Guideline for the Management of Venous Thromboembolism including the management of patients receiving low molecular weight heparin

This guidance does not override the individual responsibility of health professionals to make an appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

1.0 INTRODUCTION

Venous thromboembolism (VTE), manifested as deep vein thrombosis (DVT) and pulmonary embolism (PE), is a major cause of morbidity and mortality. VTE presents with a broad range of clinical signs and symptoms, from asymptomatic calf vein thrombosis to life-threatening, acute, massive PE. Important changes in prevention and treatment of VTE have occurred over the last few years and have been reflected in local, national and international guidelines. This guideline covers the management of adult patients with venous thromboembolism.

For VTE occurring in pregnancy refer to:
Guidelines for the treatment of venous thromboembolism occurring in pregnancy (2010) WAHT-OBS-013.
For thromboprophylaxis and risk assessment refer to:
Thromboprophylaxis Guideline (2011) WAHT-HAE-015.

THIS GUIDELINE IS FOR USE BY THE FOLLOWING STAFF GROUPS:
This guideline is designed for use by clinical and nursing staff managing patients who have symptoms suggesting VTE or diagnosed with VTE.

Education and Training
Education and training for Clinical staff using this guideline is gained during professional education and training, it is the responsibility of all individuals to maintain their professional accountability, ensure they are up to date and maintain knowledge and skills in all aspects of thrombosis management.

This guideline also covers the use of low molecular weight heparin (LMWH), and it applies to all health professionals who are involved with initiating, prescribing, administering, monitoring and dosing injectable LMWH anticoagulant therapy.

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Approved by Medicines Optimisation Expert forum on:	22/08/2017
Review Date:	13/08/2019

This is the most current document and is to be used until a revised version is available:

Key amendments to the guideline:

Date	Amendment	By:
10/04/2012	D Dimer result amended according to laboratory changes. Monitoring audit tool amended	Dr Crowther L Hancox
25/08/2012	Cut off of pre-test score for allowing d-dimer to be used changed from 0 to 1.	M Crowther
25/08/2012	For both DVT and PE instructions on how to request a d-dimer, how to request imaging, roles and responsibilities and ideal timescales is added.	M Crowther
25/08/2012	Suggested follow-up investigations for GPs are added	M Crowther
18/12/2012	Suggested rules for rescanning patients with possible DVT changes	M Crowther U Udeshi
18/12/2012	Reminder for those discharging patients on LMWH to provide sharps box	M Crowther
18/12/2012	Removed need to monitor platelet count for those on LMWH	M Crowther
24/01/2014	Re-write to include the use of rivaroxaban	M Crowther
15/09/2017	Re-write to include changes to the licensed dose of enoxaparin	M. Crowther
05/12/17	Sentence added in at the request of the Coroner	

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2.0 PURPOSE OF THE GUIDELINE

The purpose of this guideline is to provide good practice guidance for staff managing patients with venous thromboembolism (VTE). This guideline must be used in conjunction with a clinical assessment and other national and local guidelines, policies and procedures.

Priority Aims:

1. Improve accurate diagnosis and prompt treatment of venous thromboembolism (VTE).
2. Prevent progression or recurrence of thromboembolic disease.
3. Reduce the risk of complications from anticoagulation therapy.
4. Improve the safety by reducing the likelihood of patient harm associated with the use of anticoagulation therapy.

3.0 DETAILS OF GUIDELINE

This guideline covers patients admitted to Worcestershire Acute Hospitals NHS Trust with diagnosis or symptoms of VTE. It highlights the safe management of anticoagulation therapy and the importance of prompt treatment in patients receiving LMWH.

3.1 Scope and Target Population

Adult patients age 18 and over with VTE, excluding those with familial bleeding disorders or pregnancy.

3.2 Deep vein thrombosis (DVT)

3.2.1 Clinical features of a DVT

A diagnosis of DVT is usually suspected in patients who complain of a painful swollen limb. However, the clinical picture can vary widely and no clinical feature is sufficiently specific to be diagnostic. Less than a third of patients referred for tests, after initial history and clinical examination, have a DVT. Clinical diagnosis is notoriously difficult.

Common Presenting Features:

- Pain or tenderness of the leg
- Swelling of calf or leg
- Pitting oedema
- Palpable venous thrombosis
- Increased temperature in the leg
- Fever
- Discoloration or erythema of the leg
- Venous distension

3.2.2 Diagnosis of DVT

Patients suspected of having a DVT should have a pre-test probability score performed. This consists of scoring points if a clinical feature is present; the score is added at the end:

3.2.2.1 Pre-test probability scoring for DVT

Clinical feature	Score
Active cancer (treatment ongoing or within previous 6 months or palliative)	1
Paralysis, paresis, or recent plaster immobilisation of the lower extremities	1
Recently bedridden for more than 3 days or major surgery, within 4 weeks	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling by more than 3cm when compared with the asymptomatic leg (measured 10cm below tibial tuberosity)	1
Pitting oedema (greater in the symptomatic leg)	1
Collateral superficial veins (non-varicose)	1
Previous documented DVT	1
Alternative diagnosis as likely or greater than that of a DVT	-2

3.2.2.2 D-dimers

If the score is one or less a D-dimer should be performed, if this is negative then a DVT can be excluded at this point. If the D-dimer is positive the patient should be referred for imaging.

If the score is two or more the patient should be referred for imaging without having a D-dimer performed.

Patients on anticoagulation and pregnant ladies may have falsely low D-dimers and should not have them performed and progress straight to imaging.

D-dimers are requested through the ICE OrderComms system, they require a single sodium citrate tube and are sent to haematology. The average turnaround time for a D-dimer, from arrival at the laboratory, is one hour. D-dimer requests require a pre-test score written on the form. D-dimers will be reported as positive or negative. It is the requester's responsibility to chase the result on the ICE system as the result is not routinely telephoned. The haematology laboratory is CPA accredited and takes part in internal and external quality control therefore all D-dimer results can be assumed to be accurate enough on which to base clinical practice.

3.2.2.3 Ultrasound Scan

Ultrasound scan (USS) has become the investigation of choice in the diagnosis of DVT. It will detect more than 90% of proximal DVTs (i.e. popliteal vein and above). It is less sensitive for calf vein thrombosis (about only 50% are detected) but pulmonary embolism from this site is rare and unlikely to cause significant haemodynamic disturbance even if it occurs.

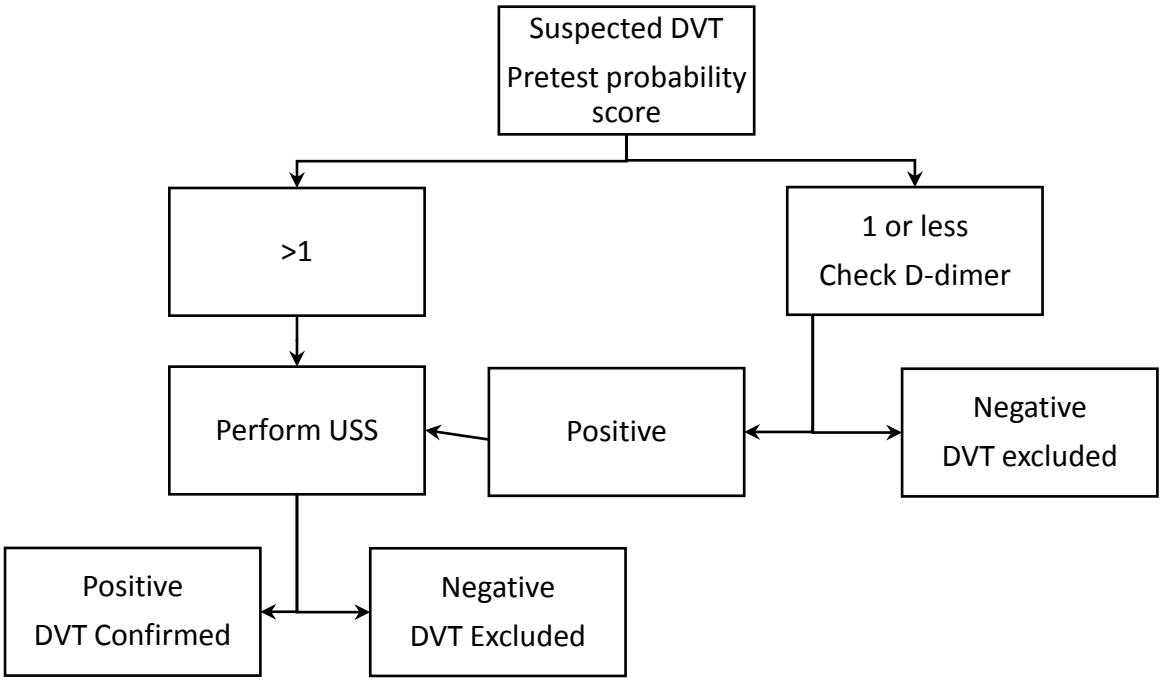
Urgent ultrasounds can be requested by discussing the case with the ultrasound radiologist/radiographer and by completing the form on ICE OrderComms. Less urgent scans can be requested on ICE OrderComms. The ultrasound report will appear on the ICE system shortly after the scan has been performed (within 1 hour) or written in the patient

notes. It is the requester's role to check for the result, it will not be routinely telephoned. All sonographers/radiologists performing ultrasound scans are appropriately trained.

All patients with a suspected DVT, a negative ultrasound scan and no other explanation for their symptoms should have a clinical review after 1 week. If there is progression of symptoms or continuing clinical concern regarding a DVT a repeat ultrasound scan can be considered.

Patients with borderline scans or scans which demonstrate clot(s) that cannot be aged should be considered for a venogram.

3.2.2.4 DVT Flow Chart



Patients who are to be referred for scanning should start treatment dose anticoagulation (as long as there is no exclusions) if the scan is likely to be more than four hours distant or there are significant symptoms. The anticoagulation can be stopped if the scan is negative but if an inpatient they should be assessed for thromboprophylaxis. Anticoagulation can be either treatment dose low molecular weight heparin (LMWH) or a Direct Oral Anticoagulant Drug (DOAC) (the choice is discussed below in section 3.2.3). The results of all investigations which change management should be documented in the notes.

3.2.2.5 Ambulatory patients

Patients who do not meet the following criteria may be discharged home on anticoagulation while awaiting imaging:

- Elderly patients with no support at home
- Recent stroke patients
- Patients with previous haemorrhagic stroke proven on CT scan
- Patients with acute gastric or duodenal ulceration
- Patients with severe hepatic failure or renal failure
- Patients with uncontrolled hypertension
- Patients with familial or acquired bleeding disorders
- Any patient with possible pulmonary embolism (see ambulatory PE)
- Any patient with a recent head trauma or brain surgery
- Patients with previous history of Heparin Induced Thrombocytopaenia (HIT)
- Patients with excessive alcohol consumption
- Patients requiring more aggressive investigation or management e.g. Thrombolysis

It is the clinician's reasonability to ensure that the patient has been fully informed of the likely diagnosis and follow-up arrangements. The patient should be given 'DVT Information Sheet 1 – Suspected DVT'. Seven day packs of either LMWH or rivaroxaban are available.

3.2.2.6 Timescales

Patients with a suspected DVT should be initially risk assessed. If a D-dimer is appropriate this should be taken within 1 hour and before any anticoagulation is given. The patient should be informed of the result, and the further plan, within 4 hours of the D-dimer being taken. If the patient requires imaging then they should be informed of the likely time for the scan and whether they require treatment with anticoagulation. The scan should be no more than 72 hours from the time of requesting. The patient should be informed of the result of the scan within 4 hours of the scan. The time of all patient contact events should be recorded in the notes.

These steps should only be performed by a doctor, nurse practitioner or a nurse from the DVT clinic apart from the D-dimer which can be taken by a trained phlebotomist. The patient should be initially assessed in hospital, the patient should only be sent home if a DVT has been excluded or diagnosed or they are awaiting imaging and have been treated with anticoagulation. The results of investigations should be given to the patient in hospital in person by the doctor, nurse practitioner or a nurse from the DVT clinic. The time of all patient contacts should be documented in the patient's notes.

Where the patient's care is referred to another department for further investigation/ management it is assumed that, on accepting the patient, the department will continue to follow the appropriate pathway and arrange all further investigations/treatments/referrals.

3.2.2.7 Information Sheets

The following information sheets are available for patients and should be used:

- DVT Information Sheet 1 – Suspected DVT
- DVT Information Sheet 2 – Confirmed DVT
- DVT Information Sheet 3 – No DVT

3.2.3 Treatment of DVT

The treatment of DVT is either with LMWH (treatment guidelines below) alone, LMWH or unfractionated heparin (UFH) converting to warfarin (LMWH must be given for at least five days and until warfarin is therapeutic for 2 days) or a DOAC. Patients should be given a seven day supply and asked to attend their GP for further supplies. If they are being started on warfarin then an appointment at either the hospital or a community anticoagulation clinic should be made and the warfarin started only on the advice of that clinic.

The length of anticoagulation is determined by the risk of recurrence and the risk of bleeding, this is individual to the patient but as a guide:

- First unprovoked proximal DVT – 3 months (except antiphospholipid syndrome then lifelong)
- Second unprovoked proximal DVT – lifelong
- Provoked DVT (oestrogen containing pill, hormone replacement, post-surgery or limb immobilisation) – 3 months (or longer if provoking factor still present)
- Intravenous catheter associated – 6 weeks
- Calf DVT – 3 months
- Cancer associated thrombosis – see below
- Intravenous drug abuser who is actively injecting into the affected leg – 6 weeks

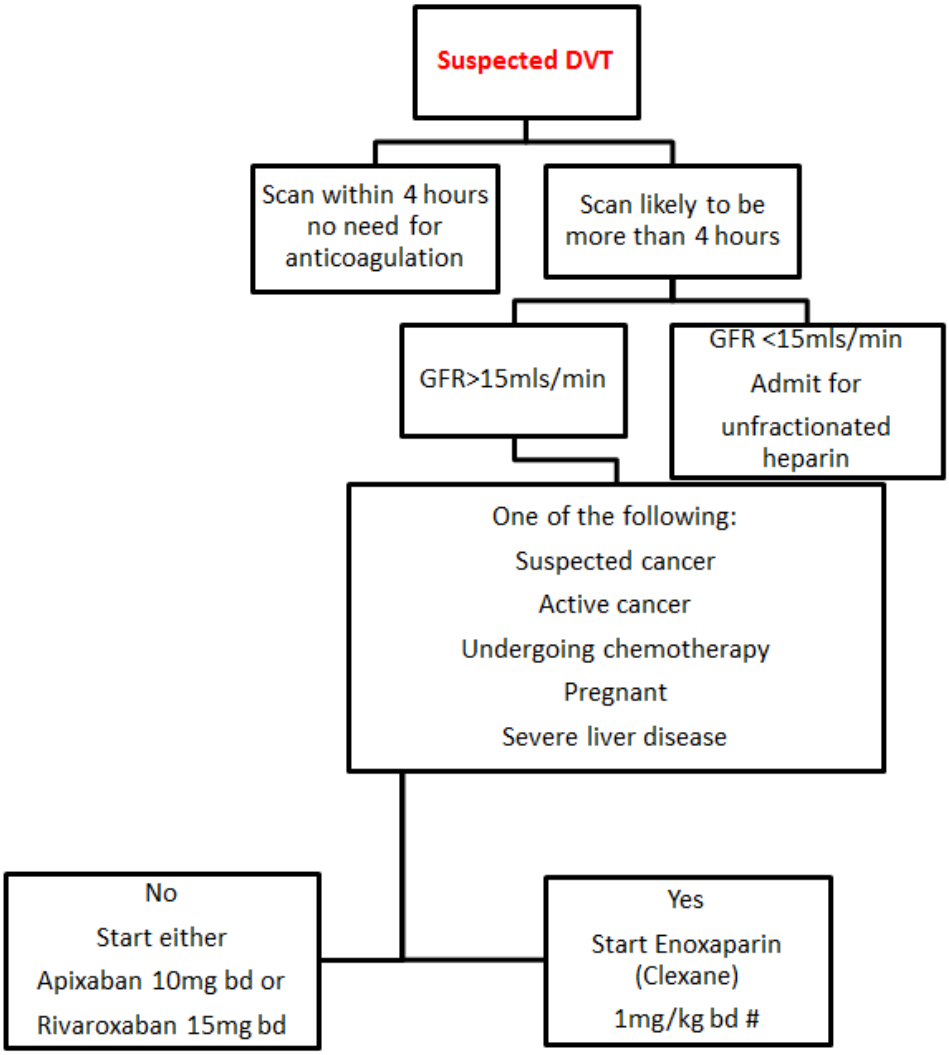
The patient should be fully counselled for the risk of bleeding while on anticoagulation. They should also be counselled on the signs/symptoms of recurrence to report and what high risk actions to avoid (prolonged immobility without prophylaxis, oestrogen containing medications) and to always inform medical staff of their past medical history if they attend hospital or become pregnant. First degree female relatives of patients with unprovoked DVT should be advised to avoid oestrogen containing medications.

3.2.3.1 Compression stockings

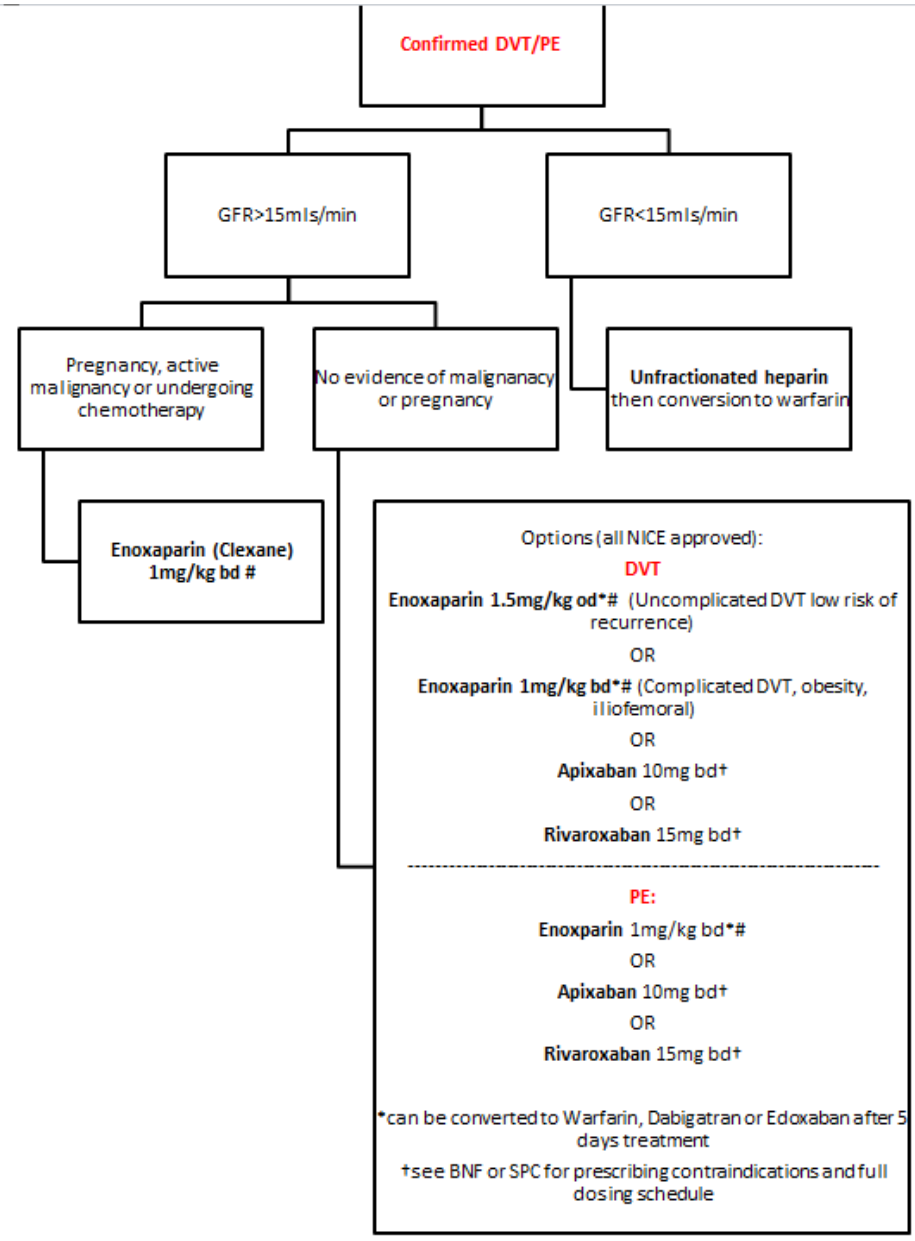
Patients with a confirmed DVT and without contraindications should be advised to wear appropriately fitting below knee compression stockings for 2 years following the event on the affected leg. This significantly reduces the risk of post-phlebitic syndrome.

3.2.3.2 Treatment options for DVT

The choice of the most appropriate treatment is a decision between the clinician and the patient. For the majority of patients there is no clearly superior product. Treatment suggestions are found in the figure below.



for CrCl 15-30ml/minute use 1mg/kg OD



for CrCl 15-30ml/minute use 1mg/kg OD

For those patients who are to be considered for a DOAC (Apixaban, Dabigatran, Edoxaban and Rivaroxaban) a discussion between the patient and the prescriber is required.
Patient likely to benefit most from warfarin:

- Indication not covered by DOAC e.g. valvular AF, prosthetic valves
- Severe renal failure (GFR<30mls/min) or high chance of significant deterioration
- Hepatic dysfunction
- Arterial grafts
- Patient concerns over long term safety data
- Concomitant use of other medicines which interact with DOACs
- Other medical conditions where data on the use of DOACs is limited
- Use of unusual drugs where experience of them alongside DOACs is limited

There may be more benefit to treatment of DVT/PE with a DOAC compared to AF as the majority of patients are treated for a short period of time, therefore long term side-effects are less of a problem. Also the highest risk of bleeding on warfarin is in the first three months and that is when the majority of blood tests are.
Patient likely to benefit most from DOAC:

- Regularly prescribed drugs that interferes with warfarin e.g. COPD patient with multiple courses of antibiotics
- Difficulty attending INR clinics (personal or medical reasons)

Likely poor compliance is not a reason for choosing a DOAC, the relative short half-life means missed doses leaves the patients without anticoagulation until the next dose is taken, the relative long half-life of warfarin means an occasional missed dose is unlikely to affect the INR.

3.2.3.3 Thrombolysis for DVT

Thrombolysis leads to more rapid clot breakdown and a lower rate of post-phlebitic syndrome however it comes with the increased risk of bleeding and possibly death. Thrombolysis should be limited to patients who:

- Have a low risk of bleeding
- Have a life-expectancy >1 year
- Have a good performance status

And have one or more of the following:

- Bilateral DVT
- DVT extends as far as renal veins causing renal dysfunction
- Significant thrombosis causing whole leg swelling and significant pain
- The viability of the leg is compromised

Thrombolysis is usually performed with the cooperation of the vascular surgeons and the interventional radiologists. If thrombolysis is to be considered then UFH should be used initially instead of either LMWH or a DOAC. Once thrombolysis is complete the patient can then be converted to LMWH or a DOAC.

3.2.3.4 Inferior vena cava filters

Inferior vena cava filters prevent the embolism of clots from the lower limbs to the lungs. They can however become thrombosed and may migrate to the lungs. Inferior vena cava filters should only be considered if there is a contra-indication to anticoagulation e.g. recent haemorrhage or requirement of emergency surgery. They should be ideally removed once full dose anticoagulation has been reinstated.

3.2.3.5 Recommended follow-up of DVT patients

Follow-up is usually with the GP. The following is a suggested follow-up regimen:

Diagnosis	Ensure patient understands condition and treatment. Alert patient to what signs/symptoms should prompt them to contact medical services. Ensure DVT patients have stockings (need to wear for 2 years).
1 week	Ensure patient understands condition and treatment. Alert patient to what signs/symptoms should prompt them to contact medical services. Consider further investigations if symptoms not improving.
4 weeks	Symptoms should be much improved/gone, consider further investigations if symptoms not improved. Ensure compliance. Patients with line associated and IVDU thrombosis should be advised to stop after six weeks if symptoms resolved. Consideration should be given to prophylaxis if indwelling line present.
8 weeks	Check patients have no problems
3 months	Provoked event (post-surgery, oestrogen therapy, pregnancy, plaster cast, long haul flight etc.). Stop anticoagulation if provoking factor removed (if not consider prophylaxis). Encourage patient to present if recurrence of symptoms. Encourage to wear stockings for 2 years. Unprovoked DVT – The decision has to be made whether to stop anticoagulation or continue long term. Indications for long term anticoagulation would be those with a high risk of recurrence (second unprovoked event, severe post-phlebitic syndrome, active cancer and a strong family history of recurrence) who have not had significant problems with anticoagulation. For those stopping anticoagulation a lupus anticoagulant and anticardiolipin antibodies should be checked 1 week after stopping anticoagulation and if positive referred to haematology. Encourage patient to present if recurrence of symptoms. **All patients continuing anticoagulation – ensure compliance, determine any signs or symptoms of thrombosis or anticoagulation.**
6 monthly for those still on anticoagulation	Ensure compliance and determine any suggestion or recurrence or problems with the anticoagulation. If there are problems with the anticoagulants then consideration should be given to changing them or stopping. U&E's should be checked annually for those with a normal renal function and 6 monthly for those with abnormal renal function.

3.2.3.6 Recurrent DVT

Symptoms of recurrent DVT should be investigated as in section 3.2.2 above. Confirmed recurrent DVT should be managed as follows:

- Recurrence when not receiving anticoagulation – treat as described in 3.2.3
- Recurrence when receiving anticoagulation – if being treated with warfarin (target INR 2.5) and patient within target range when recurrence happened consider increasing target INR to 3.5, if being treated with LMWH or a DOAC consider changing to warfarin with target INR 3.5, if being treated with warfarin target INR 3.5 and within range options are changing to or adding LMWH or adding aspirin (this should be discussed with haematology).

3.3 Thrombophlebitis

Superficial phlebitis is inflammation of a superficial vein while the term superficial thrombophlebitis is used when there is also clot present. Suppurative (thrombo)phlebitis is where there is bacterial infection of the vein and surrounding tissue. Superficial phlebitis is common with predisposing factors being venous catheters, malignancy, varicose veins, trauma, ablation surgery and thrombophilia.

The majority of cases of superficial phlebitis are benign and self-limiting but it is important that both coexisting deep vein thrombosis and suppurative phlebitis are excluded as these require treatment to prevent serious complications.

3.3.1 Diagnosis of Thrombophlebitis

Superficial phlebitis presents as pain, tenderness, induration and swelling along the course of a superficial vein. The vein itself will often be palpable as a thickened cord. There may be a mild pyrexia.

A clinical diagnosis of superficial phlebitis can be made if the above is present and the swelling and erythema does not extend for more than 5cm from the vein.

Suppurative phlebitis should be considered if there is a high fever, fluctuant swelling and/or erythema spreading for more than 5cm from the vein. Investigations may reveal raised inflammatory markers with a high ESR and CRP. Suppurative phlebitis is usually associated with previous cannulation or puncture of the vein.

Deep vein thrombosis (DVT) should be excluded with Doppler ultrasound scanning if there is either:-

- Risk factors for DVT (a past or family history of thrombosis, recent long-haul travel, immobility, malignancy, pregnancy, oral contraceptive or hormone replacement therapy use)
- Affecting the great or lesser saphenous vein
- Limb swelling
- The diagnosis is not clear.

If a DVT is suspected and the scan is likely to be more than 12 hours later then treatment dose enoxaparin (1.5mg/kg) can be given subcutaneously, ensuring there are no contra-indications to its use.

Ultrasound scanning should determine if there is clot present in either the superficial or deep veins. The scan may demonstrate other causes of symptoms or if there is a collection of pus.

Because of the confusion when the term superficial femoral vein is used, which is a deep vein, care should be taken when reading the report. Where clot is demonstrated in a superficial vein a diagnosis of superficial thrombophlebitis can be made.

3.3.2 Treatment of superficial phlebitis

IF AT ANY TIME A PATIENT WITH SUPERFICIAL PHLEBITIS HAS EVIDENCE OF CLOT IN A DEEP VEIN THEN THIS SHOULD BE TREATED AS A DEEP VEIN THROMBOSIS.

Clinically diagnosed superficial phlebitis
Treatment of clinically diagnosed superficial phlebitis should be with symptomatic with pain relief, anti-inflammatory medications (unless there are contra-indications) and compression stockings. The patient should be counselled that symptoms may persist for several weeks but that they must present to medical services if there is failure to improve or progression of their symptoms. The patient should be reassessed after seven days to ensure that there have not been any significant changes.

Superficial thrombophlebitis
Superficial thrombophlebitis can be split into:-

- Clot lying within 5cm of a junction with a deep vein or >5cm long. This requires treatment with enoxaparin 40mg subcutaneously once a day for 6 weeks as long as there are no contra-indications. If there are contra-indications to anticoagulation then a referral should be made to vascular surgery for tying off of the vein. The scan should be repeated after seven days to ensure there hasn't been progression. The patient should be encouraged to represent if there is worsening of symptoms.
- Clot lying greater than 5cm from a junction with a deep vein. This is managed as clinically diagnosed superficial phlebitis. If there is progression then anticoagulation, as above, should be initiated. The patient should be encouraged to represent if there is worsening of symptoms.

Suppurative phlebitis
Suppurative phlebitis should be treated with antibiotics. Before starting antibiotics blood cultures should be taken. Any exudates from the wound should also be swabbed. Antibiotic choice should be guided by the 'Skin and soft tissue infections' section of the trust guideline Worcestershire Secondary Care Adult Antibiotic Prescribing Policy (WRH-PHA-001). Surgical drainage should be considered where there are either systemic symptoms, severe pain or a fluctuant mass. Any puncture wound should be kept clean and dry.

Recurrent episodes of thrombophlebitis
Recurrent episodes should be referred to the vascular surgery for consideration of surgical intervention.

3.4 Pulmonary embolus

A PE is obstruction of the pulmonary artery or one of its branches by an embolus. The embolus usually is a blood clot developing in a deep vein.

3.4.1 Signs & Symptoms

Dyspnoea
Pleuritic chest pain
Sub sternal chest pain
Cough
Haemoptysis
Syncope
Tachypnoea (≥20/min)
Tachycardia (>100/min)
Signs of DVT
Cyanosis
Pyrexia
Pulseless electrical activity

3.4.2 Diagnosis of a PE

All patients with possible PE should have clinical probability assessed and documented. An alternative clinical explanation should always be considered at presentation and sought when PE is excluded. Baseline investigations should include full blood count (FBC), clotting screen, electrolytes and creatinine, liver function tests, glucose, arterial blood gases (ABG), ECG and Chest X-Ray (CXR).

3.4.2.1 Clinical scoring system

Clinical feature	Score
Age >65	1
Previous DVT or PE	3
Unilateral lower limb pain	3
Pain on lower limb deep venous palpation and unilateral oedema	4
Heart rate 75-94	3
Heart rate >95	5
Active malignancy	2
Haemoptysis	2
Surgery or fracture within 1 month	2

If the score is ten or less a D-dimer should be performed, if this is negative then a PE can be excluded at this point. If the D-dimer is positive the patient should be referred for imaging. D-dimers cannot be performed on patients who are receiving anticoagulation.

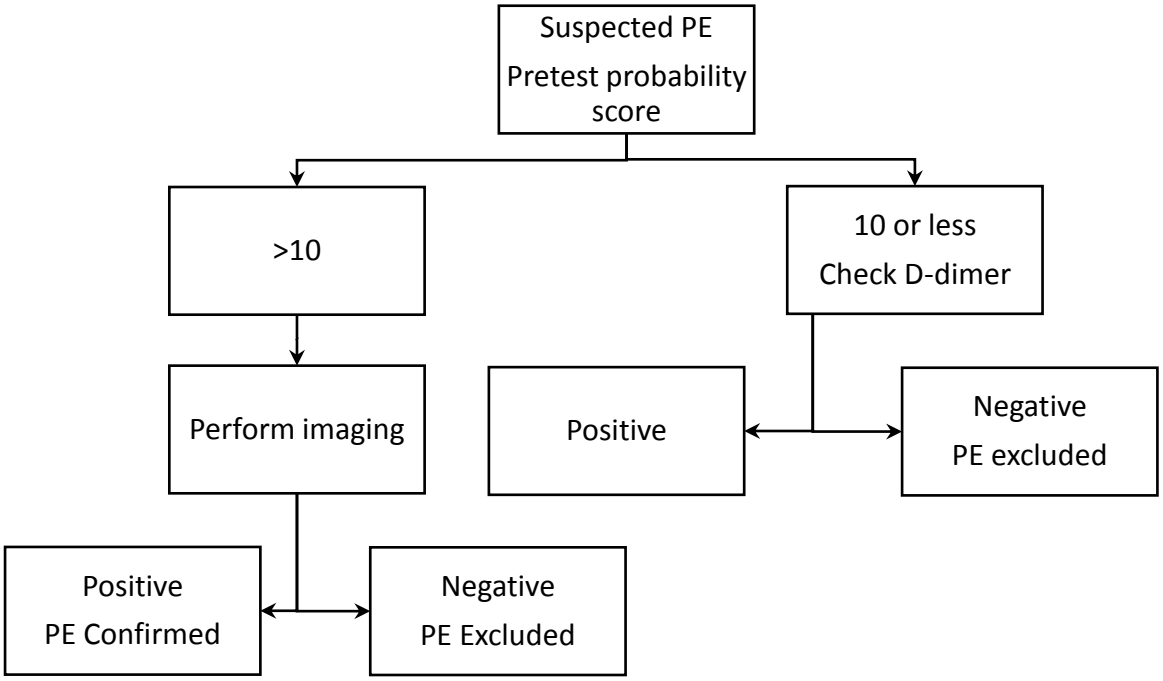
If the score is >10 then the patient should be referred for imaging without having a D-dimer performed.

Patients who are to be referred for scanning should start on either treatment dose LMWH, UFH or a DOAC (as long as there is no exclusions), see below.

D-dimers are requested through the ICE OrderComms system, they require a single sodium citrate tube and are sent to haematology. The average turnaround time for a D-dimer, from

arrival to the lab, is one hour. D-dimer requests require a pre-test score written on the form. D-dimers will be reported as positive or negative. It is the requester's responsibility to chase the result on the ICE system as the result is not routinely telephoned. The haematology laboratory is CPA accredited and takes part in internal and external quality control therefore all D-dimer results can be assumed to be accurate enough on which to base clinical practice.

3.4.2.2 PE diagnosis flow chart



3.4.2.3 Investigations for PE

There are several modalities available for diagnosing PE:

- Ventilation/perfusion can be used in patients with a normal chest X-ray and no existing cardiopulmonary disease. If normal a PE can be excluded. Low, intermediate and high probabilities require confirmation with a CTPA.
- CT pulmonary angiogram (CTPA) can be used to diagnose/exclude PE in the majority of cases; the patient must have good renal function due to the use of intravenous contrast.
- Pulmonary angiography is the gold standard but is invasive.
- Echocardiography is useful in diagnosing PE in the emergency situation and it has no side-effects.

CTPAs or V/Q scans can be requested by discussing the case with the duty radiologist and by completing the form on ICE OrderComms. Less urgent scans can be requested on ICE OrderComms. The report will appear on the ICE system shortly after the scan has been performed (within 2 hours) or written in the patient notes, it is the requester's role to check for the result, it will not be routinely telephoned. All radiologists performing the scans are appropriately trained.

The results of any investigations which change management should be documented in the notes. In emergency situations the ICE OrderComms audit trail will determine when the result was viewed, except when the result is given verbally when it should be documented in the notes at the first opportunity.

3.4.2.4 Outpatient management of PE

Patients who meet the following inclusion criteria and do not have any of the exclusion criteria may be discharged home on anticoagulation while awaiting imaging:

Inclusion criteria:

- Age <80
- Fully understands nature of condition
- Able to return for further investigation

Exclusion criteria:

- Hypoxia
- Hypotension
- Heart rate >100bpm
- Respiratory rate >30bpm
- Significant haemoptysis
- Hypothermia (temp <36°C)
- Uncontrolled chest pain
- No support at home
- Recent stroke patients
- Patients with previous haemorrhagic stroke proven on CT scan
- Patients with acute gastric or duodenal ulceration
- Patients with severe hepatic failure or renal failure
- Patients with uncontrolled hypertension
- Patients with familial or acquired bleeding disorders
- Any patient with a recent head trauma or brain surgery
- Patients with previous history of Heparin Induced Thrombocytopaenia (HIT)
- Patients with excessive alcohol consumption
- Patients requiring more aggressive investigation or management e.g. Thrombolysis

It is the clinician's responsibility to ensure that the patient has been fully informed of the likely diagnosis and follow-up arrangements. The patient should be given 'PE Information Sheet 1 – Suspected PE'. Seven day packs of either LMWH or rivaroxaban are available.

3.4.2.5 Timescales

Patients with a suspected PE should be initially risk assessed. If a D-dimer is appropriate this should be taken within 1 hour and before anticoagulation. The patient should be informed of the result, and the further plan, within 4 hours of the D-dimer being taken. If the patient requires imaging then they should be informed of the likely time for the scan. The scan should be no more than 72 hours from the time of requesting. The patient should be informed of the result of the scan within 4 hours of the scan. The time of all patient contact events should be recorded in the notes.

These steps should only be performed by a doctor or nurse practitioner apart from the D-dimer which can be taken by a trained phlebotomist. The patient should be initially assessed in hospital, the patient should only be sent home if a PE has been excluded or diagnosed or they are awaiting imaging and have been treated with LMWH and are felt by a Specialist Registrar or Consultant to be safe to be managed as an outpatient. The results of investigations should be given to the patient in hospital in person by a doctor or a nurse practitioner.

Where the patient's care is referred to another department for further investigation/ management it is assumed that, on accepting the patient, the department will continue to follow the appropriate pathway and arrange all further investigations/treatments/referrals.

3.4.2.6 Information Sheets

The following information sheets are available for patients and should be used:

- PE Information Sheet 1 – Suspected PE
- PE Information Sheet 2 – Confirmed PE
- PE Information Sheet 3 – No PE

3.4.3 Treatment of PE

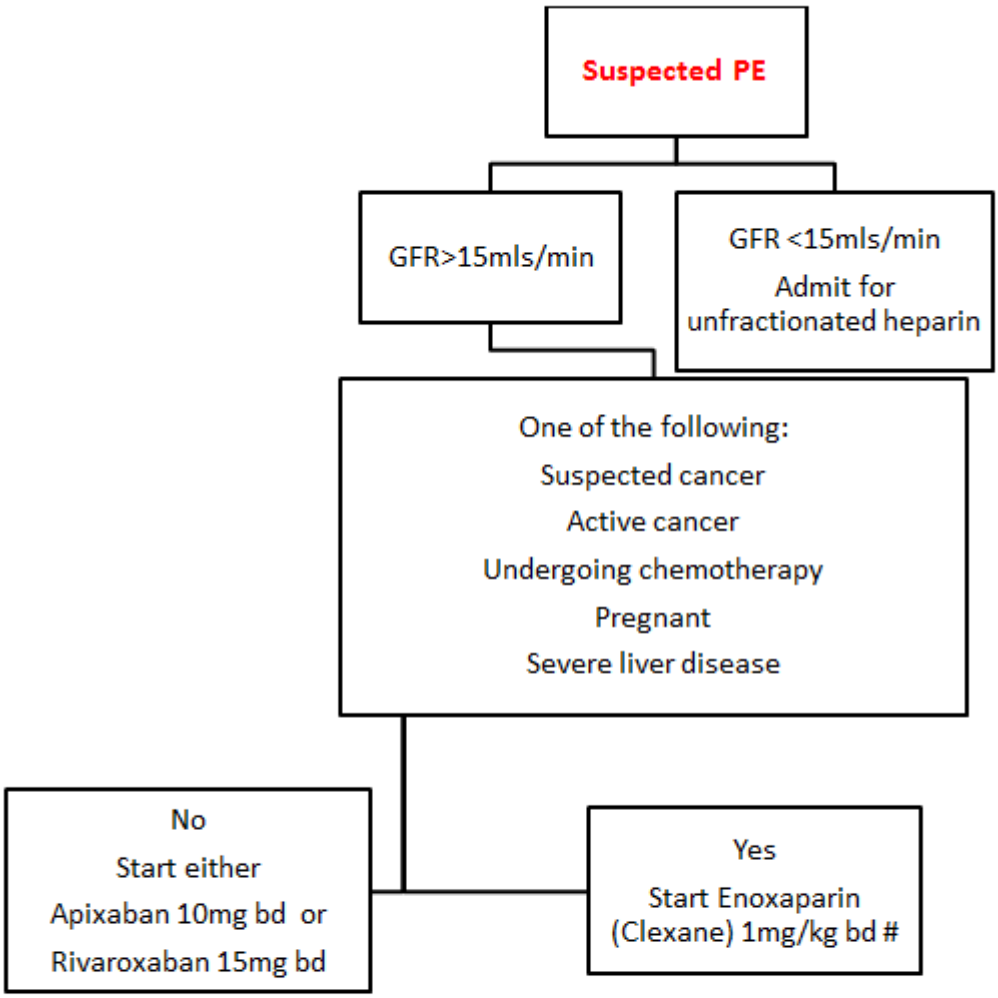
Initial treatment of PE is with LMWH, see below for prescribing guidelines, UFH or a DOAC. If being converted to warfarin the alternative anticoagulant is given for a minimum of five days with Warfarin until the INR is >2.0 for 2 days. Patients should be given a seven day supply of either LMWH or a DOAC and asked to attend their GP for further supplies. If they are being started on warfarin then an appointment at either the hospital or a community anticoagulation clinic should be made and the warfarin started only on the advice of that clinic.

Treatment of a first episode of PE is usually with six months of anticoagulation. Patients with antiphospholipid syndrome and life-threatening PE should be considered for lifelong anticoagulation. Cancer associated thrombosis is usually treated with LMWH for 6 months and then continued until the cancer is in remission.

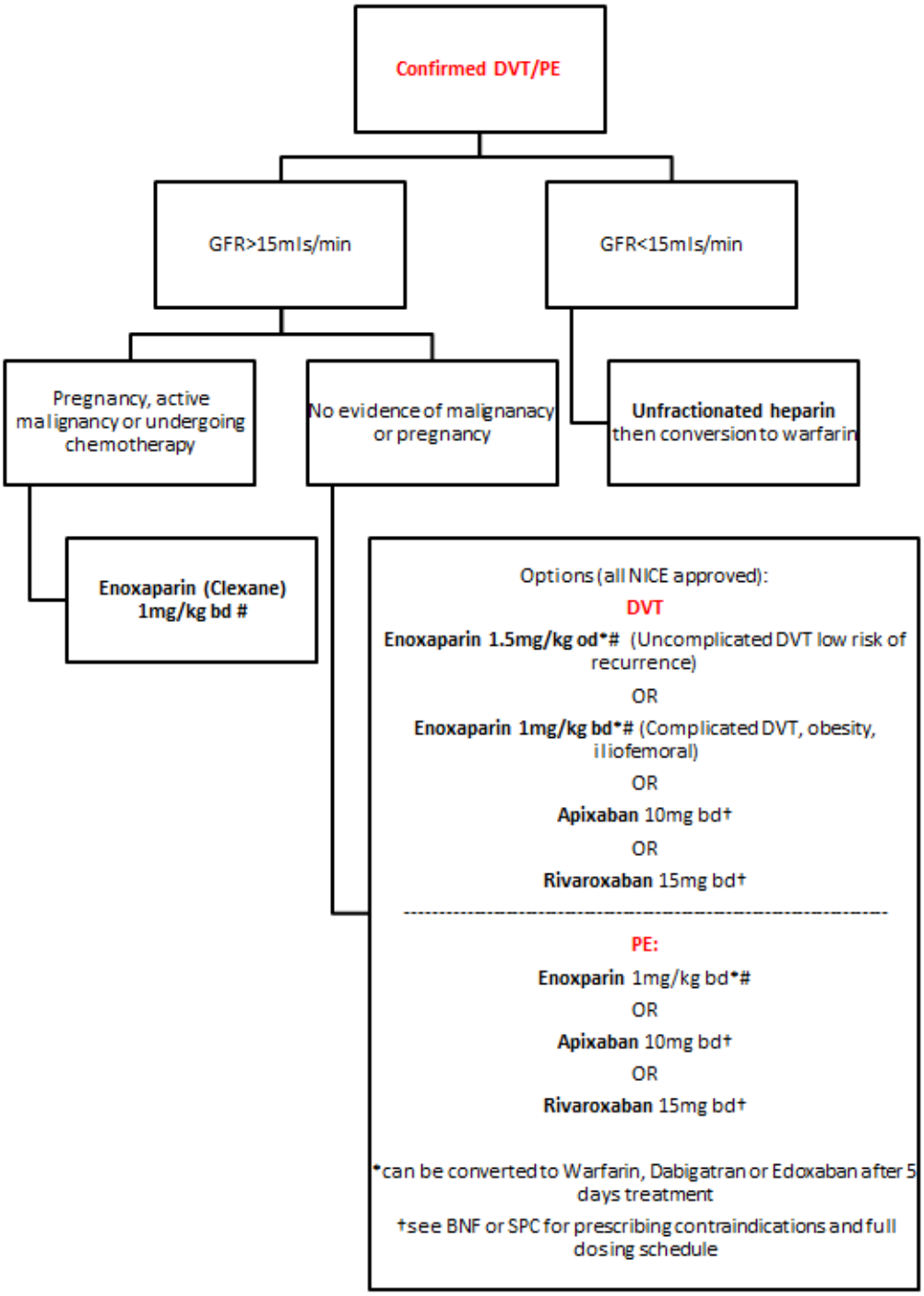
The patient should be fully counselled about the risk of bleeding while on anticoagulation. They should also be counselled on the signs/symptoms of recurrence to report and what high risk actions to avoid (prolonged immobility without prophylaxis, oestrogen containing medications) and to always inform medical staff of their past medical history if they attend hospital. First degree female relatives of patients with unprovoked PE should be advised to avoid oestrogen containing medications.

3.4.3.1 Treatment choices

The choice of the most appropriate treatment is a decision between the clinician and the patient. For the majority of patients there is no clearly superior product for all patients. Treatment suggestions are found in the figure below.



for CrCl 15-30ml/minute use 1mg/kg OD



for CrCl 15-30ml/minute use 1mg/kg OD

For those patients who are to be considered for a DOAC (Apixaban, Dabigatran, Edoxaban and Rivaroxaban) a discussion between the patient and the prescriber is required.
Patient likely to benefit most from warfarin:

- Indication not covered by DOAC e.g. valvular AF, prosthetic valves
- Severe renal failure (GFR<30mls/min) or high chance of significant deterioration
- Hepatic dysfunction
- Arterial grafts
- Patient concerns over long term safety data
- Concomitant use of other medicines which interact with DOACs
- Other medical conditions where data on the use of DOACs is limited
- Use of unusual drugs where experience of them alongside DOACs is limited

There may be more benefit to treatment of DVT/PE with a DOAC compared to AF as the majority of patients are treated for a short period of time, therefore long term side-effects are less of a problem. Also the highest risk of bleeding on warfarin is in the first three months and that is when the majority of blood tests are.
Patient likely to benefit most from DOAC:

- Regularly prescribed drugs that interferes with warfarin e.g. COPD patient with multiple courses of antibiotics
- Difficulty attending INR clinics (personal or medical reasons)

Likely poor compliance is not a reason for choosing a DOAC, the relative short half-life means missed doses leaves the patients without anticoagulation until the next dose is taken, the relative long half-life of warfarin means an occasional missed dose is unlikely to affect the INR.

3.4.3.2 Follow-up arrangements for PE

Follow-up is usually with the GP. The following is a suggested follow-up regimen:

Diagnosis	Ensure patient understands the condition and treatment. Alert patient to what signs/symptoms should prompt them to contact medical services.
1 week	Ensure patient understands the condition and treatment. Alert patient to what signs/symptoms should prompt them to contact medical services. Consider further investigations if symptoms not improving.
4 weeks	Symptoms should be much improved/gone, consider further investigations if symptoms not improved. Ensure compliance.
8 weeks	Check patients have no problems (could be over telephone)
6 months	Patients should have ECG/PFTs/Echo arranged to exclude pulmonary hypertension. The decision has to be made whether to stop anticoagulation or continue long term. Indications for long term anticoagulation are those with a high risk of recurrence (second unprovoked event, active cancer, ongoing symptoms, poor lung reserve and a strong family history of recurrence) who have not had significant problems with anticoagulation. For those stopping anticoagulation a lupus anticoagulant and anticardiolipan antibodies should be checked 1 week after stopping anticoagulation and if positive referred to haematology. Those who stop anticoagulation can be discharged. Encourage patient to present if recurrence of symptoms.

6 monthly for those continuing anticoagulation	**All patients continuing anticoagulation – ensure compliance, determine any signs or symptoms of thrombosis or anticoagulation. Check U&Es in those whose baseline renal function was abnormal.** Ensure compliance and determine any suggestion of recurrence or problems with the anticoagulation. If there are problems with the anticoagulants then consideration should be given to changing them or stopping. U&E's should be checked annually for those with a normal renal function and 6 monthly for those with abnormal renal function.

3.4.3.3 Recurrent PE

Symptoms of recurrent PE should be investigated as in section 3.4.2 above. Confirmed recurrent PE should be managed as follows:

- Recurrence when not receiving anticoagulation – treat as described in 3.4.3
- Recurrence when receiving anticoagulation – if being treated with warfarin (target INR 2.5) and patient within target range when recurrence happened consider increasing target INR to 3.5, if being treated with LMWH or a DOAC consider changing to warfarin with target INR 3.5, if being treated with warfarin target INR 3.5 and within range the options are changing to or adding LMWH or adding aspirin (this should be discussed with haematology).

3.4.4 Life-threatening PE

Patients that demonstrate significant hypotension (systolic BP<90mmHg), a history suggestive of symptomatic hypotension e.g. dizziness or syncope or are in a peri-arrest situation should be considered for thrombolysis. Contra-indications include:

- history of haemorrhagic stroke,
- active intracranial neoplasm,
- recent (<2 months) history of intracranial surgery or trauma and
- active or recent internal bleeding (last six months).

Care should be taken if there is a bleeding diathesis, uncontrolled hypertension, non-haemorrhagic stroke in the last two months, surgery in the previous 10 days or a platelet count $<100x10^9$/L.

Patients who are felt to require thrombolysis but have a contraindication could be considered for catheter or open thrombolectomy (not currently performed at WAHT).

See Appendix 3 – Emergency Department guideline for thrombolysis in massive PE

3.5 Thrombosis and Cancer

Venous thrombosis and thromboembolism is a complication for patients with cancer who have a substantial risk of recurrent VTE and bleeding complications. Oral anticoagulant therapy is often problematic in patients with cancer due to drug interactions, malnutrition and vomiting. Liver dysfunction can lead to unstable levels of anticoagulation causing INR's to become erratic. Invasive procedures and thrombocytopenia caused by chemotherapy often require interruption of anticoagulant therapy. Lee, A (2003) demonstrated improved survival in cancer patients given LMWH compared to warfarin. Unlike vitamin K antagonists, low

molecular weight heparins have predictable pharmacokinetic properties and drug interactions. Cancer patients who have proven VTE should be treated with LMWH for at least six months and until the cancer is in remission, it is possible to reduce the dose to prophylaxis after six months.

Patients diagnosed with VTE have an increased rate of cancer diagnosis in the year following their DVT. At diagnosis a history and examination should be made looking for cancer. Routine tests should include a full blood count, liver function and bone profile. Smokers should have a CXR performed. Further investigations are only necessary if these initial measures reveal abnormalities.

3.6 Guidelines for the Management of patients receiving low molecular weight heparin (LMWH)

LMWH produces an immediate anticoagulant effect whereas oral anticoagulants act slowly and their effect builds up over 2-3 days. As a consequence, initially LMWH, followed by oral anticoagulation, is associated with significantly less extension of thrombosis and embolism than in oral anticoagulation therapy alone.

Treatment dose Enoxaparin (Clexane™) is given on a weight-adjusted basis of either 1.5mg/kg by subcutaneous injection once daily or 1.0mg/kg by subcutaneous injection twice daily

Patients are commenced on daily LMWH and continue on daily doses for at least 5 days while warfarin is commenced, and until the INR reaches 2.0 or above for two consecutive days/tests.

To ensure consistency of approach within primary and secondary health care the LMWH of choice in Worcestershire for the treatment of DVT & PE is enoxaparin (Clexane™).

Heparin is the most widely used parenteral anticoagulant. It is available as unfractionated heparin (UFH) and low molecular weight heparins (LMWHs).

Different heparins are not bioequivalent and should not be interchanged during treatment without the authority of the prescriber (BNF).

Advantages of LMWHs include ease of administration, no need for monitoring in most cases, fewer side effects and possibly improved efficacy. LMWH's are characterized by higher bioavailability and longer half-life, and do not require laboratory monitoring (Hirsh & Levine 1992). For patients within the Worcestershire Acute Hospital Trust, LMWH is the drug of choice where inpatients are receiving venous thromboembolism prophylaxis or treatment for DVT or PE. LMWHs are also used in the management of myocardial infarction and unstable angina and in the management of venous thromboembolism in pregnancy.

3.6.1 Cautions/Contraindications of Heparins

- Active bleeding
- Active peptic ulcer disease
- Known bleeding disorder (e.g. haemophilia)
- Thrombocytopenia (including heparin induced thrombocytopenia) (usually platelets $<50x10^9/L$)
- Severe renal disease (CKD 4 and 5, eGFR < 30 ml/min), creatinine clearance <30 ml/min or where a patient is suspected to have this degree of renal impairment.
- Hepatic failure
- Recent cerebral haemorrhage
- Recent eye/neurosurgery
- Uncontrolled severe hypertension
- Acute bacterial endocarditis
- Known allergy to unfractionated or low molecular weight heparin

See latest British National Formulary (BNF)

3.6.2 Prescribing LMWH

Weigh patient and document weight on patient drug chart, admission sheet and anticoagulant/warfarin chart if warfarin is prescribed.

The patient's weight must be established in kilograms (kg) at the start of therapy and, where applicable, during treatment. The weight must be accurately recorded. Renal function must be considered to reduce the risk of adverse effects from LMWH's in renal impaired patients.

Blood tests:

- Full blood count (FBC), INR, Liver function tests (LFTs)
- Renal function - urea & electrolytes (U&Es)
- Check for history of bleeding risk, acute peptic symptoms or other contraindications
- Check if patient is on drugs that may prolong bleeding time or affect platelet function (e.g. aspirin, NSAIDs, clopidogrel)

NB Delays in obtaining blood results should not delay initiation of the first dose but every effort must be made to base subsequent dosing on these results

Renal function should also be assessed prior to treatment. The renal function test should not delay the first dose of treatment but every effort should be made to base subsequent dosing on these results. Patients with an e-GFR of <30ml/min will require dose adjustment. In these patients, seek specialist advice before prescribing LMWH.

3.6.3 Administering LMWH

All staff caring for patients and administering LMWH should have the necessary training and competencies to ensure safe practice. Any gaps in competencies must be addressed by their line manager.

All staff involved in training patients to self-administer subcutaneous LMWH injections should have the necessary training/experience and competency to provide the teaching and training to the patient. They must ensure that the patient is observed and safe to take on the responsibility of injections.

3.6.3 The procedure

Inject into the S/C tissue of the anterolateral or posterolateral abdominal girdle, alternating from left to right side.

Do not expel the air bubble in the syringe. Vertically introduce the whole length of the needle into the thickness of the skin held between thumb and forefinger

Hold the skin throughout the procedure

Do not rub the injection site

The used needle should be disposed of in a sharps bin. When patients are discharged on LMWH they must be provided with a sharps box. The sharps boxes can be provided from ward stock and also the manufacturers of enoxaparin (Sanofi) will also supply sharps boxes

on request. The sharps boxes can then be disposed of through a community pharmacy and if necessary more sharps boxes obtained on prescription from their GP.

3.6.4 Side effects

Side effects of LMWH include bleeding, thrombocytopenia (low platelets), osteoporosis, hyperkalaemia, injection site reactions, and allergic reactions
(including urticaria, angioedema and anaphylaxis).

3.6.5 Monitoring of platelet counts

The risk of antibody-mediated heparin-induced thrombocytopenia also exists with LMWH's. Should thrombocytopenia occur, it usually appears between the 5th and 21st day following the beginning of LMWH treatment. Therefore, it is recommended that the platelet counts be measured before the initiation of therapy with LMWH. No routine measurement of platelet counts are required for patients on LMWH.

3.6.6 Heparin Induced Thrombocytopenia (HIT)

HIT is an uncommon but potentially life threatening complication; it is less likely to occur with LMWH. HIT should be considered under the following circumstances:

- Fall in platelet count of 50% or more from baseline, occurring 4-14 days after heparin commenced (N.B. may occur earlier if patients have received heparin within the past 100 days)
- Arterial or venous thrombosis occurring while patient on heparin
- Acute systemic reaction to IV bolus of heparin
- Skin lesions at heparin injection site

Refer to known patient allergies prior to prescribing

Where the patient has been admitted in the past 100 days to hospital and given heparin they have increased risk of HIT. HIT is rare after 14 days of treatment. If suspected, do not give further doses of LMWH until treatment discussed with Haematologist.

3.6.7 Haemorrhage

As with other anticoagulants, bleeding may occur at any site (see BNF for Adverse Effects). If bleeding occurs, the origin of the haemorrhage should be investigated and appropriate treatment instituted.

4.0 MONITORING TOOL

An audit following the described management will be carried out by the DVT/Anticoagulation Nurse at least annually using the standards within this guideline and the findings reported to the Haematology Directorate which will monitor progress against any action plans.

STANDARDS	%	CLINICAL EXCEPTIONS
All patients on treatment dose LMWH will have a weight documented	100	None
All suspected DVT diagnoses will follow the algorithm	75	None
All suspected PE diagnoses will follow the algorithm	75	None
All DVT's suitable for anticoagulation will be treated as per the policy	90	None
All PE's suitable for anticoagulation will be managed as per the policy	90	None
All patients are informed of the result of investigations within 2 hours	90	None

The monitoring will be performed by a retrospective review of patient notes. This will determine if the correct pathway is followed. Timing of requests will be found from the notes and the audit trails on WinPath and ICE OrderComms.

5.0 CONTRIBUTION LIST

Key individuals involved in developing the document

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Circulated to the following individuals for comments

Name	Designation

Circulated to the following Divisional Medical Directors for comment and circulation to their Directorates

Name	Division

Circulated to the chair of the following Committee's / Groups for comments

Name	Committee / Group

Worcestershire Acute Hospitals NHS Trust

DVT Information Sheet 1 – Suspected Deep Vein Thrombosis

You have shown signs that you might have a blood clot in the leg, a deep vein thrombosis (DVT). To confirm this we are awaiting an ultrasound scan of your leg. The scan should be in the next couple of days but until then we feel you can go home.

While at home there are a few precautions you must take and certain things to look out for:

- The leg may be painful and it is okay to take painkillers like paracetamol and codeine but you must not use aspirin or non-steroidal anti-inflammatory drugs (NSAID) e.g. ibuprofen, diclofenac, indomethacin.
- Try to rest the leg and not do too much walking or significant physical activity.
- If the leg becomes either more painful, more swollen, blue in colour or cold then you must contact the hospital immediately.
- If you develop any bleeding or bruising you must contact the hospital immediately.
- If you develop chest pain, shortness of breath or spit with blood in it you must attend A&E immediately.

Your follow-up is:

- Attend_____

  at_____am/pm on the _____/_____/20___

- Please telephone_____

  at_____am/pm on the _____/_____/20___

Your emergency contact is:

_____

DVT Information Sheet 2 – Deep Vein Thrombosis

You have been found to have a blood clot in your leg (deep vein thrombosis). About 1 in 1000 people each year get a DVT. The blood clot in the leg slows down the blood flow leading to pain, swelling and discolouration. Most DVTs are picked up because of leg swelling or pain but occasionally found when scans are done for other reasons. DVTs may be 'provoked' where something has caused it for example pregnancy, the oral contraceptive pill, operations, immobility and cancer, or 'unprovoked' where no obvious cause is found.

To stop the clot getting bigger or spreading you have been started on a drug to thin the blood. The blood clot will slowly dissolve over the next few weeks to months which should improve the pain and swelling. Wearing 'compression' stockings on the affected leg for two years will help the leg improve faster and reduce the chances of long term problems with the leg. Once the blood thinning treatment is finished and even when on treatment there is a chance of the blood clot getting worse or coming back therefore if the symptoms get worse or return then you must contact medical services.

You will be given a drug to thin the blood. It is important that you read the information that comes with the drugs which will discuss possible side-effects. The main side-effect we worry about is bleeding.

You should contact your GP if:

- You notice any bruising where you cannot remember knocking yourself or bleeding.
- Notice blood when you pass urine or move your bowel.

You should attend A&E if:

- You have the bruising or bleeding mentioned above and feel weak, dizzy or lightheaded.
- You bang your head and you have a headache or feel unwell.
- You cough up blood, get short of breath or have chest pain.
- You are sick and there is sick in the blood.
- You develop weakness, slurred speech or you lose feeling in your face or arm or leg.

The length of treatment will be decided by your GP but will depend if it is a provoked or unprovoked DVT, other medical problems and if how well you got on with the blood thinning drugs. It might be worth making an appointment in about a week's time with your GP so you can talk things through. If you attend an outpatient appointment or come into hospital it is important that you tell the doctor or nurse looking after you that you have had a DVT in the past. If you think you are pregnant it is important to see your doctor as soon as possible, this is especially important if you are still on warfarin.

First degree relatives (brothers, sisters, parents and children) are also at increased risk of DVTs if you have had an unprovoked DVT. They should also tell nurses or doctors if they come to hospital. Any female first degree relatives should avoid oestrogen containing contraceptive pills or hormone replacement therapy.

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DVT Information Sheet 3 – No deep vein thrombosis

It was thought that you may have had a blood clot in your leg (deep vein thrombosis (DVT)). The tests that we have performed have not shown any evidence of a DVT. The hospital staff looking after you should have told you why they think your leg is how it is and may have given some treatment or arranged further tests. It is now okay for you to go home but we would like you to take the following precautions:

- The leg may be painful and it is okay to take painkillers like paracetamol and codeine but you must not use aspirin or non-steroidal anti-inflammatory drugs (NSAID) (e.g. ibuprofen, diclofenac, indomethacin) for at least 24 hours if you have been given an injection of heparin or a tablet called rivaroxaban.
- If the leg is no better after a week then you should attend your GP.
- If the leg becomes either more painful, more swollen, blue in colour or cold then you must contact your GP or out of hours GP service.
- If you develop chest pain, shortness of breath or spit with blood in it you must attend A&E immediately.

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PE Information Sheet 1 – Suspected Pulmonary Embolism

You have shown signs that you might have a blood clot in your lung, a pulmonary embolism (PE). To confirm this we are awaiting a scan of your lung. The scan should be in the next couple of days but until then we feel you can go home.

While at home there are a few precautions you must take and certain things to look out for:

- Your chest may be painful and it is okay to take painkillers like paracetamol and codeine but you must not use aspirin or non-steroidal anti-inflammatory drugs (NSAID) e.g. ibuprofen, diclofenac, indomethacin.
- Try to rest and not do too much walking or significant physical activity.
- If your legs become either painful, swollen, blue in colour or cold then you must contact the hospital immediately.
- If you develop any bleeding or bruising you must contact the hospital immediately.
- If you develop worsening or new chest pain, worsening or new shortness of breath or spit with blood in it you must attend A&E immediately.

Your follow-up is:

- Attend_____

  at_____am/pm on the _____/_____/20___

- Please telephone_____

  at_____am/pm on the _____/_____/20___

Your emergency contact is:

Worcestershire NHS
Acute Hospitals NHS Trust

PE Information Sheet 2 – Pulmonary embolism

You have been found to have a blood clot in your lung (pulmonary embolism (PE)). About 1 in 3000 people each year get a PE. The blood clot in the lung slows down the blood flow leading to pain, shortness of breath and occasionally spit with blood in it. Most PEs are picked up because of shortness of breath or pain but occasionally found when scans are done for other reasons. PEs may be 'provoked' where something has caused it for example pregnancy, the oral contraceptive pill, operations, immobility and cancer, or 'unprovoked' where no obvious cause is found.

To stop the clot getting bigger or spreading you have been started on a drug to thin the blood. The blood clot will slowly dissolve over the next few weeks to months which should improve the pain and shortness of breath. Once the blood thinning treatment is finished and even when on treatment there is a chance of the blood clot getting worse or coming back therefore if the symptoms get worse or return then you must contact medical services.

You will be given a drug to thin the blood. It is important that you read the information that comes with the drugs which will discuss possible side-effects. The main side-effect we worry about is bleeding.

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You should contact your GP if:

- You notice any bruising where you cannot remember knocking yourself or bleeding.
- Notice blood when you pass urine or move your bowel.

You should attend A&E if:

- You have the bruising or bleeding mentioned above and feel weak, dizzy or lightheaded.

- You bang your head and you have a headache or feel unwell.
- You have new or worsening chest pain, shortness of breath or blood in your spit.
- You are sick and there is sick in the blood.
- You develop weakness, slurred speech or you lose feeling in your face or arm or leg.

The length of treatment will be decided by your GP but will depend if it is a provoked or unprovoked PE, other medical problems and if how well you got on with the blood thinning drugs. It might be worth making an appointment in about a week's time with your GP so you can talk things through. If you attend an outpatient appointment or come into hospital it is important that you tell the doctor or nurse looking after you that you have had a PE in the past. If you think you are pregnant it is important to see your doctor as soon as possible, this is especially important if you are still on warfarin.

First degree relatives (brothers, sisters, parents and children) are also at increased risk of PEs if you have had an unprovoked PE. They should also tell nurses or doctors if they come to hospital. Any female first degree relatives should avoid oestrogen containing contraceptive pills or hormone replacement therapy.

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PE Information Sheet 3 – No pulmonary embolism

It was thought that you may have had a blood clot in your lung (pulmonary embolism (PE)). The tests that we have performed have not shown any evidence of a PE. The hospital staff looking after you should have told you why they think you are unwell and may have given some treatment or arranged further tests. It is now okay for you to go home but we would like you to take the following precautions:

- The chest may be painful and it is okay to take painkillers like paracetamol and codeine but you must not use aspirin or non-steroidal anti-inflammatory drugs (NSAID) (e.g. ibuprofen, diclofenac, indomethacin) for at least 24 hours if you have been given an injection of heparin or a tablet called rivaroxaban.
- If your problems are no better after a week then you should attend your GP.
- If the leg becomes painful, more swollen, blue in colour or cold then you must contact your GP or out of hours GP service.
- You have new or worsening chest pain, shortness of breath or blood in your spit you must attend A&E immediately.