Guideline Number & Full Title:	2786 - Guideline on the management of pulmonary embolism (PE Pathway)
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Scope ***(Target audience, state if Trust wide):***	Trust Wide
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Explicit definition of patient group to which it applies ***(e.g. inclusion and exclusion criteria, diagnosis):***	All Adults
Changes from previous version ***(not applicable if this is a new guideline, enter below if extensive):***	Updated thrombolysis slide, alteplase now recommended first line again in all scenarios due to improved supply situation. Updated wording/formatting to appendix 1 on the use of streptokinase for thrombolysis due to resolving national shortage of alteplase.
NICE guidance reference:	NICE NG158
Summary of evidence base this guideline has been created from: (other than NICE)	• BTS Guideline on outpatient management of PEs • BTS Guidelines for the management of suspected acute pulmonary embolism • BNF & SPC licensed dosing and information • Enhanced using Medusa IV guide • MOPETT Trial for half dose alteplase dosing • Expert Local Advice

This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date or outside of the Trust.

PE Pathway

This document comprises 6 simple flow charts to assist clinicians in the investigation and treatment of suspected or confirmed Acute Pulmonary Emboli. The pathway has been put together using up to date evidence from American (ACP), European (ESC) and National (NICE NG158 updated from CG144 in 2020, BTS and RCOG) Guidelines. It has been reviewed locally by clinicians from Acute Medicine, Respiratory Medicine, Emergency Medicine, Haematology and Interventional Radiology.

The charts are listed as follows:

1. **Telephone Triage Management of Suspected Acute PE**
2. **Investigation of Suspected Acute PE in Hospital**
3. **Management of Confirmed Acute PE in Hospital**
4. **Thrombolytic therapy in PE**
5. **Investigation and Treatment of Suspected Acute PE in Pregnancy**
6. **Follow up of Acute PE**

Appendix 1 - Protocol for the Use of Streptokinase in Massive PE During Alteplase Stock Shortage

Acute PE is a condition around which there is a lack of clinical confidence because it is common, presentation overlaps with many other conditions, it has a high mortality rate and is an area around which there have been clinical governance issues and medicolegal cases. Following some of the advice within this pathway should help clinicians standardise and rationalise the way that suspected acute PE is investigated and treated to follow best available evidence. As in most areas of medicine, however, there are few absolutes and clinical judgement needs to be applied.

1. Telephone Triage Management of Suspected Acute PE

Box 1 PERC Criteria

If a patient is considered low risk by gestalt impression (<15% pre-test probability) then provided age <50, pulse<100, Sats >94 and no history of haemoptysis, oestrogen use, prior DVT, present signs of DVT and no history of trauma / surgery within 4 weeks then PE can be safely ruled out without further tests (NICE NG158).

Box 2

Simplified PESI

Low risk = 0, High > 0

Clinical question	Score
Age >80	1
Tachycardia (>110)	1
Systolic BP <100mmHg	1
SaO2 <90	1
Chronic lung or heart disease	1
Cancer (history or active)	1

Clinical suspicion of PE

Shocked? Hypoxic?

No

Yes

PE Rule Out (PERC) Criteria (See Box 1)

ED Resus via 999

Not met

Met

PE excluded (GP to reassess)

sPESI / PESI (PE severity Index) (See Box 2)

Low

High

Assessment of social and co-morbid clinical history

Unable to manage at home

Admit to AMRA

Reassess (See flowchart 2)

Able to manage at home

2 Level Wells for PE Document result in notes (See Box 3)

≤4

>4

1. GP to request D Dimer
2. Give 24hr DOAC or LMWH cover

Give 24hr DOAC or LMWH cover

Normal age-adjusted D dimer (Box 4)

D dimer elevated

PE excluded (GP to reassess)

Admit to AMRA next day for imaging

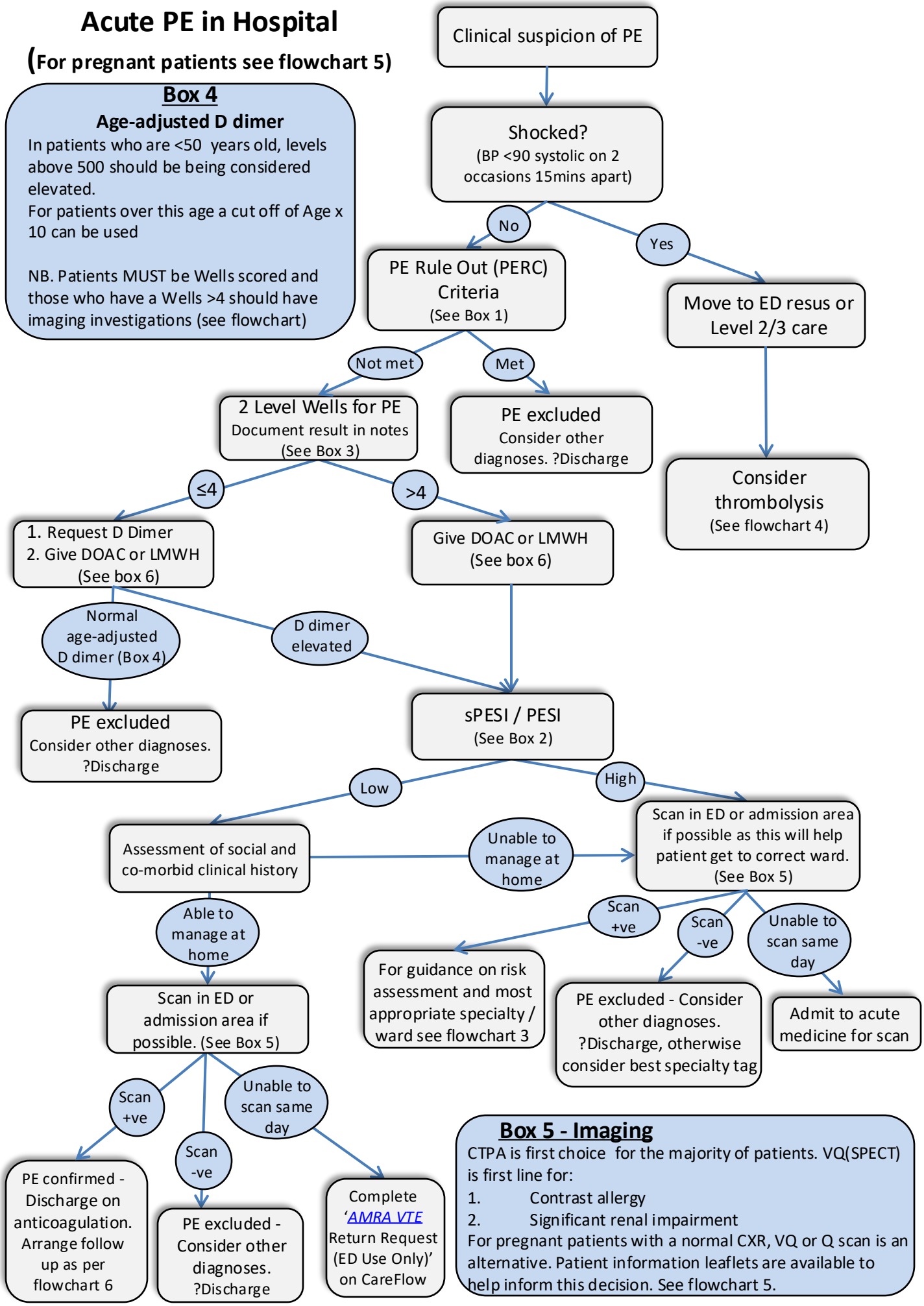
Box 3

2 Level Wells for PE

Clinical question	Score
Clinical signs and symptoms of DVT	3
PE most likely diagnosis	3
Tachycardia (>100)	1.5
Immobilisation or surgery in previous 4 weeks	1.5
Past Hx DVT or PE	1.5
Haemoptysis	1
Active malignancy (palliative, on treatment or treated in past 6 months)	1

2. Investigation of Suspected Acute PE in Hospital

(For pregnant patients see flowchart 5)



3. Management of Confirmed Acute PE in Hospital

(For pregnant patients see flowchart 5)

Box 6

Anticoagulation

NICE recommends starting the anticoagulation intended for on-going treatment from the outset, including while waiting for imaging to confirm diagnosis. Apixaban or Rivaroxaban which can be used without LMWH are preferred. LMWH remains an option initially when DOACs are contraindicated (body weight, drug interactions, renal failure etc.), as these patients may need to be started on Warfarin if PE confirmed.

Helpful documents on the acute medicine intranet page and the haemostasis and thrombosis section of NUH's clinical guidelines include:

1. Oral anticoagulant checklist. http://nuhnet/acute_medicine/acutemedicine/Acute%20Med%20Education/Anticoagulation%20-%20DOAC%20counselling%20and%20checklist.docx
2. DOAC – Quick reference . http://nuhnet/nuh_documents/Guidelines/Trust%20Wide/Trust%20Wide/2455.pdf

On rare occasions where PE confirmed but anticoagulation is contraindicated, consider insertion of a removable IVC filter until anticoagulation can be started safely.

PE confirmed on imaging

1. Ensure anticoagulated (See Box 6)
2. Shocked? (BP <90 systolic on 2 occasions 15mins apart)

Yes → Move to ED resus or Level 2/3 care depending on senior clinical judgment → Consider thrombolysis (See flowchart 4)

No → sPESI / PESI (See Box 2)

Low → Assessment of social and co-morbid clinical history

- Able to manage at home → Discharge on anticoagulation (Arrange follow up as per flowchart 6)
- Unable to manage at home → If in ED, admit to Respiratory Medicine

High →

1. Troponin
2. Review CTPA for right heart strain
3. If diagnosed on VQ consider ECHO

→ Risk Assess
RV strain on imaging +/-ve
Trop elevated +/-ve

- Intermediate-low (both –ve or either +ve) → If in ED or AMRA admit to Respiratory Medicine Likely 48 hour stay
- Intermediate-high (both +ve) → Admit to area with cardiac monitoring (ARCU at QMC (L1 if full), ACU or CCD at NCH) Close monitoring for deterioration over first 48 hours (See Box 7)

  - No deterioration → Reassess PESI at 48 hours. Step down if stable
  - Deterioration → Consider rescue thrombolysis (See flowchart 4)

Box 7

Deterioration

If a patient with intermediate-high risk PE develops any of the following during monitoring:

1. Hypotension (<90 systolic)
2. Significant increase in oxygen requirements
3. Further significant elevation of troponin
4. Increasing lactate

They will need prompt senior review and clinical decision regarding suitability for rescue thrombolysis (see flowchart 4). This may be more likely to happen in those with large DVT

4. Thrombolytic therapy in PE

Box 8: Indications for consideration of thrombolysis

1. Cardiac arrest with confirmed or suspected Acute PE
2. High clinical suspicion of PE with cardiovascular instability at presentation (Systolic BP <90mmHg repeated after 15 min interval)
3. Confirmed PE within 14 days deemed to be "high risk" i.e. Systolic BP <90mmHg repeated after 15 min interval
4. Confirmed "intermediate-high risk" PE (elevated troponin and right heart strain on imaging) who deteriorates despite anticoagulation (Box 6)
5. Type A right atrial thrombus ("worm-like") and not crossing to left atrium (ECHO first)

Patient Status	**CARDIAC ARREST**	**NON–CARDIAC ARREST**			
Special circumstances?	**N/A**	**NO SPECIAL CIRCUMSTANCES**	**PREGNANT**	**MAJOR BLEEDING RISK**	**AGE >75**
Thrombolysis or clot removal	**Alteplase**: 50mg in 50mls water for injection (WFI) as a bolus.	**Alteplase**: Recon each 50mg vial with 50ml WFI and: If ≥65kg – give 10mg as a bolus, then 90mg over 2 hours If <65kg – give a total dose of 1.5mg/kg. 10mg as a bolus then the remainder of the dose over 2 hours	**Alteplase**: Recon each 50mg vial with 50ml WFI and: If ≥65kg – give 10mg as a bolus, then 90mg over 2 hours If <65kg – give a total dose of 1.5mg/kg. 10mg as a bolus then the remainder of the dose over 2 hours	**Consider options:** **1. Half dose alteplase:** Recon 1 x 50mg vial in 50ml WFI and: If ≥ 50kg – give 10mg as a bolus, then 40mg over 2 hours If <50kg – give a total dose of 0.5mg/kg. 10mg as a bolus then the remainder of the dose over 2 hours **2. Catheter-based clot disruption and removal** - Discuss with interventional radiology	**Half dose alteplase:** Recon 1 x 50mg vial in 50ml WFI and: If ≥ 50kg – give 10mg as a bolus, then 40mg over 2 hours If <50kg – give a total dose of 0.5mg/kg. 10mg as a bolus then the remainder of the dose over 2 hours
	Only consider **streptokinase** if alteplase is unavailable – see appendix 1 for more information if required.				
Initial anticoagulation	**If no prior anticoagulation:** Give unfractionated heparin (UFH) as 5000 unit loading dose immediately followed by infusion **If prior DOAC or low molecular weight heparin (LMWH)**: Give UFH following the same protocol as above, but starting at the point when the next dose of anticoagulation would have been due (12 or 24 hours) **If started on UFH infusion prior:** Pause the UFH infusion prior to administration of thrombolysis. Then check the APTT ratio every 2 hours following completion of thrombolysis and restart UFH infusion when the APTT ratio is <2. Restart the UFH infusion at the same rate that was being given prior to thrombolysis (do not give another loading dose).				
Other considerations	CPR should be continued for >1 hour to give time for response. Discuss with AICU	N/A	Involve obstetrics in all decision-making	Even where there is an absolute contraindication to thrombolysis (box 9), mechanical clot retrieval could still be considered	N/A
Destination	AICU	ARCU, Level 1 or Level 2 bed			
Care beyond thrombolysis / clot disruption	**Assess response:** 48 hours continuous monitoring in an appropriate bed Vitals every 15 mins for 2 hours, then 30 mins for 2 hours, then hourly **If stable:** UFH for first 24 hours post thrombolysis then LMWH if stable and no bleeding, otherwise continue UFH **If deterioration:** Consider catheter-based clot disruption and removal e.g. FlowTriever – D/W interventional radiology				

Box 9 – Contraindications to thrombolysis

Note: if a patient has received low molecular weight heparin or DOAC, this is NOT a contraindication for thrombolysis

Absolute

1. Haemorrhagic stroke or stroke of unknown origin at any time
2. Ischaemic stroke within 6 months
3. Major trauma /surgery/head injury within 3 weeks
4. CNS damage or neoplasms
5. Gastrointestinal bleeding within 1 month
6. Aortic dissection

Note: absolute CIs might become relative if life-threatening PE

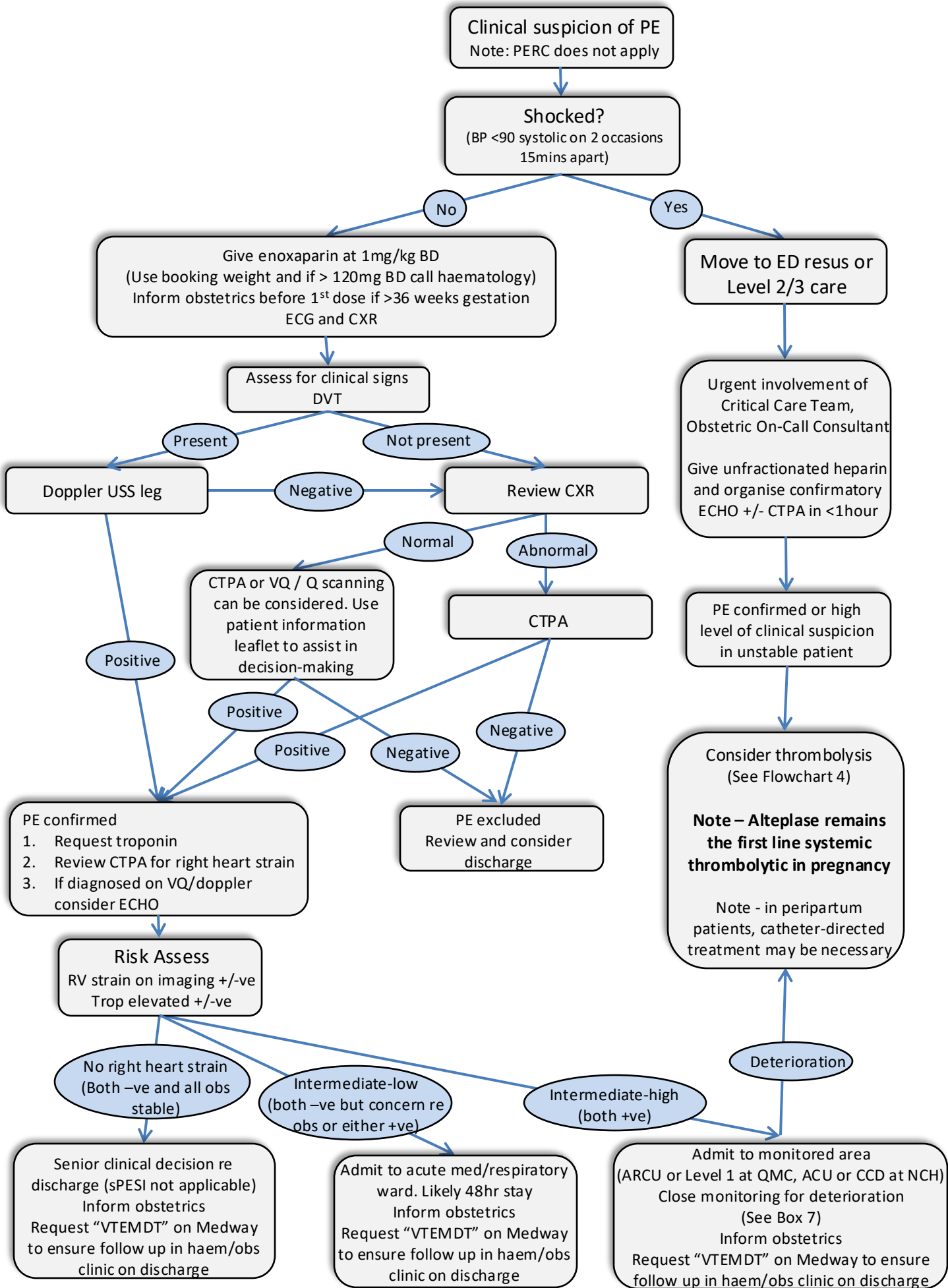
Relative (Should be discussed)

1. TIA within 6 months
2. Oral anticoagulant therapy
3. Non-compressible vascular puncture
4. Pregnancy or within 1 week postpartum
5. Refractory hypertension (>180 systolic)
6. Advanced liver disease
7. Infective endocarditis
8. Active peptic ulcer disease
9. Disseminated malignancy
10. Known bleeding disorders

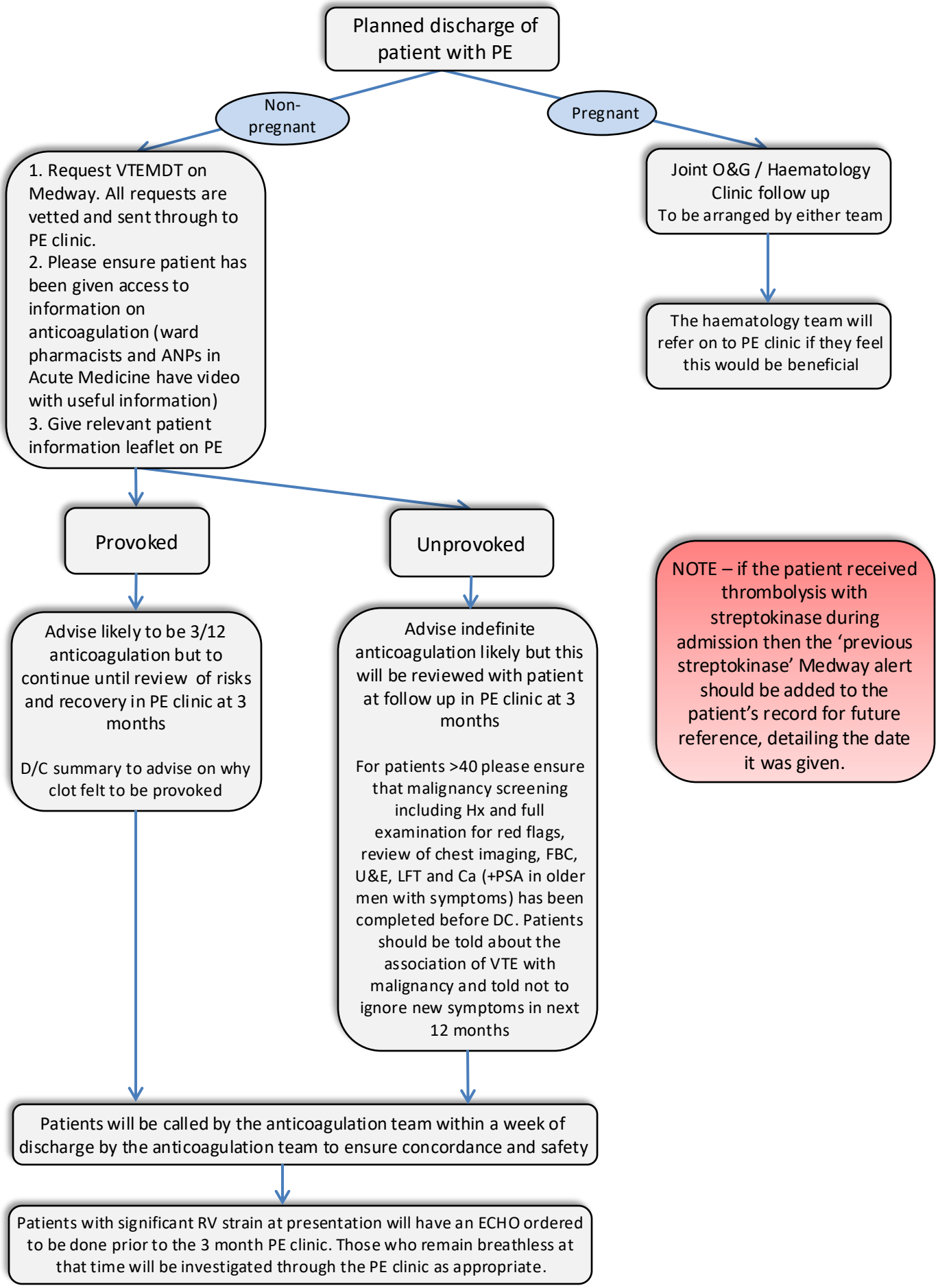
Bleeding Risks

The risk of intracranial bleeding is around 2% and non-intracranial bleeding is 6.3% from all forms of thrombolysis . Both increase with age.

5. Investigation and Treatment of Suspected Acute PE in Pregnancy



6. Follow up of Acute PE



Appendix 1 - Protocol for the Use of Streptokinase in Massive PE During Alteplase Stock Shortage

NHS Nottingham University Hospitals NHS Trust

Streptokinase for the treatment of massive PULMONARY EMBOLISM

Indication

Massive pulmonary embolism

To only be used as a 2nd line thrombolytic in an emergency, if alteplase is unavailable.

Important Considerations – please read:

1. There is limited information or experience on the use of streptokinase in pregnancy – involve obstetrics in decision making.
2. Repeat treatment with streptokinase administered more than 5 days and less than 12 months after initial treatment may not be effective. This is because of the increased likelihood of resistance due to antistreptokinase antibodies.
3. Also, the therapeutic effect may be reduced in patients with recent streptococcal infections such as streptococcal pharyngitis, acute rheumatic fever and acute glomerulonephritis.
4. If patient has had a dose of lower molecular weight heparin or DOAC this is not a contraindication to thrombolysis should it become indicated.

For further details on considerations, contraindications and ongoing management and anticoagulation surrounding systemic thrombolysis refer back to section 4 in the "Pulmonary Embolism – Management" guidelines

Dosing

1,500,000 units by intravenous infusion over 1 - 2 hours

NB - In an arrest situation, bolus administration of 50-100% of the dose may be considered at the discretion of the resus team leader (unlicensed).

Infusion Preparation and Administration

Streptokinase is usually stocked in the emergency drug cupboards (AICU at QMC and Morris ward at City)
See the emergency drug list or contact pharmacy
http://nuhqpharm01/reports/emergencydrugslist - or scan the QR code →

Instructions for Reconstitution:

1. Add 5mL of sodium chloride 0.9% to the vial (all strengths). Swirl the solution gently to facilitate quick reconstitution, but care should be taken to avoid foaming.
2. After reconstitution, a clear, colourless to yellowish solution is obtained in the following concentrations:
   - 250,000unit vial = 50,000units in 1mL.
   - 750,000unit vial = 150,000units in 1mL.
   - 1.5million unit vial = 300,000units in 1mL.
3. Dilute further before administration

Instructions for Dilution and Administration

1. Reconstitute dose using the vials of streptokinase available as per the instructions above (ideally 1 x 1.5million units vial if available OR 2 x 750,000 unit vials OR 6 x 250,000 unit vials)
2. Make up the reconstituted solution to a suitable volume of sodium chloride 0.9% e.g. 50mL - 100mL
3. Infuse over 1-2 hours via peripheral cannula or CVC

NB - In an arrest situation, bolus administration of 50-100% of the dose may be considered at the discretion of the resus team leader (unlicensed).

Flushing:

- To avoid adverse effects resulting from an unintentional 'bolus' dose flush with sodium chloride 0.9% at the same rate the medicine was administered.
- Discard the IV administration set before flushing the cannula.
- Peripheral cannula: Flush if it is to remain in situ.
- Central venous access device: Aspirate the cannula contents before flushing.

Infusion Compatibilities:

Sodium chloride 0.9%, glucose 5%, Hartmann's / compound sodium lactate (Ringer's lactate)

Monitoring

There is a relatively high risk of **ANAPHYLAXIS** with this drug. Observe patient closely throughout infusion and ensure resuscitation facilities available.

Adverse effects:

- Anaphylactic reactions common.
- Hypotension and arrhythmias commonly seen at the beginning of therapy. Arrhythmias may also occur due to reperfusion.
- Fever and chills are common.
- Haemorrhage at the injection site (and other puncture sites) and bruising are common.

Monitor:

- Signs of anaphylaxis e.g. rash, flushing, itching, urticaria, angioneurotic oedema, dyspnoea, bronchospasm and hypotension.
- Pulse, blood pressure, ECG & temperature.

At the beginning of therapy, a fall in blood pressure, tachycardia or bradycardia (in individual cases going as far as shock) are commonly observed.

Follow up and Additional Information

- The prescribing clinician must add the "cardiology - previous streptokinase" Medway alert to the patient's record for future reference detailing the date streptokinase was administered
- If arterial puncture (e.g. ABG) is needed during or immediately after thrombolysis, upper extremity approach (e.g. radial) is preferable and more compression than usual may be needed afterwards – manufacturer recommends 30min with compression bandage.

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