Whittington Health NHS

Venous Thromboembolic Disease (VTE) including Pulmonary Embolism & Deep Vein Thrombosis

Diagnosis & Management

Subject:	Venous thromboembolism – diagnosis and management
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Key Words:	VTE, pulmonary embolism, deep vein thrombosis (DVT)

Version Control Sheet

Version	Date	Author	Status	Comment
1.0	November 2015 (consultation from November 2014)	Dr Farrukh Shah, Consultant Haematologist, Dr Rodric Jenkin, Consultant Physician Dr Alison Thomas, Dr Rizwan Kaiser (Consultant Respiratory Physician)	Live	New guideline approved at November 25 meeting of the Clinical Guidelines Committee

➢ Criteria for use

➢ This guideline is for use only with **NON-PREGNANT ADULT PATIENTS** with suspected pulmonary embolism or deep vein thrombosis.

Please see Whittington Health Guideline
"Venous Thromboembolism in Pregnancy and the Puerperium: Acute Management."

➢ 1. 1 Introduction

Guidelines for the management of suspected acute pulmonary embolism (PE) and deep vein thrombosis were published NICE guidance published in 2012 [2]

The diagnosis and management of VTE consists of a number of stages:

- Establishing a diagnosis:
  - Clinical evaluation and pre-test probability score (Wells score)
  - D-dimer for diagnosis exclusion in low risk patients
  - Imaging to confirm diagnosis (Doppler ultrasound, V/Q scan (ventilation perfusion scan or CTPA (CT pulmonary angiogram)
- For PE: risk stratification to determine management location (inpatient vs. outpatient) and treatment escalation in massive and sub-massive PE
- Immediate therapy: initiation of heparin anticoagulation
- VTE classification (provoked vs. unprovoked vs. cancer-related) and longer term management.

➢ 1.2 Risk Factors for VTE

PROVOKING	***OTHER:***
Active cancer or receiving cancer treatment	Previous VTE or family history of VTE
Surgery within past 12 weeks	Obesity (Body mass index >30kg/m^2)
Hospitalisation within past 12 weeks	Known thrombophilia
Pregnancy or recent childbirth	Medical co-morbidities including: heart disease, lung disease, inflammatory disorders, metabolic/endocrine disorders
Hormone replacement therapy or oestrogen containing contraceptive	Sickle cell disease or thalassaemia
Intravenous drug use	Nephrotic syndrome
Central venous catheter (in situ or recent)	Varicose veins with phlebitis
Lower limb fracture/ immobilisation	
Immobilisation >3 days	
Long distance travel >4 hours	

➢ 1. 3 Is VTE likely?

The following must be considered during clinical assessment:

- Presenting features suggestive of PE or DVT
- Is there another diagnosis that may account for the symptoms/signs? E.g.
    - **PE:** Pneumonia, cardiac failure, pneumothorax, exacerbation COPD, myocardial infarction, pericarditis
    - **DVT:** Cellulitis, cardiac failure, lymphoedema, dependent oedema

➢ 2 Pulmonary Embolism (PE)

➢ 2.1 Presenting features of PE

PE classically has several patterns of presentation: -

- Sudden circulatory collapse with acute right heart failure, in a previously well patient or in a patient with poor cardiorespiratory reserve (15%)
- Pulmonary infarction syndrome i.e. pleuritic chest pain +/- haemoptysis (60%)
- Isolated breathlessness (25%)

97% patients with PE will have ≥ 1 of dyspnoea/tachypnoea/pleuritic chest pain.

The overall predictive value of any single clinical feature in the diagnosis or exclusion of PE is less than 80% [3]. The commonest symptoms and signs are:-

Symptoms		**Signs**	
Breathlessness	73%	Tachypnoea $\geq$ 20/min	70%
Pleuritic chest pain	66%	Crackles	51%
Cough	20%	Tachycardia $\geq$ 100/min	30%
Haemoptysis	11%		

Less common signs include: Wheeze, pleural rub, Loud pulmonary 2nd HS, pyrexia

➢ 2.2 Basic initial tests for suspected PE

- Arterial Blood Gas (ABG) on air if O_2 Sats < 94% (note O_2 Sats may be in normal range in young healthy adults
- ECG – commonest finding is sinus tachycardia, look for changes of R heart Strain : anteroseptal T wave inversion or ST depression, RBBB, S1 Q3 T3 pattern
- CXR to look for alternative cause. In PE often normal, but the following may be seen :
  - Linear/wedge shaped shadows
  - Small pleural effusion
  - Localised subtle paucity of vasculature
- Troponin T – may be elevated in acute PE (correlates with increased short term mortality and risk of adverse outcome) **[7]**
- Pregnancy test: must be performed in all women of childbearing age. If positive refer to separate guideline relating to VTE diagnosis and management in pregnancy.

➢ 2.3 Clinical Probability Scoring in PE – Two level Wells score

Two-level PE Wells Score [4]	
Criterion	Points
Clinical signs of DVT (i.e. leg swelling, pain)	+3
Alternative diagnosis **less likely** than PE	+3
Heart rate > 100/minute	+1.5
Immobilization (>3 days) or surgery < 4 weeks ago	+1.5
Previous DVT or PE	+1.5
Haemoptysis	+1
Cancer	+1

Total score

- 4 points or less : PE unlikely
- > 4 points : PE likely

➢ 2.4 D-dimer in diagnosis of PE

D-dimers are breakdown products from fibrinolysis and are raised in a number of circumstances including active thrombosis, disseminated intravascular coagulation, inflammation, cancer and pregnancy.

They are only useful for EXCLUSION of VTE in patients already deemed to be at low risk clinically using the Wells score i.e.: PE Wells clinical probability score is 4 points or less (PE unlikely score)

- D-dimer should **not** be performed if:
  - PE or DVT Wells clinical probability score is high.
  - Inpatients, pregnancy and sickle cell patients with vaso-occlusive crisis. These patients should proceed directly to imaging.

- Negative D-dimer test (<250 ng/ml FEU) test reliably excludes PE/DVT in patients with **LOW** clinical probability scores. Further tests for PE or DVT are not indicated.

D-dimer goes in a citrate bottle (**light blue top**). The Wells score is required on the request form.
For the current Sysmex Innovance assay a cut off value of ≥ 250 ng/ml FEU has been set, whereby a value to ≥ 250 ng/ml FEU is considered **POSITIVE**

➢ 2.5 Chest x-ray (CXR)

- Good quality PA (posteroanterior) CXR should be obtained.
- Aim to get a formal review of CXR by a radiologist. Within working hours review by hot seat radiology. Outside of working hours, CXR must be reviewed by a senior clinician (registrar grade or above)
- Look specifically for other diagnoses i.e. pneumonia, pneumothorax, heart failure,
- Features of chronic airflow obstruction (e.g. hyperinflation).

➢ 2.6 VQ or CTPA

VQ should be considered 1st line if:

- Age < 40 years and <u>provided CXR is normal & no history of chronic respiratory disease</u>
- History of contrast allergy
- Severe renal impairment

CTPA should be considered 1st line if:

- Age > 40 years
- Abnormal CXR or history of chronic respiratory disease
- Any age and massive or submassive PE suspected (haemodynamic instability and/or severe hypoxaemia)

Definitive investigation for PE **<u>must occur within 24 hours</u>** of presentation, ideally the same day. Within working hours arrange test via radiology hot seat.

- VQ available Monday - Friday only – MUST INFORM NUCLEAR MEDICINE (x5517) BY 12 pm FOR POSSIBLE SAME DAY VQ SCAN.

- Weekends – CTPA only, unless patient presents on a Sunday and can wait for VQ on Monday (discuss with radiologist on call).

- If out of hours and/or same day scan not possible - if patient is suitable for ambulatory care with no exclusion criteria (see ambulatory care pathway), then patient can be treated with LMWH and return to Ambulatory Clinic for next day scan and review. See Ambulatory Care Pathway Guideline.

- Treat patient with LMWH whilst awaiting imaging, unless imaging to be performed within 1 hour of patient's presentation.

A normal VQ scan and good quality negative CTPA exclude PE. However, if there is discordant very high clinical probability and no alternative cause for symptoms, then further imaging maybe indicated. If there is clinical suspicion of DVT then perform leg Dopplers. Discuss all such cases with Thoracic Radiology Consultant and Respiratory Consultant.

Radiation to patient

- CXR 0.02 mSv
- VQ scan 1.4 mSv (70 CXR)
- CTPA 5mSv (250 CXR)
- Background (annual) 2mSv (100 CXR)

Pulmonary Embolism – Investigation Pathway

Clinically suspected Pulmonary Embolism
→ Breathlessness ± Pleuritic chest pain ± Haemoptysis

If hypotensive, and massive PE suspected – Urgent CTPA or portable ECHO (if not clinically stable for transfer to CT)

History/Examination/ ECG/ CXR
Bloods (FBC, U&E, CRP, Clotting, Trop T +/- ABG

Assess Clinical Probability (2 Level Wells Score)

PE unlikely (≤ 4 points)

PE likely (>4 points)

Check D-dimers

D-dimer -ve

D-dimer

PE excluded
Consider alternative diagnoses

Give treatment dose LMWH (Tinzaparin 175 mg/kg)

Arrange PE investigation (as per algorithm below)

If clinically stable assess suitability for Ambulatory Care

Wells Clinical Probability Score

	Points
Clinical Signs of DVT	3
Alternative diagnosis less likely than PE	3
Immobilisation (>3 days) or surgery previous 4 weeks	1.5
Previous DVT or PE	1.5
HR > 100 /min	1.5
Haemoptysis	1
Active Cancer	1

Total score > 4 points : PE likely
Total score 4 points or less : PE unlikely

Diagnostic Test Algorithm for Pulmonary Embolism

Contrast allergy Or severe renal impairment

Age < 40

Age > 40

Any age and massive/ submassive PE suspected (Haemodynamically unstable and/or significant hypoxaemia)

CXR abnormal OR Chronic resp disease

No

Yes

VQ (SPECT) Scan

CTPA

➢ 2.7 Risk Stratification of confirmed PE

Risk stratification is used to determine which subgroups may be at highest risk of clinical deterioration and therefore may benefit the most from more intense monitoring or perhaps even the administration of thrombolytic therapy. Likewise low risk patients may be suitable for outpatient ambulatory care [5;6]

PE can be classified as:

- High Risk (= Massive PE, > 15% PE related mortality) – accounts for 5% of all cases
  → manifests as haemodynamic instability (cardiogenic shock or hypotension).

- Intermediate Risk (= Submassive PE, 3-10% PE related mortality) – 15-20% of all PE cases
  → Patient haemodynamically stable on presentation, but with evidence of right ventricular strain.

- Low Risk (<1% mortality) – 75% of all cases
  → Haemodynamically stable and no signs of right ventricular strain.

Patients who are haemodynamically stable at presentation should be risk stratified using a combination of a clinical severity score (PESI score – see below) and assessment for right ventricular dysfunction using imaging (CT, Echo) and cardiac biomarkers [5-7]

Table 1 - Pulmonary Embolism Severity Index (PESI) Score

Criteria	**Points**	**Patients Score**
Age	1 point per year	
Male sex	10	
Active cancer (last 6 months)	30	
Heart failure	10	
Chronic lung disease	10	
Pulse > 110 /min	20	
Systolic BP < 100 mmHg	30	
Resp Rate > 30 /min	20	
Body temp < 36 C	20	
Altered mental state	60	
Oxygen Sats <90% on air	20	
	Total score	

Score	**Severity Index**	**30 day mortality**
< 65	I – very low risk	0.7%
66-85	II – low risk	1.2%
86-105	III – intermediate risk	4.8%
106-125	IV – high risk	13.6%
>125	V – very high risk	24.5%

Markers of right ventricular dysfunction should be assessed to stratify risk:

- Elevation of Troponin T (due to RV myocardial injury)

- CTPA features of Right Heart Strain (RV dilatation with RV:LV ratio >0.9).
  ALL CTPA reports should comment on the presence/absence of right heart strain

- ECHO features : RV dilatation or RV systolic dysfunction, paradoxical septal wall motion
  (*ECHO should be requested in cases where the CTPA suggests Right Heart Strain, or the Trop T is positive in combination with a High PESI score or significant central clot burden*)

➢ 2.8 Submassive (Intermediate Risk) PE

Defined as significant acute pulmonary embolism, with evidence of right ventricular dysfunction and/or myocardial injury but without hypotension (SBP <90mmHg or ≥40mmHg drop from baseline, for more than 15 minutes)

Management

- If eGFR >20mls/min: Administer bolus dose of IV Unfractionated Heparin (80 Units/kg), followed by daily s/c LMWH (Tinzaparin 175 mg/kg)

- If eGFR <20 ml/min: Commence IV Heparin infusion at 1000U/hr and adjust as per activated partial thromboplastin time (APTT) ("See **Therapeutic Anticoagulation in Adults Guideline**" target APTT 1.5-2.5).

- Monitor anti-Xa level if eGFR 20-30ml/min and patient given LMWH.

At present there is no definitive evidence that thrombolysis improves mortality in patients without shock, hypotension or cardiac arrest, compared to Heparin alone [5].

In general, these patients should be monitored very closely for the initial 48-72 hours (on CCU, HDU or AAU monitored bed), and thrombolysis considered early at signs of haemodynamic decompensation.

In cases of submassive PE where BP is maintained but multiple adverse prognostic indicators are present (extensive central clot burden on imaging, significant RV dysfunction on ECHO, severe hypoxaemia, positive Troponin, High Risk PESI score III-V, coexisting proximal DVT, and age <75 years), thrombolysis can be considered but only on a case by case basis following discussion with Medical Consultant on call.

If thrombolysis would be contraindicated due to bleeding risk, then patient should be electively transferred to the Bart's Health.

Patients with submassive PE at presentation will require a repeat Echocardiogram at 3 months, and respiratory follow up, as there is a risk of developing chronic thromboembolic pulmonary hypertension.

➢ 2.9 Massive (High Risk) PE & Thrombolysis

- **Discuss all cases of massive PE with the medical consultant on call.**

- **Massive PE is PE so severe as to cause circulatory collapse and is due to acute right heart failure.** It is defined as PE with hypotension (either systolic BP <90 mmHg or a pressure drop ≥40 mmHg, for more than 15 mins), that is not caused by a cardiac arrhythmia, hypovolaemia or sepsis.

- The diagnosis of PE should be confirmed by an urgent CTPA. If clinically unstable for transfer to CT, an urgent portable ECHO showing either acute right ventricular dysfunction (where there is no other explanation for RV dysfunction) or a free floating thrombus in the right atrium or right ventricle. For urgent portable ECHO, within working hours contact cardiac technician or cardiology SpR. Out of hours contact ED or ITU SpR. If out of hours ECHO expertise is not available, then patient should be stabilized with inotropic support and an urgent CTPA then performed.

- Patients should be treated with unfractionated IV heparin (UFH) whilst waiting for tests to confirm PE (Bolus dose of 80 IU/kg, and maintenance infusion 1000U/hr, adjusted to APTT 1.5-2.5, see "**Therapeutic anticoagulation in adults guideline**")

- Thrombolysis is the first line treatment for massive PE. The expected therapeutic benefit should always be weighed up carefully against the risk of bleeding. The risk of major bleeding with thrombolysis is ~ 10%, with intracranial haemorrhage 2-3%. Risks and benefits should be discussed with patient when feasible. Thrombolysis may be instituted on clinical grounds alone if cardiac arrest is imminent.

- Give thrombolysis <u>peripherally</u> not centrally as increased risk of bleeding.

- <u>Administration for PE causing cardiac arrest or peri-arrest :</u>
  50 mg IV bolus of **alteplase** (tPA) over 1-2 minutes

- <u>Administration for massive PE but not in cardiac or peri-arrest</u> :
  - 100mg **alteplase** diluted in 2mg/ml of water for injection
  - 10 mg given as bolus over 1-2 minutes
  - Remaining 90 mg over 2 hours via syringe driver.
  - N.B In patients less than 65kg, the total dose should not be more than 1.5mg/kg (but bolus dose of 10mg remains the same)
  - Discontinue Heparin infusion whilst thrombolytic being administered

- Follow thrombolysis with IV Heparin infusion. Immediately check APTT :
  - If APTT ratio < 2, commence/resume IV heparin infusion (Maintenance Infusion 1000 U/hr). If APTT ratio is >2, wait and repeat after 4 hours
  - Adjust to aim for an APTT ratio of around 2 (range 1.5-2.5) (see "Therapeutic anticoagulation in adults guideline'' for dosing adjustments")
  - Check APTT 6 hours after any dose change
  - Commence Warfarin day 3, continue heparin for at least 5 days and until INR > 2 for 2 consecutive days
  - **N.B.If patient had received dose of LMWH prior to thrombolysis, Heparin infusion should only be commenced 18 hours after time of LMWH dose.**

All patients should be transferred to Intensive Care Unit, but thrombolysis should not be delayed whilst awaiting a bed.

If thrombolysis is contraindicated, or there is failure to respond to thrombolysis, therapeutic options include surgical or catheter thromboembolectomy. All cases should be discussed with the cardiothoracic surgeon on call at the Bart's Health. Mechanical treatment rather than repeat thrombolysis is favoured for persistent obstructing clot.

Contraindications to Thrombolysis

Absolute*

- Known history of intracranial haemorrhage at any time
- Ischaemic stroke in preceding 6 months
- Known cerebral neoplasm, arteriovenous malformation, or intracranial aneurysm
- Active internal bleeding
- Recent head trauma/ brain or spinal surgery/ head injury (within 8 weeks)
- Known bleeding diathesis

Relative

- Recent surgery (within 2 weeks)
- Oral anticoagulant therapy
- Prolonged traumatic resuscitation
- Non compressible blood vessel puncture in past 7 days
- Refractory Hypertension (systolic > 180 mmHg)
- Advanced liver disease
- Pregnancy or within 1 week post-partum
- Infective endocarditis
- Active peptic ulcer disease

*Contraindications to thrombolysis that are considered absolute might become relative in a patient with immediately life threatening massive PE where alternative therapy not immediately available.

Discuss difficult cases with admitting consultant and Haematology Consultant on call.

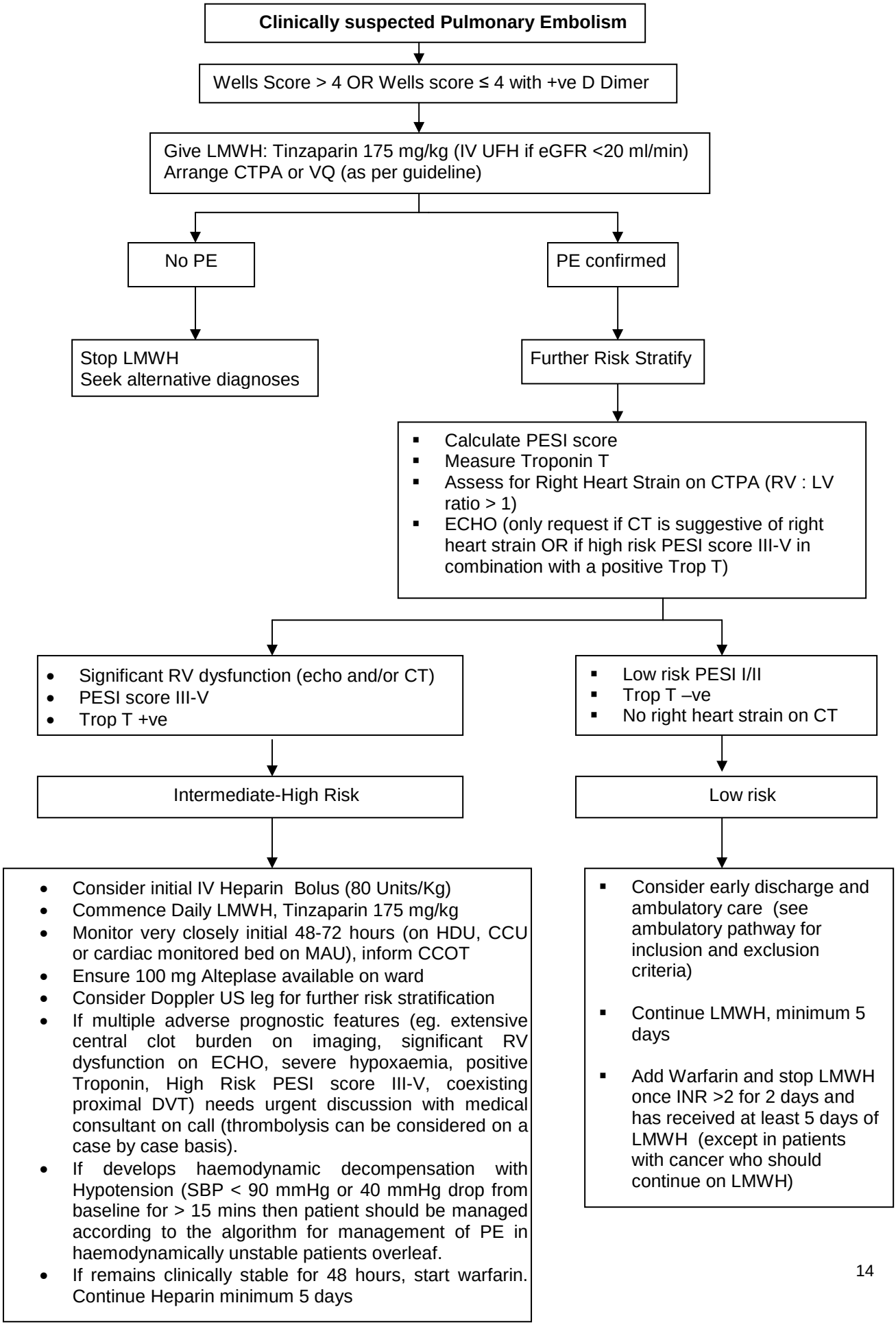
➢ 2.10 Oxygen therapy and Pulmonary Embolism

Prescribe oxygen for all patients admitted with PE using appropriate target saturations for that individual. In general, target saturation range should be:

- 95-98% for patients without underlying respiratory disease
- 90-94% for patients with chronic respiratory disease without Type II resp failure
- 88-92% for those with COPD and Type II respiratory failure, or obesity hypoventilation

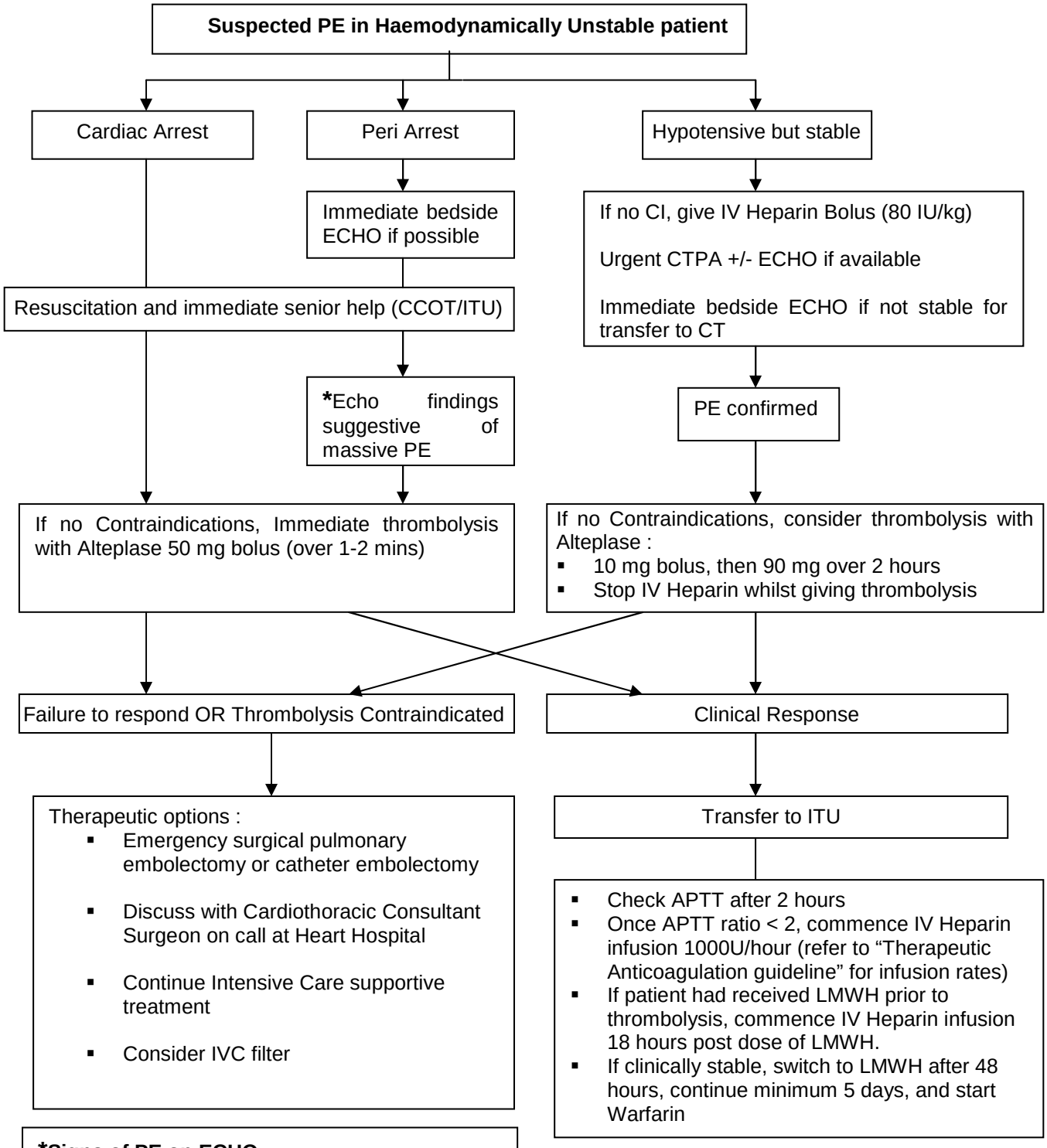
	**Please see Whittington Health Guideline:** Safe Oxygen Therapy in Adult Patients Guideline

Algorithm for Management of suspected PE in Haemodynamically Stable (SBP >90mmHg)



Algorithm for Management of suspected PE in Haemodynamically Unstable Patients

(SBP <90mmHg or drop of >40mmHg from baseline for >15 mins, and not due to hypovolaemia/sepsis/arrhythmia)



***Signs of PE on ECHO**

Indirect:
Right ventricular dysfunction – dilatation, impaired systolic function, free wall hypokinesia, paradoxical septal wall motion

Direct:
Thrombi in right atrium, right ventricle, or pulmonary artery

➢ 3. Deep Vein Thrombosis (DVT)

➢ 3.1 Presentation and assessment of DVT (including use of D-dimer)

Proximal deep vein thrombosis: thrombosis involving the popliteal, femoral or iliac veins.
Distal vein thrombosis: thrombus limited to calf veins (gastrocnemius, soleus, anterior and posterior tibial veins).

Initial clinical assessment should evaluate both risk factors for VTE as well as the potential for alternative diagnoses.

Pre-test probability score should be performed in all patients using the Two level **DVT** Wells score:

Two-level DVT Wells Score(2;8)

Criterion	Points
Active cancer (treatment ongoing or within last 6 months or metastatic disease/ palliative)	+1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	+1
Immobilization (>3 days) or surgery < 12 weeks ago	+1
Localised tenderness along distribution deep venous system	+1.
Entire leg swollen	+1
Calf swelling >3cm larger than unaffected leg	+1
Pitting oedema confined to symptomatic leg	+1
Collateral superficial veins (non-varicose)	+1
Previously documented DVT	+1
An alternative diagnosis is at least as likely as DVT	-2

Total score:

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

Patients with a low risk score (1 or less) should have a D-dimer test performed.

The combination of low initial clinical suspicion, a **low risk** score and a negative D-dimer excludes a DVT and further imaging is not required.

All patients with a Wells DVT score of 2 or more or those with a positive D-dimer require further imaging with compression ultrasonography.

➢ 3.2 Compression ultrasonography for DVT diagnosis

Compression ultrasonography of the leg is the investigation of choice and imaging should be performed **within 24 hours**, ideally the same day.

Ultrasound is available on a daily basis, booked via ambulatory care or after discussion with radiology hot seat.

If scanning is not available within 4 hours the patient should receive an initial treatment dose of LMWH (see 4.2). For paients in the Emergency department or outpatients, if a same day scan is not available and the patient is suitable they can return to ambulatory care the following morning for a scan (please ensure the scan is arranged and patient knows when and where to attend)

In patients with a high clinical suspicion of DVT/ "DVT likely" Wells score and negative ultrasound scan a D-dimer should be performed. Those with a positive D-dimer should have a repeat scan at 6-8 days but should not receive anticoagulation in this period.

If the second USS is negative, a DVT is considered to be excluded [2].

➢ 3.3 Distal/ calf vein thrombosis

Imaging of the distal calf veins is not routinely performed. The risk of extension of these clots into the proximal system is low (approximately 3%) and if occurs, is usually visible after 7 days on repeat scanning of the proximal veins. Patients in whom a distal DVT is suspected who have a normal initial scan of the proximal venous system should have a repeat scan performed at 6-8 days [8]

If a distal calf vein thrombosis is seen, anticoagulation should be considered particularly if the thrombosis is large (>5cm) or in close proximity to the popliteal vein. The current recommendation is for 3 months anticoagulation [8;9].

➢ 3.4 Massive acute onset deep vein thrombosis

The treatment of choice for DVT is LMWH.

Catheter-directed thrombolysis can be considered for patients who fulfil ALL the following criteria:

- extensive symptomatic iliofemoral thrombus
- acute symptoms (<14 days duration)
- good functional status
- expected life expectancy of over 1 year
- low risk of bleeding.

Such patients should initially be discussed with the senior physician (consultant or DMR out of hours) then discussed with the on call vascular surgery SpR at the Royal Free Hospital for consideration of transfer to RFH for catheter directed thrombolysis.

➢ 3.5 Superficial vein thrombosis

Patients with lower limb superficial vein thrombosis (SVT) of the long or short saphenous vein should have an ultrasound assessment to exclude DVT, particularly if the proximal long saphenous is affected [10;11].

Patients with confirmed superficial vein thrombosis within 3cm of the saphenofemoral junction should be considered for **therapeutic** anticoagulation for 3 months.

Patients with SVT >5cm, particularly if severe symptoms OR above knee OR prior VTE OR active cancer OR recent surgery should be considered for **prophylactic** dose tinzaparin for 6 weeks.

Radiological parameters (including length of segment affected and distance to saphenofemoral junction) may not always be available in which case anticoagulation dose and duration would be a clinical decision.

Other patients should be managed symptomatically with non-steroidal anti-inflammatory drugs and/or paracetamol. Consider a repeat scan if no improvement at 1 week or earlier if progressive symptoms.

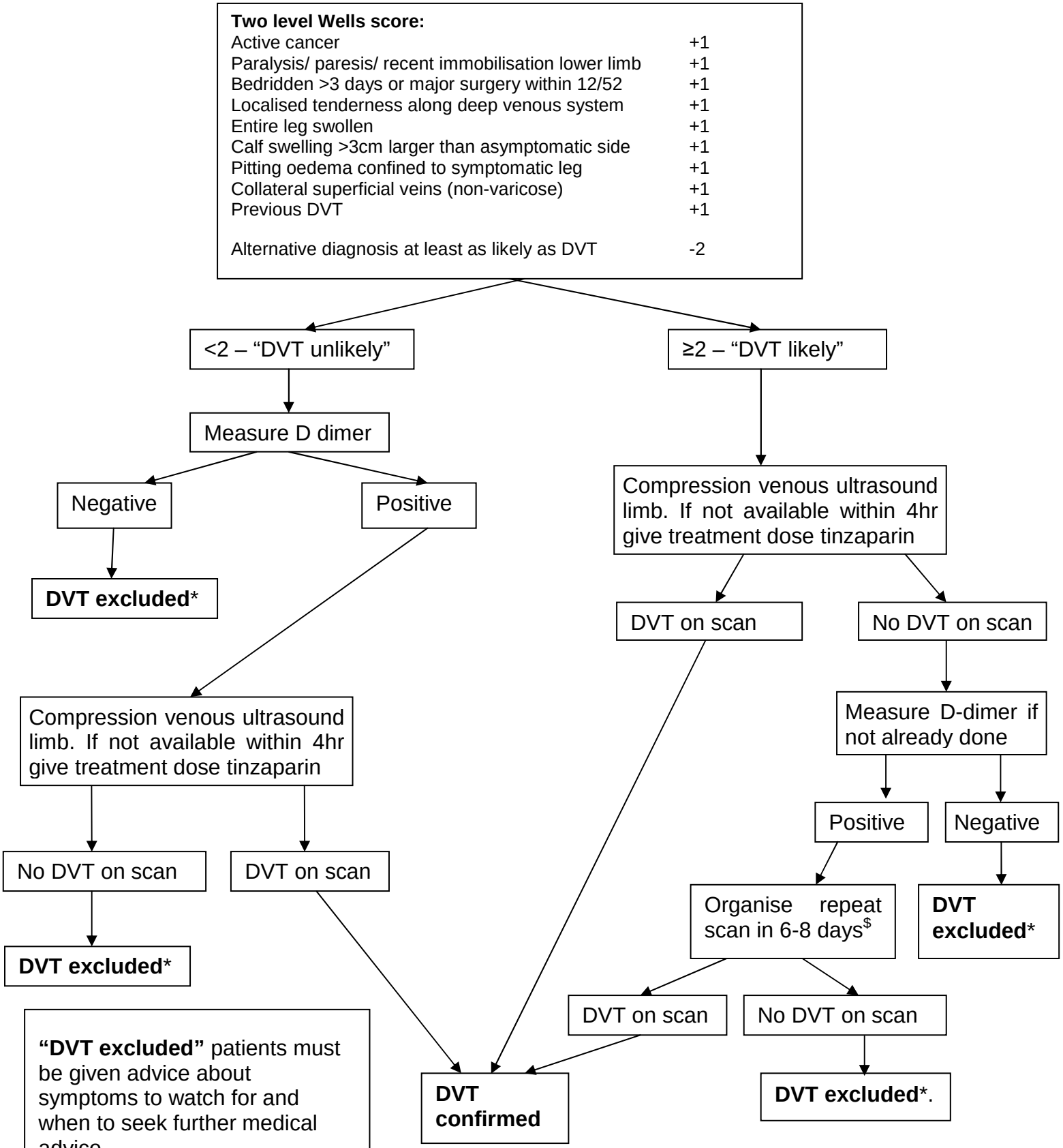
➢ 3.6 Graduated compression stockings

A recommendation should be provided in the discharge letter for GP to consider Graduated compression stockings for patients with proximal DVT. These should be worn on the affected leg. They have been demonstrated to provide symptomatic relief of symptoms of venous congestion. The role of compression stockings in the prevention of post thrombotic syndrome (PTS) is equivocal [12] but the current NICE guidelines states that Graduated compression stockings should be worn for at least 2 years and be replaced 2-3 times per year.

Contra-indications to compression stockings include:

- Swelling not sufficiently reduced to enable stocking fitting
- Peripheral arterial disease or ankle: brachial pressure index <0.8
- Severe peripheral neuropathy
- Oedema secondary to congestive cardiac failure
- Local skin/ soft tissue conditions e.g. infection, ulceration, recent skin graft
- Extreme deformity of leg

➢ Pathway for assessment of clinically suspected DVT



"DVT excluded" patients must be given advice about symptoms to watch for and when to seek further medical advice.

If clinical concern and/or no clear alternate diagnosis, seek senior support and consider offering patient a one week review appointment in ambulatory care.

$ - For high risk patients who have a negative initial ultrasound and a subsequent positive d-dimer, please ensure they are discussed with the consultant on the day as in certain circumstances additional imaging will be considered.

➢ 4.1 Classification of VTE causality

Discerning the likely causality of the VTE is important for determining treatment duration:

A **PROVOKED** VTE is defined as a VTE or PE in a patient with an antecedent (within 3 months) major transient risk factor for VTE [2]. Examples include:

- Surgery
- Trauma
- Acute medical illness
- Significant immobility (bedbound, unable to walk unaided or spending a substantial proportion of day in bed/chair)
- Long haul flight (>4 hours)
- Pregnancy or puerperium
- Hormone therapy (HRT or oral contraceptives)

An **UNPROVOKED** VTE is defined as a VTE in a patient with no antecedent major transient risk factor. These patients should be reviewed in haematology clinic at 3 months post event and considered for extended duration/ indefinite anticoagulation. They should remain on anticoagulation until reviewed.

A **CANCER-RELATED** VTE is defined as a VTE in a patient with known active malignancy (diagnosed within 6 months, receiving chemotherapy/ radiotherapy, recurrent, inoperable or metastatic disease). These patients should be treated with LMWH instead of warfarin and treatment duration determined by their oncologist/haematologist. Patients with skin squamous cell or basal cell carcinomas are not included in this definition.

➢ 4. 2 Anticoagulation for treatment of VTE

Please see Whittington Health Guideline:

'Therapeutic Anticoagulation in Adults"

INDICATION & DURATION FOR ANTICOAGULATION

- All patients commenced on therapeutic anticoagulation must have a clear indication for therapeutic anticoagulation explained to them, documented in their medical notes and conveyed to their general practitioner(9;13)
- The planned duration for anticoagulation or a review date regarding duration must be clearly documented

ASSESSMENT OF BLEEDING RISKS

- Bleeding risk must be assessed and documented in all patients prior to commencement of anticoagulation (Table 1)
- In patients deemed at increased risk of bleeding advice should be sought from a senior member of the patient's team and haematology

Table 1: Bleeding risks

Recent acute stroke (haemorrhagic or ischaemic)
History of GI bleed/ peptic ulcer
Blood pressure >200 mmHg systolic or >120 mmHg diastolic
Severe liver disease (prolonged prothrombin time or known varices)
Severe renal disease (creatinine clearance <30ml/min) with significant uraemia
Recent surgery or major trauma (especially to eye or nervous system)
Spinal intervention (e.g. lumbar puncture, spinal or epidural) planned or performed within 24 hours
Undergoing procedure with high risk of bleeding
Platelet count <100 (discuss with haematology)
Haemophilia or other known bleeding disorder (discuss with haematology)

BASELINE INVESTIGATIONS

The following must be performed prior to initiation of anticoagulation:

- Urea, creatinine and electrolytes
- Full blood count
- Liver function tests
- Coagulation screen
- Patient weight (**all patients commencing LMWH must have an actual weight measured)[14]**
- Pregnancy test (women of child-bearing age)

PATIENT COUNSELLING

All patients must be counselled regarding the risks, benefits and appropriate management of anticoagulation and written consent obtained using the form in **Appendix 1 "Therapeutic Anticoagulation in Adults".** Patients commencing warfarin should be counselled using the checklist in **Appendix 2**. Copies of the form should be given to the patient and sent to the general practitioner. The original should be retained in the patient's medical notes.

WHEN TO CONTACT HAEMATOLOGY FOR INITIAL ANTICOAGULATION ADVICE:

- Patients with an increased bleeding risk. Consideration may be given to split dosing of LMWH (87.5U/kg BD) or reduced dose tinzaparin
- Obese patients (weight >110kg): start on 175U/kg OD but consider monitoring anti-Xa levels to ensure adequate anticoagulation achieved
- Patients with confirmed VTE on therapeutic anticoagulation
- Patients with a history of allergic reactions to heparin or heparin-induced thrombocytopenia
- Patients with an e-GFR <30ml/min:
    - eGFR 20-30ml/min: 175U/kg (100% dose) with anti-Xa monitoring
    - eGFR <20ml/min: unfractionated heparin infusion

TINZAPARIN PRESCRIBING:

Cautions and contra-indications to LMWH:

Contra-indications	Cautions
History of heparin-induced thrombocytopenia	On oral vitamin K antagonist with therapeutic INR
Hypersensitivity to UFH or any LMWH	On treatment dose oral direct thrombin or Xa inhibitor (eg. rivaroxaban or dabigatran)
Major or uncontrolled active bleeding	Increased bleeding risk (see Table 1)
	eGFR <30ml/min

Dosing:
The standard therapeutic dose is 175 IU/kg once daily subcutaneously. The following chart should be used to select the correct dose and syringe size:

VTE Treatment: 175 IU/kg once daily SC (20 000 IU/ml formulation)			
	Weight (kg)	**Prescribed dose**	**Injection volume (ml)**
0.5ml syringe (RED)	37-42	7000	0.35
	43-48	8000	0.40
	49-53	9000	0.45
	54-59	10 000	0.50
0.7ml syringe (YELLOW)	60-65	11 000	0.55
	66-70	12 000	0.60
	71-76	13 000	0.65
	77-82	14 000	0.70
0.9ml syringe (BLUE)	83-88	15 000	0.75
	89-93	16 000	0.80
	94-99	17 000	0.85
	100-105	18 000	0.90
Multi-dose vial (GREEN)	106-110	19 000	0.95
	111-116	20 000	1.00
	117-122	21 000	1.05
	123-128	22 000	1.10
	129-133	23 000	1.15
	134-139	24 000	1.20
	140-145	25 000	1.25

Renal failure:

Intravenous UFH infusion is the preferred heparin for patients with eGFR<20ml/min (Cockcroft Gault creatinine clearance must be calculated for patients at extremes of body weight). Where it is felt that UFH cannot be safely administered to the patient and therapeutic anticoagulation with tinzaparin is essential, then discuss with haematology for consideration of reduced dose tinzaparin with anti-Xa monitoring.

Monitoring of anti-coagulant activity:

- Most patients receiving LMWH do not require monitoring.
- The following groups of patients may benefit from anti-Xa monitoring. **These patients must be discussed with haematology**:
    - Renal failure (eGFR <30ml/min).
    - Pregnancy
    - Obesity (weight >105kg)

How to take an anti-Xa level:

- Request on ICE including details of indication for monitoring, current dose, time of last dose and correct contact details of team to relay results. (Inform lab in advance if sample will arrive out of hours or at weekend)
- Sample must be taken **4 hours** post dose into a citrate vacutainer
- Hand deliver sample to lab (sample to be immediately centrifuged and frozen by lab before being sent to Royal Free hospital for analysis)

Monitoring for heparin induced thrombocytopenia (HIT):

Most patients do not require monitoring for HIT [15;16]. The platelet monitoring required for patients receiving LMWH or UFH is shown in Table 2.

Table 2: Platelet monitoring for heparin-induced thrombocytopenia

Patient type	Platelet monitoring for HIT
LMWH and post cardiothoracic surgery OR cancer patients undergoing surgery	• Baseline platelet count • Once between days 4-7 post starting LMWH • Once again between days 10-14 if still on LMWH
UFH during in-patient episode, now on LMWH	• Baseline platelet count • Once between days 4-7 post starting UFH • Once again between days 10-14 if still on LMWH
ANY type of heparin within previous 100 days	• Baseline platelet count • Check at 24 hours • Thereafter as per other categories as appropriate
UFH infusion	• Baseline platelet count • Check at 24 hours if UFH/LMWH in previous 100 days • Every 2-3 days from days 4-14 or until UFH stopped (whichever is earlier)
LMWH and patient does not fall into any category above	• Baseline platelet count • Subsequent monitoring not required

- Suspect HIT if the platelet count falls by 50% or more from baseline (even if the platelet count remains within the normal range)
- Consider the possibility of HIT if patient develop venous/arterial thrombosis on heparin or skin lesions at heparin injection site

- If HIT suspected **stop LMWH/UFH immediately and contact haematology urgently for advice**

Patients with active cancer (cancer-related VTE):
In patients with cancer-related VTE, LMWH is the anticoagulant of choice instead of vitamin K antagonists.

COMMENCING PATIENTS ON WARFARIN:

If patients are being commenced on warfarin as an inpatient or through ambulatory care rather than the anticoagulation clinic:

REFER TO THE "THERAPEUTIC ANTICOAGULATION IN ADULTS GUIDELINE"

- Counselling and consent
- Loading algorithm
- Patients must receive at least 5 days LMWH AND have an INR >2.0 on two consecutive days before the LMWH is stopped.

➢ 4. 3 Inferior vena cava (IVC) Filters

IVC filters are rarely indicated but consider if:

- Anticoagulation is contra-indicated. A retrievable IVC filter should be used if short term contraindication to anticoagulation
- Patients on therapeutic anticoagulation who have confirmed new VTE
- Pre-operative patient with PE (within 2 months) in whom anticoagulation must be interrupted and surgery cannot be delayed.

Discussions on a case by case basis should occur with Vascular Consultant Radiologist (Dr Kumaradevan), Consultant Respiratory Physician and Haematologists

➢ 4.4 Discharge Checklist

- € Written patient information leaflet on PE/DVT provided
- € Patient questions/concerns about PE/DVT discussed and addressed.
- € Reason for anticoagulation, expected duration of therapy
- € Patient consented for anticoagulation therapy (**Appendix 1 "Therapeutic Anticoagulation in Adults" guideline**)
- € Referral to anticoagulant clinic, date and time of appointment.
- € Discharge letter to GP with information on : duration, indication, target INR
- € Request letter to GP for graduated compression stockings if DVT.
- € Unprovoked VTE:
    - o further assessment for malignancy undertaken
    - o additional investigations requested if appropriate
    - o plan in place to follow up on results
    - o Red top referral made to haematology for discussion of long term anticoagulation (to be seen 3 months post event)

➢ 4.5 Follow up arrangements

Referrals to Respiratory Medicine

All patients with PE require follow up in 3 months. Patients should leave hospital with a referral made to, and new patient appointment for respiratory outpatients.

The risk of developing chronic thromboembolic pulmonary hypertension is approximately 4% at 2 years [17]. Patients who remain symptomatic at 3 months with breathlessness will require further assessment with an Echocardiogram, Pulmonary Function tests and possibly repeat imaging.

Patients with massive PE and submassive PE at presentation will require a repeat ECHO at 3 months to monitor for resolution of right heart dysfunction. This should be requested at the time of discharge.

Referrals to Haematology:

- All patients with an unprovoked or recurrent VTE should be referred to Haematology outpatients for discussion regarding anticoagulation duration and consideration of long term anticoagulation therapy. They will be seen 3 months post event.
- Patients who may benefit from rivaroxaban as an alternative to warfarin
- Patients with unusual site thrombosis (e.g. upper extremity, portal vein).

Referrals to Oncology:

All patients with active cancer (diagnosed within last 6 months, receiving chemotherapy/ radiotherapy, recurrent, inoperable or metastatic disease) should continue on LMWH therapy and their treating oncologist be informed. LMWH therapy should continue for at least 6 months when the need for on-going anticoagulation should be re-assessed.

➢ 4.6 Duration of anticoagulation

Decisions regarding duration should be made on a case by case basis with reference to whether or not a first episode of venous thrombosis was provoked or not, other risk factors such as risk of anticoagulation related bleeding

		Target INR range
1st unprovoked PE Review by consultant haematologist at this time to discuss long term anticoagulation	≥ 6 months, consider indefinite	2.5 (2-3)
1st PE with precipitating factors (provoked) (eg trauma, surgery, pregnancy)	6 months*	2.5 (2-3)
1st provoked DVT	3 months	2.5 (2-3)
1st unprovoked proximal DVT	3months, consider indefinite	2.5 (2-3)
Distal DVT (where decision to treat)	3 months	2.5 (2-3)
Recurrent VTE	Long term	2.5 (2-3)
VTE whilst taking warfarin with therapeutic INR	Long term	3.5 (3-4)
Cancer-related VTE	≥6 months	Remain on LMWH

*could consider 3 months if concerns about bleeding risk, provided patient is asymptomatic, has been adequately anticoagulated (with therapeutic INR >75% of time), and not had significant PE at presentation (massive/submassive PE)

➢ 4.7 Unprovoked VTE and screening for occult malignancy

All patients who experience an unprovoked PE or DVT should be investigated for occult malignancy as follows:

- Comprehensive history and full examination
- Chest X-ray, liver function tests, renal function, calcium, urinalysis

If Age > 40 and dependent on the initial clinical evaluation consideration should be given to performing a CT abdomen/pelvis and/or referral to the one-stop breast clinic (female patients if concern regarding possible breast cancer).

If there are no concerning findings in the history, examination or initial work up (above) then the yield of scans in this scenario is low [18].

These investigations must be requested by the team which initially assesses the patient (e.g. ambulatory care) and be performed within 2 weeks. The team is responsible for following up on the results.
Should initial tests suggest underlying malignancy, the patient must be referred to the appropriate specialist clinic for further evaluation via the 2 week wait system.

➢ 4.8 Thrombophilia testing

There is no role for thrombophilia screening in patients with provoked VTE or in patients with unprovoked events where the decision has already been made to consider long term anticoagulation.

Thrombophilia testing is ONLY performed by haematologists.

➢ 4.9 Low risk patients and Ambulatory Care Management of PE

	Please see Whittington Health Guideline: **Ambulatory PE Pathway Guideline**

Selected patients at low risk of adverse outcome can be considered for outpatient/ambulatory investigation and treatment.
Patients must have been:

- Reviewed by a senior clinician (Consultant or Duty Medical Registrar) who agrees that patient is appropriate for outpatient management.
- Carefully selected for ambulatory outpatient management according to strict criteria

The following are exclusion criteria for ambulatory management. Any patients meeting an exclusion criteria must be admitted for inpatient investigation and management.

High Clinical Risk

- Intermediate or High Risk PESI Score (Class III-V)
- Positive Troponin T
- Evidence of RV Dysfunction on CT or ECHO
- Haemodynamically Unstable – Systolic BP < 100 mmHg, or Pulse > 110 /min
- Respiratory compromise – O_2 Sats < 94% on air, and/or RR > 24 /min
- Co-existing major proximal DVT (high segment femoral and above)

High Bleeding Risk

- Platelets < 75 or severe coagulopathy
- Active bleeding
- Recent GI Bleed (within 2 weeks)
- Recent stroke (within 2 weeks)
- Recent eye or CNS surgery (within 2 weeks)
- Uncontrolled hypertension (systolic >180/ diastolic >120mmHg)

Problems related to LMWH

- Severe renal dysfunction (eGFR <30 ml/min), necessitating IV UFH
- Allergy to Heparin
- Previous heparin induced thrombocytopenia
- Morbid Obesity (> 150 kg)

Ambulatory Treatment not feasible in terms of:

- Adherence unlikely (alcoholic/drug dependence, homeless, acute mental illness)
- Immobility or unable to obtain transport to and from the hospital
- Cognitive impairment (unaware of adverse symptoms and how to obtain help)
- Unable to access telephone at home

➢ 5.0 Reporting of hospital acquired VTE

There is a requirement to report and investigate hospital acquired VTE. All patients diagnosed with a PE or proximal DVT as an inpatient or within 90 days of a hospital admission (even if admission was to a different hospital) should be notified to the VTE CQUIN working group by e-mailing the details to:
Whh-tr.VTE-Enquiries@nhs.net

➢ Contacts

- Consultant Respiratory Physician (via switchboard or Respiratory secretaries ext 5353 or 5354)
- Respiratory team SpRs (bleep 3359/3049).

- Haematology consultants via Switchboard
- Haematology SpRs (bleep 3060 and 3037)
- Cardiothoracic Surgeon on call at Bart's Health (via Switchboard)

Out of hours:

- Medical registrar (bleep 3300)
- Consultant physician on-call (via switch)
- Haematologist on-call (via switch)

➢ References

(1) British Thoracic Society guidelines for the management of suspected acute pulmonary embolism. Thorax 2003 Jun;58(6):470-83.

(2) NICE. Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing. Clinical Guideline 144. London: National Institute for Clinical Excellence; 2012.

(3) Hoellerich VL, Wigton RS. Diagnosing pulmonary embolism using clinical findings. Arch Intern Med 1986 Sep;146(9):1699-704.

(4) Wells PS, Anderson DR, Rodger M, Ginsberg JS, Kearon C, Gent M, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. Thromb Haemost 2000 Mar;83(3):416-20.

(5) Konstantinides S, Torbicki A, Agnelli G, Danchin N , Fitzmaurice D et al.. Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). Eur Heart J. Published Online Aug 2014; 1-48.

(6) Jaff MR, McMurtry MS, Archer SL, Cushman M, Goldenberg N, Goldhaber SZ, et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association. Circulation 2011 Apr 26;123(16):1788-830.

(7) Jimenez D, Uresandi F, Otero R, Lobo JL, Monreal M, Marti D, et al. Troponin-based risk stratification of patients with acute nonmassive pulmonary embolism: systematic review and metaanalysis. Chest 2009 Oct;136(4):974-82.

(8) Bates SM, Jaeschke R, Stevens SM, Goodacre S, Wells PS, Stevenson MD, et al. Diagnosis of DVT: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012 Feb;141(2 Suppl):e351S-e418S.

(9) Keeling D, Baglin T, Tait C, Watson H, Perry D, Baglin C, et al. Guidelines on oral anticoagulation with warfarin - fourth edition. Br J Haematol 2011 Aug;154(3):311-24.

(10) Tait C, Baglin T, Watson H, Laffan M, Makris M, Perry D, et al. Guidelines on the investigation and management of venous thrombosis at unusual sites. Br J Haematol 2012 Oct;159(1):28-38.

(11) NICE. Clinical Knowledge Summary: Thrombophlebitis - superficial. London: National Institute for Clinical Excellence; 2014.

(12) Kahn SR, Shapiro S, Wells PS, Rodger MA, Kovacs MJ, Anderson DR, et al. Compression stockings to prevent post-thrombotic syndrome: a randomised placebo-controlled trial. Lancet 2014 Mar 8;383(9920):880-8.

(13) National Patient Safety Agency. Patient safety alert No. 18: Actions that can make anticoagulation safer. London: NPSA; 2007.

(14) National Patient Safety Agency. Rapid response report No 14 - reducing treatment dose errors with low molecular weight heparins. London: NPSA; 2010.

(15) North Central London Joint Formulary Committee. Low Molecular Weight Heparin. 2014. NCL JFC. 15-11-2014.

Ref Type: Online Source

(16) Watson H, Davidson S, Keeling D. Guidelines on the diagnosis and management of heparin-induced thrombocytopenia: second edition. Br J Haematol 2012 Dec;159(5):528-40.

(17) Pengo V, Lensing AW, Prins MH, Marchiori A, Davidson BL, Tiozzo F, et al. Incidence of chronic thromboembolic pulmonary hypertension after pulmonary embolism. N Engl J Med 2004 May 27;350(22):2257-64.

(18) Carrier M, Lazo-Langner A, Shivakumar S, Tagalakis V, Zarychanski R, Solymoss S, et al. Screening for Occult Cancer in Unprovoked Venous Thromboembolism. N Engl J Med. 2015 Aug 20;373(8):697-704.

		Yes/No	Comments
1.	**Does the procedural document affect one group less or more favourably than another on the basis of:**		
	• Race	No	
	• Ethnic origins (including gypsies and travellers)	No	
	• Nationality	No	
	• Gender	No	
	• Culture	No	
	• Religion or belief	No	
	• Sexual orientation including lesbian, gay and bisexual people	No	
	• Age	No	
	• Disability - learning disabilities, physical disability, sensory impairment and mental health problems	No	
2.	**Is there any evidence that some groups are affected differently?**	No	
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	No	
4.	**Is the impact of the procedural document likely to be negative?**	No	
5.	**If so can the impact be avoided?**	N/A	
6.	**What alternatives are there to achieving the procedural document without the impact?**	N/A	
7.	**Can we reduce the impact by taking different action?**	N/A	

If you have identified a potential discriminatory impact of this procedural document, please refer it to the Director of Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact the Director of Human Resources.

Checklist for the Review and Approval of Procedural Document

To be completed and attached to any procedural document when submitted to the relevant committee for consideration and approval.

	Title of document being reviewed:	Yes/No	Comments
1.	**Title**		
	Is the title clear and unambiguous?	Yes	
	Is it clear whether the document is a guideline, policy, protocol or standard?	Yes	
2.	**Rationale**		
	Are reasons for development of the document stated?	Yes	
3.	**Development Process**		
	Is it clear that the relevant people/groups have been involved in the development of the document?	Yes	
	Are people involved in the development?	Yes	
	Is there evidence of consultation with stakeholders and users?	Yes	Respiratory, haematology, pathology, ambulatory care
4.	**Content**		
	Is the objective of the document clear?	Yes	
	Is the target population clear and unambiguous?	Yes	
	Are the intended outcomes described?	Yes	
5.	**Evidence Base**		
	Are key references cited in full?	N/A	
	Are supporting documents referenced?	N/A	
6.	**Approval**		
	Does the document identify which committee/ group will approve it?	Yes	
7.	**Dissemination and Implementation**		
	Is there an outline/plan to identify how this will be done?	Yes	
8.	**Document Control**		
	Does the document identify where it will be held?	Yes	
9.	**Process to Monitor Compliance and Effectiveness**		
	Are there measurable standards or KPIs to	Yes	

	Title of document being reviewed:	Yes/No	Comments
	support the monitoring of compliance with and effectiveness of the document?		
	Is there a plan to review or audit compliance with the document?	Yes	
10.	**Review Date**		
	Is the review date identified?	Yes	
	Is the frequency of review identified? If so is it acceptable?	Yes	
11.	**Overall Responsibility for the Document**		
	Is it clear who will be responsible for co-ordinating the dissemination, implementation and review of the document?	Yes	

Executive Sponsor Approval			
If you approve the document, please sign and date it and forward to the author. Procedural documents will not be forwarded for ratification without Executive Sponsor Approval			
Name		Date	
Signature			
Relevant Committee Approval			
The Director of Nursing and Patient Experience's signature below confirms that this procedural document was ratified by the appropriate Governance Committee.			
Name		Date	
Signature			
Responsible Committee Approval – only applies to reviewed procedural documents with minor changes			
The Committee Chair's signature below confirms that this procedural document was ratified by the responsible Committee			
Name		Date	
Name of Committee		Name & role of Committee Chair	
Signature			

Tool to Develop Monitoring Arrangements for Policies and guidelines

What key element(s) need(s) monitoring as per local approved policy or guidance?	Who will lead on this aspect of monitoring? Name the lead and what is the role of the multidisciplinary team or others if any.	What tool will be used to monitor/check/observe/Assess/inspect/ authenticate that everything is working according to this key element from the approved policy?	How often is the need to monitor each element? How often is the need complete a report? How often is the need to share the report?	What committee will the completed report go to?
Element to be monitored	**Lead**	**Tool**	**Frequency**	**Reporting arrangements**
Appropriate requesting of D-dimers in DVT & PE	Ambicare Team	Wells score and action taken following D-dimer result	Within 3 months of implementation; then annually	
Thrombolysis for massive PE	Respiratory Lead for VTE	Review of management in accordance with guideline	Annually	
Cancer screening for VTE	?Oncology (Pauline Leonard)	Compliance with guideline and detection rate of occult malignancy	Within 6 months of implementation, then annually	