoagulants can affect the interpretation of thrombophilia test results
1.6.3 Consider testing for hereditary thrombophilia in patients who have had unprovoked DVT or PE and who have a first-degree relative who has had DVT or PE if it is planned to stop anticoagulation treatment. **[2012]** [1.6.3]	1.9.4 Consider testing for hereditary thrombophilia in people who have had unprovoked DVT or PE and who have a first-degree relative who has had DVT or PE if it is planned to stop anticoagulation treatment, but be aware that these tests are affected by anticoagulants and specialist advice may be needed. **[2012, amended 2020]**	Wording has been added to ensure clinicians are aware that anticoagulants can affect the interpretation of thrombophilia test results.

Terms used in this guideline **Unprovoked DVT or PE** DVT or PE in a patient with: • no antecedent major clinical risk factor for VTE (see provoked deep vein thrombosis or pulmonary embolism) who is not having hormonal therapy (oral contraceptive or hormone replacement therapy) or • active cancer, thrombophilia or a family history of VTE, because these are underlying risks that remain constant in the patient.	**Terms used in this guideline** **Unprovoked DVT or PE** Deep vein thrombosis or pulmonary embolism in a person with no recent major clinical risk factor for VTE (see provoked DVT or PE) who is not having hormonal therapy (oral contraceptive or hormone replacement therapy).	Amended to reflect the 2020 guideline committee's use of the term.

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1 **Table 4 Minor changes to recommendation wording (no change to intent)**

Recommendation numbers in current guideline	Comment
All recommendations	'Patient' has been changed to 'people' in line with NICE's current style for guideline recommendations.
Section 1.1., all recommendations	The wording has been simplified and re-ordered for clarity.
1.1.1	'such as a swollen or painful leg' has been added to clarify signs or symptoms of DVT.
1.1.7 and 1.1.20	'Consider' has been changed to 'Think about' for clarity and in line with NICE's current use of 'consider' as an indication of certainty in guideline recommendations. The bullet points have been re-ordered for clarity.
1.1.15	'such as chest pain, shortness of breath or coughing up blood' has been added to clarify signs or symptoms of PE.
1.5.1	'Monitoring their anticoagulant treatment' has been changed to 'any monitoring needed for their anticoagulant treatment' to reflect the inclusion in the 2020 update of recommendations for treatment with direct oral anticoagulants that do not require frequent monitoring.
1.4.2	The reference to an 'anticoagulant information booklet' has been changed to 'anticoagulation information', and 'specific to their treatment' has been added to reflect the inclusion of direct anticoagulants in the 2020 update.
1.7.6	'If offering elastic graduated compression stockings to manage leg symptoms after DVT' has been added for clarification and to reflect recommendation 1.7.5, in which stockings are not advised for preventing post-thrombotic syndrome or VE recurrence after DVT.
Terms used in this guideline	The definition of 'proximal DVT' has been changed from 'DVT in the popliteal vein or above. Proximal DVT is sometimes referred to as 'above-knee' DVT' to 'DVT at or above the level of the popliteal trifurcation area' for clarification.
Terms used in this guideline	The following terms were deleted because they are now well known: D-dimer, haemodynamically stable PE, INR, PE, right ventricular dysfunction. In addition, 'renal impairment was deleted because it is now defined in the recommendations.

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