

# Venous thromboembolic diseases: diagnosis, management and thrombophilia testing

NICE guideline

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## Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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This guideline is the basis of QS29.

## Overview

This guideline covers diagnosing and managing venous thromboembolic diseases in adults. It aims to support rapid 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.

The guideline does not cover pregnant women.

## 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

# Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in [NICE's information on 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

NICE has also produced a [visual summary](#) of the recommendations on diagnosis and initial management of suspected deep vein thrombosis (DVT) and pulmonary embolism (PE).

### Signs or symptoms of DVT

- 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

Clinical feature	Points
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 at least as likely as DVT	-2
Clinical probability simplified score	Points
DVT likely	2 points or more
DVT unlikely	1 point or less

Adapted with permission from Wells 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:

- a D-dimer test, then
- interim therapeutic anticoagulation (see the section on [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]

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

- offer or continue anticoagulation treatment (see the section on [anticoagulation treatment for confirmed DVT or PE](#)) or
- if anticoagulation treatment is contraindicated, offer a mechanical intervention (see the section on [mechanical interventions](#)).

For people with symptomatic iliofemoral DVT see the section on [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 the section on [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 the section on [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 the section on [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 these 2020 recommendations and how they might affect practice, see the [rationale and impact section on D-dimer testing](#).

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 PE

- 1.1.15 For people who present with signs or symptoms of 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 (the clinician estimates the likelihood of PE to be less than 15% based on the overall clinical impression, and other diagnoses are feasible), 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 and how it might affect practice, see the [rationale and impact section on the PERC rule](#).

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]

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
<b>Clinical probability simplified score</b>	<b>Points</b>
PE likely	More than 4 points

Clinical feature	Points
PE unlikely	4 points or less

Adapted with permission from Wells 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](#) 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 the section on [interim therapeutic anticoagulation for suspected DVT or PE](#)). [2012, amended 2020]

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

- offer or continue anticoagulation treatment (see the section on [anticoagulation treatment for confirmed DVT or PE](#)) or
- if anticoagulation treatment is contraindicated, consider a mechanical intervention (see the section on [mechanical interventions](#)).

For people with PE and haemodynamic instability see the section on [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 the section on [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 the section on [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:
  - 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]

## Signs or symptoms of both DVT and PE

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 PE

- 1.2.1 Consider outpatient treatment for suspected or confirmed low-risk PE, using a validated risk stratification tool to determine the suitability of outpatient treatment. [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 the recommendations in the section on [anticoagulation treatment for confirmed DVT or PE](#). [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 and how they might affect practice, see the [rationale and impact section on outpatient treatment for low-risk PE](#).

Full details of the evidence and the committee's discussion are in [evidence review E: outpatient treatment of low-risk pulmonary embolism](#)

## 1.3 Anticoagulation treatment for suspected or confirmed DVT or PE

NICE has also produced a [visual summary](#) of the recommendations on anticoagulation treatment for DVT or PE.

- 1.3.1 When offering anticoagulation treatment, follow the recommendations on shared decision making and supporting adherence in the [NICE guidelines on medicines optimisation](#), [medicines adherence](#) and [patient experience in adult NHS services](#). [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 the section on [diagnosis and initial management](#). [2020]
- 1.3.3 If possible, choose an interim anticoagulant that can be continued if DVT or PE is confirmed (see the section on [anticoagulation treatment for confirmed DVT or PE](#)). [2020]

In March 2020, direct-acting anticoagulants and some low molecular weight heparins (LMWHs) were off label for the treatment of suspected DVT or PE. See [NICE's information on prescribing medicines](#).

- 1.3.4 When using interim therapeutic anticoagulation for suspected proximal DVT or PE:
- carry out baseline blood tests including full blood count, renal and hepatic function, prothrombin time (PT) and activated partial thromboplastin time (APTT)
  - do not wait for the results of baseline blood tests before starting anticoagulation treatment
  - review, and if necessary act on, the results of baseline blood tests within 24 hours of starting interim therapeutic anticoagulation. [2020]

## Anticoagulation treatment for confirmed DVT or PE

- 1.3.5 Offer anticoagulation treatment for at least 3 months to people with confirmed proximal DVT or PE. For recommendations on treatment after 3 months see the section on [long-term anticoagulation for secondary prevention](#). [2020]
- 1.3.6 If not already done, carry out baseline blood tests, as outlined in recommendation 1.3.4, when starting anticoagulation treatment. [2020]

- 1.3.7 When offering anticoagulation treatment, take into account comorbidities, contraindications and the person's preferences.

Follow the recommendations on anticoagulation treatment in the sections on:

- DVT or PE in people at extremes of body weight
- PE with haemodynamic instability
- DVT or PE with renal impairment or established renal failure
- DVT or PE with active cancer
- DVT or PE with triple positive antiphospholipid syndrome. [2020]

- 1.3.8 Offer either apixaban or rivaroxaban to people with confirmed proximal DVT or PE (but see recommendations 1.3.11 to 1.3.20 for people with any of the clinical features listed in recommendation 1.3.7). If neither apixaban nor rivaroxaban is suitable offer:

- LMWH for at least 5 days followed by dabigatran or edoxaban 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]

- 1.3.9 Do not routinely offer unfractionated heparin (UFH) with a VKA to treat confirmed proximal DVT or PE unless the person has renal impairment or established renal failure (see recommendations 1.3.13 and 1.3.14) or an increased risk of bleeding. [2020]

- 1.3.10 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 DVT or PE in people at extremes of body weight

- 1.3.11 Consider anticoagulation treatment with regular monitoring of therapeutic levels for people with confirmed proximal DVT or PE who weigh less than 50 kg or more than 120 kg, to ensure effective anticoagulation.

Note the cautions and requirements for dose adjustment and monitoring in the medicine's summary of product characteristics (SPC), and follow locally agreed

protocols or advice from a specialist or multidisciplinary team. [2020]

## Anticoagulation treatment for PE with haemodynamic instability

- 1.3.12 For people with confirmed PE and haemodynamic instability, offer continuous UFH infusion and consider thrombolytic therapy (see the section on [thrombolytic therapy](#)). [2020]

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

In March 2020, some LMWHs were off label for the treatment of DVT or PE in people with severe renal impairment ([estimated creatinine clearance](#) 15 ml/min to 30 ml/min) or established renal failure (estimated creatinine clearance less than 15 ml/min). See [NICE's information on prescribing medicines](#).

- 1.3.13 Offer people with confirmed proximal DVT or PE and renal impairment ([estimated creatinine clearance](#) between 15 ml/min and 50 ml/min) one of:
- apixaban
  - rivaroxaban
  - LMWH for at least 5 days followed by:
    - edoxaban or
    - dabigatran if estimated creatinine clearance is 30 ml/min or above
  - LMWH or UFH, given concurrently with a 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.

Note the cautions and requirements for dose adjustment and monitoring in the medicine's SPC, and follow locally agreed protocols or advice from a specialist or multidisciplinary team. [2020]

- 1.3.14 Offer people with confirmed proximal DVT or PE and established renal failure ([estimated creatinine clearance](#) less than 15 ml/min) one of:
- LMWH



- UFH
- LMWH or UFH concurrently with a 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.

Note the cautions and requirements for dose adjustment and monitoring in the medicine's SPC, and follow locally agreed protocols or advice from a specialist or multidisciplinary team. [2020]

## Anticoagulation treatment for DVT or PE with active cancer

In March 2020, most anticoagulants were off label for the treatment of DVT or PE in people with active cancer. See [NICE's information on prescribing medicines](#).

- 1.3.15 Offer people with [active cancer](#) and confirmed proximal DVT or PE anticoagulation treatment for 3 to 6 months. Review at 3 to 6 months according to clinical need. For recommendations on treatment after 3 to 6 months see the section on [long-term anticoagulation for secondary prevention](#). [2020]
- 1.3.16 When choosing anticoagulation treatment for people with active cancer and confirmed proximal DVT or PE, take into account the tumour site, interactions with other drugs including those used to treat cancer, and the person's bleeding risk. [2020]
- 1.3.17 Consider a direct-acting oral anticoagulant (DOAC) for people with active cancer and confirmed proximal DVT or PE. [2020]
- 1.3.18 If a DOAC is unsuitable consider LMWH alone or LMWH concurrently with a 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]
- 1.3.19 For people with confirmed DVT or PE and cancer that is in remission, follow the recommendations in the section on [anticoagulation treatment for confirmed DVT or PE](#). [2020]

## Anticoagulation treatment for DVT or PE with triple positive antiphospholipid syndrome

- 1.3.20 Offer people with confirmed proximal DVT or PE and an established diagnosis of triple positive antiphospholipid syndrome LMWH concurrently with a 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]

## Treatment failure

- 1.3.21 If anticoagulation treatment fails:

- check adherence to anticoagulation treatment
- address other sources of hypercoagulability
- increase the dose of anticoagulant or change to an anticoagulant with a different mode of action. [2020]

## NICE technology appraisal guidance on anticoagulation treatment for confirmed DVT or PE

For NICE technology appraisal guidance 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.](#)

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

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 G: economic modelling report for pharmacological treatment](#) also underpins recommendations 1.3.8, 1.3.9, 1.3.17 and 1.3.18.

## 1.4 Long-term anticoagulation for secondary prevention

- 1.4.1 Assess and discuss the benefits and risks of continuing, stopping or changing the anticoagulant with people who have had anticoagulation treatment for 3 months (3 to 6 months for people with [active cancer](#)) after a [proximal DVT](#) or PE. Follow the recommendations on shared decision making and supporting adherence in the [NICE guidelines on medicines optimisation, medicines adherence and patient experience in adult NHS services](#). [2020]
- 1.4.2 Consider stopping anticoagulation treatment 3 months (3 to 6 months for people with active cancer) after a [provoked DVT or PE](#) if the provoking factor is no longer present and the clinical course has been uncomplicated. If anticoagulation treatment is stopped, give advice about the risk of recurrence and provide:
- 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 Consider continuing anticoagulation beyond 3 months (6 months for people with active cancer) after an [unprovoked DVT or PE](#). Base the decision on the balance between the person's risk of venous thromboembolism (VTE)

recurrence and their risk of bleeding. Discuss the risks and benefits of long-term anticoagulation 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 HAS-BLED score for major bleeding risk 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]
- 1.4.7 Take into account the person's preferences and their clinical situation when selecting an anticoagulant for long-term treatment. [2020]
- 1.4.8 For people who do not have renal impairment, active cancer, established triple positive antiphospholipid syndrome or extreme body weight (less than 50 kg or more than 120 kg):
- offer continued treatment with the current anticoagulant if it is well tolerated or
  - if the current treatment is not well tolerated, or the clinical situation or person's preferences have changed, consider switching to apixaban if the current treatment is a direct-acting anticoagulant other than apixaban. [2020]
- 1.4.9 For people with renal impairment, active cancer, established triple positive antiphospholipid syndrome or extreme body weight (less than 50 kg or more than 120 kg), consider carrying on with the current treatment if it is well tolerated. [2020]
- 1.4.10 If anticoagulation treatment fails follow the recommendation on treatment failure. [2020]
- 1.4.11 For people who decline continued anticoagulation treatment, consider aspirin 75 mg or 150 mg daily.

In March 2020, the use of aspirin for secondary prevention of DVT or PE was off label. See [NICE's information on prescribing medicines](#). [2020]

- 1.4.12 Review general health, risk of VTE recurrence, bleeding risk and treatment preferences at least once a year for people taking long-term anticoagulation treatment or aspirin. [2020]

For a short explanation of why the committee made the 2020 recommendations on reviewing anticoagulation treatment and how they might affect practice, see the [rationale and impact section on long-term anticoagulation for secondary prevention](#).

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

- [evidence review F: what factors determine the optimum duration of pharmacological treatment for DVT or PE in people with a VTE?](#)
- [evidence review D: pharmacological treatment in people with suspected or confirmed deep vein thrombosis and/or pulmonary embolism](#) (for recommendations 1.4.1 and 1.4.7 to 1.4.11).

[Evidence review G: economic modelling report for pharmacological treatment](#) also underpins recommendation 1.4.8.

## 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 because of a religious or ethical belief, or a food intolerance, see the section on [giving information and planning for discharge in the NICE guideline on venous thromboembolism in over 16s](#). [2012, amended 2020]

## 1.6 Thrombolytic therapy

### DVT

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]

See [NICE interventional procedures guidance on ultrasound-enhanced, catheter-directed thrombolysis for deep vein thrombosis](#).

### PE

1.6.2 Consider pharmacological systemic thrombolytic therapy for people with PE and haemodynamic instability(see also the section on [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 the section on [anticoagulation treatment for DVT or PE](#)). If the person develops haemodynamic instability, refer to recommendation 1.6.2. [2015]

See [NICE interventional procedures guidance on ultrasound-enhanced, catheter-directed thrombolysis for pulmonary embolism](#).

## 1.7 Mechanical interventions

### Inferior vena caval filters

- 1.7.1 Do not offer an inferior vena caval (IVC) filter to people with [proximal DVT](#) or 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 an 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 taking the steps outlined in the recommendation on [treatment failure](#). [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 and how they might affect practice, see the [rationale and impact section on IVC filters](#).

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

## 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]

## Percutaneous mechanical thrombectomy

See [NICE interventional procedures guidance on percutaneous mechanical thrombectomy for acute deep vein thrombosis of the leg](#).

## 1.8 Investigations for cancer

- 1.8.1 For people with [unprovoked DVT or PE](#) who are not known to have cancer, review the medical history and baseline blood test results including full blood count, renal and hepatic function, PT and APTT, and offer a physical examination. [2020]
- 1.8.2 Do not offer further investigations for cancer to people with unprovoked DVT or PE unless they have relevant clinical symptoms or signs (for further information see the [NICE guideline on suspected cancer](#)). [2020]

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

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 can be 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 can be 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

### Active cancer

Receiving active antimitotic treatment; or diagnosed within the past 6 months; or recurrent or metastatic; or inoperable. Excludes squamous skin cancer and basal cell carcinoma.

### Estimated creatinine clearance

Creatinine clearance estimated using the Cockcroft and Gault formula; see the [BNF's information on prescribing in renal impairment](#).

### Provoked DVT or PE

DVT or PE 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 (combined oral contraceptive pill or hormone replacement therapy).

## Proximal DVT

DVT at or above the level of the popliteal trifurcation area.

## Unprovoked DVT or PE

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

## Wells score

Clinical prediction rule for estimating the probability of DVT or PE. 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 venous thromboembolism

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

For a short explanation of why the committee made the recommendation for research, see the [rationale on inferior vena caval filters](#).

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

### 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 (DOACs) compared with each other, with low molecular weight heparin (LMWH) plus a vitamin K antagonist (VKA), with LMWH alone, with placebo and with aspirin for the initial and long-term treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE) based on individual patient data from existing trials? [2020]

For a short explanation of why the committee made the recommendation for research, see the [rationale on anticoagulation treatment for confirmed DVT or PE](#).

Full details of the evidence and the committee's discussion are in [evidence review D: pharmacological treatment in people with suspected or confirmed DVT and/or PE](#).

### 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]

For a short explanation of why the committee made the recommendation for research, see the [rationale on long-term anticoagulation for secondary prevention](#).

Full details of the evidence and the committee's discussion are in [evidence review F: what factors determine the optimum duration of pharmacological treatment for DVT or PE in people with a VTE?](#)

### 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]

For a short explanation of why the committee made the recommendation for research, see the [rationale on anticoagulation treatment for DVT or PE in people who use intravenous drugs](#).

Full details of the evidence and the committee's discussion are in [evidence review D: pharmacological treatment in people with suspected or confirmed DVT and/or PE](#).

## 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]

For a short explanation of why the committee made the recommendation for research, see the [rationale on long-term anticoagulation for secondary prevention](#).

Full details of the evidence and the committee's discussion are in [evidence review F: what factors determine the optimum duration of pharmacological treatment for DVT or PE in people with a VTE?](#)

## 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, a cost-effectiveness analysis showed that the additional cost may be offset by faster results that reduce the need for additional GP time and unnecessary interim anticoagulation.

Evidence on fully quantitative point-of-care D-dimer tests for deep vein thrombosis (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 pulmonary embolism (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 venous thromboembolism

(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.

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## Pulmonary embolism rule-out criteria (the PERC rule)

[Recommendation 1.1.16](#)

### Why the committee made the recommendation

In people with signs or symptoms of 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. The committee noted that the studies evaluating PERC all took place in emergency departments but they could see no reason why its use should be limited to this setting or why the diagnostic accuracy of PERC would differ in other settings.

## 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.

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## 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. They noted that specialist services with expertise in thrombosis are not available at all times and agreed that it is important for people with VTE to know who they can contact if they need advice outside normal service hours.

### 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.



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

[Recommendations 1.3.1 to 1.3.21](#)

## 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 also noted that continuing the same anticoagulant treatment after diagnosis offers benefits in terms of safety and convenience. However, they acknowledged that local protocols or availability of anticoagulants for suspected VTE may necessitate the use of different anticoagulants before and after diagnosis.

The committee agreed that when choosing an interim anticoagulant, clinicians should always take individual clinical circumstances into account, including whether the person is at an extreme of body weight, has PE with haemodynamic instability, renal impairment, [active cancer](#) or established triple positive antiphospholipid syndrome.

### 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 low molecular weight heparin (LMWH) and a vitamin K antagonist (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 is 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. Sensitivity analyses were carried out varying the drug prices but these analyses did not change any of the conclusions from the economic model.

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 a VKA. The committee also made a recommendation for research on DOACs compared with each other and with other anticoagulants.

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.

Unfractionated heparin (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 DVT or PE in people at extremes of body weight (less than 50 kg or more than 120 kg)**

Body weight can influence the absorption, distribution and elimination of anticoagulants, and their therapeutic effect can be altered at extremes of body weight. Because of this, and based on their knowledge and experience, the committee agreed that body weight should be taken into account and therapeutic monitoring considered when choosing anticoagulation for people whose weight is outside the range of 50 kg to 120 kg.

There was little evidence on the comparative effectiveness of different anticoagulants for people at extremes of body weight, and the evidence was limited to obesity defined as a body mass index of 30 kg/m<sup>2</sup> and above rather than body weight. However, the committee noted that the summaries of product characteristics (SPCs) for several anticoagulants specify body weight rather than obesity and agreed that using the same criterion as the SPCs would make the recommendations clearer and easier to implement.

Because of the uncertainty about the most effective anticoagulant treatment for this group, the committee included a subgroup based on body weight in their recommendation for research on

DOACs compared with each other and with other anticoagulants.

## 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 SPC for each treatment, the committee agreed that LMWH, UFH or 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 ml/min to 29 ml/min) based on its SPC. For people with estimated creatinine clearance less than 15 ml/min the main options are UFH or LMWH given either on their own or with a VKA until oral anticoagulation is established and in the therapeutic range. 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 active cancer

There was very little evidence available on the duration of anticoagulation treatment for people with DVT or PE and active cancer. The committee agreed, based on the evidence and their experience, that anticoagulation treatment should continue for 3 to 6 months and then be reviewed. They noted that most of the evidence on VTE in people with active cancer looked at treatment over a period of 6 months, but agreed that some people need shorter treatment durations and it is good practice to determine the length of treatment on a case-by-case basis.

The effectiveness of 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 active cancer and VTE, rivaroxaban, edoxaban and LMWH were found to be similarly effective, although bleeding complications were more frequent with DOACs. 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 based on 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 active cancer but, because of the limitations of the evidence, they could not be more specific about the choice of DOAC.

The committee noted the potential for interactions between anticoagulants and other drugs people with active cancer may be taking, such as chemotherapy drugs, and the possibility of an increased risk of bleeding with some types of tumours. The evidence suggested a higher rate of gastrointestinal and genitourinary bleeds in people with active cancer having treatment with a DOAC compared with those having LMWH. The committee agreed that DOACs may be unsuitable for people with tumours that are associated with an increased risk of these types of bleeds (such as people with gastrointestinal malignancies). However, they agreed that treatment decisions for people with active cancer need to be made on a case-by-case basis.

The committee made provision for people with active cancer if a DOAC is not suitable by including LMWH alone and LMWH with a VKA as alternatives. Although LMWH alone is commonly used in practice and is the only licensed option to treat VTE in active cancer, it is not cost effective compared with DOACs and reducing its use would be beneficial in conserving NHS resources. Sensitivity analyses were carried out varying the drug prices but these analyses did not change any of the conclusions from the economic model.

The committee recognised that there are circumstances in which LMWH is the most suitable treatment option and agreed that it could be considered when this is the case. They were aware that LMWH with a VKA is often impractical for people with active cancer because of difficulties with INR monitoring and maintaining INR within the therapeutic range. They agreed that it is less clinically effective than LMWH alone but is less costly and remains a suitable option in some circumstances.

## Anticoagulation treatment for people with DVT or PE and triple positive antiphospholipid syndrome

The committee were aware of an MHRA safety alert warning of an increase in VTE recurrence in people with diagnosed triple positive antiphospholipid syndrome taking a DOAC compared with those taking LMWH and a VKA. Although people with antiphospholipid syndrome were not included in the evidence review, the committee agreed that it is important to include a recommendation highlighting the need to offer LMWH with a VKA to this group.

## Anticoagulation treatment for DVT or PE in people who use intravenous drugs

VTE can be difficult to treat in people who use intravenous drugs. They often have problems with access to medical care and adherence to prescribed treatments. There is a lack of good evidence on the comparative clinical and cost effectiveness of treatments and doses for VTE in this population. The committee made a recommendation for research with the aim of improving VTE treatment in people who use intravenous drugs.

## Treatment failure

The committee acknowledged that VTE can recur despite anticoagulant treatment and used their knowledge and experience to outline steps that can be taken if treatment fails.

## 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.

Current VTE management for people at extremes of body weight is not expected to change substantially.

For people with haemodynamically unstable PE, UFH is currently used in clinical practice and the recommendation is not expected to affect the frequency of its use in this group.

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.

For people with active 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.

For people with VTE and antiphospholipid syndrome, the use of DOACs is expected to decrease.

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## Long-term anticoagulation for secondary prevention

[Recommendations 1.4.1 to 1.4.12](#)

### Why the committee made the recommendations

The committee agreed that the benefits of anticoagulation treatment become less certain over time, and that after 3 months (or 3 to 6 months in people with active cancer) treatment needs to be reviewed and a decision made about whether to continue or stop treatment. They agreed that, at this point, the aim of anticoagulation changes from treatment to reducing the risk of recurrence.

### 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](#) if the provoking factor is no longer present, 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 person. 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. For bleeding risk, 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. For VTE recurrence, there was very limited evidence, and that evidence suggested that these tools are not sufficiently accurate to be used in practice.

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 for VTE recurrence and major bleeding combined and research 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 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 if it is well tolerated.

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. Sensitivity analyses were carried out varying the drug prices but these analyses did not change any of the conclusions from the economic model.

There was a lack of evidence on longer-term treatment for people with renal impairment, active cancer, antiphospholipid syndrome or extremes of body weight. Based on their clinical experience, the committee agreed that continuing the current treatment, if it is well tolerated, should be considered for people in these groups, 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 mg daily 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 or aspirin 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 (3 to 6 months for people with active cancer), 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.

The recommendations are not expected to change practice for people with renal impairment or extremes of body weight. For people with antiphospholipid syndrome, it is expected that DOAC use will decrease, with a concomitant increase in the use of LMWH with a VKA. For people with active cancer, DOAC use can be expected to increase, with LMWH on its own becoming a less common treatment. For people with none of these clinical features, greater use of DOACs, particularly apixaban, for long-term treatment can be expected to lower costs by reducing the need for clinical visits, INR monitoring and managing bleeding events. The use of aspirin may increase for people who decline long-term anticoagulation. This may reduce VTE recurrence in people who would otherwise not receive treatment.

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## 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 occurrence (in people with an undefined initial VTE event) 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 noted that the type of IVC filter used is the same whether it is intended to be

temporary or permanent. They agreed that, although the decision between a temporary and permanent IVC filter would be made on a case-by-case basis, most IVC filters are likely to be temporary. It is therefore prudent to have a plan in place for removal of the IVC filter at the time of fitting it, to ensure it is removed promptly when 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.

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## 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 (including previous investigations such as imaging) 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 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.

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## 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 deep vein thrombosis (DVT). The blood clot can dislodge and travel in the blood, particularly to the pulmonary arteries. This is known as pulmonary embolism (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 committee details

You can see everything NICE says on this topic in the [NICE Pathway on venous thromboembolism](#).

To find our guidance on related topics, including guidance in development, see [NICE's webpage on embolism and thrombosis](#).

For full details of the evidence and the guideline committee's discussions, see the [evidence reviews](#). You can also find information about [how the guideline was developed](#), including details of the committee.

NICE has produced [tools and resources to help you put this guideline into practice](#). For general help and advice on putting our guidelines into practice, see [resources to help you put NICE guidance into practice](#).

# Update information

## March 2020

This guideline updates and replaces NICE guideline CG144 (published June 2012, updated November 2015).

We have reviewed the evidence and made new recommendations on:

- D-dimer testing
- the PERC rule for pulmonary embolism (PE)
- outpatient management of low-risk PE
- anticoagulation treatment for suspected and confirmed deep vein thrombosis or PE
- reviewing anticoagulation treatment after deep vein thrombosis (DVT) or PE
- inferior vena caval filters
- investigations for cancer for people with suspected or confirmed DVT or PE.

These recommendations are marked [2020].

We have also made some changes without an evidence review:

- In section 1.1 on diagnosis and initial management we have:
  - replaced '24-hour dose of a parenteral anticoagulant' with 'interim therapeutic anticoagulation' because the updated guideline includes DOACs
  - amended recommendation 1.1.4 to clarify that the D-dimer test should be carried out before interim therapeutic anticoagulation is started because anticoagulation can affect the D-dimer result
  - added 'stop interim therapeutic anticoagulation' to replace '24-hour dose' and ensure that interim anticoagulation is not continued when it is no longer needed
  - added a limit of 4 hours for D-dimer test results to correspond with the limit of 4 hours recommended for proximal leg vein ultrasound scan results
  - changed 'offer a mechanical intervention' if PE is identified to 'consider a mechanical intervention' to align with the updated recommendations on mechanical interventions
  - defined renal impairment in people with suspected PE as 'severe (estimated creatinine clearance less than 30 ml/min)' to clarify that investigation with CTPA is not excluded in all degrees of renal impairment.
- In section 1.5 on information and support for people having anticoagulation treatment we have:
  - added information about animal products contained in direct-acting anticoagulants
  - updated the link to the section in the NICE guideline 'Venous thromboembolism: reducing the risk' on information for people concerned about using animal products.
- In section 1.9 on thrombophilia testing we have:
  - changed 'do not offer thrombophilia testing' to 'do not offer testing for hereditary thrombophilia' to differentiate between hereditary thrombophilia and antiphospholipid syndrome, which is an acquired form of thrombophilia. This is to align with the addition of a recommendation on anticoagulation treatment for people with triple positive antiphospholipid syndrome in the updated guideline
  - added wording to the recommendation on testing for antiphospholipid antibodies to ensure that clinicians are aware that anticoagulants can affect the interpretation of thrombophilia test results.

- In the section 'Terms used in this guideline' we have:
  - added a definition of 'active cancer' for clarification
  - amended the definition of 'unprovoked DVT or PE' to reflect the 2020 guideline committee's use of the term.

These recommendations are marked [2012, amended 2020]

Recommendations marked [2012] last had an evidence review in 2012. Those marked [2015] last had an evidence review in 2015.

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## Accreditation

