Northern Care Alliance
NHS Foundation Trust

Guideline for the Investigation and Management of Venous ThromboEmbolism (VTE)

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Contents

1. Overview

VTE is one of the top three causes of cardiovascular death.

This guideline provides evidence-based recommendations for the management of people with suspected or confirmed VTE within an inpatient and outpatient setting. Guidance is provided for the investigation, diagnosis and treatment of varying types of VTE, including deep vein thrombosis (DVT), pulmonary embolism (PE), catheter related thrombosis (CRT), superficial venous thrombosis, unusual site thrombosis (UST), cerebral venous sinus thrombosis (CVST) and cancer associated thrombosis (CAT).

This document provides instruction on the initial diagnostic pathway for all patients with suspected VTE, incorporating 2020 guidance and quality standards produced by the National Institute for Health and Care Excellence (NICE NG158 & QS201).

This document provides generic guidance on the initial management and anticoagulation of all newly diagnosed VTE, including use of the Direct Oral AntiCoagulant (DOAC) agents. For appropriate patient groups, this document provides guidance on use of ambulatory protocols.

Guidance is also provided on additional management options such as systemic reperfusion therapy (thrombolysis) and when to consider interventional radiology or surgery in the context of high-risk PE or iliofemoral deep vein thrombosis

This document provides guidance on follow up of patients with confirmed VTE, in particular regarding the decision-making process for extended duration anticoagulation (no scheduled stop date) in patients with unprovoked VTE. In addition, this document provides guidance on estimation of VTE recurrence risk, bleeding risk and thrombophilia screening which can be documented and used to inform decision making on extended duration anticoagulation

This guideline is to be used in support of (but not instead of) senior clinical decision making. The recommendations within may lack direct relevance to individual circumstances and any investigations or treatments proposed should be discussed with the individual patient.

Always remember the following:

“No decision about me, without me” – Always talk to the patient about their options and your recommendations.

and

“Guidelines guide, clinicians decide” – NICE guidance is written with an 80/20 strategy in mind; in most cases it will be correct to directly follow the guidelines. In some cases, senior clinicians may deviate from guidance with appropriate documentation and justification.

If you have any concerns about the content of this document, please contact the author or advise the Document Control Team.

2. Scope

This guidance is for use across all NCA care organisations treating adult patients. This guideline does not apply to paediatrics given the alternative pathological causes, treatment options and longer-term management strategies applicable to children.

VTE can affect anyone in the hospital or in community settings and present in a variety of ways. All staff providing care to hospitalised inpatients should be aware of the risk factors for VTE and understand when to raise concern about possible VTE diagnosis. All staff groups need to have access to and working knowledge of this guideline.

Associated Documents

Guideline documents on VTE for use in specific patient populations are linked here but can also be found on the policy hub at the VTE service page This also includes QRG templates.

- Acute Management of Thromboembolic Disease in Pregnancy & the Puerperium - CPWCO62
- Policy for the Prevention of Hospital Acquired Thrombosis Salford–TC36(07). BRO-CPSU017
- Cerebral Venous Sinus Thrombosis Policy - Salford-TWCG22(14).
- Therapeutic dose LMWH anticoagulation - Salford-P130277(02)
- Adult Loading doses Policy. BRO-EDT017
- Enoxaparin in Newly Diagnosed VTE. NCA-PGD150

3. Background

Venous thrombosis refers to the formation of potentially deadly blood clots in the deep veins of the body. Once formed, a clot can slow or block normal blood flow, or break loose and travel to the lungs. A clot that travels within the circulation to the lungs is called a pulmonary embolism. Deep vein thrombosis (DVT) and pulmonary embolism (PE) are known collectively as venous thromboembolism (VTE).

VTE is one of the top three cardiovascular killers. It has an incidence rate of approximately 1:1000, which rises to between 2-7:1000 in patients aged >70.[1] VTE associated with hospitalisation is the second highest reason for loss of disability adjusted life years (DALY) in high income countries, and the highest in low to middle income countries. It is responsible for more DALYs lost than nosocomial pneumonia, catheter related bloodstream infections and adverse drug events. It is also responsible for more patient deaths/year than trauma, AIDS and several forms of cancer combined.

The diagnosis of VTE is not always straightforward; many other conditions may have similar symptoms. Failure to diagnose a case of VTE correctly may result in a patient not receiving the correct treatment and potentially suffering a fatal Pulmonary Embolism (PE) as a result. However, the reference standard tests for VTE come with risks of radiation and other healthcare associated harms. It is important to be vigilant regarding suspicion of disease, but also use non-invasive testing methods where possible to reassure patients and mitigate the harms of over-testing. Clinical judgement should be exercised at all times and informed individual patient preferences supported. However, reasons for deviation from this guidance should be documented.

4. What is new in this version?

This document is an amalgamation of previous Salford, Pennine and Bury/Rochdale guidelines, with updates to concur with recent guidance produced from the National Institute for Health and Care Excellence (NICE), the European Society of Cardiology (ESC) the British Committee for Standards in Haematology (BCSH) and the British Thoracic Society (BTS).

This document replaces P130213(01) V4.1 and CPSU067 V1.3

Updates include a separate dedicated section on identification and hyperacute management of high risk (massive/life threatening) pulmonary embolism and iliofemoral deep vein thrombosis. This document also now contains hyperlinks to existing NCA policies for VTE management, updates on the potential use of DOAC therapies in suspected VTE, unusual site VTE and thrombophlebitis and novel scores to predict bleeding risk.

5. Guideline

Any assessment for potential VTE begins with a thorough history, clinical examination and baseline investigations (including routine blood tests, chest XR, ECG, observations as required). If a patient presents with signs or symptoms of both DVT and PE, carry out initial diagnostic investigations for either DVT or PE (not both), basing the choice of diagnostic investigations on clinical judgement.

If a patient presents with symptoms of unusual site VTE such as suspected upper limb DVT, superficial thrombophlebitis, splanchnic vein thrombosis or cerebral venous sinus thrombosis, follow the relevant section in this guideline or the hyperlink to separate NCA wide guidance help at the thrombosis hub.

Once a VTE has been diagnosed, subacute management consists of therapeutic dose anticoagulation, provocation assessment (to determine duration of therapy), further investigations for cancer if deemed necessary, documentation of bleeding risk, medication guidance and arranging appropriate follow up.

Following the initial treatment course (usually 3 months), clinical teams need to consider whether anticoagulation can stop, or whether there is a need for extended duration (no scheduled stop date) therapy. This decision is based on initial tolerance of anticoagulation, provocation status, previous VTE history and can also be guided by clinical factors / decision rules.

NICE guidelines were updated in 2020 and contain guidance on the entire patient journey for VTE.[2] They can be accessed here. European Society of Cardiology (ESC) guidelines on the management of acute pulmonary embolism were updated in 2019 to include clear definitions of haemodynamic instability, quantified radiation dosing in PE imaging and a dedicated management algorithm for high risk PE.[3] The guidelines are open access and can be found here. British Thoracic Society (BTS) guidelines on outpatient PE management were published in 2018.[4] The guidelines are open access and can be found here.

A visual summary of the recommended diagnostic and initial management process in suspected VTE has been produced by NICE and can be found here. Quality standards for VTE management produced by NICE and the BTS can be found here and here.

5.1 Investigation of Suspected DVT

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. Key risk factors within the last three months should be considered and documented as part of the initial assessment for VTE.

Bilateral leg swelling is rarely a result of VTE but should prompt consideration of other pathologies such as lymphoedema, congestive cardiac failure, iatrogenic medication side effects, cellulitis, lipodermatosclerosis and post thrombotic syndrome. Investigation of DVT in patients with bilateral leg swelling should trigger a senior review prior to referral.

If further assessment to exclude DVT is required ***Record a Dichotomised Wells score*** as per NICE guidance[5]:

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 *likely*	2 points or more
DVT *unlikely*	1 point or less

‘DVT Likely’ / High probability Wells score

Offer patients in whom DVT is suspected and with a ‘Likely’ probability Wells score a duplex compression ultrasound scan performed by a vascular sonographer.

Same day vascular imaging is available at several NCA sites and should be considered the standard of care in accordance with NICE guidance. Portable bedside imaging for inpatients can be considered when necessary. In patients with high likelihood of DVT a D-dimer should be sent to inform subsequent management (not the initial decision to ultrasound).

Contact numbers for vascular sonography are as follows:

SCO 0161 206 2144 (extension 62144 from any hospital phone)
BRO 0161 627 8497 (Oldham), 0161 778 2661 (Bury/Fairfield) and 01706 517 850 (Rochdale)

If a scan slot is not available within 4 hours and the patient is not currently anticoagulated, offer interim therapeutic anticoagulation until the scan is completed.

Consider the bleeding risks of anticoagulation and advise the patient accordingly (including omission / prophylactic dosing) if the benefits are outweighed by risks.

Recommended drug and dosing options (including common interactions, contraindications and pitfalls) for interim therapeutic anticoagulation in suspected VTE are listed in Appendix 1.

If the patient is being discharged to return for imaging at a later date, ensure they are provided with written information on the following:

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

Relevant SCO and BRO information leaflets are available on the NCA policy hub under the vascular section or generic via the Thrombosis UK website.

If a whole leg scan is reported as negative by a vascular sonographer, interim anticoagulation should be stopped, an alternative diagnosis recorded and the patient reassured. Tell the person that it is not likely they have DVT. Discuss with them the signs and symptoms of DVT and when and where to seek further medical help

There is good evidence to support the safety of withholding therapeutic anticoagulation following a single negative whole leg duplex compression ultrasound scan, without further investigation[6, 7]. These patients have a subsequent 3-month VTE event rate of <1% (0.25 to 0.89%). This event rate is similar to that seen following discharge after negative D-dimer in patients with an 'unlikely' Wells score[8]. Advise these patients 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 as required.

If a proximal ultrasound scan has been performed by a general sonographer, the scan result is inconclusive below the knee and/or ongoing suspicion of DVT remains (high Wells score and positive d-dimer), patients should be offered a repeat scan in 7-10 days, with clinical follow up. Anticoagulation should be stopped during this period unless there is another clear clinical indication. A repeat inconclusive or negative scan at this stage should be considered as excluding clinically relevant VTE and the patient reassured with no further planned investigations unless clinically indicated, as above.

If either scan result is positive for VTE, follow the appropriate 'General Management of confirmed venous thromboembolism' subsection 5.5.

‘DVT Unlikely’ / Low probability Wells score

Offer patients in whom DVT is suspected and with a low probability Wells score a D-dimer test as per NICE guidance[5].

Patients aged 50 and under → If the D-dimer is negative then DVT can be safely excluded. Advise these patients 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 as required.

Patients aged 51 and over → In this age group, there is good evidence to suggest that raising the cut point of the D-dimer assay to an age adjusted threshold in suspected VTE improves specificity without compromising sensitivity.[9-12] This practice is now recommended in NICE guidance.[2] Age adjusted thresholds can vary by assay and should be interpreted with caution, using online calculators as required. All labs across the NCA using the HaemosIL D-Dimer immunoassay with an upper limit of 230-250ng/mL can apply an age adjusted threshold (AAT) as follows:

AAT formula = Age multiplied by 5. **(**HaemosIL D-dimer immunoassay)

As an example, the cut point for an 80 year old patient becomes 400ng/mL, rather than the standard cut point of 230ng/mL. Values below 400ng/mL in this population can therefore be considered negative and DVT excluded in patients with an accompanying ‘unlikely’ DVT clinical probability score. Current research suggests using the age adjusted strategy with caution in those patients who are critically unwell (hypoxia, hypotension, shock), those who have had symptoms for longer than 7 days or those who have represented with the same symptoms.[13, 14]

If the D-dimer result is positive offer a whole leg compression ultrasound scan.

Follow the guidance on page 6/7 regarding practical arrangement of vascular ultrasound imaging and interim therapeutic anticoagulation pending scan. If the patient is being discharged to return for imaging at a later date, ensure they are provided with written information on the following:

- Symptoms and signs to look out for, including the potential complications of thrombosis and of treatment.
- Direct contact details of a healthcare professional or team with expertise in thrombosis who can discuss any new symptoms or signs, or other concerns
- information about out-of-hours services they can contact

Relevant SCO and BRO information leaflets are available on the NCA policy hub under the vascular section or generic via the Thrombosis UK website.

If the scan result is negative (or negative above but inconclusive below knee), anticoagulation should be stopped, an alternative diagnosis recorded and the patient reassured. No further imaging is necessary.

If the scan result is positive for DVT, follow the appropriate ‘General Management of confirmed venous thromboembolism’ subsection 5.5.

Bilateral Doppler USS should only be requested after senior review – these require double slots and the presence of bilateral leg swelling is likely to signal alternative diagnoses.

Suspected Upper Extremity DVT (UEDVT)

If a patient presents with signs or symptoms of UEDVT carry out an assessment of their general medical history and a physical examination to exclude other causes. Key risk factors for UEDVT within the last three months should be considered and documented, to include active malignancy, known anatomical distortion and/or recent vascular intervention (indwelling venous catheters).

Request a CXR in all patients with suspected upper limb DVT to asses for a potential contributory cause, such as cervical rib, apical tumour or other compressive lesion.

There are no validated clinical probability scores relevant to investigation of suspected UEDVT. In addition, the D-dimer assay at a standard cut point has a sensitivity of between 73 to 99% on recent evaluation[15]. As such, these methods cannot be used for exclusion of UEDVT reliably.

Offer patients in whom UEDVT is suspected a compression ultrasound scan of the affected upper extremity.

Same day vascular imaging is available at several NCA sites and should be considered the standard of care in accordance with NICE guidance. Contact numbers are provided earlier in this document.

If a scan slot is not available the same day within 4 hours and the patient is not currently anticoagulated, offer the patient a daily treatment dose of interim therapeutic anticoagulation until the scan is completed.

Consider the bleeding risks of anticoagulation and advise the patient accordingly if you feel the benefits are outweighed by the risks. Drug and dosing options (including common interactions, contraindications and pitfalls) for therapeutic anticoagulation in suspected or confirmed VTE are listed in Appendix 1. Please note, guidance from the British Society for Haematology, Haemostasis and Thrombosis Taskforce now supports the use of DOAC therapy in cases of UEDVT, within appropriate limits for weight and renal function (as per Appendix 1).[16]

If the scan result is negative, anticoagulation should be stopped, an alternative diagnosis recorded and the patient reassured.

If the scan result is inconclusive, discuss with a consultant radiologist regarding the potential for definitive imaging via CT venography or MRI.

If the scan result is positive for DVT, follow the appropriate 'General Management of confirmed venous thromboembolism' subsection 5.5.

There is no evidence regarding the safety of ambulatory pathways for investigation of suspected UEDVT. However, the embolic and complication rates from confirmed UEDVT are very low and it is unusual to admit patients for assessment/investigation. Clinical teams should consider presenting features, exclusion criteria for other VTE ambulatory pathways, patient preference and gestalt risk assessment. A shared decision with the patient regarding management should follow.

5.2 Investigation of Suspected PE

If a patient presents with signs or symptoms concerning for PE, carry out an assessment of their general medical history, a physical examination, an ECG and a chest X-ray to exclude other causes.[17, 18] Consider Key risk factors for VTE ***over the last 90 days.***

If further assessment to exclude PE is required ***record a gestalt assessment;*** this is your overall clinical impression of the likelihood of pulmonary embolism, based on the history, examination and initial investigations. ***This should be recorded as unlikely, uncertain or likely.*** If an objective score is preferred to gestalt assessment, use the Geneva score to identify those patients unlikely to have an acute PE (Score <4).

In patients with an unlikely gestalt assessment (OR a Geneva score <4), there is evidence that application of the Pulmonary Embolism Rule-out Criteria (PERC) can reduce imaging requests whilst maintaining a high sensitivity[19, 20]. This approach is supported in NICE 2020 guidance.

Apply the PERC score to these patients as below:

Clinical feature	Points
Age ≥ 50	1
Unilateral Leg Swelling	1
Heart Rate ≥ 100	1
Oxygen saturations <95% on room air	1
Prior history of venous thromboembolism	1
Trauma or Surgery within the last 4 weeks	1
Haemoptysis	1
Exogenous oestrogen therapy or pregnancy	1
Total Score	

A PERC score of 0 in patients combined with an unlikely gestalt assessment (OR Geneva score of <4) has been shown to reduce the post-test possibility of acute PE to <1.8%. These patients should be reassured and further invasive investigations avoided unless specific clinical concerns persist (such as recurring symptoms, high NEWS score or severe unexplained pleuritic pain).

In patients unsuitable for PERC (likely gestalt or Geneva >3) or those suitable for PERC with a score ≥1, offer further evaluation to exclude PE with a dichotomised Wells score[5]:

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 *likely*	More than 4 points
PE *unlikely*	4 points or less

‘PE Likely’ / High probability Wells score

In patients with high likelihood of PE the D-dimer assay offers no additional diagnostic information and should not be ordered routinely. These patients should proceed directly for definitive imaging.

Offer patients in whom PE is suspected and with a ‘PE Likely’ Wells score a CT Pulmonary Angiogram (CTPA), to be carried out immediately. For people with a specific allergy to contrast media or a high risk from irradiation (age <35 as example), consider a V/Q SPECT or V/Q Planar scan as an alternative to CTPA.

If a scan slot cannot be performed immediately (within 1 hour of referral) and the patient is not anticoagulated, offer interim therapeutic anticoagulation until the scan is completed.

Consider the bleeding risks of anticoagulation and advise the patient accordingly. Drug and dosing options (including common interactions, contraindications and pitfalls) for therapeutic anticoagulation in suspected or confirmed VTE are listed in Appendix 1.

If the scan result is negative, anticoagulation should be stopped, alternative diagnoses considered and the patient counselled and managed as appropriate.

If the scan result is positive for PE, follow the appropriate ‘General Management of confirmed venous thromboembolism’ subsection 5.5.

‘PE Unlikely’ / Low probability Wells score

Offer patients in whom PE is suspected and with a ‘PE Unlikely’ Wells score a D-dimer test.

Patients aged 50 and under → If the D-dimer is negative then PE can be safely excluded. Advise these patients that it is not likely they have PE and discuss with them the signs and symptoms of PE, and when and where to seek further medical help as required.

Patients aged 51 and over → In this age group, there is good evidence to suggest that raising the cut point of the D-dimer assay to an age adjusted threshold in suspected VTE improves specificity without compromising sensitivity.[9-12] This practice is now recommended in NICE guidance. Age adjusted thresholds can vary by assay and should be interpreted with caution, using online calculators as required. All labs across the NCA using the HaemosIL D-Dimer immunoassay with an upper limit of 230-250ng/mL can apply an age adjusted threshold (AAT) as follows:

AAT formula = Age multiplied by 5. **(**HaemosIL D-dimer immunoassay)

As an example, at SCO the cut point for an 80 year old patient becomes 400ng/mL, rather than the standard cut point of 250ng/mL. Values below 400ng/mL in this population can therefore be considered negative and DVT excluded in patients with an accompanying ‘unlikely’ DVT clinical probability score.

Current research suggests using the age adjusted strategy with caution in those patients who are critically unwell (hypoxia, hypotension, shock), those who have had symptoms for longer than 7 days or those who have represented with the same symptoms following initial reassurance.[13, 14]

If the D-dimer result is positive offer the patient a CTPA scan to further assess for PE.

For people under 35 years of age who are at low risk of deterioration and do not require hospital admission, or those with an allergy to contrast media, consider V/Q SPECT or V/Q Planar scan as a first line alternative to CTPA. For a V/Q scan to be diagnostic, the CXR must be clear and there should be no chronic lung disease or left ventricular dysfunction. If in doubt, discuss with a senior radiologist.

Where available, V/Q imaging can be ordered locally as follows:

SCO: order via EPR and contact nuclear medicine on 68525 within working hours.
BRO: discuss with nuclear medicine at NMGH

V/Q imaging scans report a probability rather than a definitive diagnosis of PE. A report indicating low probability of PE safely excludes the disease. Advise these patients that it is not likely they have PE and discuss with them the signs and symptoms of PE, and when and where to seek further medical help. VQ scans reported as high probability should be regarded as positive.

Where VQ scans are reported as moderate probability reaching a final diagnosis can be difficult. Where clinical suspicion is low (but scan shows moderate probability) approximately 16% of patients may still have pulmonary embolus. These cases should be reviewed on an individual basis to decide whether to treat as PE or pursue a CTPA for confirmation.

Outpatient Management of Suspected Pulmonary Embolism

Patients attending any acute care area (Emergency department, Same Day Emergency Care (SDEC) area, Acute Medical Unit etc..) with suspected PE requiring imaging can be managed in an ambulatory fashion if they are confirmed as low risk using any *validated* risk stratification tool. The risk of early complications in this setting can be calculated using the widely validated simplified Pulmonary Embolism Severity Index (sPESI)[21-23]. Other validated risk stratification tools are available through online calculators, such as the PESI score and HESTIA criteria.

The sPESI is calculated as follows:

Clinical feature	Points
Age >80	1
Active Cancer	1
History of chronic cardiopulmonary disease	1
Heart rate ≥ 110	1
Systolic BP ≤ 100mmHg	1
Oxygen Saturation <90% on room air	1
Total SPESI Score	

Patients with suspected PE and an SPESI score of 0 (or a PESI score <3 / HESTIA 0) should routinely be offered outpatient investigation and management. However, a score of ≥1 carries a predicted short-term mortality of 8.9% or higher and usually warrants admission for expedited imaging and observation. ***These patients must be discussed with or reviewed by a consultant/senior decision maker if ambulatory care is being considered.*** In addition to validated scoring systems, document the NEWS and social history during assessment and share the final decision on ambulatory vs inpatient care with the patient whenever possible, based on overall risk assessment and patient preference.[24]

If a decision is made to manage a person on an outpatient VTE pathway, ensure interim dosing of therapeutic anticoagulation (using Appendix 1) and arrange a scan within 24h, in line with BTS standards. Agree a plan for monitoring and follow up, provide written information on the following:

- Potential complications of VTE and treatment
- Direct contact details for the accountable clinical team who can discuss any new issues
- Information on out of hours services they can contact if their team is unavailable.

Relevant SCO ('testing for blood clots') and BRO information leaflets are available on the NCA policy hub under the vascular section or generic via the Thrombosis UK website.

A QRG for the outpatient management of pulmonary embolism can be found in Appendix 2.

5.3 Investigation of suspected VTE in pregnancy and the puerperium

Separate NCA guidelines exists for the emergency department (ED) management of people who are pregnant or have recently given birth, and for the investigation and management of suspected VTE in pregnancy and the puerperium, including guidance on breastfeeding:

Wom95(05)a V7: Pregnant and/or women who have recently given birth attending the ED
CPWC062 v6: Thromboembolic disease in pregnancy and the puerperium

Management of suspected VTE in pregnancy and the puerperium across the NCA is essentially similar to non-pregnant patients, but with specific differences as follows:

- In suspected PE, ensure a thorough clinical assessment of the lower limbs. The first imaging test should be an ultrasound lower limb scan if signs/symptoms of DVT are present.
- In suspected PE requiring lung imaging, the person should be counselled regarding the risks of irradiation and the options discussed in detail. Supporting literature with radiation estimates can be found here; in both V/Q and CTPA, the absolute risks are very small.
- **Only LMWH or UFH can be used in the Emergency Department to provide therapeutic dose anticoagulation in pregnancy and the post-partum period.**
- If required, treatment dose anticoagulation should be prescribed based on booking/early pregnancy weight. Recommendations on periprocedural breast feeding are detailed in the policy above. **All DOAC and VKA agents are absolutely contraindicated.**
- Pregnant people of any gestation with suspected VTE can be managed via normal ambulatory protocols in accordance with national guidance, if it is felt safe to do so.
- When it is considered unsafe to manage via ambulatory pathways, clinical teams should obtain the relevant diagnostic imaging on the day of attendance, to ensure timely diagnosis.
- People >20/40 gestation or within 3 weeks of birth *who require hospital admission* to facilitate imaging or for ongoing medical management ***cannot be admitted to the SCO or BRO*** sites given the lack of on-site obstetric cover; they require transfer to their booking hospital (or preferred obstetric hospital if not booked) and discussion with the obstetric team.
- If VTE is confirmed, continue therapeutic anticoagulation, inform Obstetrics at the booking hospital and discuss referral to a joint obstetric/haematology clinic.

The role of D-dimer in pregnant patients with suspected VTE remains unclear. The D-dimer is likely to rise with gestational age. However, if a pregnant person with suspected PE has a negative D-dimer many experts feel this is sufficient to exclude VTE without imaging.

A recent systematic review and meta-analysis reported a 3-month VTE rate of 0.32% (95% CI 0.06 to 1.83) in pregnant patients with suspected VTE left untreated after a negative d-dimer.[25] Pooled sensitivity for D-dimer was 99.5% (95% CI 95.0-100.0). In addition, a prospective cohort study published in NEJM reported the use of YEARS clinical criteria and D-dimer testing to result in avoidance of CTPA in 65% of pregnant patients with suspected PE attending during the first trimester.[26] However, the recent NIHR DiPEP study reports poor performance of the D-dimer as a prognostic tool in a mixed case control cohort.[27] RCOG green top guidelines do not recommend D-dimer use at present.

As such, any decision taken to exclude VTE in pregnancy without imaging based on an algorithm involving D-dimer should be approved by a consultant / senior clinician with clear documentation, shared decision making and appropriate safety netting.

5.4 When to consider and how to deliver systemic thrombolysis in VTE

High Risk (Massive) Pulmonary Embolism

All patients require immediate therapeutic anticoagulation on confirmation of PE diagnosis. Higher risk patients can also benefit from consideration of acute reperfusion strategies. High risk PE is NOT defined by clot burden or hypoxaemia. A high-risk PE is essentially one with ongoing haemodynamic instability and clinical evidence of shock.

Ongoing haemodynamic instability has been defined in the recent iteration of ESC guidance as any 1 of the following rows:

CARDIAC ARREST	Defined as any need for CPR		
OR **OBSTRUCTIVE SHOCK**	Defined as Systolic BP <90mmHg or vasopressors required to achieve a systolic BP of ≥90mmHg despite adequate filling status	**AND**	Evidence of end-organ hypoperfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate)
OR **PERSISTENT HYPOTENSION**	Defined as systolic BP <90mmHg or systolic BP drop ≥40 mmHg, lasting longer than 15 min and not caused by new-onset arrhythmia, hypovolaemia, or sepsis	**AND**	Evidence of end-organ hypoperfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate)

The first step in managing high risk PE is to Initiate immediate therapeutic anticoagulation

Start therapeutic anticoagulation for patients with high risk PE using an IV bolus followed by infusion of UnFractionated Heparin (UFH) OR a single therapeutic dose of subcutaneous LMWH (dosed as per Appendix 1). These agents can be given *in addition to* systemic thrombolysis and should not be delayed while discussions on thrombolysis are taking place.

When using UFH, treatment begins with a slow intravenous bolus of IV heparin dosed at 75 units/kg over 3-5minutes (maximum dose of 8000 units, elderly patients max 5000units, renal impairment (CrCl<30mls/min) max 2500units). A maintenance infusion follows, dosed at 18units/kg/hr adjusted at 4 hours as per APTT results and continued for at least 24 hours prior to commencing LMWH. Further guidance is available in the SCO UFH policy document, available via the NCA policy hub. Ensure accurate prescribing as per local agreements.

The second step is to consider systemic reperfusion therapy

Patients with PE who are in shock have a predicted short-term mortality of >15% [28]. This can be substantially reduced with reperfusion therapy. However, this must be balanced against the individual risk of major bleeding. Patients should be counselled where possible and understand the risks and benefits of reperfusion therapy in addition to therapeutic anticoagulation. The risk of death is approximately halved with thrombolysis in this context; the risk of haemorrhagic stroke increases by approximately 1.8%; the risk of major bleeding increases by approximately 9%.[29]

Systemic pharmacological thrombolysis should be administered using t-PA (alteplase). Alteplase can be sourced from the ED, ICU or using local systems (such as 'find that drug' online repository). For all conscious patients >65kg, deliver in 2 stages as follows:

1. Give a single 10mg bolus of alteplase (Actilyse) over 1-2 minutes
2. Commence a 90mg infusion of alteplase (Actilyse) over 2 hours via syringe pump.

In patients weighing <65kg the total dose over both stages should not exceed 1.5mg/kg as described in the table below.

Weight	IV Bolus (1-2 minutes) mg	Subsequent infusion (over 2 hours) mg
45 kgs	10	55
50 kgs	10	65
55 kgs	10	70
60 kgs	10	80
65 kgs	10	90

Alteplase comes in 50mg or 100mg vials and can be reconstituted in sterile water to a 1mg/mL or 2mg/ml solution (See Appendix 3). If cardiac arrest is imminent (peri-arrest state) or confirmed, some authors recommend giving a 50mg initial bolus followed by a 50mg infusion over the subsequent 2 hours, although evidence to support this practice is limited [30]. Prolonged CPR should be considered (60-90 mins) following thrombolysis for cardiac arrest from PE.

Contraindications to systemic thrombolysis should be considered prior to administration. In addition, specific factors suggesting a higher bleeding risk with systemic thrombolysis should be considered in the decision making process. The relative importance of contraindications/bleeding risk depends on the strength of the indication. There is equal risk to life from omitting reperfusion therapy in patients critically ill with high risk PE as there is from bleeding complications of therapy:

Major contraindications	Relative Contraindications	Increased bleeding risk with thrombolysis
Active Intracranial neoplasm	Severe uncontrolled hypertension	>75 years of age
Recent (<8 weeks) intracranial/spinal surgery	Non-haemorrhagic stroke >3 months ago	Increased BMI
Haemorrhagic stroke	Surgery within previous 10 days	High HAS-BLED score
Active bleeding or recent significant internal bleeding	Pregnancy	
	Non-haemorrhagic stroke within last 3 months	
	Active neoplastic disease	

Thrombolysis should ideally be administered in a monitored environment with rapid access to multidisciplinary senior clinicians, such as the Emergency Department resuscitation room, medical high care area, critical care/intensive care unit or theatre recovery area. If there is good clinical response to thrombolysis, convert UFH to LMWH at 24h post alteplase administration. Further guidance on anticoagulation immediately post thrombolysis can be found here.

A QRG for systemic thrombolysis in high risk PE can be found in Appendix 3.

Intermediate Risk (Submassive) Pulmonary Embolism

ESC guidelines define intermediate risk PE as those confirmed cases with a raised PESI/SPESI score, but without high risk features of haemodynamic instability.[3] Intermediate risk is further stratified into high and low based on evidence of RV dysfunction/strain, as per the table below:

Early mortality risk		Indicators of risk			
		Haemodynamic instability	PESI>2 or SPESI >0	RV dysfunction on TTE or CTPA	Elevated cardiac troponin levels
High		+	+	+	+
Intermediate	Int-High	-	+	+	+
	Int-Low	-	+	One (or none) positive	
Low		-	-	-	-

All patients with intermediate risk PE should be commenced on therapeutic anticoagulation and admitted for observation. People with Intermediate-High risk PE represent a group with RV strain who are at risk of decompensation. However, recent trial evidence reports no overall mortality benefit to systemic thrombolysis for intermediate risk PE and no improvement in longer term outcomes such as chronic pulmonary hypertension.[29, 31] These patients should be anticoagulated and carefully monitored in a higher care area initially and only considered for systemic thrombolysis in the event of clinical deterioration suggestive of shock, or at consultant discretion.

All patients with intermediate risk PE should be admitted to hospital for serial observation over 24-48 hours and consideration of cardiac monitoring.

What to do when systemic thrombolysis is absolutely contraindicated or has failed

In this scenario, ensure accurate risk stratification (CTPA/echo/cardiac biomarkers/USS proximal lower limb veins/bloods/functional assessment and frailty score) and explore alternative treatment options through consultant level discussion. This is best achieved by direct referral to local interventional radiology services or a specialist respiratory centre (Manchester Foundation Trust, Wythenshawe campus). Referral should go through the respiratory team on call at Wythenshawe initially, to discuss options and potential for transfer. If agreed, the patient should be transferred to a critical care bed at Wythenshawe to facilitate bedside review and discussion by the specialist MDT. Treatment options include the following:

- **Catheter directed clot retrieval / pharmacological thrombolysis**
  Right heart catheterisation under imaging guidance and subsequent clot extraction, ultrasound dissolution using the EKOS catheter, mechanical fragmentation or directed low dose thrombolysis are all potential treatment options in this population[32].
- **Inferior vena cava filter placement**
  Prevention of further embolic burden in cases of known DVT with an absolute contraindication to anticoagulation.
- **Surgical Embolectomy**
  Direct clot retrieval following thoracotomy and extra corporeal membrane oxygenation

These cases are complex. They require consultant level discussion on an individual case by case basis once a degree of cardiovascular stability has been achieved.

Acute iliofemoral or whole leg DVT

Use NICE 2020 guidelines to prompt referral to vascular services for consideration of advanced intervention, as below:

Consider catheter-directed thrombolytic therapy for patients with symptomatic iliofemoral DVT who have all of the following:

- ***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.***

These patients should be discussed with the responsible medical consultant and require urgent discussion on a case by case basis with the local on call vascular surgery team. Contact details are available as follows:

BRO Vascular on call team – Bleep 7424 between 8-5 then via switch on 01616240420
MFT Vascular on call team – via switchboard on 03003309444

Prior to contacting vascular surgery, ***ensure that therapeutic anticoagulation is commenced*** using Appendix 1. In the situation where a surgical procedure may be imminent, initial anticoagulation with LMWH or UFH is preferable (to ensure ease of monitoring and/or reversal) rather than DOAC therapy.

5.5 General Management of Confirmed VTE

Generic initial management of confirmed VTE consists of the following 4 pillars:

(1) Assessment of provocation and ongoing VTE risk
(2) Consideration of malignancy screening in the context of unprovoked VTE
(3) Estimating and mitigating bleeding risk
(4) Commencing therapeutic anticoagulation for an initial period of 3 months

Assessment of Provocation and Ongoing VTE Risk

The duration of treatment for all VTE and the need for ancillary investigations are influenced by a judgement on the risk of potential VTE recurrence. This depends on provocation and risk factors at the time of disease, in particular whether these risks were transient or expected to continue (permanent). VTE occurring in the context of a transient risk factor is often referred to as 'provoked'. The definition of a provoked VTE provided by the National Institute of Health and Care Excellence (NICE) in the 2020 guideline update is as follows:

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

Other provoking risk factors include active cancer, pregnancy, intravenous drug use and chronic cardiorespiratory failure.[33] Of note, the dichotomous terms of 'provoked' or 'unprovoked' VTE can sometimes lead to clinical uncertainty. It is preferable to focus on the transient or permanent nature of risk factors around the time of VTE diagnosis. A VTE in association with transient risk factors and no ongoing permanent risk factors has a low risk of recurrence. When VTE is diagnosed in the absence of transient risk factors, or in the presence of ongoing permanent risk factors (such as malignancy) then the risk of recurrence is much higher. Further guidance on provocation definitions is provided by the SSC of the ISTH in an open access publication here.[34]

When diagnosis of VTE has been confirmed, an early assessment of provocation and evaluation of risk factors (both transient and permanent) should be undertaken and documented by the treating clinician.

Consideration of Malignancy Screening in the context of unprovoked VTE

NICE guidelines were revised in 2020 to de-emphasise early CT imaging for malignancy screening in the setting of unprovoked VTE, following robust trial evidence demonstrating negligible benefit.[35]

After diagnosis of an unprovoked VTE, current NICE guidance now recommends taking a medical history, performing a physical examination and sending baseline blood tests. Further investigations for cancer (mammography/CT Imaging/PSA etc..) should only be pursued if relevant clinical symptoms or signs are clinically detected.

Estimating and mitigating bleeding risk

Initial therapeutic anticoagulation for VTE is usually essential to reduce the risks of propagation, embolization, long term consequences (such as post thrombotic syndrome or pulmonary hypertension) and death. However, therapeutic anticoagulation increases the risk of bleeding.

A history and examination should be taken to elucidate bleeding risks and ensure patients are adequately counselled prior to commencing anticoagulation. This process can also identify and target modifiable risk factors for bleeding and provide an opportunity for intervention. Modifiable risk factors can be identified through assessment of hepatic and renal function, haemoglobin and platelet levels, blood pressure, drug adherence and use of over the counter medication.

Objective bleeding scores such as HASBLED have been validated for prediction of bleeding risk in VTE patients and can also be used to provide a quantifiable risk for discussion:[36]

Clinical feature	Points
Hypertension (uncontrolled >160mmHg systolic)	1
Renal Disease (Dialysis, transplant, creatinine >200 or eGFR <30)	1
Liver Disease (Established chronic liver disease, or acute transaminase rise >3* normal limit and Bilirubin >2* normal limit)	1
History of stroke	1
Prior major bleeding or predisposition to bleeding	1
Labile INR (Consistently high, unstable or Time in Therapeutic Range <60%)	1
Age >65	1
Antiplatelet use / Anti-inflammatory drug use	1
Excessive Alcohol Use (≥8 drinks per week)	1
Total Score	

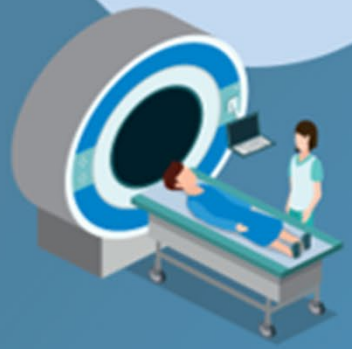
The corresponding bleeding risks associated with this score are as follows:

HAS-BLED score of 0-1 *Bleeding risk of 1.1%/100 patient years*
HAS-BLED score of 2 *Bleeding risk of 1.9%/100 patient years*
HAS-BLED score of 3 or more *Bleeding risk of 4.9%/100 patient years*

A score of 3 or more should prompt consideration of intervention to modify risk factors for bleeding (such as platelet transfusion, antihypertensive therapy or discontinuation of other medications). This score also identifies patients with renal or hepatic contraindications to some commonly used anticoagulants (described in more detail in Appendix 1). In patients with a HAS-BLED score of 3 or more and no modifiable risk factors, consideration should be given to other therapeutic approaches dependent on the severity of VTE and predicted clinical trajectory. Options include antiplatelet therapy only, prophylactic dose anticoagulation, referral for IVC filter insertion, or reduced/intermediate dose anticoagulation. Discuss these cases as an MDT with haematology referral as necessary.

A practical approach to assessing and managing risk of bleeding during anticoagulant therapy in patients with VTE can be found overleaf, with accompanying text review here.[37]

Practical approach for assessing and managing risk of bleeding during anticoagulant therapy in patients with venous thromboembolism



1

At diagnosis

- Rule out absolute contraindications for anticoagulant treatment

2

Upon discharge

- Choose optimal drug class (prevent relevant interaction with comedication and considering renal function and comorbid conditions)
- Choose optimal drug dose (dose reduction according to label)
- Identify and target modifiable risk factors for bleeding

3

At three months

- Establish optimal duration of anticoagulation by weighing risk of bleeding (using a validated risk score) versus risk of recurrent venous thromboembolism
- Establish optimal dose of long-term anticoagulant treatment (consider reduced dose in patients with higher risk of bleeding)
- Identify and target modifiable risk factors for bleeding

4

Long term follow-up

- Assess drug tolerance and adherence regularly
- Identify and target modifiable risk factors for bleeding
- Evaluate appropriateness of continued anticoagulation (longitudinal assessment of validated bleeding risk score)

How to identify modifiable risk factors for bleeding

Assess

- *Hepatic and renal function*
- *Haemoglobin level and platelet count*
- *Blood pressure*
- *Drug adherence*
- *Use of (over the counter) comedication*

Commencing therapeutic anticoagulation for an initial period of 3 months.

When the diagnosis of VTE has been confirmed and a decision made to treat, patients should be established on therapeutic dose anticoagulation as soon as possible.

The choice of agent for short term therapeutic anticoagulation is based on the type and location of VTE, in addition to relevant associated clinical factors, clinical experience, patient preference and patient safety initiatives at local sites (such as using different DOACs for different conditions).

NICE 2020 guidance supports the primary use of either rivaroxaban or apixaban as first line therapies in both suspected and confirmed VTE and in patients with certain types of cancer. Options, local preferences and their relative contraindications are summarised in Appendix 1.

If the diagnosis of VTE occurs *on established treatment dose anticoagulation despite good adherence to oral therapy,* discuss the case with the local haematology service. Options include changing the modality of anticoagulation to long term LMWH or bridging to warfarin therapy with individualised target INR.

When commenced on therapeutic anticoagulation, patients should be counselled appropriately and provided with written information on indication, duration and common complications. NICE guidance provides specific recommendations as follows:

Give people having anticoagulation treatment verbal and written information about:

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

There are no restrictions to mobilising patients with a diagnosis of VTE who are established on therapeutic anticoagulation. Relevant evidence suggests benefit (rather than risk) to early mobilisation.[38]

Relevant SCO and BRO information leaflets are available on the NCA policy hub under the vascular section or generic via the Thrombosis UK website (DOAC fact sheet, VTE overview, DVT diagnosis etc.). Example guidance leaflets on use of rivaroxaban and apixaban for the management of acute VTE produced by other NHS trusts can be found here and here.

Treatment Failure

Treatment failure (propagation or VTE recurrence despite treatment) often warrants discussion with the on-call haematology service. NICE guidelines recommend checking adherence, addressing other sources of hypercoagulability and/or increasing the dose of anticoagulant or change to an anticoagulant with a different mode of action. These cases can be complex; have a low threshold for discussion with haematology on call services.

5.6 Specific Management Issues Following the Diagnosis of DVT

Isolated Proximal DVT

Proximal DVT refers to clot at the level of or above the popliteal trifurcation (popliteal vein). Inform the accountable senior clinician, initiate immediate therapeutic anticoagulation for 3 months and follow the general guidance in section 5.5 on early management of confirmed VTE. Refer to section 5.9 for advice on what to do after the 3-month initial period of anticoagulation.

If the person has an iliofemoral DVT, refer to section 5.4 and consider discussion with vascular surgery.

Isolated Distal DVT

Distal DVT refers to clot below the level of the popliteal trifurcation, commonly found in the peroneal, tibial or gastrocnemial veins. The 90-day risk of propagation and/or embolization is between 5 and 11% in recent literature[39-42]. The risk of major bleeding with 3 months therapeutic anticoagulation at baseline is between 2 and 3%[43]. A recent Cochrane review supports the use of therapeutic anticoagulation to reduce the risks of recurrence and propagation, with no increase in major bleeding events.[44] As such, the majority of these cases should be treated with 3 months therapeutic anticoagulation as per isolated proximal DVT.

In the event of contraindications to anticoagulation or patient preference for conservative management, alternative treatment options include the following:

- Therapeutic anticoagulation for 6 weeks, followed by clinical review
- Serial sonography (a repeat scan between day 10 and 14) with therapeutic anticoagulation *only* in the event of propagation within the calf veins or to the level of the popliteal vein.
- Prophylactic dose anticoagulation for 6 weeks, followed by clinical review

Factors suggesting a higher likelihood of propagation include extensive thrombus (>5cm, involving multiple veins), unprovoked disease, active malignancy, history of VTE, inpatient status or particularly severe symptoms. Patients should be counselled regarding the risks and benefits of these options, following assessment of provocation, severity and bleeding risk.

Please note that chronic thrombus is often found on whole leg CUS; this is not an indication for anticoagulation. Only treat mixed age or acute thrombus. If a decision is made to treat, follow the general guidance in section 5.5.

Upper limb DVT

Upper limb DVT refers to clot in the axillary, subclavian or internal jugular veins. This should be managed as per isolated proximal DVT. Inform the accountable senior clinician, initiate immediate therapeutic anticoagulation for 3 months and follow the general guidance in section 5.5 on early management of confirmed VTE. Refer to section 5.9 for advice on what to do after the 3-month initial period of anticoagulation.

A high proportion of upper limb DVT cases are related to indwelling catheters. If the VTE is line related, also take note of the specific guidance for catheter (line) related thrombosis in the section 5.8.

When to consider an Inferior Vena Cava (IVC) filter

The use of IVC filters is broadly discouraged by national bodies given the lack of evidence and the potential for harm. NICE guidance has several recommendations on the topic:

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

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

There are only 2 potential indications for consideration of IVC filter placement and both are consider (not offer) recommendations in updated NICE guidance, representing the limited evidence base:

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

Consider an IVC filter for people with proximal DVT or PE who have a PE while taking anticoagulation treatment only after taking the steps outlined in the recommendation on treatment failure. ***[2020]***

Absolute contraindications to anticoagulation are best determined clinically by the treating team but could include the following: active bleeding, haemorrhagic stroke, non-haemorrhagic stroke within last 3 months, intracranial neoplasm and recent (<8 weeks) intracranial/spinal surgery bleeding. Discuss with the haematology team for expert advice if required.

An IVC filter is also a *temporising measure* only; as such there should be a clear plan in place for removal of the filter at the earliest possible opportunity, as soon as the patient becomes eligible for anticoagulant treatment.

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

IVC filters require placement under X-Ray guidance in a theatre environment by an interventional radiologist. If filter placement is under consideration, discuss with local interventional radiology services at Oldham or Manchester NHS Foundation Trust.

When to mobilise after a diagnosis of DVT

There is evidence to support early mobilisation after a diagnosis of DVT to reduce the risk of post thrombotic syndrome. Despite concerns regarding the potential for embolic phenomena, a network meta-analysis reported no risk of VTE progression or death with early ambulation.[38]

When assessing the patient to mobilise, ensure patients have commenced treatment for their DVT and are aware of the symptoms of PE including shortness of breath, chest pain, haemoptysis and sudden collapse. Initial exercise should be gentle and accommodate any pain issues relating to the DVT.

5.7 Specific Management Issues Following the Diagnosis of PE

All patients require immediate therapeutic anticoagulation on confirmation of PE diagnosis providing there are no absolute contraindications. Inform the senior accountable clinician and follow the general guidance in sections 5.5 on commencing therapeutic dose anticoagulation.

In patients with confirmed PE who appear unwell, send cardiac troponin and blood gases, consider ancillary investigations as indicated (echo, proximal leg vein ultrasound) and assign a risk category as per section 5.4. The ESC approach to risk stratification is repeated below:

Early mortality risk		Indicators of risk			
		Haemodynamic instability	PESI>2 or SPESI >0	RV dysfunction on TTE or CTPA	Elevated cardiac troponin levels
High		+	+	+	+
Intermediate	Int-High	-	+	+	+
	Int-Low	-	+	One (or none) positive	
Low		-	-	-	-

Haemodynamic instability is defined previously in section 5.4 and links to the SPESI/PESI scoring systems and guidance for intermediate risk patients are provided in section 5.4.

Outpatient management of confirmed low risk PE

Low risk patients with confirmed PE should be considered for early outpatient management. Use a validated scoring system to evaluate suitability (as described in section 5.2) and offer outpatient management if the score is appropriately low (SPESI 0, PESI <3 or HESTIA 0).

In addition to validated scoring systems, document the NEWS and social history during assessment and share the final decision on ambulatory vs inpatient care with the patient whenever possible, based on overall risk assessment, feasibility and patient preference.

If the person would prefer outpatient management despite a raised SPESI/PESI or NEWS score (>2) the case ***must be discussed with a consultant/senior decision maker.***

If a decision is made to manage a person with confirmed PE on an outpatient pathway, ensure appropriate therapeutic anticoagulation (using Appendix 1) and agree a plan for monitoring and follow up in line with BTS guidance, which **must include an initial review within 7 days of discharge** (telephone/face to face). Written information should be provided on the following:

- The potential complications of VTE and treatment
- Direct contact details for the accountable clinical team who can discuss any new issues
- Information on out of hours services the person can access if their team is unavailable.

Patients should also be referred for a follow up review at 3-6 months. Follow usual pathways for outpatient referral, or at SCO through direct email referral to pulmonary.embolismFU@nca.nhs.uk

A QRG for the outpatient management of pulmonary embolism can be found in Appendix 2.

5.8 Specific management issues regarding thrombosis at unusual sites

Guidance on the investigation and management of venous thrombosis at unusual sites is taken from local specialty protocols and the BSH Taskforce guidelines, published in 2012 and updated in 2022. Both articles are open access.[16]

Catheter (Line) Related Thrombosis

Thrombotic complications with indwelling central venous catheters are seen in between 5 and 20% of cases. [45, 46] They occur with both directly inserted central venous catheters (CVC) and peripherally inserted central catheters (PICC). They can also occur with extended dwell cannula's such as the midline or powerwand devices.

Catheter Related Thrombosis (CRT) refers principally to thrombosis with axillary vein involvement (or more proximal, such as subclavian or jugular vein) in the upper extremity, or involving femoral venous catheters in the lower extremity. Isolated brachial, cephalic and other forearm thrombi should be managed as superficial venous thrombosis in line with the relevant section of this guidance.

The management of CRT differs in agent and duration of therapy decisions and the impact on the life of the line itself.

All patients with confirmed CRT should be commenced on therapeutic anticoagulation with LMWH on diagnosis, providing no contra-indications are present. For those at high risk of bleeding, consider using a prophylactic dose of LMWH

Subsequent duration of therapy depends on whether the catheter is to remain in situ or be removed. Current guidance suggests that the catheter can remain in situ if still required, provided the following occur:

- The catheter is not infected
- The catheter is functional
- There is resolution of symptoms in the affected limb with treatment, on surveillance.

If a decision is taken to remove the catheter, this should not be performed until the patient has received at least 3-5 days of anticoagulation

Following the decision to remove the catheter, offer patients the following duration of therapy:

All patients with confirmed CRT with the catheter remaining in situ should continue anticoagulation for 3 months.[45]

If the catheter is removed following confirmed diagnosis of CRT, continue therapeutic anticoagulation for 2 to 6 weeks, dependent on symptoms and clinical trajectory.[47]

Following the initial 5 days of therapeutic anticoagulation with LMWH, various pharmacological options are available as per Appendix A. ***Patients who are critically ill, with impaired renal function, active cancer or with the catheter remaining in situ should receive LMWH anticoagulation as a preferred agent for the duration of therapy***

Cerebral Venous Sinus Thrombosis

A separate comprehensive guideline is available on this topic written by the neurology services and available via the VTE service (Salford) webpage on the trust intranet.

Additionally, please note that BSH guidance now supports the use of DOAC therapy in selected cases of CVST following initial treatment with LMWH (for 5-10 days), as an alternative to the more commonly used oral VKA.[16] Treatment decisions should be taken in consult with neurology services and based on individual circumstances.

Superficial Venous Thrombosis (thrombophlebitis)

Superficial Venous Thrombosis refers to a thrombus in a peripheral vein, usually affecting the lower limbs. It occurs more often than DVT and can have potentially serious consequences. Prospective research on patients with a new thrombophlebitis of >5cm suggests that around 1:25 patients will have a concurrent symptomatic PE and 1:10 will show a proximal DVT on compression ultrasound[48]. Untreated thrombophlebitis is associated with a 3.1% symptomatic VTE rate, a 3.3% extension rate and a 1.9% recurrence rate in the initial 3 months [49].

Further large studies have suggested a particular increase in risk amongst thrombophlebitis patients with any of the following features:

- Clot involving the greater saphenous vein
- Clot extending to within 10cm of the saphenofemoral junction
- Clot above the knee
- Clot occurring in patients with a previous history of SVT or other VTE
- Clot in the context of active cancer
- Clot in the context of recent surgery

In patients with thrombophlebitis of the thigh, significant symptoms or raised d-dimer, consider early duplex compression imaging of the leg in keeping with investigation strategies for DVT (section 5.1).

In patients with* thrombophlebitis *>5cm in length confirmed on ultrasound and any of the above risk factors, consider the use of prophylactic dose anticoagulation for 6 weeks. Current evidence supports use of either LMWH or unlicensed DOAC therapy (rivaroxaban 10mg only) for this indication.[50]

If thrombophlebitis is unprovoked, then follow up may be warranted to assess ongoing thrombosis risk at the discretion of the treating clinician. These patients do not require further imaging after initial diagnostics unless relevant and should usually be referred back to primary care.

For patients without risk significant factors as above, symptomatic treatment can be provided using standard anti-inflammatory medications via topical or oral routes. Anticoagulation is in general not used to treat thrombophlebitis related to an IV infusion; in this instance the peripheral cannula should be removed and symptomatic relief provided. Ongoing symptoms following these measures should prompt sonographic evaluation of the affected area.Patients being treated conservatively without anticoagulation should be warned regarding the symptoms and signs of VTE and written information provided.

Cancer-associated Thrombosis

People with cancer related thrombosis should be commenced on therapeutic anticoagulation for 3-6 months initially. There is now reasonable evidence suggesting good clinical effectiveness for DOAC therapy in cancer related VTE related to certain types of cancer. NICE guidance was updated in 2020 to recommend the following:

When choosing anticoagulation treatment for people with active cancer and confirmed proximal DVT or PE, take into account the tumour site, interactions with other drugs including those used to treat cancer, and the person's bleeding risk. **[2020]**

Consider a direct-acting oral anticoagulant (DOAC) for people with active cancer and confirmed proximal DVT or PE. **[2020]**

Evidence outside of NICE guidance suggests DOAC therapy are *not recommended* as first line therapy in the following people with cancer:[51]

- Creatinine clearance <30 mL/min
- Luminal gastrointestinal lesion
- Luminal genitourinary lesion
- Recent (<3 months) history of peptic ulcer disease or other bleeding lesion
- Anticancer therapies that significantly affect P-glycoprotein, CYP3A4, or CYP2J2 pathways
- Severe hepatic impairment with coagulopathy
- Surgery or invasive procedure imminent

If a DOAC is unsuitable consider LMWH alone or LMWH concurrently with a VKA for at least 5 days and/or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own. **[2020]**

After 3-6 months of therapy, the continuing use of treatment should be reassessed, including an estimation of bleeding risk and clarification of cancer management plan. Whilst cancer remains ‘active’, there is supporting evidence for extended duration therapeutic anticoagulation even in the presence of high bleeding risk. However, this decision should be taken with the patient. In the event of a decision to continue anticoagulation, this decision should be revisited annually.

Occasionally, cancer associated thrombosis will present as an asymptomatic finding at imaging. These patients should be managed by immediate initiation of therapeutic anticoagulation as above. Treatment can commence in the community, in hospital or in an ambulatory fashion through the emergency department as dictated by clinical need and access to medication.

Anticoagulation treatment for DVT or PE with triple positive antiphospholipid syndrome

There is recent evidence to suggest that DOAC therapy is inferior to LMWH/VKA therapy in patients with triple positive antiphospholipid syndrome.[52-54] As such, the following recommendations from NICE should be considered during initial treatment and management decisions.
Offer people with confirmed proximal DVT or PE and an established diagnosis of triple positive antiphospholipid syndrome LMWH concurrently with a VKA for at least 5 days and/or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own. **[2020]**

Splanchnic Vein Thrombosis (SVT)

In cirrhotic patients with symptomatic acute splanchnic vein thrombosis, we suggest therapeutic dose LMWH, and a switch to VKAs or DOACs, if not contraindicated by severity of liver dysfunction.[55] Oesophageal or fundic varices, are not a contraindication for anticoagulation, but adequate prophylactic treatment (with β-blockers, endoscopic ligation, etc.) should precede anticoagulation. We suggest LMWH in patients with luminal gastrointestinal cancer, active gastrointestinal mucosal abnormalities, genitourinary cancer at high risk of bleeding, or receiving current systemic therapy with potentially relevant drug-drug interactions with DOACs.

In non-cirrhotic patients with symptomatic acute splanchnic vein thrombosis who have no signs of active bleeding, consider full therapeutic dose of DOACs, and consider LMWH and VKAs with INR range of 2.0-3.0 in patients who cannot tolerate or have contraindications for DOACs.

In patients with symptomatic acute splanchnic vein thrombosis, we recommend the use of anticoagulant therapy for at least 3 to 6 months, irrespective of thrombosis extension and underlying risk factors; patients with transient risk factors (surgery, infections) may discontinue treatment after 3 months of anticoagulation, but patients with cirrhosis, active cancer, MPNs, and other thrombophilic conditions should undergo extended anticoagulation while weighing its risks and benefits. In every circumstance, gastrointestinal bleeding should be monitored before or during anticoagulation and should be properly controlled.

We recommend longer courses of anticoagulation or indefinite anticoagulant treatment in patients with thrombosis progression or recurrence after treatment discontinuation, unprovoked splanchnic vein thrombosis, or persistent risk factors. Reduced doses of LMWH or DOACs may be used to minimize bleeding risk as for usual site venous and withholding anticoagulation in patients with poor short-term prognosis.

5.9 Longer term management of VTE (>3 months)

The majority of patients with confirmed VTE should be commenced on therapeutic anticoagulation for a treatment duration of 3 months in the first instance.

NICE guidance now recommends to consider stopping anticoagulation treatment 3 months (3 to 6 months for people with active cancer) after a provoked DVT or PE if the provoking factor is no longer present and the clinical course has been uncomplicated. If anticoagulation treatment is stopped, give advice about the risk of recurrence and provide:

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

Consider continuing anticoagulation beyond 3 months after an unprovoked DVT or PE. Base the decision on the balance between the person's risk of venous thromboembolism (VTE) recurrence and their risk of bleeding. Discuss the risks and benefits of long-term anticoagulation with the person, and take their preferences into account. **[2020]**

The risks of VTE recurrence and bleeding can be estimated using the tools below:

Estimating the risk of recurrence

Factors associated with an increased risk of VTE recurrence following cessation of treatment include male sex, raised d-dimer levels (3-5 weeks after cessation of anticoagulation) age and site of index event. Other less robust characteristics that may suggest an increased recurrence risk include obesity, post thrombotic symptoms, ongoing immobility or hormone therapy[56].

Several prognostic models have been derived to produce quantifiable estimates of recurrence risk, including the DASH score, Vienna prediction model and the HERDOO2 rule [57-59]. The DASH score is the simplest of these and calculated as per the table below:

Clinical feature	Points
D-Dimer abnormal (measured 1 month after cessation of anticoagulation)	2
Age ≤ 50	1
Male sex	1
Hormone use at VTE onset	-2
Total DASH Score	

A rising DASH score corresponds to increasing annualised recurrence rate as follows:

DASH Score	Annualised VTE recurrence rate
-2	1.8%
-1	1.0%
0	2.4%
1	3.9%
2	6.3%
3	10.8%
4	19.9%

The authors of the score suggest that in patients with a DASH score <2 lifelong anticoagulation can potentially be avoided.

Other scores such as the Vienna risk prediction model have online calculators available and incorporate 1,3 and 5 year recurrence risk predictions. None of these scores have been extensively validated in the literature – as such clinicians can only use them as a supplemental tool to clinical assessment and expertise.

Estimating the risk of bleeding

The average risk of major bleeding on therapeutic anticoagulation in the first year is between 2-3%. The fatal bleeding rate is estimated at 0.37%[43]. While these rates appear to be slightly reduced with DOAC use as compared to VKA therapy, the risks of long term treatment need to clearly explained to the patient and balanced in the overall decision on duration of therapy[60].

A bleeding risk score for use during extended duration anticoagulation has now been developed, and validated for use in a general population (**VTE BLEED**).[61, 62] The score is described below.

VTE Bleed Score	
Criteria	**Points**
Active Cancer	2
Male patient with uncontrolled hypertension (systolic BP >140mmHg)	1
Anaemia (Hb<130g/L in patients identifying as male, <120g/L in patients identifying as female or non-binary)	1.5
Recent history of major or non-major clinically relevant bleeding	1.5
Renal dysfunction (CrCl 30 to 60ml/min)	
Age ≥60 years	1.5
Total Score	**Outcome**
<2	Low bleed risk
≥2	High bleed risk

The ACCP guideline also provides clear tabulated information on recognised bleeding factors and the associated increase in risk following 3 months therapeutic anticoagulation as below[63]:

Recognised Risk Factors (RF) for bleeding		
Age >65	Prior bleeding	Active cancer
Renal failure	Liver failure	Thrombocytopenia
Prior stroke	Diabetes	Anaemia
Antiplatelet therapy	Significant comorbidity	Recent surgery
Alcohol abuse	Frequent falls	

Estimated absolute risk of major bleeding (in %/year)			
	Low risk (0 RF)	Moderate risk (1 RF)	High risk (>1 RF)
0-3 months	1.6	3.2	12.8
After 3 months	0.8	1.6	>6.5

Other scores include the RIETE score, and the outpatient bleeding risk index[64, 65]. No score is perfect and clinicians should use the above resources to estimate, document, discuss and mitigate the risk of bleeding where feasible.

A high bleeding risk score is not necessarily a contra-indication to anticoagulation if the VTE recurrence risk is considerable, but should prompt a discussion on risk to raise awareness, identify any modifiable factors and explore other options.

For people who decline or have reservations about continued anticoagulation treatment after counselling, consider reduced dose DOAC therapy or aspirin 75 mg or 150 mg daily.

Reducing the longer-term dose of anticoagulation after 6 months

When DOAC medication is continued >6months as prophylaxis against recurrent VTE, there is good evidence to support dose reduction.[66-68]

If DOAC therapy is being continued long term with no scheduled stop date, the BNF recommends a 50% dose reduction of both apixaban (to 2.5mg BD) and rivaroxaban (to 10mg OD) following completion of at least 6 months therapeutic dose anticoagulation.

The decision to reduce the dose of anticoagulation should be shared with the involved person, taking into account recurrence risk, bleeding risk, compliance and preferences. The duration of overall therapy should be individualised after careful assessment of the treatment benefit against the risk for bleeding, as described in the SPC for DOAC medications.

Longer term follow up (>1year)

Referral to specialist clinics for complex decision making around VTE is available through respiratory, haematology and acute medical services as needed on a case by case basis. All people on long term anticoagulation or aspirin for VTE prevention should have routine primary care follow up as per NICE guidance. The aim should be to review general health, risk of VTE recurrence, bleeding risk and treatment preferences at least once a year for people taking long-term anticoagulation treatment or aspirin.

Thrombophilia screening

Do not offer thrombophilia testing to people who have had provoked DVT or PE. Do not offer testing for hereditary thrombophilia to people who are continuing anticoagulation treatment. Consideration of thrombophilia testing is only warranted in patients with ***unprovoked VTE*** where, following 3-month review a plan has been made *to stop* anticoagulation. In this circumstance, NICE and BSH guidance should be followed as below[5]:

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

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

6. Roles & Responsibilities

Thrombosis Committee – to disseminate the guideline, consider feedback from committees and individuals, to revise as required and promote uptake of best practice. To work with thrombosis leads across NCA sites to standardise care and share best practice.

Directors of Nursing – to ensure the guideline is available to Divisional Directors of Nursing for dissemination.

Divisional Directors of Nursing - to ensure that guideline is disseminated and to ensure that general adherence to the policy and all relevant staff groups are educated to the level required, whilst keeping up to date with current practice. To review and respond to issues highlighted by the guideline.

Assistant Director of Nursing / Lead Nurses - to ensure that delivery of care to all patients within the Division adheres to the guideline and all relevant staff groups are educated to the level required, whilst keeping up to date with current practice.

Ward Managers - to ensure that delivery of care to all patients within the ward is in keeping with the guideline and all relevant staff groups are educated to the required level, whilst keeping up to date with current practice.

Nursing ward teams - to ensure that delivery of care to all patients within the ward/department adheres to the guideline and keeps up to date with current practice.

Clinicians - to ensure that all in-patients under their care have full adherence to the guideline and all staff groups are educated to the level required, whilst keeping up to date with current practice. To review and respond to issues highlighted by the policy.

7. Monitoring Document Effectiveness

The table below details the implementation strategy for this policy.

Objective	Action	Responsibility	Date to be completed
Cascade and briefing	Cascade via Trust Communications channels, e.g., Weekly Update, Team Brief, screen savers, display as feature intranet home page. Share across division via direct email	Communication team	July 2023
Training and development	Key trainers from clinical teams to be identified to assist with intensive training and raising awareness campaign prior to launch and week following launch in each clinical area.		July 2023
	Policy to be available on Trust Intranet for staff to view		June 2023
	Updates to mandatory training packages		July 2023
	Promotion through junior doctor and advanced practice networks via thrombosis committee representatives.		June 2023
Audit	Ongoing audit of VTE care through established thrombosis committee process – VTE case data ascertainment monthly with root cause analysis where indicated, established governance report at thrombosis committee meetings, cross site NCA wide thrombosis committee discussions and reporting to the national exemplar network.	Thrombosis committee leads	ongoing

Any deviation from this guideline leading to deterioration of the patient requires completion of an incident report at the level of which will be determined on a patient specific basis.

The policy document will be formally reviewed every five years. In the event of any VTE related incidents, the document will be reviewed, and addendums added in response to the learning that arises from such events.

8. Abbreviations & Definitions

AAT	Age Adjusted threshold
ACCP	American College of chest Physicians
AIDS	Acquired Immune Deficiency Syndrome
APTT	Activated Partial Thromboplastin Time
BCO	Bury Care Organisation
BCSH	British Committee for Standards in Haematology
BD	Twice Daily
BMI	Body Mass Index
BNF	British National Formulary
BP	Blood Pressure
BRO	Bury, Rochdale and Oldham Care Organisation
BSH	British Society for Haematology
BTS	British Thoracic Society
BW	Body weight
CAT	Cancer Associated Thrombosis
CCU	Coronary Care Unit
CI	Confidence Interval
CM	Centimetre
CPR	Cardiopulmonary Resuscitation
CrCl	Creatine Clearance
CRT	Catheter Related Thrombosis
CT	Computerised Tomography
CTPA	CT Pulmonary Angiography
CUS	Compression Ultrasonography
CVST	Cerebral venous sinus thrombosis
DALY	Disability Adjusted life Years
DiPEP	Diagnosis of PE in Pregnancy
DOAC	Direct Oral Anticoagulant
DVT	Deep Vein Thrombosis
eGFR	Estimated Glomerular Filtration Rate
ECG	Electrocardiogram
EKOS	Ekosonic Endovascular System
EPR	Electronic Patient Record
ESC	European Society of Cardiology
G/L	Gram/litre
HB	Haemoglobin
INR	International Normalised Ratio
IV	Intravascular
IVC	Inferior Vena Cava
Kg	Killogram
LMWH	Low Molecular Weight Heparin
MDT	Multi-Disciplinary Team
Mg	Milligrams
Mins	Minutes
Ml/MIN	Millimetre per minutes
Mls	Millilitres
mmHg	Millimetres of Mercury
MPN	Myeloproliferative neoplasms
MRI	Magnetic Resonance Imaging
NEWS	New Early Warning Score

NCA	Northern Care Alliance
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
Ng/ml	Nanogrames per mililitre
OCO	Oldham Care Organisation
OD	Once Daily
PE	Pulmonary embolism
PERC	Pulmonary Embolism Rule Out Criteria
PESI	Pulmonary Embolism Severity Index
PSA	Prostate Specific Antigen
QRG	Quick Reference guide
RF	Risk Factor
RCO	Rochdale Care Organisation
RCOG	Royal College of Obstetricians and Gynaecologist
RV	Right Ventricle
SDEC	Same Day Emergency Care
SCO	Salford Care Organisation
SPC	Summary of Product Characteristcs
sPESI	simplified Pulmonary Embolism Severity Index
SVT	Superficial Venous Thrombosis
t-pa	Tissue Plasminogen Activator
U	Units
UEDVT	Upper Extremity Deep Vein Thrombosis
USS	Ultrasound Scan
UFH	Unfractionated Heparin
VKA	Vitamin K Antagonist
VTE	Venous Thromboembolism
VQ	Ventilated Perfusion Scan
XR	Xray

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10. Document Control Information

Part 1: Lead Author, Consultation Details, Communication Plan

Name of lead author	Daniel Horner
Job title	Consultant in Emergency and Intensive Care Medicine
Contact number	01612068793
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Consultation:

Name/s of person or group	State which Care Organisations/ corporate services/staff groups the person or group represents	Date	Response: FU/FNU/NR
Charlotte Ward	SCO Acute Medicine CD	27/3/23	FU
Sam Decalmer	SCO Respiratory Medicine	27/3/23	FU
Alan Field	SCO Pharmacy	27/3/23	FU
Martin Thomas	SCO Emergency Medicine CD	27/3/23	FU
Usmaan Hamid	BRO Pharmacy	27/3/23	FU
Emma Boxall	SCO Pharmacy	27/3/23	FU
Kathryn Gow	BRO Acute and Respiratory Med	27/3/23	FU
Nicola Rothwell	BRO Acute Medicine CD	27/3/23	FU
Kate Swainson	BRO Radiology	27/3/23	FU
Mark Livingstone	BRO Pharmacy	27/3/23	FU
Diane Elford	BRO Pharmacy	27/3/23	FU
Nawres Aldafai	BRO Pharmacy	27/3/23	FU
Helen March	BRO Pharmacy	27/3/23	FU
Khowla Hashaishi	SCO Haematology	27/3/23	FU
Sheila Ramjug	SCO Respiratory Medicine and pulmonary HTN lead	27/3/23	FU

Equality Impact Assessment sign off: See Section 11.

Name (Lead from EDI team)	J McMahon
Date	28/06/2023

Communication plan:

See sections 6 and 7 above

Part 2: Committee Approval

Approval date	12/6/2023
Method of approval	Provisionally approved at MOC 12/05/2023 Amendments submitted to MOC chair 12/6/2023
Name of approving Committee	Medicines Optimisation Committee
Chairperson Name / Role	Dr Richard Cooper, MOC Chair
Amendments approval: Name of approver, version number and date. Do not amend above details	

Part 3: Search Terms and Review Arrangements

Keywords & phrases	Deep vein thrombosis, DVT, Pulmonary embolism, PE , Venous Thromboembolism, VTE, anticoagulation, clot, bleeding, thrombolysis, IVC filter.
Document review arrangements	Review will occur by Thrombosis Committee leads, or nominated representatives within five years or earlier should a change in legislation, best practice or other change in circumstance dictate.
Special requests	For trust wide dissemination.

11. Equality Impact Assessment (EqIA) tool

- The below tool must be completed at the start of any new or existing policy, procedure, or guideline development or review. For ease, all documents will be referred to as 'policy'. The EqIA should be used to inform the design of the new policy and reviewed right up until the policy is approved and not completed simply as an audit of the final policy itself.
- All sections of the tool will expand as required.
- EqIAs must be sent for review prior to the policy being sent to committee for approval. Any changes made at committee after an EqIA has been signed off must result in the EqIA being updated to reflect these changes. Policies will not be published without a completed and quality reviewed EqIA.

Help and guidance available:

- Equality Impact Assessment Help Resource
- Email the EDI Team: eqia@nca.nhs.uk for advice or training information.
- Submit documents requiring EqIA sign off to: eqia@nca.nhs.uk. Allow an initial four-week turnaround.
- Where there is a statutory or significant risk, requests to expedite the review process can be made by exception to the Group Equality & Inclusion Programme Managers: Yasmin.bukhari@nca.nhs.uk or stephanie.chadwick@nca.nhs.uk

Part 1: Possible Negative Impacts		
Protected Characteristic	**Possible Impact**	**Action/Mitigation**
Age	Increasing age often results in increased morbidity, impaired functional/cognitive status, all of which may impact on the ability to diagnose and manage VTE	All reasonable steps should be taken facilitate the safe and timely assessment, monitoring and response to a patient with suspected VTE in accordance with Trust policies and procedures. This will ensure that patient safety and timely treatment is delivered. Communication aids should be used as required.
Disability	Impaired functional and cognitive status can have varying degrees of impact on the diagnosis and management of VTE	
Ethnicity	Language barriers could have varying degrees of impact on the patients ability to maintain their own safe fluid status	The use of interpreters and communication aids should support care.
Gender	Staff members may not always appropriately reference a patient's chosen gender during care, which could cause offence and result in a negative patient experience.	Staff members should confirm how patients wish to be identified and addressed. Wording of pregnant person used throughout document.
Marriage/Civil Partnership	No impact anticipated.	
Pregnancy/Maternity	Challenges within this area include limited diagnostic modalities, increased radiation risk and necessary co-ordination of care for people approaching their delivery date.	Links to a separate approved policy with independent EQIA published within this guideline
Religion & Belief	There may be limitations in relation to use of porcine derived medications, however this is usually limited within hospital settings, following a Fatwa guidance supporting use in life threatening circumstances.	Exploration of alternative therapeutic options highlighted in this guidance.
Sexual Orientation	No impact anticipated.	

Trans	Staff members may not always appropriately reference a patient's chosen gender care which could cause offence and result in a negative patient experience	Patients should always be addressed/referred to by their chosen gender.
Other Under Served Communities (Including Carers, Low Income, Veterans)	Difficulties in accessing outpatient pathways/transport should be considered in determining initial diagnostic strategy and ongoing management strategies in VTE	Options for inpatient and outpatient investigation are provided, along with guidance on suitability and multiple management options including less restrictive drug regimens.

Part 2: Possible Opportunity for Positive Impacts		
Protected Characteristic	**Possible Impact**	**Action/Mitigation**
Age	Having a comprehensive VTE guideline that is applied to all patients irrespective of their protected characteristic(s) will improve the patient experience, quality, and safety of the care they receive. It also facilitates staff by providing structure and guidance for the safe and appropriate management of patients, including those people with contraindications, reservations or concerns regarding specific treatment options.	
Disability		
Ethnicity		
Gender		
Marriage/Civil Partnership		
Pregnancy/Maternity		
Religion & Belief		
Sexual Orientation		
Trans		
Other Under Served Communities (Including Carers, Low Income, Veterans)		

Part 3: Combined Action Plan

Action *(List all actions & mitigation below)*	Due Date	Lead *(Name & Job Role)*	From Negative or Positive Impact?
Mitigation stated in section 1	July 2023	NCA Thrombosis Committee leads	**Negative**
Mitigation stated in section 1	July 2023	NCA Thrombosis Committee leads	**Positive**

Part 4: Information Consulted and Evidence Base *(Including any consultation)*

Protected Characteristic	Name of Source	Summary of Areas Covered	Web link/contact info
Age	See extensive reference list above.		
Disability			
Ethnicity			
Gender			
Marriage/Civil Partnership			
Pregnancy/Maternity			
Religion & Belief			
Sexual Orientation			
Trans			
Other Under Served Communities (Including Carers, Low Income, Veterans)			

Part 5: EqIA Update Log (Detail any changes made to EqIA as policy has developed and any additional impacts included)

Date of Update	Author of Update	Change Made
23/06/202323	Prof Daniel Horner	Sections 1 - 6

6. Have all of the negative impacts you have considered been fully mitigated or resolved? *(If the answer is no, please explain how these don't constitute a breach of the Equality Act 2010 or the Human Rights Act 1998)*
Impact has been mitigated as described above in sections 1 & 2

7. Please explain how you have considered the duties under the accessible information standard if your document relates to patients?
As stated in section 1. The policy will be available to staff in different formats, including large print, enlarged on computer screen and/or on different colour paper, and via Read & Write software. This would also include all Appendices.

8. Equality Impact Assessment completed and signed off? *(Insert named lead from EDI Team below). Please also add this information to Section 10 Part 1.*
Name:  **Date:** 28/06/2023

12. Appendices

Appendix 1

Direct Oral Anticoagulant (DOAC/NOAC) Agents

These agents are recommended as initial first line treatment in VTE patients who are not pregnant or breastfeeding and without severe renal or hepatic impairment. Current evidence suggests previous weight restrictions may lack validity. A recent updated communication (2021) from the ISTH SSC subcommittee on control of anticoagulation concluded the following "For treatment of VTE, we suggest that standard doses of rivaroxaban or apixaban are among appropriate anticoagulant options regardless of high BMI and weight".[69] In people <50kg, >120kg or BMI>40kg/m^2, consider MDT evaluation, individual assessment and shared decision making; DOACs may still be the most appropriate option on balance. www.medicines.org.uk.

	Generic name	Brand name	Drug Action	Initial LMWH	Dosing for therapeutic anticoagulation in acute VTE	Avoid	Caution
SCO preferred agent	Rivaroxaban	Xarelto™	Direct inhibitor of activated factor X	No	15mg twice a day for 21 days then 20mg once daily. Reduce to 10mg OD after 6 months if continuing.	CrCl <15mls/min **Liver disease Pregnancy Breast feeding**	CrCl 15-49mls/min. Weight <50kg or >120kg. See SpC for dose adjustment or seek pharmacy/haematology advice.
BRO preferred agent	Apixaban	Eliquis™	Direct inhibitor of activated factor X	No	10mg twice a day for 7 days then 5mg twice a day. Reduce to 2.5mg BD after 6 months if continuing.	CrCl <15mls/min **Liver disease Pregnancy Breast feeding**	Caution with CrCl 15-29mls/min Weight <50kg or >120kg. See SpC for dose adjustment or seek pharmacy/haematology advice.
Alternative options	Dabigatran	Pradaxa™	Direct thrombin inhibitor	Yes, for minimum of 5 days	Adult 18-74: 150mg BD Adult 75-79: 110-150mg BD Adult 80+: 110mg BD	CrCl<30mls/min **Liver disease Pregnancy Breast feeding**	Consider reduced dose if CrCl 30-50mls/min. See SpC for dose adjustment or seek pharmacy/haematology advice.
	Edoxaban	Lixiana™	Direct inhibitor of activated factor X	Yes, for minimum of 5 days	60mg daily	CrCl <15mlsmin **Liver disease Pregnancy Breast feeding**	CrCl 15 - 50 mL/min Body weight ≤60kg or >120kg. See SpC for dose adjustment or seek pharmacy/haematology advice.

Avoid concomitant use with strong inhibitors of both CYP3A4 and P-gp e.g. ketoconazole, itraconazole, voriconazole or HIV protease inhibitors Caution with strong CYP3A4 inducers e.g. rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort as they may lead to reduced anticoagulant concentrations. A specific table of interactions follows at the end of this appendix.

Warfarin / Vitamin K Receptor Antagonists

These agents are recommended for patients with triple phase antiphospholipid syndrome and acute VTE, those who encounter treatment failure on DOAC agents, those who would benefit from ease of rapid reversal, patients previously established successfully on warfarin, patients declining to use DOAC therapy after informed discussion or those circumstances where clear and reliable monitoring of compliance could be beneficial.

	Generic name	Brand name	Drug Action	Initial LMWH required	Usual treatment dose for DVT/PE	Avoid	Caution
Often the best choice for lifelong anticoagulation, or when monitored compliance is beneficial	Warfarin		Vitamin K antagonist	Yes, for minimum of 5 days; usually given until INR is within therapeutic range	Variable, to achieve stable target INR of 2.5 (2-3). Loading nomograms are available in the BNF and online	**Pregnancy** Liver disease	eGFR <15mls/min Intercurrent illness Concurrent medications and herbal products need to be carefully checked for interactions with warfarin prior to prescription as below.
Rarely used in cases of warfarin allergy	Acenocoumarol	Sinthrome	Vitamin K antagonist	Yes, as above.	As above	As above	As above Roughly three times as potent as warfarin so lower doses required.

Warfarin loading can be prescribed through EPR (SCO) or anticoagulant paper chart WPH544 (BRO).

Patients should be advised to refrain from heavy alcohol intake, use of herbal remedies such as St Johns Wort and ingestion of cranberry/grapefruit juice. Common drug interactions with warfarin listed in the current SPC can be found below:

Examples of drugs which potentiate the effect of warfarin
allopurinol, capecitabine, erlotinib, disulfiram, azole antifungals (ketoconazole, fluconazole etc) omeprazole paracetamol (prolonged regular use), propafenone amiodarone tamoxifen methylphenidate, zafirlukast fibrates statins (not pravastatin, predominantly associated with fluvastatin), macrolides (e.g clarithromycin and erythromycin) quinolones (e.g. ciprofloxacin) sulfamethoxazole metronidazole
Examples of drugs which antagonise the effect of warfarin
Barbiturates, primidone, carbamazepine, griseofulvin, oral contraceptives, rifampicin, azathioprine, phenytoin
Examples of drugs with variable effect
Corticosteroids, nevirapine, ritonavir

Low Molecular Weight Heparin (LMWH) Agents

These agents are recommended as initial first line treatment for pregnant people with VTE and those with certain forms of cancer (see section 5.8)
In pregnancy, dosing should commence based on pre-pregnancy or early booking weight.
Full prescribing information is available for individual drugs in the Summary of Product Characteristics at www.medicines.org.uk

	Generic name	Brand names	Drug Action	Usual treatment dose for DVT/PE	Avoid	caution
First choice LMWH at SCO for patients with CrCl>30mls/min	Tinzaparin	Innohep™	Potentiates the inhibition of factor XA via antithrombin	175IU/kg once daily dose.	Patients with hypersensitivity or previous heparin induced thrombocytopaenia/thrombosis (HITT)	eGFR <15mls/min Hyperkalaemia Platelet count <50
First choice for all patients at BRO First choice at SCO for patients with CrCl <30mls/min	Enoxaparin	Clexane™ Inhixa™	Potentiates the inhibition of factor XA via antithrombin	1.5mg/kg once daily in normal renal function. 1mg/kg once daily in patients with CrCl <30mls/min	Patients with hypersensitivity or previous heparin induced thrombocytopaenia/thrombosis (HITT)	eGFR <15mls/min Hyperkalaemia Platelet count <50

Avoid in patients with a platelet count <50 or those with a known history of heparin induced thrombocytopaenia. Note that LMWH agents are of porcine origin. This should be disclosed to patients where relevant as per BNF guidance. Dosing of tinzaparin for patients >105kg often requires the use of two injections – see the SCO dedicated LMWH policy for dosing tables and further guidance on monitoring for HITT.

Unfractionated Heparin Infusion

Occasionally used in cases where eGFR is <5ml/min and anticoagulation necessary. Refer to the dedicated trust policy online.

Argatroban, fondaparinux and other rarely used agents

Refer to the dedicated trust policy on rarely used alternative anticoagulant agents (P130211). Also consider discussion with a haematology specialist.

Notable drug interactions for Direct Oral Anticoagulant (DOAC/NOAC) Agents (also see https://bnf.nice.org.uk/; SPC: www.medicines.org.uk)

Class	Drugs	Rivaroxaban	Edoxaban	Apixaban	Dabigatran
		Rivaroxaban is metabolised by cytochrome P450 and is also a substrate for P-glycoprotein. Interactions can occur with inhibitors or inducers of both P-gp and CYP3A4.	Edoxaban is metabolised by hydrolysis and cytochrome P450 and is also a substrate for P-glycoprotein. Interactions can occur with inhibitors or inducers of both P-gp and CYP3A4.	Apixaban is metabolised by cytochrome P450 and is also a substrate for P- glycoprotein. Interactions can occur with inhibitors or inducers of both P-gp and CYP3A4.	Dabigatran is a pro-drug not metabolised by the cytochrome P450 system and has no *in vitro* effects on human cytochrome P450 enzymes. Dabigatran is however a substrate at P-glycoprotein receptors (P-gp). Interaction can occur with P-gp inhibitors or inducers.
Strong inhibitors ofP-gp and CYP3A4	Ketoconazole Itraconazole Posaconazole Voriconazole (see below for fluconazole)	Levels of rivaroxaban increased by up to 160%. Contraindicated	Levels of edoxaban likely to increase. Ketoconazole requires dose reduction to 30 mg once daily.	Levels of apixaban increased by 100% for some, no data availablefor others. Contraindicated.	Levels of dabigatran increased. Levels of dabigatran increased by ~150% for ketoconazole. Contraindicated.
Strong P-gp inhibitor and moderate CYP3A4inhibitor	Dronedarone	Levels of rivaroxaban increased by up to 160%. Contraindicated.	Levels of edoxaban likely to increase. Requires dose reduction to 30 mg once daily.	Levels of apixaban increased by 100% for some, no data availablefor others. Contraindicated.	Levels of dabigatran increased by ~100% for dronedarone. Contraindicated.
Strong P-gp inhibitor/inducer and strong inhibitorof CYP3A40	HIV protease inhibitors	Levels of rivaroxaban increased by up to 160%. Contraindicated.	Levels of edoxaban likely to increase. Contraindicated.	Levels of apixaban increased by 100% for some, no data availablefor others. Contraindicated.	May increase or decrease risk of bleeding. Avoid combination.
Strong P-gp inhibitors and moderate CYP3A4 inhibitors	Ciclosporin	Predicted to increase exposure, increasing rivaroxaban effect.	Levels of edoxaban increased. Requires dose reduction to 30 mg once daily.	Predicted to increase exposure, increasing apixaban effect.	Contraindicated.

	Tacrolimus	Extent of interaction unknown.	Interaction expected. Avoid.	Extent of interaction unknown.	Combination contraindicated.
Mild to moderate P-gp inhibitor and moderate CYP3A4 inhibitor	Amiodarone Quinidine Verapamil		Levels of edoxaban increased. Does not require dose reduction based on clinical data.	Levels of apixaban increased but to a lesser extent than with the strong inhibitors. Monitor for signs of bleeding, no dose adjustment required.	Levels of dabigatran increased by ~50 - 60%. Reduce dose to 110 mg twice daily. Due to the long half-life of amiodarone, the potential for interaction may persist for several weeks after stopping amiodarone. Reduce dose to 110 mg twice daily, advise patient to take simultaneously, monitor carefully. Largest increase in dabigatran levels observed when verapamil administered one hour prior to dabigatran with no significant increase when administered two hours after dabigatran.
	Diltiazem			Levels of apixaban increased but to a lesser extent than with the strong inhibitors. Monitor for signs of bleeding, no dose adjustment required.	
Moderate CYP3A4 inhibitor	Fluconazole	Levels of rivaroxaban increased by 40%. Not considered clinically significant.	No data	Not considered clinically significant.	No data
Strong CYP3A4 and moderate P- gp inhibitor	Clarithromycin	Levels of rivaroxaban increased by 50%. Not considered clinically significant. No dose reduction required. Monitor closely. Consider use of azithromycin (safer alternative).	Predicted to increase exposure to edoxaban. Not considered clinically significant.	Expected increase in levels of apixaban. Not considered clinically significant.	Levels of dabigatran increased by ~20%. No dose reduction required. Monitor closely. Consider use of azithromycin (safer alternative).

Moderate CYP3A4 and moderate P- gp inhibitor	Erythromycin	Levels of erythromycin increased by 30%. Not considered clinically significant. No dose reduction required. Monitor closely. Consider use of azithromycin (safer alternative).	Levels of edoxaban increased. Requires dose reduction to 30 mg once daily.	Might increase in levels of apixaban. Not considered clinically significant.	Levels of dabigatran increased by ~20%. No dose reduction required. Monitor closely. Consider use of azithromycin (safer alternative).
Strong P-gp inducer and strong CYP3A4 inducer	Rifampicin Carbamazepine Phenytoin Phenobarbital St John's Wort	Reduces area under curve (AUC) of rivaroxaban by 50% causing a reduced anticoagulation effect. Contraindicated.	Levels of edoxaban reduced, 35%. Avoid.	Levels of apixaban reduced, 50% reduction with rifampicin. Combination contraindicated.	Levels of dabigatran decreased. Combination contraindicated.

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Outpatient Management of Pulmonary Embolism

National guidance now supports outpatient management in both suspected and confirmed PE, providing the risk of complications is low. People attending the Emergency Department, Same Day Emergency Care (SDEC), or any Acute Medical Review area with suspected PE can be managed in an ambulatory fashion if identified as low risk by a *validated* risk stratification tool.

The risk of early complications in this setting can be calculated using the widely validated Simplified Pulmonary Embolism Severity Index (SPESI). Other validated risk stratification tools are available through online calculators, such as the PESI score and HESTIA criteria.

Patients with suspected PE and an SPESI score of 0 (or a PESI score <3 / HESTIA 0 at clinical discretion) should routinely be offered initial outpatient investigation and management.

In addition to validated scoring systems, document the NEWS score (should be <3) and social history during assessment and share the final decision on ambulatory vs inpatient care with the patient whenever possible, based on overall risk assessment and patient preference.

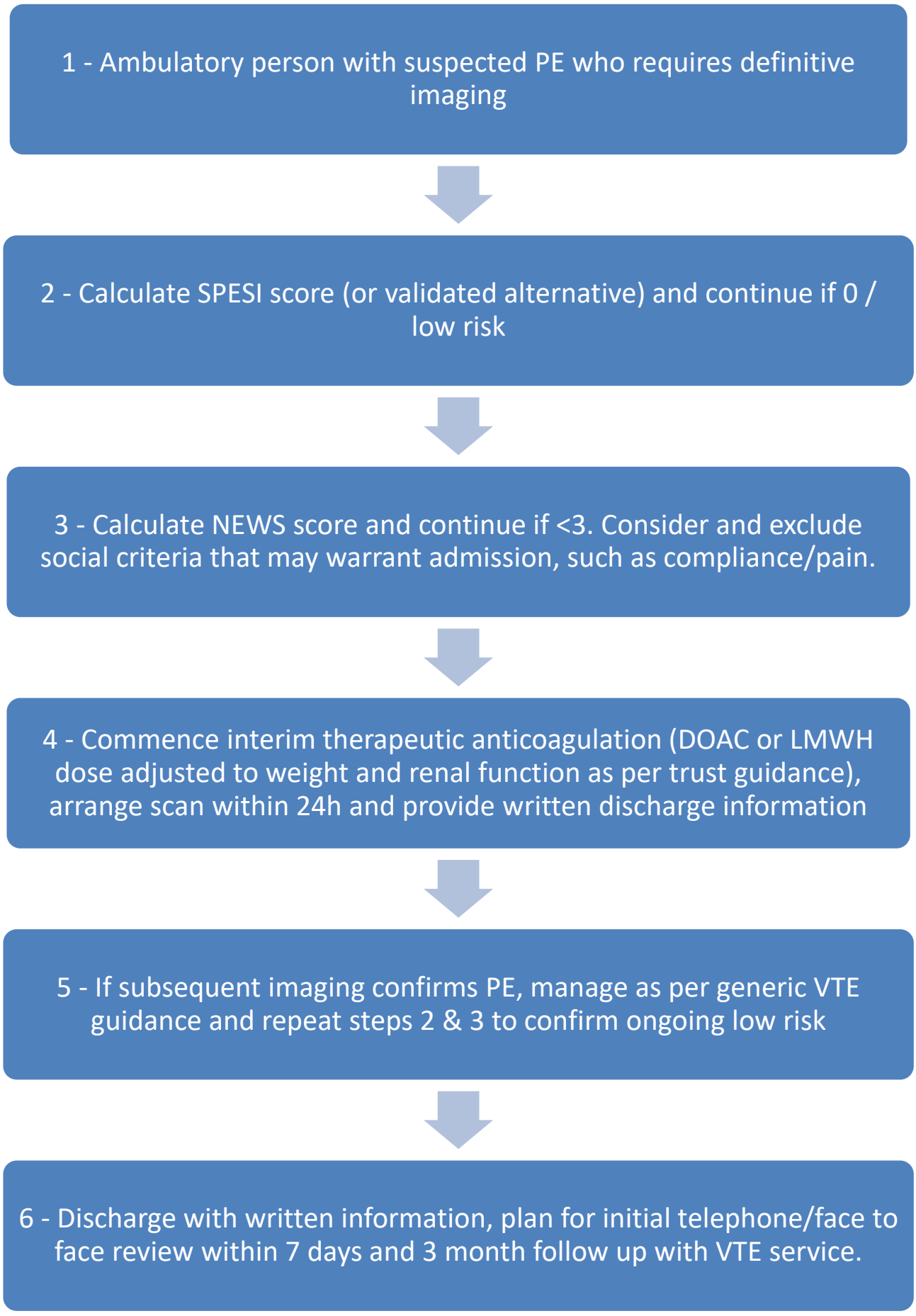
A raised SPESI/HESTIA score of ≥1 or PESI >2 carries a predicted short-term mortality risk of >8.9% and usually warrants hospital admission. ***These patients must be discussed with or reviewed by a consultant/senior decision maker if ambulatory care is being considered.***

If a decision is made to manage a person with *suspected* PE on an outpatient VTE pathway, ensure interim dosing of therapeutic anticoagulation and arrange a scan within 24h as per national BTS and NICE guidance. Agree a plan for review and provide written information on the potential complications of VTE and treatment, direct contact details for the accountable clinical team who can discuss any new issues and information on out of hours services they can contact.

If subsequent imaging confirms PE, follow the generic trust guidance on initial management of confirmed VTE including the following key points:

1. assessment of provocation
2. consideration of malignancy screening in the context of unprovoked VTE,
3. estimating and mitigating bleeding risk
4. commence therapeutic anticoagulation for an initial period of 3 months

If a decision is made to manage a person with *confirmed* PE on an outpatient pathway, ensure appropriate therapeutic anticoagulation and agree a plan for monitoring and follow up in line with BTS guidance, which **must include an initial telephone or face to face review within 7 days of discharge**. Patients should also be referred for 3-month follow up to a dedicated VTE service. At SCO this can be achieved through direct email referral to pulmonary.embolismFU@nca.nhs.uk


1 - Ambulatory person with suspected PE who requires definitive imaging
2 - Calculate SPESI score (or validated alternative) and continue if 0 / low risk
3 - Calculate NEWS score and continue if <3. Consider and exclude social criteria that may warrant admission, such as compliance/pain.
4 - Commence interim therapeutic anticoagulation (DOAC or LMWH dose adjusted to weight and renal function as per trust guidance), arrange scan within 24h and provide written discharge information
5 - If subsequent imaging confirms PE, manage as per generic VTE guidance and repeat steps 2 & 3 to confirm ongoing low risk
6 - Discharge with written information, plan for initial telephone/face to face review within 7 days and 3 month follow up with VTE service.

SPESI Score

Clinical feature	Points
Age >80	1
Active Cancer	1
History of chronic cardiopulmonary disease	1
Heart rate ≥ 110	1
Systolic BP ≤ 100mmHg	1
Oxygen Saturation <90% on room air	1
Total SPESI Score	

How to arrange an outpatient scan and subsequent follow up in SDEC/Outpatient Clinic

SCO	OCO	BCO	RCO
1. Order the relevant scan (CTPA or V/Q) on EPR.	Order the CTPA/ V/Q scan via Health views.	Order the CTPA/ V/Q scan via Health views.	Order the CTPA/ V/Q scan via Health views.
2. Use the 'Outpatient management of VTE' document or liaise with the RMO to book scan time and SDEC review	If no slots available same day, CT will contact the patient to come in. The patient then self presents at SDEC after the scan	CT will contact SDEC with appointment and patient will then be contacted by SDEC services	Put in SDEC diary and email medical secretary for details to be inputted on the Tracker system. Provide written safety netting advice and SDEC contact details
3. Provide a 'testing for blood clots' leaflet with details of the review and guidance on what to do in the event of complications	Provide written safety netting advice and SDEC contact details	Provide written details on discharge with review details (Time date and location) and safety netting advice.	CT will contact patient for appt – if cannula required, CT will send to SDEC for this to be completed. Patient will be contacted to attend on the day/ next day when results are available (checked daily via Tracker)

What should I use for therapeutic dose interim anticoagulation and on confirmation of PE

Rivaroxaban OR apixaban are now recommended in NICE 2020 guidance as preferred initial first line treatment in patients with suspected/confirmed PE who are not pregnant or breastfeeding, without severe renal or hepatic impairment, or at extremes of weight (<50 or >120kg). Doses are below:

Rivaroxaban – 15mg BD initially until scan. If PE confirmed, to complete 21 days total at 15mg BD, then 20mg OD for remainder of 3 months.
Apixaban – 10mg BD initially until scan. If PE confirmed, to complete 7 days total at 10mg BD, then 5mg BD for remainder of 3 months.

For patients who cannot take the above, use once daily LMWH dosed according to weight and renal function as interim anticoagulation. See Appendix 1 of the VTE investigation and management NCA guideline for further options and detailed notes on prescribing.

Where can I find national guidelines on this topic?

British Thoracic Society guidelines - https://thorax.bmj.com/content/73/Suppl_2/ii1
BTS quality standards - https://bmjopenrespres.bmj.com/content/7/1/e000636
NICE - https://www.nice.org.uk/guidance/ng158/chapter/Recommendations#outpatient-treatment-for-low-risk-pe

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Systemic Thrombolysis in Pulmonary Embolism

All patients require immediate therapeutic anticoagulation on confirmation of PE diagnosis. Higher risk patients can also benefit from consideration of acute reperfusion strategies. **High risk PE** is NOT defined by clot burden or hypoxaemia. A **high-risk PE** is defined by haemodynamic instability and clinical evidence of shock as outlined by 2019 ESC guidance below:

Early mortality risk		Indicators of risk			
		Haemodynamic instability	PESI>2 or SPESI >0	RV dysfunction (on echo or CTPA)	Elevated cardiac troponin levels
High		+	+	+	+
Intermediate	Int-High	-	+	+	+
	Int-Low	-	+	One (or none) positive	
Low		-	-	-	-

Ongoing haemodynamic instability is defined as any of the following rows / clinical scenarios:

CARDIAC ARREST	Defined as any need for CPR		
OR **OBSTRUCTIVE SHOCK**	Defined as Systolic BP <90mmHg or vasopressors required to achieve a systolic BP of ≥90mmHg despite adequate filling status	**AND**	Evidence of end-organ hypoperfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate)
OR **PERSISTENT HYPOTENSION**	Defined as systolic BP <90mmHg or systolic BP drop ≥40 mmHg, lasting longer than 15 min and not caused by new-onset arrhythmia, hypovolaemia, or sepsis	**AND**	Evidence of end-organ hypoperfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate)

The first step in managing high risk PE is to Initiate immediate therapeutic anticoagulation

The second step is to consider systemic reperfusion therapy with thrombolysis based on individualised bleeding risk, patient preference and clinical trajectory.

See the flow chart below for guidance on considering systemic thrombolysis in high risk PE.

1 - Patient with confirmed PE or strong suspicion of PE but too unstable to image

2 - If not commenced already, start therapeutic anticoagulation immediately using unfractionated heparin (UFH) bolus/infusion or subcutaneous LMWH

3 - Review ESC criteria in table 1 & 2 - only continue if meets definition of high risk PE

4 - Consider the relative contraindications and bleeding risk with additional systemic thrombolysis - involved the named consultant whenever possible. Higher rates of major bleeding post thrombolysis occur in those >75, high BMI and with high HASBLED scores

5 - If decision is made to thrombolyse - administer a 10mg bolus of alteplase followed by a 90mg infusion over 2h. Total dose is 100mg in >65kg.

6 - If cardiac arrest is imminent or occurs during preparation, adjust the dose delivery to 50mg bolus over 1 minute followed by 50mg infusion over 2h. In this situation, prolonged CPR (60-90 mins) should be considered. Total dose remains 100mg.

Therapeutic anticoagulation in high risk PE

In patients with clear evidence of shock and tissue hypoperfusion, IV UFH is preferred as the initial anticoagulation modality due to certainty of absorption/uptake and ease of reversal. The initial bolus of UFH = 75U/Kg titrated over 3-5 minutes (max 8000U). A maintenance infusion follows. Further guidance is available in the dedicated trust policy document. If there is a good clinical response to thrombolysis, convert UFH to LMWH after 24h.

For all other patients with intermediate PE, therapeutic anticoagulation should be commenced with LMWH given the lower bleeding risk and more predictable pharmacokinetics. Further guidance is available in the dedicated trust policy document.

DO NOT stop or reverse therapeutic anticoagulation to deliver systemic thrombolysis.

Bleeding considerations with thrombolysis:

Major contraindications	**Relative Contraindications**	**Increased bleeding risk with thrombolysis**
Active Intracranial neoplasm	Severe uncontrolled hypertension	>75 years of age
Recent (<8 weeks) intracranial/spinal surgery	Non-haemorrhagic stroke >3 months ago	Increased BMI
Haemorrhagic stroke	Surgery within previous 10 days	High HAS-BLED score
Active bleeding or recent significant internal bleeding	Pregnancy	
	Non-haemorrhagic stroke within last 3 months	
	Active neoplastic disease	

How to reconstitute and administer alteplase

Reconstitute alteplase 100 mg vial with preservative-free sterile water, provided using the transfer set in same package. Swirl the alteplase vial gently to remove bubbles.

	Volume to be administered according to concentration	
WEIGHT≥65KG	1mg/ml	2mg/ml
10 mg as an intravenous bolus over 1 - 2 minutes, immediately followed by	10ml	5ml
90 mg as an intravenous constant rate infusion over 2 hours until the maximum total dose of 100 mg	90ml	45ml
WEIGHT <65KG		
10 mg as an intravenous bolus over 1 - 2 minutes, immediately followed by	10ml	5ml
an intravenous constant rate infusion over 2 hours up to a maximum total dose of 1.5 mg/kg actual body weight	1.5ml/Kg actual body weight	0.75ml/Kg actual body weight

Further instructions on alteplase reconstitution (including images) can be found via the electronic medicines compendium and the online injectable medicines guide (Medusa).