

Venous thromboembolic diseases:
the management of venous thromboembolic diseases
and the role of thrombophilia testing

**Support for education and
learning**

**Deep vein thrombosis:
Clinical case scenarios**

June 2012

These clinical case scenarios accompany the clinical guideline: 'Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing' (available at www.nice.org.uk/guidance/CG144). Issue date: June 2012.

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Introduction

Venous thromboembolism (VTE) is a condition in which a blood clot (a thrombus) forms in a vein, most commonly in the deep veins of the legs or pelvis. This is known as deep vein thrombosis, or DVT. The thrombus 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.

Venous thromboembolic diseases cover a spectrum ranging from asymptomatic calf vein thrombosis to symptomatic DVT. They can be fatal if they lead to PE, in which the blood supply to the lungs is badly blocked by the thrombus. Non-fatal VTE can cause serious long-term conditions such as post-thrombotic syndrome.

Thrombophilia is a major risk factor for VTE. It is an inherited or acquired prothrombotic state that predisposes to venous thromboembolism. Other major risk factors for VTE include a history of DVT, age over 60 years, surgery, obesity, prolonged travel, acute medical illness, cancer, immobility and pregnancy.

Failure to diagnose and treat VTE correctly can result in fatal PE. However, diagnosis of VTE is not always straightforward. The NICE clinical guideline on [Venous thromboembolic diseases](#) includes advice on the Wells score, D-dimer measurement, ultrasound and radiological imaging. It also offers guidance on the management of VTE, investigations for cancer in patients 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.

To ensure comprehensive management and continuity when developing a programme of care for patients who are at risk of or who develop VTE, users of this guideline are encouraged to refer to NICE guidance on

[Venous thromboembolism: reducing the risk](#) (NICE clinical guideline 92)

[Rivaroxaban for the prevention of venous thromboembolism after total hip or total knee replacement in adults](#) (NICE technology appraisal guidance 170)

[Dabigatran etexilate for the prevention of venous thromboembolism after hip or knee replacement surgery in adults](#) (NICE technology appraisal guidance 157)

[Medicines adherence](#) (NICE clinical guideline 76)

[Patient experience in adult NHS services](#) (NICE clinical guideline 138)

(see also section 6 of the VTE diseases NICE clinical guideline).

Key to terms

The following terms are used in these clinical case scenarios and the NICE guideline.

International normalised ratio (INR) A standardised laboratory measure of blood coagulation used to monitor the adequacy of anticoagulation in patients who are having treatment with a vitamin K antagonist (VKA).

Provoked deep vein thrombosis (DVT) or pulmonary embolism (PE)

DVT or PE in a patient with an antecedent (within 3 months) and transient major clinical risk factor for VTE – for example 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 patient who is having hormonal therapy (oral contraceptive or hormone replacement therapy).

Proximal DVT DVT in the popliteal vein or above. Proximal DVT is sometimes referred to as 'above-knee DVT'.

Renal impairment Reduced renal function that may be acute or chronic. An estimated glomerular filtration rate of less than 90 ml/minute/1.73 m² 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 clinical guideline 73]).

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' above) 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.

Wells scores Clinical prediction rules for estimating the probability of DVT and PE. There are a number of versions of Wells scores available. This guideline recommends the two-level DVT Wells score and the two-level PE Wells score.

Clinical case scenarios: deep vein thrombosis

Clinical case scenarios are an educational resource that can be used for individual or group learning. They are also available in [slide set format](#) to support group learning. Each question should be considered by the individual or group before referring to the answers.

These clinical case scenarios are an essential component of the workshop set out in the [Deep Vein Thrombosis training plan](#). They have been put together to improve your knowledge of '[Venous thromboembolic diseases](#): the management of venous thromboembolic diseases and the role of thrombophilia testing' (NICE clinical guideline CG144) and its application in practice. They illustrate how the DVT-related recommendations from the NICE guideline can be applied to the care of adults presenting to the acute care setting. These cases assume that you are the lead clinician throughout the patient's acute phase. Although it is acknowledged that in reality this is not likely, they have been developed in this way to facilitate learning and understanding of the whole diagnosis and management pathway. They may also be informative for those in primary care who may be the initial point of contact for a person with signs and symptoms of VTE diseases and who may be involved in the care of their VTE disease after discharge from the acute setting.

You will need to refer to the NICE guideline to help you decide what steps you would need to follow to diagnose and manage each case, so make sure that users have access to a copy (either online at www.nice.org.uk/guidance/CG144 or as a printout). You may also want to refer to the VTE NICE pathway (<http://pathways.nice.org.uk/pathways/venous-thromboembolism>) and the topic page on NHS Evidence (www.evidence.nhs.uk/topic/venous-thromboembolism).

Each case scenario includes details of the person's initial presentation. The clinical decisions about recognition, referral, diagnosis and management are then examined using a question and answer approach. Relevant recommendations from the NICE guideline are quoted in the text (after the answer), with corresponding recommendation numbers.

This resource has been developed to illustrate the application of the recommendations in 'Venous thromboembolic diseases' (NICE clinical guideline 144) in practice and should only be used to support learning. The recommendations and these cases only cover the scope of the NICE guideline. It is acknowledged that when a patient presents with suspected venous thromboembolism there are multiple considerations including those beyond the scope of the NICE guideline. These cases do not reflect treatment plans for actual patients and should not be used as such. If an individual clinician has any queries or concerns about the relationship between NICE guidance and this educational resource they should always refer to the original guidance published by NICE, and this should in all cases be regarded as the only definitive statement of the guidance. The NICE clinical guideline may be found at <http://www.nice.org.uk/CG144>

Case scenario 1: John

Presentation

John is a 75-year-old man with a recent (4 weeks ago) admission to hospital for hip replacement. The procedure was performed under general anaesthetic. During admission John received the following VTE prophylaxis (to be continued until John no longer had significantly reduced mobility):

- antiembolism stockings
- pharmacological VTE prophylaxis.

John reports that his right leg has been swollen for over 2 weeks. He thought it was healing after the operation, which is why he has not told anyone sooner. He presented to his GP and the GP has referred him to your accident and emergency (A&E) department.

1.1 Question

You believe John has symptoms of DVT. What would you do next?

1.1 Answer

Carry out an assessment of John's general medical history and a physical examination to exclude other causes.

Relevant recommendations

- If a patient presents with signs or symptoms of deep vein thrombosis (DVT), carry out an assessment of their general medical history and a physical examination to exclude other causes. **[KPI 1.1.1]**
- See [Venous thromboembolism: reducing the risk](#) (NICE clinical guideline 92) for VTE prophylaxis recommendations.

1.2 Question

John reports that he had a DVT 20 years ago and that he has osteoarthritis.

On admission he is afebrile with a temperature of 37°C and his right calf and ankle are red, blotchy and swollen with pitting oedema. His heart rate is 80 beats per minute, respiratory rate 15 breaths per minute, blood pressure is 136/80 mmHg and SpO₂ 96% in air.

You suspect DVT: what would you do next?

1.2 Answer

Even though John received VTE prophylaxis the diagnosis of DVT should still be highly considered. Use the two-level DVT Wells score to estimate the clinical probability of DVT.

Relevant recommendation

- If DVT is suspected, use the two-level DVT Wells score (see [appendix 1](#) or table 1 in the NICE clinical guideline) to estimate the clinical probability of DVT. [1.1.2]

1.3 Question

John's two-level DVT Wells score is 3 (DVT likely):

- Major surgery within 12 weeks requiring general or regional anaesthesia = 1.
- Pitting oedema confined to symptomatic leg = 1.
- Previously documented DVT = 1.

You do not consider that an alternative diagnosis is at least as likely as DVT.

You suspect DVT: what would you do next?

1.3 Answer

Organise a proximal leg vein ultrasound scan. Unfortunately in your organisation this scan is not available within 4 hours of being requested. Therefore, you offer a D-dimer test, an interim 24-hour dose of a parenteral anticoagulant and a proximal leg vein ultrasound scan carried out within 24 hours of being requested.

The D-dimer test is positive and the proximal leg vein ultrasound scan is also positive.

Relevant recommendation

- Offer patients in whom DVT is suspected and with a **likely** two-level DVT Wells score **either**:
 - a proximal leg vein ultrasound scan carried out within 4 hours of being requested and, if the result is negative, a D-dimer test **or**
 - a D-dimer test and an interim 24-hour dose of a parenteral anticoagulant (if a proximal leg vein ultrasound scan cannot be carried out within 4 hours) and a proximal leg vein ultrasound scan carried out within 24 hours of being requested.

Repeat the proximal leg vein ultrasound scan 6–8 days later for all patients with a positive D-dimer test and a negative proximal leg vein ultrasound scan. **[KPI 1.1.3]**

1.4 Question

What would you do next?

1.4 Answer

Diagnose DVT and start treatment with low molecular weight heparin (LMWH) as soon as possible and continue it for at least 5 days or until the INR is 2 or above for at least 24 hours, whichever is longer.

Also start VKA within 24 hours of diagnosing DVT and arrange for John to return to the outpatient clinic in 3 months to assess whether to continue VKA.

Relevant recommendations

- Diagnose DVT and treat (see section 1.2 of the NICE guideline) patients with a positive proximal leg vein ultrasound scan. **[1.1.5]**
- Offer a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed proximal DVT or PE, taking into account comorbidities, contraindications and drug costs, with the following exceptions:
 - For patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 ml/minute/1.73 m²) offer unfractionated heparin (UFH) with dose adjustments based on the APTT (activated partial thromboplastin time) or LMWH with dose adjustments based on an anti-Xa assay.
 - For patients with an increased risk of bleeding consider UFH.
 - For patients with PE and haemodynamic instability, offer UFH and consider thrombolytic therapy (see recommendations 1.2.7 and 1.2.8 in the NICE guideline).Start the LMWH, fondaparinux or UFH as soon as possible and continue it for at least 5 days or until the international normalised ratio (INR) (adjusted by a vitamin K antagonist [VKA]; see recommendation 1.2.3) is 2 or above for at least 24 hours, whichever is longer. **[KPI 1.2.1]**
- Offer a VKA to patients with confirmed proximal DVT or PE within 24 hours of diagnosis and continue the VKA for 3 months. At 3 months, assess the risks and benefits of continuing VKA treatment (see recommendations 1.2.4 and 1.2.5). **[1.2.3]**

Related recommendations

- Offer a VKA beyond 3 months to patients with an unprovoked PE, taking

into account the patient's risk of VTE recurrence and whether they are at increased risk of bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment. **[KPI 1.2.4]**

- Consider extending the VKA beyond 3 months for patients with unprovoked proximal DVT if their risk of VTE recurrence is high and there is no additional risk of major bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment. **[KPI 1.2.5]**
- Consider pharmacological systemic thrombolytic therapy for patients with PE and haemodynamic **instability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.7]**
- Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic **stability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.8]**

Additional information

When offering a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed proximal DVT or PE (recommendation 1.2.1) the guidance developers noted that it is very important to consider the individual patient circumstances, such as comorbidities and contraindications in order to offer the most suitable agent for the patient. Important considerations include:

- **Renal status:** Dose adjustment and monitoring may be required as patients with renal impairment may accumulate excessive amounts of these drugs in the body. LMWH and fondaparinux should be used with caution for people with renal impairment, and UFH should be considered as an alternative. UFH has a short half-life and is predominantly metabolised in the liver compared to LMWHs that are predominantly excreted through the kidneys. UFH therefore may be more suitable for patients who are at risk of bleeding or have renal impairment.
- **Risk of bleeding or need for surgery or thrombolysis:** As in renal impairment patients, UFH is an alternative option for patients with uncertain risk of bleeding or if the patient may have to undergo surgical procedures or

thrombolysis. Unfractionated heparin has a shorter half-life and is more easily reversed if required.

- **Risk of HIT:** Based on clinical experience the guidance developers identified that there may be a lower risk of HIT in people receiving LMWH compared to UFH. If the patient has a history of HIT, fondaparinux is an alternative option because it is a synthetic pentasaccharide and not associated with HIT.
- **Appropriate dose:** Dosing errors in administering LMWH to patients have been the subject of a National Patient Safety Agency alert ([NPSA Rapid response 14](#)); doses were frequently not adjusted to the appropriate clinical indication, weight or renal function. Patients should be weighed prior to receiving LMWH to ensure that they are prescribed the correct dose, especially in obese patients. Renal function should also be considered in all patients, although renal function testing should not delay the first dose it should be taken into account for subsequent doses.
- **Patient preferences:** Both UFH and LMWH are of porcine origin. This may be a concern to some patients. If this is a concern, fondaparinux may be considered as a suitable alternative for some of these patients.
- **Route of administration for UFH:** Both the intravenous route and the subcutaneous route were included for UFH in the evidence review. However, the main group of patients where UFH is likely to be used are those with risk of bleeding or accumulation due to severe renal impairment. The intravenous route has advantages over the subcutaneous route in patients where accumulation or bleeding may be problematic. If problems arise, the action of UFH can be limited by turning off the infusion. Protamine sulphate can be administered as indicated.

1.5 Question

Would you consider catheter-directed thrombolytic therapy and/or an inferior vena caval filter for John?

1.5 Answer

No, do not consider catheter-directed thrombolytic therapy for John because he reports that his symptoms have existed for longer than 14 days.

Do not offer John an inferior vena caval filter because he is able to have anticoagulation treatment and does not have recurrent PE or DVT.

Relevant recommendations

- Consider catheter-directed thrombolytic therapy for patients with symptomatic iliofemoral DVT who have:
 - symptoms of less than 14 days' duration **and**
 - good functional status **and**
 - a life expectancy of 1 year or more **and**
 - a low risk of bleeding. **[KPI 1.2.6]**
- Offer temporary inferior vena caval filters to patients with proximal DVT or PE who cannot have anticoagulation treatment, and remove the inferior vena caval filter when the patient becomes eligible for anticoagulation treatment. **[1.2.10]**
- Consider inferior vena caval filters for patients with recurrent proximal DVT or PE despite adequate anticoagulation treatment only after considering alternative treatments such as:
 - increasing target INR to 3–4 for long-term high-intensity oral anticoagulant therapy **or**
 - switching treatment to LMWH. **[1.2.11]**

Related recommendation

- Ensure that a strategy for removing the inferior vena caval filter at the earliest possible opportunity is planned and documented when the filter is placed, and that the strategy is reviewed regularly. **[1.2.12]**

1.6 Question

In addition to the pharmacological treatment you have started, what other treatment should be offered to John to treat the DVT?

1.6 Answer

A week after diagnosis, or when swelling is reduced sufficiently, John should be offered below-knee graduated compression stockings with an ankle pressure greater than 23 mmHg, if there are no contraindications.

By this point it is likely that John will have left the acute setting, so to ensure he receives this treatment refer him at the time of diagnosis to the relevant healthcare professional/department responsible for providing stockings (this may be his GP or the orthotic department).

Also ask his GP to ensure that the stockings are worn for at least 2 years and are replaced two or three times a year or in line with the manufacturer's instructions.

Relevant recommendation

- Offer below-knee graduated compression stockings with an ankle pressure greater than 23 mmHg to patients with proximal DVT a week after diagnosis or when swelling is reduced sufficiently and if there are no contraindications¹, and:
 - advise patients to continue wearing the stockings for at least 2 years
 - ensure that the stockings are replaced two or three times per year or according to the manufacturer's instructions
 - advise patients that the stockings need to be worn only on the affected leg or legs. **[KPI 1.2.9]**

1.7 Question

What information would you give John about his treatment? Would you offer John self-management of his INR?

¹ Prescribers should refer to specific product information and contraindications before offering graduated compression stockings.

1.7 Answer

Offer John verbal and written information about his anticoagulant treatment, including monitoring, side effects, interactions and lifestyle impacts. Provide him with an anticoagulant information booklet and an anticoagulant alert card. Advise him to carry the anticoagulant alert card at all times.

You would not routinely offer John self-management of his INR.

Relevant recommendations

- Give patients having anticoagulation treatment verbal and written information about:
 - how to use anticoagulants
 - duration of anticoagulation treatment
 - possible side effects of anticoagulant treatment and what to do if these occur
 - the effects of other medications, foods and alcohol on oral anticoagulation treatment
 - monitoring 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. **[1.3.1]**
- Provide patients who are having anticoagulation treatment with an ‘anticoagulant information booklet’ and an ‘anticoagulant alert card’ and advise them to carry the ‘anticoagulant alert card’ at all times. **[1.3.2]**
- 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 clinical guideline 92).] **[1.3.3]**
- Advise patients about the correct application and use of below-knee graduated compression stockings, how long they should be worn and when

they should be replaced. **[1.3.4]**

- Do not routinely offer self-management or self-monitoring of INR to patients who have had DVT or PE and are having treatment with a VKA. **[1.4.1]**

1.8 Question

Are there any further tests or investigations you would organise in relation to John's diagnosis of DVT?

1.8 Answer

No further investigations are required. John's DVT is [provoked](#), probably as a result of immobility caused by his elective hip replacement surgery. If John's DVT had been [unprovoked](#), and depending on future anticoagulation plans, the NICE guideline recommends screening for cancer and thrombophilia.

Relevant recommendation

- Do not offer thrombophilia testing to patients who have had provoked DVT or PE. **[1.6.4]**

Related recommendations

- Offer all patients diagnosed with unprovoked DVT or PE who are not already known to have cancer the following investigations for cancer:
 - a physical examination (guided by the patient's full history) **and**
 - a chest X-ray **and**
 - blood tests (full blood count, serum calcium and liver function tests) **and**
 - urinalysis. **[1.5.1]**
- Consider further investigations for cancer with an abdomino-pelvic CT scan (and a mammogram for women) in all patients aged over 40 years with a first unprovoked DVT or PE who do not have signs or symptoms of cancer based on initial investigation (see recommendation 1.5.1 above). **[KPI 1.5.2]**
- Do not offer thrombophilia testing to patients who are continuing anticoagulation treatment. **[1.6.1]**
- Consider testing for antiphospholipid antibodies in patients who have had unprovoked DVT or PE if it is planned to stop anticoagulation treatment. **[1.6.2]**
- 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. **[1.6.3]**
- Do not routinely offer thrombophilia testing to first-degree relatives of people with a history of DVT or PE and thrombophilia. **[1.6.5]**

Case scenario 2: Susan

Presentation

Susan is a 50-year-old woman who presents to your A&E department following GP referral. Susan complains of pain in her left calf, which has been present for a week. Three weeks ago she had acute appendicitis with hospital admission. For the last day her left thigh has been painful.

2.1 Question

You believe Susan has symptoms of a suspected DVT. What would you do next?

2.1 Answer

Carry out an assessment of Susan's general medical history and a physical examination to exclude other causes.

Relevant recommendation

- If a patient presents with signs or symptoms of deep vein thrombosis (DVT), carry out an assessment of their general medical history and a physical examination to exclude other causes. **[KPI 1.1.1]**

2.2 Question

You have noted Susan's presentation and recent medical history. Her medical records do not indicate that she received VTE prophylaxis while in hospital. She has no significant past medical history.

On examination her entire left leg is swollen. Left calf 38 cm, right calf 34 cm, left thigh 56 cm, right thigh 52 cm. Her heart rate is 70 beats per minute, respiratory rate 14 breaths per minute, blood pressure 120/80 mmHg, temperature 36°C and SpO₂ 99% in air.

You suspect DVT: what would you do next?

2.2 Answer

You would use the two-level DVT Wells score to estimate the clinical probability of DVT.

Relevant recommendations

- If DVT is suspected, use the two-level DVT Wells score (see [appendix 1](#)) to estimate the clinical probability of DVT. [1.1.2]
- See [Venous thromboembolism: reducing the risk](#) (NICE clinical guideline 92) for VTE prophylaxis recommendations.

2.3 Question

Susan's two-level DVT Wells score is 3 (DVT likely):

- Recent bedridden for more than 3 days = 1.
- Entire leg swollen = 1.
- Calf swelling 3 cm larger than asymptomatic side = 1.

You do not think an alternative diagnosis is at least as likely as DVT.

You suspect deep vein thrombosis . With a 'DVT likely' score, what would you do next?

2.3 Answer

Offer an immediate proximal leg vein ultrasound, because this is available within 4 hours of you requesting it.

Relevant recommendation

- Offer patients in whom DVT is suspected and with a **likely** two-level DVT Wells score **either**:
 - a proximal leg vein ultrasound scan carried out within 4 hours of being requested and, if the result is negative, a D-dimer test **or**
 - a D-dimer test and an interim 24-hour dose of a parenteral anticoagulant (if a proximal leg vein ultrasound scan cannot be carried out within 4 hours) and a proximal leg vein ultrasound scan carried out within 24 hours of being requested.

Repeat the proximal leg vein ultrasound scan 6–8 days later for all patients with a positive D-dimer test and a negative proximal leg vein ultrasound scan. **[KPI 1.1.3]**

2.4 Question

The proximal leg vein ultrasound scan identifies an occlusive clot in the common femoral vein. What would you do next?

2.4 Answer

Diagnose DVT and start treatment with LMWH as soon as possible and continue it for at least 5 days or until the INR is 2 or above for at least 24 hours, whichever is longer.

In addition to the LMWH, you should consider catheter-directed thrombolytic therapy for Susan because she is otherwise well, has a normal life expectancy, has a low risk of bleeding and the DVT is of less than 14 days' duration. Expert clinical opinion suggests that when considering catheter-directed thrombolytic therapy, in addition to considering the eligibility criteria above, you should take into account the availability of adequate monitoring facilities and patient preferences. On this occasion the appropriate facilities are available to safely administer and monitor catheter-directed thrombolytic therapy for Susan.

You would also start VKA within 24 hours of diagnosing DVT and arrange for Susan to return to the outpatient clinic in 3 months to assess whether to continue VKA.

Relevant recommendations

- Diagnose DVT and treat (see section 1.2 of the NICE guideline) patients with a positive proximal leg vein ultrasound scan. **[1.1.5]**
 - Offer a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed proximal DVT or PE, taking into account comorbidities, contraindications and drug costs, with the following exceptions:
 - For patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 ml/minute/1.73 m²) offer unfractionated heparin (UFH) with dose adjustments based on the APTT (activated partial thromboplastin time) or LMWH with dose adjustments based on an anti-Xa assay.
 - For patients with an increased risk of bleeding consider UFH.
 - For patients with PE and haemodynamic instability, offer UFH and consider thrombolytic therapy (see recommendations 1.2.7 and 1.2.8 in the NICE guideline).
- Start the LMWH, fondaparinux or UFH as soon as possible and continue it

for at least 5 days or until the international normalised ratio (INR) (adjusted by a vitamin K antagonist [VKA]; see recommendation 1.2.3) is 2 or above for at least 24 hours, whichever is longer. **[KPI 1.2.1]**

- Consider catheter-directed thrombolytic therapy for patients with symptomatic iliofemoral DVT who have:
 - symptoms of less than 14 days' duration **and**
 - good functional status **and**
 - a life expectancy of 1 year or more **and**
 - a low risk of bleeding. **[KPI 1.2.6]**
- Offer a VKA to patients with confirmed proximal DVT or PE within 24 hours of diagnosis and continue the VKA for 3 months. At 3 months, assess the risks and benefits of continuing VKA treatment (see recommendations 1.2.4 and 1.2.5). **[1.2.3]**

Related recommendations

- Offer a VKA beyond 3 months to patients with an unprovoked PE, taking into account the patient's risk of VTE recurrence and whether they are at increased risk of bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment. **[KPI 1.2.4]**
- Consider extending the VKA beyond 3 months for patients with unprovoked proximal DVT if their risk of VTE recurrence is high and there is no additional risk of major bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment. **[KPI 1.2.5]**
- Consider pharmacological systemic thrombolytic therapy for patients with PE and haemodynamic **instability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.7]**
- Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic **stability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.8]**

Additional information

When offering a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed proximal DVT or PE (recommendation 1.2.1) the guidance developers noted that it is very important to consider the individual patient circumstances, such as comorbidities and contraindications in order to offer the most suitable agent for the patient. Important considerations include:

- **Renal status:** Dose adjustment and monitoring may be required as patients with renal impairment may accumulate excessive amounts of these drugs in the body. LMWH and fondaparinux should be used with caution for people with renal impairment, and UFH should be considered as an alternative. UFH has a short half-life and is predominantly metabolised in the liver compared to LMWHs that are predominantly excreted through the kidneys. UFH therefore may be more suitable for patients who are at risk of bleeding or have renal impairment.
- **Risk of bleeding or need for surgery or thrombolysis:** As in renal impairment patients, UFH is an alternative option for patients with uncertain risk of bleeding or if the patient may have to undergo surgical procedures or thrombolysis. Unfractionated heparin has a shorter half-life and is more easily reversed if required.
- **Risk of HIT:** Based on clinical experience the guidance developers identified that there may be a lower risk of HIT in people receiving LMWH compared to UFH. If the patient has a history of HIT, fondaparinux is an alternative option because it is a synthetic pentasaccharide and not associated with HIT.
- **Appropriate dose:** Dosing errors in administering LMWH to patients have been the subject of a National Patient Safety Agency alert ([NPSA Rapid response 14](#)); doses were frequently not adjusted to the appropriate clinical indication, weight or renal function. Patients should be weighed prior to receiving LMWH to ensure that they are prescribed the correct dose, especially in obese patients. Renal function should also be considered in all patients, although renal function testing should not delay the first dose it should be taken into account for subsequent doses.

- **Patient preferences:** Both UFH and LMWH are of porcine origin. This may be a concern to some patients. If this is a concern, fondaparinux may be considered as a suitable alternative for some of these patients.
- **Route of administration for UFH:** Both the intravenous route and the subcutaneous route were included for UFH in the evidence review. However, the main group of patients where UFH is likely to be used are those with risk of bleeding or accumulation due to severe renal impairment. The intravenous route has advantages over the subcutaneous route in patients where accumulation or bleeding may be problematic. If problems arise, the action of UFH can be limited by turning off the infusion. Protamine sulphate can be administered as indicated.

2.5 Question

Would you offer Susan an inferior vena caval filter?

2.5 Answer

No, because Susan is able to have anticoagulation treatment.

Relevant recommendations

- Offer temporary inferior vena caval filters to patients with proximal DVT or PE who cannot have anticoagulation treatment, and remove the inferior vena caval filter when the patient becomes eligible for anticoagulation treatment. **[1.2.10]**
- Consider inferior vena caval filters for patients with recurrent proximal DVT or PE despite adequate anticoagulation treatment only after considering alternative treatments such as:
 - increasing target INR to 3–4 for long-term high-intensity oral anticoagulant therapy **or**
 - switching treatment to LMWH. **[1.2.11]**

Related recommendation

- Ensure that a strategy for removing the inferior vena caval filter at the earliest possible opportunity is planned and documented when the filter is placed, and that the strategy is reviewed regularly. **[1.2.12]**

2.6 Question

In addition to the pharmacological treatment you have started, what other treatment should be offered to Susan to treat the DVT?

2.6 Answer

A week after diagnosis, or when swelling is reduced sufficiently, Susan should be offered below-knee graduated compression stockings with an ankle pressure greater than 23 mmHg, if there are no contraindications.

By this point it is likely that Susan will have left the acute setting, so to ensure she receives this treatment refer her at the time of diagnosis to the relevant healthcare professional/department responsible providing stockings (this may be his GP or the orthotic department).

Also ask her GP to ensure that the stockings are worn for at least 2 years, are replaced two or three times a year and are worn in line with the manufacturer's instructions.

Relevant recommendation

- Offer below-knee graduated compression stockings with an ankle pressure greater than 23 mmHg to patients with proximal DVT a week after diagnosis or when swelling is reduced sufficiently and if there are no contraindications², and:
 - advise patients to continue wearing the stockings for at least 2 years
 - ensure that the stockings are replaced two or three times per year or according to the manufacturer's instructions
 - advise patients that the stockings need to be worn only on the affected leg or legs. **[KPI 1.2.9]**

2.7 Question

What information would you give Susan about her treatment? Would you offer Susan self-management of her INR?

² Prescribers should refer to specific product information and contraindications before offering graduated compression stockings.

2.7 Answer

Offer Susan verbal and written information about her anticoagulant treatment, including monitoring, side effects, interactions and lifestyle impacts. Provide her with an anticoagulant information booklet and an anticoagulant alert card. Advise her to carry the anticoagulant alert card at all times.

You would not routinely offer Susan self-management of her INR.

Relevant recommendations

- Give patients having anticoagulation treatment verbal and written information about:
 - how to use anticoagulants
 - duration of anticoagulation treatment
 - possible side effects of anticoagulant treatment and what to do if these occur
 - the effects of other medications, foods and alcohol on oral anticoagulation treatment
 - monitoring 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. **[1.3.1]**
- Provide patients who are having anticoagulation treatment with an ‘anticoagulant information booklet’ and an ‘anticoagulant alert card’ and advise them to carry the ‘anticoagulant alert card’ at all times. **[1.3.2]**
- 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 clinical guideline 92).] **[1.3.3]**
- Advise patients about the correct application and use of below-knee graduated compression stockings, how long they should be worn and when

they should be replaced. [1.3.4]

- Do not routinely offer self-management or self-monitoring of INR to patients who have had DVT or PE and are having treatment with a VKA. [1.4.1]

2.8 Question

Are there any further tests or investigations you would organise in relation to Susan's diagnosis of DVT?

2.8 Answer

No further investigations are required. Susan's PE is [provoked](#), probably as a result of immobility caused by her episode of appendicitis and apparent lack of prophylaxis. If Susan's DVT had been [unprovoked](#), and depending on future anticoagulation plans, NICE recommends screening for cancer and thrombophilia.

Relevant recommendation

- Do not offer thrombophilia testing to patients who have had provoked DVT or PE. **[1.6.4]**

Related recommendations

- Offer all patients diagnosed with unprovoked DVT or PE who are not already known to have cancer the following investigations for cancer:
 - a physical examination (guided by the patient's full history) **and**
 - a chest X-ray **and**
 - blood tests (full blood count, serum calcium and liver function tests) **and**
 - urinalysis. **[1.5.1]**
- Consider further investigations for cancer with an abdomino-pelvic CT scan (and a mammogram for women) in all patients aged over 40 years with a first unprovoked DVT or PE who do not have signs or symptoms of cancer based on initial investigation (see recommendation 1.5.1 above). **[KPI 1.5.2]**
- Do not offer thrombophilia testing to patients who are continuing anticoagulation treatment. **[1.6.1]**
- Consider testing for antiphospholipid antibodies in patients who have had unprovoked DVT or PE if it is planned to stop anticoagulation treatment. **[1.6.2]**
- 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. **[1.6.3]**
- Do not routinely offer thrombophilia testing to first-degree relatives of people with a history of DVT or PE and thrombophilia. **[1.6.5]**

Case scenario 3: Nita

Presentation

Nita is a 31-year-old woman who presents to your A&E department with pain and swelling in her right leg. She also reports that the back of her calf appears red. She plays regular sport and says this pain feels different from previous muscle injuries.

3.1 Question

You believe Nita has symptoms of a suspected DVT. What would you do next?

3.1 Answer

Carry out an assessment of Nita's general medical history and a physical examination to exclude other causes.

Relevant recommendation

- If a patient presents with signs or symptoms of deep vein thrombosis (DVT), carry out an assessment of their general medical history and a physical examination to exclude other causes. **[KPI 1.1.1]**

3.2 Question

You have noted Nita's presentation. She has no significant past medical history, but reports she has taken a combined oral contraceptive pill for the past 10 years. On examination her lower right leg is swollen. Left calf 34 cm, right calf 37 cm, left thigh 50 cm, right thigh 50 cm. Heart rate 60 beats per minute, respiratory rate 11 breaths per minute, blood pressure 122/75 mmHg, temperature 37⁰c and SpO₂ 99% in air.

You suspect DVT: what would you do next?

3.2 Answer

Use the two-level DVT Wells score to estimate the clinical probability of DVT.

Relevant recommendation

- If DVT is suspected, use the two-level DVT Wells score (see [appendix 1](#) or table 1 in the NICE clinical guideline) to estimate the clinical probability of DVT. [1.1.2]

3.3 Question

Nita's two-level DVT Wells score is 0 (DVT unlikely):

- Localised tenderness along the distribution of the deep venous system = 1.
- Calf swelling 3 cm larger than asymptomatic side = 1.
- An alternative diagnosis is at least as likely as DVT = -2 (you are considering a ruptured Baker's cyst).

You still suspect DVT: what would you do next?

3.3 Answer

Offer Nita a D-dimer test.

Relevant recommendation

- Offer patients in whom DVT is suspected and with an **unlikely** two-level DVT Wells score a D-dimer test and if the result is positive offer **either**:
 - a proximal leg vein ultrasound scan carried out within 4 hours of being requested **or**
 - an interim 24-hour dose of a parenteral anticoagulant (if a proximal leg vein ultrasound scan cannot be carried out within 4 hours) and a proximal leg vein ultrasound scan carried out within 24 hours of being requested.

[KPI 1.1.4]

3.4 Question

Nita's D-dimer test is negative: what would you do next?

3.4 Answer

Take into consideration alternative diagnoses. Advise Nita that it is not likely she has a DVT, and discuss with her the signs and symptoms of DVT and when and where to seek further medical help.

Based on initial investigations, you believe this is likely to be a muscle strain and therefore arrange further appropriate investigations³.

Relevant recommendation

- Take into consideration alternative diagnoses in patients with:
 - an **unlikely** two-level DVT Wells score **and**
 - ◇ a negative D-dimer test **or**
 - ◇ a positive D-dimer test and a negative proximal leg vein ultrasound scan.
 - a **likely** two-level DVT Wells score **and**
 - ◇ a negative proximal leg vein ultrasound scan and a negative D-dimer test **or**
 - ◇ a repeat negative proximal leg vein ultrasound scan.

Advise patients in these two groups that it is not likely they have DVT, and discuss with them the signs and symptoms of DVT and when and where to seek further medical help. **[1.1.6]**

³ This action is beyond the scope of the NICE guideline but has been added to replicate the usual diagnosis process.

Case scenario 4: Gary

Please note this case scenario also appears in the PE clinical case scenarios.

Presentation

Gary is a 52-year-old man who is an endurance cyclist. He presents to your A&E department following referral from his GP. He reports shortness of breath at rest and chest pain. On direct questioning he admits to pain in the right calf for a month, which he put down to muscle sprain.

4.1 Question

You believe Gary has symptoms of a suspected PE and DVT. Which diagnostic route should you take?

4.1 Answer

Take into consideration the 'additional information' below in making your decision.

Because of Gary's chest pain and shortness of breath, you decide to carry out initial diagnostic investigations for PE.

Relevant recommendation

- If a patient presents with signs or symptoms of both DVT (for example a swollen and/or painful leg) and PE (for example chest pain, shortness of breath or haemoptysis), carry out initial diagnostic investigations for either DVT or PE, basing the choice of diagnostic investigations on clinical judgement. **[1.1.14]**

Additional information

When developing the guideline the developers discussed the advantages and disadvantages to the patient in following each pathway (either DVT or PE):

- The ultrasound scan used in the DVT algorithm avoids radiation exposure and the administration of contrast compared with CTPA which is used in the PE diagnostic algorithm. A CTPA is approximately equivalent to 3.6 years of natural background radiation (UK average 2.2 mSv per year taken from referral guideline from the Royal College of Radiologists)
- One advantage of CTPA is that it also looks at all of the other structures within the chest including whether there is evidence of right ventricular dilatation which has prognostic implications and can identify other causes for the patient's symptoms.
- The DVT diagnosis algorithm may be chosen for a patient with a possible provoked DVT and PE because there will be no change to the pharmacological treatment as a result of diagnosis and they would be exposed to no radiation or intravenous contrast.

4.2 Question

What would you do next to diagnose PE?

4.2 Answer

Carry out an assessment of his general medical history, a physical examination and a chest X-ray to exclude other causes.

Relevant recommendation

- If a patient presents with signs or symptoms of PE, carry out an assessment of their general medical history, a physical examination and a chest X-ray to exclude other causes. **[1.1.7]**

4.3 Question

On admission Gary's SpO₂ is 93% in air, heart rate is 102 beats per minute, respiratory rate 17 breaths per minute, blood pressure 110/70 mmHg, temperature 37⁰c. You still suspect PE: what would you do next?

4.3 Answer

Use the two-level PE Wells score to estimate the clinical probability of PE.

Relevant recommendation

- If PE is suspected, use the two-level PE Wells score (see [appendix 2](#) or table 2) to estimate the clinical probability of PE. [1.1.8]

4.4 Question

You calculate the two-level PE Wells score to be 7.5 (PE likely)⁴:

- Clinical signs and symptoms of DVT = 3.
- Alternative diagnosis less likely than PE = 3.
- Heart rate >100 beats per minute = 1.5.

You suspect PE. With this Wells score result, what would you do next?

⁴ It is acknowledged that the implementation of recommendations 1.1.7 and 1.1.8 are likely to happen simultaneously. For example, it is not likely that in reality the clinician would wait for the chest X-ray result before commencing a Wells score. The cases have been presented in this manner in order to illustrate implementation of each of the recommendations

4.4 Answer

Offer CTPA.

On this occasion immediate CTPA is available so you offer this.

Relevant recommendation

- Offer patients in whom PE is suspected and with a **likely** two-level PE Wells score **either**:
 - an immediate computed tomography pulmonary angiogram (CTPA) **or**
 - immediate interim parenteral anticoagulant therapy followed by a CTPA, if a CTPA cannot be carried out immediately.

Consider a proximal leg vein ultrasound scan if the CTPA is negative and DVT is suspected. **[1.1.9]**

Related recommendation

- 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 interim parenteral anticoagulant therapy. **[1.1.11]**

4.5 Question

The CTPA is positive showing several pulmonary emboli. What would you do next?

4.5 Answer

Diagnose PE and start treatment.

Based on your clinical decision you offer LMWH immediately and continue this for at least 5 days or until the INR is 2 or above for at least 24 hours (whichever is longer). You also start VKA within 24 hours of diagnosis of the PE and continue this for 3 months. You also ensure an outpatient appointment is booked for Gary in 3 months' time to assess benefits and risks of continuing the VKA.

Relevant recommendations

- Diagnose PE and treat (see section 1.2 of the NICE guideline) patients with a positive CTPA or in whom PE is identified with a V/Q SPECT or planar scan. **[1.1.12]**
 - Offer a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed proximal DVT or PE, taking into account comorbidities, contraindications and drug costs, with the following exceptions:
 - For patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 ml/minute/1.73 m²) offer unfractionated heparin (UFH) with dose adjustments based on the APTT (activated partial thromboplastin time) or LMWH with dose adjustments based on an anti-Xa assay.
 - For patients with an increased risk of bleeding consider UFH.
 - For patients with PE and haemodynamic instability, offer UFH and consider thrombolytic therapy (see recommendations 1.2.7 and 1.2.8 below).
- Start the LMWH, fondaparinux or UFH as soon as possible and continue it for at least 5 days or until the international normalised ratio (INR) (adjusted by a vitamin K antagonist [VKA]; see recommendation 1.2.3) is 2 or above for at least 24 hours, whichever is longer. **[KPI 1.2.1]**
- Offer a VKA to patients with confirmed proximal DVT or PE within 24 hours of diagnosis and continue the VKA for 3 months. At 3 months, assess the risks and benefits of continuing VKA treatment (see recommendations 1.2.4

and 1.2.5). **[1.2.3]**

Related recommendations

- Offer a VKA beyond 3 months to patients with an unprovoked PE, taking into account the patient's risk of VTE recurrence and whether they are at increased risk of bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment. **[KPI 1.2.4]**
- Consider extending the VKA beyond 3 months for patients with unprovoked proximal DVT if their risk of VTE recurrence is high and there is no additional risk of major bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment. **[KPI 1.2.5]**
- Consider pharmacological systemic thrombolytic therapy for patients with PE and haemodynamic **instability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.7]**
- Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic **stability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.8]**

Additional information

When offering a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed proximal DVT or PE (recommendation 1.2.1) the guidance developers noted that it is very important to consider the individual patient circumstances, such as comorbidities and contraindications in order to offer the most suitable agent for the patient. Important considerations include:

- **Renal status:** Dose adjustment and monitoring may be required as patients with renal impairment may accumulate excessive amounts of these drugs in the body. LMWH and fondaparinux should be used with caution for people with renal impairment, and UFH should be considered as an alternative. UFH has a short half-life and is predominantly metabolised in the liver compared to LMWHs that are predominantly excreted through the kidneys. UFH therefore may be more suitable for patients who are at risk of bleeding or have renal impairment.

- **Risk of bleeding or need for surgery or thrombolysis:** As in renal impairment patients, UFH is an alternative option for patients with uncertain risk of bleeding or if the patient may have to undergo surgical procedures or thrombolysis. Unfractionated heparin has a shorter half-life and is more easily reversed if required.
- **Risk of HIT:** Based on clinical experience the guidance developers identified that there may be a lower risk of HIT in people receiving LMWH compared to UFH. If the patient has a history of HIT, fondaparinux is an alternative option because it is a synthetic pentasaccharide and not associated with HIT.
- **Appropriate dose:** Dosing errors in administering LMWH to patients have been the subject of a National Patient Safety Agency alert ([NPSA Rapid response 14](#)); doses were frequently not adjusted to the appropriate clinical indication, weight or renal function. Patients should be weighed prior to receiving LMWH to ensure that they are prescribed the correct dose, especially in obese patients. Renal function should also be considered in all patients, although renal function testing should not delay the first dose it should be taken into account for subsequent doses.
- **Patient preferences:** Both UFH and LMWH are of porcine origin. This may be a concern to some patients. If this is a concern, fondaparinux may be considered as a suitable alternative for some of these patients.
- **Route of administration for UFH:** Both the intravenous route and the subcutaneous route were included for UFH in the evidence review. However, the main group of patients where UFH is likely to be used are those with risk of bleeding or accumulation due to severe renal impairment. The intravenous route has advantages over the subcutaneous route in patients where accumulation or bleeding may be problematic. If problems arise, the action of UFH can be limited by turning off the infusion. Protamine sulphate can be administered as indicated.

4.6 Question

Would you offer Gary systemic thrombolytic therapy, catheter-directed thrombolytic therapy or an inferior vena caval filter to treat his PE and DVT?

4.6 Answer

No, do not offer systemic thrombolytic therapy to treat Gary's PE because he is not haemodynamically unstable.

Do not offer an inferior vena caval filter because Gary is able to have anticoagulation treatment.

Relevant recommendations

- Consider catheter-directed thrombolytic therapy for patients with symptomatic iliofemoral DVT who have:
 - symptoms of less than 14 days' duration **and**
 - good functional status **and**
 - a life expectancy of 1 year or more **and**
 - a low risk of bleeding. **[KPI 1.2.6]**
- Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic **stability** (see also recommendation 1.2.1 in the NICE guideline). **[1.2.8]**
- Offer temporary inferior vena caval filters to patients with proximal DVT or PE who cannot have anticoagulation treatment, and remove the inferior vena caval filter when the patient becomes eligible for anticoagulation treatment. **[1.2.10]**
- Consider inferior vena caval filters for patients with recurrent proximal DVT or PE despite adequate anticoagulation treatment only after considering alternative treatments such as:
 - increasing target INR to 3–4 for long-term high-intensity oral anticoagulant therapy **or**
 - switching treatment to LMWH. **[1.2.11]**

Related recommendations

- Ensure that a strategy for removing the inferior vena caval filter at the earliest possible opportunity is planned and documented when the filter is placed, and that the strategy is reviewed regularly. **[1.2.12]**
- Consider pharmacological systemic thrombolytic therapy for patients with PE and haemodynamic **instability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.7]**

- Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic **stability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.8]**

4.7 Question

A few days after Gary's admission the acute PE phase has been managed and Gary is stable. You noted on admission that Gary complained of a sore leg. You now note that his entire leg is swollen, he has calf swelling of more than 3 cm on his sore leg. You are still concerned about DVT: what would you do next?

4.7 Answer

The anticoagulation treatment for pulmonary embolism is very similar to that for deep vein thrombosis. Therefore if Gary does have a DVT, the treatment he has been receiving would also be treating any possible DVT. However, the treatment for DVT also includes graduated compression stocking to prevent the development of post thrombotic limb. It is therefore helpful to confirm if Gary has a DVT. You would therefore offer a proximal leg vein ultrasound.

Relevant recommendation

- Offer patients in whom DVT is suspected and with a **likely** two-level DVT Wells score **either**:
 - a proximal leg vein ultrasound scan carried out within 4 hours of being requested and, if the result is negative, a D-dimer test **or**
 - a D-dimer test and an interim 24-hour dose of a parenteral anticoagulant (if a proximal leg vein ultrasound scan cannot be carried out within 4 hours) and a proximal leg vein ultrasound scan carried out within 24 hours of being requested.

Repeat the proximal leg vein ultrasound scan 6–8 days later for all patients with a positive D-dimer test and a negative proximal leg vein ultrasound scan. **[KPI 1.1.3]**

4.8 Question

The proximal leg vein ultrasound scan shows a proximal DVT. What would you do next? Would you consider catheter-directed thrombolytic therapy?

4.8 Answer

Do not offer Gary catheter-directed thrombolytic therapy because he has had symptoms for longer than 14 days. Additionally the ultrasound did not identify iliofemoral DVT.

In addition to the LMWH and VKA (see answer 4.5), a week after diagnosis or when swelling is reduced sufficiently Gary should be offered below-knee graduated compression stockings with an ankle pressure greater than 23 mmHg, if there are no contraindications.

By this point it is likely that Gary will have left the acute setting, so to ensure he receives this treatment refer him at the time of diagnosis to the relevant healthcare professional/department responsible for providing stockings (this may be his GP or the orthotic department).

Also ask his GP to ensure that the stockings are worn for at least 2 years, are replaced two or three times a year and are worn in line with the manufacturer's instructions.

Relevant recommendations

- Consider catheter-directed thrombolytic therapy for patients with symptomatic iliofemoral DVT who have:
 - symptoms of less than 14 days' duration **and**
 - good functional status **and**
 - a life expectancy of 1 year or more **and**
 - a low risk of bleeding. **[KPI 1.2.6]**
- Offer below-knee graduated compression stockings with an ankle pressure greater than 23 mmHg to patients with proximal DVT a week after diagnosis or when swelling is reduced sufficiently and if there are no contraindications⁵, and:
 - advise patients to continue wearing the stockings for at least 2 years
 - ensure that the stockings are replaced two or three times per year or according to the manufacturer's instructions

⁵ Prescribers should refer to specific product information and contraindications before offering graduated compression stockings.

– advise patients that the stockings need to be worn only on the affected leg or legs. **[KPI 1.2.9]**

4.9 Question

What information would you give to Gary about his treatment? Would you offer him self-management of his INR?

4.9 Answer

Offer Gary verbal and written information about his anticoagulant treatment including monitoring, side effects, interactions and lifestyle impacts. Provide him with an anticoagulant information booklet and an anticoagulant alert card. Advise him to carry the anticoagulant alert card at all times.

You would not routinely offer Gary self-management of his INR.

Relevant recommendations

- Give patients having anticoagulation treatment verbal and written information about:
 - how to use anticoagulants
 - duration of anticoagulation treatment
 - possible side effects of anticoagulant treatment and what to do if these occur
 - the effects of other medications, foods and alcohol on oral anticoagulation treatment
 - monitoring 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. **[1.3.1]**
- Provide patients who are having anticoagulation treatment with an ‘anticoagulant information booklet’ and an ‘anticoagulant alert card’ and advise them to carry the ‘anticoagulant alert card’ at all times. **[1.3.2]**
- 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 clinical guideline 92).] **[1.3.3]**
- Advise patients about the correct application and use of below-knee graduated compression stockings, how long they should be worn and when

they should be replaced. [1.3.4]

- Do not routinely offer self-management or self-monitoring of INR to patients who have had DVT or PE and are having treatment with a VKA. [1.4.1]

4.10 Question

Following this recent episode of [unprovoked](#) PE and DVT, are there any further tests you would offer Gary?

4.10 Answer

Yes, offer the following investigations for cancer: a physical examination (guided by his full history) and a chest X-ray and blood tests (full blood count, serum calcium and liver function tests) and urinalysis.

If these tests do not identify signs and symptoms of cancer in Gary, consider further investigation with an abdomino-pelvic CT scan for cancer.

If active cancer is identified it may be necessary to re-assess Gary's PE and DVT treatment plan.

If the plan is to stop anticoagulant treatment you should also consider thrombophilia testing.

Relevant recommendations

- Offer all patients diagnosed with unprovoked DVT or PE who are not already known to have cancer the following investigations for cancer:
 - a physical examination (guided by the patient's full history) **and**
 - a chest X-ray **and**
 - blood tests (full blood count, serum calcium and liver function tests) **and**
 - urinalysis. **[1.5.1]**
- Consider further investigations for cancer with an abdomino-pelvic CT scan (and a mammogram for women) in all patients aged over 40 years with a first unprovoked DVT or PE who do not have signs or symptoms of cancer based on initial investigation (see recommendation 1.5.1 above). **[KPI 1.5.2]**
- Do not offer thrombophilia testing to patients who are continuing anticoagulation treatment. **[1.6.1]**
- Consider testing for antiphospholipid antibodies in patients who have had unprovoked DVT or PE if it is planned to stop anticoagulation treatment. **[1.6.2]**
- 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. **[1.6.3]**

Related recommendations

- Do not routinely offer thrombophilia testing to first-degree relatives of people with a history of DVT or PE and thrombophilia. **[1.6.5]**
- Offer LMWH to patients with active cancer and confirmed proximal DVT or PE, and continue the LMWH for 6 months⁶. At 6 months, assess the risks and benefits of continuing anticoagulation⁷. **[KPI 1.2.2]**

⁶ At the time of publication (June 2012) some types of LMWH do not have a UK marketing authorisation for 6 months of treatment of DVT or PE in patients with cancer. Prescribers should consult the summary of product characteristics for the individual LMWH and make appropriate adjustments for renal impairment. Informed consent for off-label use should be obtained and documented.

⁷ Although this use is common in UK clinical practice, at the time of publication (June 2012) none of the anticoagulants has a UK marketing authorisation for the treatment of DVT or PE beyond 6 months in patients with cancer. Informed consent for off-label use should be obtained and documented.

Case scenario 5: Jane

Presentation

Jane is a 65-year-old woman with inoperable ovarian cancer and poor functional status. She presents to your A&E department following a referral from the oncology outpatient clinic. She complains of pain along the length of her left leg with her left calf feeling particularly painful. She also reports that her left calf feels hot.

5.1 Question

You believe Jane has symptoms of a suspected DVT. What would you do next?

5.1 Answer

You would carry out an assessment of her general medical history and a physical examination to exclude other causes.

Relevant recommendation

- If a patient presents with signs or symptoms of deep vein thrombosis (DVT), carry out an assessment of their general medical history and a physical examination to exclude other causes. **[KPI 1.1.1]**

5.2 Question

You have noted Jane's presentation and recent medical history. She has no other significant past medical history. Her heart rate is 90 beats per minute, respiratory rate 13 breaths per minute, blood pressure 135/60 mmHg, temperature 37.5⁰c, SpO₂ 96% in air.

You suspect DVT: what would you do next?

5.2 Answer

You would use the two-level DVT Wells score to estimate the clinical probability of DVT.

Relevant recommendation

- If DVT is suspected, use the two-level DVT Wells score ([see appendix 1](#)) to estimate the clinical probability of DVT. **[1.1.2]**

5.3 Question

Jane's two-level DVT Wells score is 2 (DVT likely):

- Active cancer = 1.
- Localised tenderness along the distribution of the deep venous system = 1

You suspect DVT: what do you do next?

5.3 Answer

A proximal leg vein ultrasound is available to you within 4 hours of you requesting it, so you offer Jane a proximal leg vein ultrasound.

Relevant recommendation

- Offer patients in whom DVT is suspected and with a **likely** two-level DVT Wells score **either**:
 - a proximal leg vein ultrasound scan carried out within 4 hours of being requested and, if the result is negative, a D-dimer test **or**
 - a D-dimer test and an interim 24-hour dose of a parenteral anticoagulant (if a proximal leg vein ultrasound scan cannot be carried out within 4 hours) and a proximal leg vein ultrasound scan carried out within 24 hours of being requested.

Repeat the proximal leg vein ultrasound scan 6–8 days later for all patients with a positive D-dimer test and a negative proximal leg vein ultrasound scan. **[KPI 1.1.3]**

5.4 Question

The proximal leg vein ultrasound scan identifies a DVT. What would you do next?

5.4 Answer

Diagnose DVT and start treatment with LMWH. This should continue for 6 months. Ensure that an outpatient appointment is booked for Jane for 6 months' time to assess the risks and benefits of continuing anticoagulation. When developing their recommendations, the GDG noted that current international guidelines and UK clinical practice recommend continuing anticoagulation lifelong in patients with active cancer, based on expert clinical experience, case series and opinion, in the absence of randomised controlled trials.

Relevant recommendations

- Diagnose DVT and treat (see section 1.2 of the NICE guideline) patients with a positive proximal leg vein ultrasound scan. **[1.1.5]**
- Offer LMWH to patients with active cancer and confirmed proximal DVT or PE, and continue the LMWH for 6 months⁸. At 6 months, assess the risks and benefits of continuing anticoagulation⁹. **[KPI 1.2.2]**

Additional information

The evidence suggested that using LMWH instead of VKAs offered an overall benefit, for patients with proximal DVT or PE and active cancer (recommendation 1.2.2). However, this means that patients will be having daily subcutaneous injections instead of taking oral tablets. Therefore, patient preference and practicalities, such as whether patients can reliably self-inject or have a carer (such as a relative or district nurse) to help to administer the injection needs to be taken into account. The ability of patients to adhere to the treatment plan is important for its success.

⁸ At the time of publication (June 2012) some types of LMWH do not have a UK marketing authorisation for 6 months of treatment of DVT or PE in patients with cancer. Prescribers should consult the summary of product characteristics for the individual LMWH and make appropriate adjustments for renal impairment. Informed consent for off-label use should be obtained and documented.

⁹ Although this use is common in UK clinical practice, at the time of publication (June 2012) none of the anticoagulants has a UK marketing authorisation for the treatment of DVT or PE beyond 6 months in patients with cancer. Informed consent for off-label use should be obtained and documented.

Additional benefits to LMWH for people with cancer:

- It is difficult to maintain good INR control (which puts patients at risk of bleeding or more VTE events) while patients are on chemotherapy. This makes it a strong case for the use of LMWH for those patients with new VTE, and active cancer, particularly if undergoing chemotherapy.
- Patients with cancer have a higher risk of major bleeding on anticoagulation compared to patients without cancer, which may relate to the underlying cancer and propensity for bleeding (e.g. ulcerated gastric cancer).
- Patients with impaired renal function can receive LMWH at a reduced dose, and would therefore not be excluded. There may be an additional cost to Factor X monitoring for such patients, however probably few actual tests need to be conducted when patients are stabilised.

At 6 months, the need to continue anticoagulation should be reassessed and discussed with the patient. The current recommendation of international guidelines and UK clinical practice is to continue anticoagulation lifelong in patients with active cancer, based on expert clinical experience, case series and opinion, in the absence of randomised controlled trials (Khorana AA, Streiff MB, Farge D, Mandala M, Debourdeau P, Cajfinger F et al. Venous thromboembolism prophylaxis and treatment in cancer: a consensus statement of major guidelines panels and call to action. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*. 2009; 27(29):4919-4926.)

5.5 Question

Would you offer catheter-directed thrombolytic therapy or an inferior vena caval filter to Jane?

5.5 Answer

No, do not offer Jane catheter-directed thrombolytic therapy because her functional status indicates her life expectancy is less than 1 year.

Do not offer an inferior vena caval filter because Jane is able to have anticoagulation treatment.

Relevant recommendation

- Consider catheter-directed thrombolytic therapy for patients with symptomatic iliofemoral DVT who have:
 - symptoms of less than 14 days' duration **and**
 - good functional status **and**
 - a life expectancy of 1 year or more **and**
 - a low risk of bleeding. **[KPI 1.2.6]**

Related recommendations

- Offer temporary inferior vena caval filters to patients with proximal DVT or PE who cannot have anticoagulation treatment, and remove the inferior vena caval filter when the patient becomes eligible for anticoagulation treatment. **[1.2.10]**
- Consider inferior vena caval filters for patients with recurrent proximal DVT or PE despite adequate anticoagulation treatment only after considering alternative treatments such as:
 - increasing target INR to 3–4 for long-term high-intensity oral anticoagulant therapy **or**
 - switching treatment to LMWH. **[1.2.11]**
- Ensure that a strategy for removing the inferior vena caval filter at the earliest possible opportunity is planned and documented when the filter is placed, and that the strategy is reviewed regularly. **[1.2.12]**

5.6 Question

What information would you give Jane about her treatment?

5.6 Answer

Offer Jane verbal and written information about her anticoagulant treatment, including monitoring, side effects, interactions and lifestyle impacts. Provide her with an anticoagulant information booklet and an anticoagulant alert card. Advise her to carry the anticoagulant alert card at all times.

Relevant recommendations

- Give patients having anticoagulation treatment verbal and written information about:
 - how to use anticoagulants
 - duration of anticoagulation treatment
 - possible side effects of anticoagulant treatment and what to do if these occur
 - the effects of other medications, foods and alcohol on oral anticoagulation treatment
 - monitoring 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. **[1.3.1]**
- Provide patients who are having anticoagulation treatment with an ‘anticoagulant information booklet’ and an ‘anticoagulant alert card’ and advise them to carry the ‘anticoagulant alert card’ at all times. **[1.3.2]**
- 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 clinical guideline 92).] **[1.3.3]**

5.7 Question

Jane’s DVT is considered to be [unprovoked](#). Bearing this in mind, are there any other further investigations and tests you would organise?

5.7 Answer

No further tests are required. Even though Jane's DVT is considered '[unprovoked](#)' by the definition in the NICE guideline, further testing for cancer or thrombophilia are not required because Jane is known to have active cancer.

Relevant recommendations

- Offer all patients diagnosed with unprovoked DVT or PE who are not already known to have cancer the following investigations for cancer:
 - a physical examination (guided by the patient's full history) **and**
 - a chest X-ray **and**
 - blood tests (full blood count, serum calcium and liver function tests) **and**
 - urinalysis. **[1.5.1]**
- Consider further investigations for cancer with an abdomino-pelvic CT scan (and a mammogram for women) in all patients aged over 40 years with a first unprovoked DVT or PE who do not have signs or symptoms of cancer based on initial investigation (see recommendation 1.5.1 above). **[KPI 1.5.2]**
- Do not offer thrombophilia testing to patients who are continuing anticoagulation treatment. **[1.6.1]**
- Consider testing for antiphospholipid antibodies in patients who have had unprovoked DVT or PE if it is planned to stop anticoagulation treatment. **[1.6.2]**
- 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. **[1.6.3]**

Related recommendation

- Do not routinely offer thrombophilia testing to first-degree relatives of people with a history of DVT or PE and thrombophilia. **[1.6.5]**

Other implementation tools

NICE has developed tools to help organisations implement the clinical guideline on Venous thromboembolic diseases. These are available on the NICE website (www.nice.org.uk/guidance/CG144).

- PE training plan, clinical case scenarios and slide set.
- Costing statement – details of the likely costs and savings when the cost impact of the guideline is not considered to be significant.
- Audit support including electronic data tools – for monitoring local practice.

Acknowledgements

NICE would like to thank the National Clinical Guideline Centre and the Guideline Development Group, especially

- Gerard Stansby, Professor of Vascular Surgery, Freeman Hospital and Newcastle University
- Susan Ballard
- David Berridge, Consultant Vascular Surgeon, Leeds General Infirmary
- Richard Day, Consultant Physician (Geriatrics), Poole Hospital NHS Foundation Trust
- Beverley Hunt, Professor of Thrombosis and Haemostasis, King's College, London and Medical Director of Lifeblood
- David Keeling, Consultant Haematologist, Oxford University Hospitals NHS Trust
- Steven Moser, Consultant Radiologist, Imperial College Healthcare NHS Trust, London
- Karen Sheares, Respiratory Consultant with an interest in pulmonary vascular diseases, Papworth Hospital NHS Foundation Trust

Appendix 1 Two-level DVT Wells score^a

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 at least as likely as DVT	-2
Clinical probability simplified score	
DVT <i>likely</i>	2 points or more
DVT <i>unlikely</i>	1 point or less
^a Adapted with permission from Wells PS et al. (2003) Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis.	

[A template patient record Two-level PE Wells score](#) which you can print, complete and then add to patient records can be downloaded from the NICE website

Appendix 2 Two-level PE Wells score^a

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 > 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 <i>likely</i>	More than 4 points
PE <i>unlikely</i>	4 points or less
^a 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.	

[A template patient record Two-level PE Wells score](#) which you can print, complete and then add to patient records can be downloaded from the NICE website