Thromboembolic disease in pregnancy and the puerperium

Classification :	Guideline
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Departments/Group this Document applies to:	Maternity

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Guideline to be followed by (target staff):

To be read in conjunction with the following documents:
Thromboprophylaxis in Pregnancy and Puerperium Guideline

Are there any eCARE implications? No

CQC Fundamental standards:
Regulation 9 – person centred care
Regulation 10 – dignity and respect
Regulation 11 – Need for consent
Regulation 12 – Safe care and treatment
Regulation 13 – Safeguarding service users from abuse and improper treatment
Regulation 14 – Meeting nutritional and hydration needs
Regulation 15 – Premises and equipment
Regulation 16 – Receiving and acting on complaints
Regulation 17 – Good governance
Regulation 18 – Staffing
Regulation 19 – Fit and proper

Disclaimer

Since every patient's history is different, and even the most exhaustive sources of information cannot cover every possible eventuality, you should be aware that all information is provided in this document on the basis that the healthcare professionals responsible for patient care will retain full and sole responsibility for decisions relating to patient care; the document is intended to supplement, not substitute for, the expertise and judgment of physicians, pharmacists or other healthcare professionals and should not be taken as an indication of suitability of a particular treatment for a particular individual.

The ultimate responsibility for the use of the guideline, dosage of drugs and correct following of instructions as well as the interpretation of the published material **lies solely with you** as the medical practitioner.

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Guideline Statement

To enable staff to care for women with thromboembolic disease in pregnancy and the puerperium.

Executive Summary

Venous thromboembolism (VTE) remains the leading cause of direct maternal death, with no evidence of a consistent decrease in mortality over the past 20 years.

The subjective, clinical assessment of deep venous thrombosis (DVT) and pulmonary thromboembolism (PE) is particularly unreliable in pregnancy and a minority of women with clinically suspected VTE have the diagnosis confirmed when objective testing is employed.

VTE is up to ten times more common in pregnant women than in non-pregnant women of the same age and can occur at any stage of pregnancy but the puerperium is the time of highest risk. Acute VTE should be suspected during pregnancy in women with symptoms and signs consistent with possible VTE, particularly if there are other risk factors for VTE.

The symptoms and signs of VTE include leg pain and swelling (usually unilateral), lower abdominal pain, low-grade pyrexia, dyspnea, chest pain, hemoptysis and collapse.

1.0 Roles and Responsibilities:

Doctors, midwives, nurses and MCA's must be aware that women are at risk of thromboembolism from the very beginning of pregnancy. Therefore, at booking, a full risk assessment must be undertaken before maternity care plans are decided. Obese women with a BMI of 35 or more are unsuitable for midwife-only care. Further full risk assessments should be completed and documented on admission in labour and following the birth.

2.0 Implementation and dissemination of document

Guideline to be published on the intranet.

3.0 Processes and procedures

3.1 How is acute VTE diagnosed in pregnancy?

Any woman with signs and symptoms suggestive of VTE should have objective testing performed expeditiously and treated with low-molecular-weight heparin (LMWH) until the diagnosis is excluded by objective testing, unless treatment is strongly contraindicated (see below). Treatment must be started by a doctor.

Contraindications (In these cases discuss with haematology consultant on call)

- Bleeding disorders
- Undiagnosed bleeding
- Renal impairment

3.2 Investigations needed for the diagnosis of an acute DVT

- **Compression duplex ultrasound** (doppler of the legs) should be undertaken where there is clinical suspicion of DVT. This is undertaken in the Radiology department. If ultrasound is

negative and there is a low level of clinical suspicion, anticoagulant treatment can be discontinued.

- If ultrasound is negative and a high level of clinical suspicion exists, anticoagulant treatment should be discontinued but the ultrasound should be repeated on days 3 and 7.
- V/Q scanning carries a slightly increased risk of childhood cancer compared with Computed Tomography Pulmonary Angiogram (CTPA)1/280,000 versus less than 1/1,000,000) but carries a lower risk of maternal breast cancer (lifetime risk increased by up to 13.6% with CTPA.

3.3 Diagnosis of acute PE

Women presenting with symptoms and signs of an acute PE should have an electrocardiogram (ECG) and a chest X-ray (CXR) performed.

In women with suspected PE who also have symptoms and signs of DVT, compression duplex ultrasound should be performed. If compression ultrasonography confirms the presence of DVT, no further investigation is necessary and treatment for VTE should continue.

In women with suspected PE without symptoms and signs of DVT, a ventilation/perfusion (V/Q) lung scan or a computerized tomography pulmonary angiogram (CTPA) should be performed.

When the chest X-ray is abnormal and there is a clinical suspicion of PE, CTPA should be performed in preference to a V/Q scan.

Alternative or repeat testing should be carried out where V/Q scan or CTPA is normal but the clinical suspicion of PE remains. Note that VQ are done in Northampton. It is best mentioning availability when weighing up which to use.

Anticoagulant treatment should be continued until PE is definitively excluded.

Women with suspected PE should be advised that, compared with CTPA, V/Q scanning may carry a slightly increased risk of childhood cancer but is associated with a lower risk of maternal breast cancer; in both situations, the absolute risk is very small.

- V/Q scanning carries a slightly increased risk of childhood cancer compared with CTPA (1/280,000 versus less than 1/1,000,000) but carries a lower risk of maternal breast cancer (lifetime risk increased by up to 13.6% with CTPA.

- Chest X-ray may identify other pulmonary disease such as pneumonia, pneumothorax or lobar collapse. Whilst the X-ray is normal in over 50% of pregnant women with objectively proven PE, abnormal features caused by PE include atelectasis, effusion, focal opacities, regional oligemia or pulmonary edema. The radiation dose to the fetus from a chest X-ray performed at any stage of pregnancy is negligible.

- Where feasible, women should be involved in the decision to undergo CTPA or V/Q scanning.

- **If the clinical suspicion of acute PE is still high despite normal tests then anticoagulant treatment should be continued until PE is definitely excluded.**

- Women should be managed on an individual basis regarding intravenous unfractionated heparin, thrombolytic therapy or thoracotomy and surgical embolectomy.
- Management should involve a multidisciplinary team including senior physicians, obstetricians and radiologists.
- Intravenous unfractionated heparin is the preferred, initial treatment in massive PE with cardiovascular compromise.
- The on-call medical team should be contacted immediately. An urgent portable echocardiogram or CTPA within 1 hour of presentation should be arranged. If massive PE is confirmed, or in extreme circumstances prior to confirmation, immediate thrombolysis should be considered

3.4 Baseline blood investigations

Before anticoagulant therapy is commenced-

- Do full blood count, coagulation screen, urea and electrolytes and liver function tests.

Anticoagulant therapy can be influenced by renal and hepatic function. Discuss with haematology consultant if there is renal/hepatic impairment.

Performing a thrombophilia screen prior to therapy is not routinely recommended. Discuss with consultant hematologist if need arises.

D-dimer testing should not be done as it is not useful in pregnancy as it is not unusual for it to be raised in healthy pregnant women.

Anaesthetic referral should be done for all women on therapeutic LMWH antenatally.

3.5 Initial anticoagulant treatment of VTE in pregnancy

LMWH should be given in doses titrated against the woman's **booking or early pregnancy weight**. There is insufficient evidence to recommend whether the dose of LMWH should be given once daily or in two divided doses.

Table 2. Antenatal therapeutic doses of low-molecular-weight heparin

Booking or early pregnancy weight in kg	Initial dose of Dalteparin in IU*

<50kg	5000 IU twice daily
50-69kg	7500 IU AM / 5000 IU PM - BD dose
70-89kg	7500 IU twice daily
90–109kg	10 000 IU twice daily
110–125 kg	12 500 IU twice daily
>125 kg	Discuss with hematologist

Antenatal dose of enoxaparin	
<50 kg	40mg twice daily or 60mg once daily
50-69 kg	60mg twice daily or 90mg once daily
70-89kg	80mg twice daily or 120 once daily
90-109kg	100 mg twice daily or 150mg once daily
110-125kg	120 mg twice daily or 180mg once daily
>125kg	Discuss with hematologist

Routine measurement of peak anti-Xa activity for patients on LMWH for treatment of acute VTE in pregnancy or postpartum is not essential but can be requested at the discretion of the supervising consultant. It is useful for women at extremes of body weight (less than 50 kg and 90 kg or more) or with other complicating factors (for example with renal impairment or recurrent VTE). It should be done 4 hours after the heparin dose. Target anti Xa is 0.5-1 (BD dose) or 0.8-1.2 (OD) dose. If the dose needs to be modified this should be done with consultant input.

When VTE occurs at term, consider use of intravenous heparin which has a shorter half- life.

Routine platelet count monitoring is not recommended. Obstetric patients who are postoperative and receiving unfractionated heparin should have platelet count monitoring performed every 2–3 days from days 4 to 14 or until heparin is stopped.

If a massive PE is suspected, the on-call medical registrar should be contacted immediately. An urgent portable echocardiogram or CTPA within 1 hour of presentation should be arranged. If massive PE is confirmed, or in extreme circumstances prior to confirmation, immediate thrombolysis should be considered.

In the initial management of DVT, the leg should be elevated. Mobilisation should be encouraged. Graduated elastic compression stockings can be prescribed to help with symptoms (e.g pain and oedema) but there is no evidence they reduce the rate of post thrombotic syndrome or VTE recurrence if on anticoagulation.

Consideration should be given to the use of a temporary inferior vena cava filter for patients with iliac vein DVT, in the peripartum period, to reduce the risk of PE or in patients with proven DVT and who have recurrent PE despite adequate anticoagulation or other patients with recent DVT who need their anticoagulation stopping temporarily. This should be discussed a with a hematology consultant.

3.6 Maintenance treatment

- All women who require treatment for a diagnosis of VTE should have an individual management plan documented on eCare.

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- Treatment with therapeutic doses of subcutaneous LMWH should be employed during the remainder of the pregnancy.

- Arrangements should be made to allow safe disposal of needles and syringes. Outpatient follow-up should include clinical assessment and advice with assessment of blood platelets and peak anti-Xa levels if appropriate (see sections 3.5 and below).

- Women receiving therapeutic-dose unfractionated heparin should have their platelet count monitored at least every other day until day 14 or until the unfractionated heparin is stopped, whichever occurs first.

- Pregnant women who develop heparin-induced thrombocytopenia or have heparin allergy and require continuing anticoagulant therapy should be managed with danaparoid sodium or fondaparinux, under hematologist advice

- Because of their adverse effects on the fetus, vitamin K antagonists, such as warfarin, and the direct oral anticoagulants should not be used for antenatal VTE treatment.

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- Women with antenatal VTE can be managed with subcutaneous LMWH for the remainder of the pregnancy using LMWH. If LMWH therapy requires monitoring, (for example, extremes of body weight or renal impairment, aim is to achieve a peak anti-Xa 4 hours post-injection, of 0.5–1 units/ml (BD dose), 0.8-1.2 (OD dose)).

- Subcutaneous LMWH appears to have advantages over APTT-monitored unfractionated heparin in the maintenance treatment of VTE in pregnancy. The simplified therapeutic regimen for LMWH is convenient and allows outpatient treatment. Women should be taught to self-inject and can then be managed as outpatients until delivery.

- Consideration should be given to the use of newer anticoagulants (fondaparinux, argatroban or r-hirudin) in pregnant women who are unable to tolerate heparin (LMWH or unfractionated heparin) or danaparoid and who require continuing anticoagulant therapy after discussing with hematology consultant.

3.7 Anticoagulant therapy during labour and delivery

- The woman taking LMWH for maintenance therapy should be advised that once she is established in labour or thinks that she is in labour, she should not inject any further heparin.

- If a woman presents in labour shortly after taking LMWH they should be reassured bleeding complications are rare. Discuss with consultant obstetrician and haematologist on call

- When VTE occurs at term, consideration should be given to the use of intravenous unfractionated heparin which is more easily manipulated.

- Where delivery is planned, LMWH maintenance therapy should be discontinued 24 hours before planned delivery.

- Active management of third stage with 40 units of oxytocin infusion in 500ml of normal saline at rate of 125ml/hr is required when woman has been on antenatal dalteparin.

- Regional anaesthetic or analgesic techniques should not be undertaken until at least 24 hours after the last dose of therapeutic LMWH.

- The epidural catheter should not be removed within 12 hours of the most recent injection.

- LMWH should not be given for 4 hours after the use of spinal anesthesia or after the epidural catheter has been removed, and the epidural catheter should not be removed within 12 hours of the most recent injection.

- Wound drains and interrupted sutures or staples should be considered for women undergoing caesarean section on therapeutic anticoagulation

- Any woman who is considered to be at high-risk of haemorrhage, and in whom continued heparin treatment is considered essential, should be managed with intravenous, unfractionated heparin until the risk factors for haemorrhage have resolved.

- Risk factors include major antepartum haemorrhage, coagulopathy, progressive wound hematoma, suspected intra-abdominal bleeding and postpartum haemorrhage. Unfractionated heparin has a shorter half-life than LMWH and its activity is more completely reversed with protamine sulphate

3.8 Postnatal anticoagulation

- Treatment doses of LMWH should be based on current, postnatal weight

- Give weight appropriate prophylactic dose of LMWH 4-6 hours after delivery (as long as no concerns about haemostasis) and then start weight appropriate treatment dose LMWH at 12/24 hours post delivery

- Therapeutic anticoagulant therapy should be continued for the duration of the pregnancy and for at least 6 weeks postnatally and until at least 3 months of treatment has been given in total. The final decision to stop treatment should be made by the hematologist.

- Women should be offered a choice of LMWH or warfarin for postnatal therapy after discussion about the need for regular blood tests for monitoring of warfarin, particularly during the first 10 days of treatment. Single LMWH dose postnatally is adequate unless indicated to administer BD due to extreme obesity.

- Women should be advised that neither heparin (unfractionated or LMWH) nor warfarin is contraindicated if breastfeeding. DOACs are contraindicated if breast feeding

- Postpartum warfarin should be avoided until at least the fifth day and for longer in women at increased risk of postpartum hemorrhage. [New 2015]

3.9 Prevention of post-thrombotic leg syndrome

- Women should be advised that prolonged use of LMWH (more than 12 weeks) is associated with a significantly lower chance of developing post-thrombotic syndrome.
- Graduated compression stockings can be prescribed for symptomatic relief of pain or oedema but there is no evidence that wearing them reduces the rate of post thrombotic syndrome and NICE do not recommend them.

3.10 Postnatal clinic review

- Postnatal review for patients who develop VTE during pregnancy or the puerperium should, whenever possible, be at an obstetric medicine clinic or a joint obstetric haematology clinic.

- Thrombophilia testing should be performed once anticoagulant therapy has been discontinued **only** if it is considered that the results would influence the woman's future management.

3.11 How should massive life-threatening PE in pregnancy be managed?

Collapsed, shocked patients need to be assessed by a team of experienced clinicians, including the on-call Consultant obstetrician and medical team who should decide on an individual basis whether a woman receives intravenous unfractionated heparin, thrombolytic therapy or thoracotomy and surgical embolectomy.

Intravenous unfractionated heparin is the preferred treatment in massive PE with cardiovascular compromise.

The on-call medical registrar should be contacted immediately. An urgent portable echocardiogram or CTPA within 1 hour of presentation should be arranged.

If massive PE is confirmed or, in extreme circumstances prior to confirmation, immediate thrombolysis should be considered. Management should involve a multidisciplinary resuscitation team including senior physicians, obstetricians and radiologists.

Maternal resuscitation should commence following the principles of ABC and, if cardiac arrest occurs, cardiopulmonary resuscitation should be performed with the woman in a left lateral tilt.

A perimortem caesarean section should be performed by 5 minutes if resuscitation is unsuccessful and the pregnancy is more than 20 weeks.

Intravenous unfractionated heparin is the traditional method of heparin administration in acute VTE and remains the preferred treatment in massive PE because of its rapid effect and extensive experience of its use in this situation.

Please see appendix 3 for regimen for the administration of intravenous, unfractionated heparin.

4.0 Statement of evidence/references

References:

MBRACE, UK: Saving Lives, Improving Mothers' Care
Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2014–16

CEMACH (2007) Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer – 2003-2005.

CEMACH (2004) Why Mothers Die 2000-2002. RCOG Press

Milton Keynes Hospital NHS Foundation Trust (2008) Anticoagulation Guidelines for Adults.

RCOG Guideline no 37a (April 2015) Thromboembolic disease in pregnancy and the puerperium: reducing the risk

RCOG Guideline no 37b (April 2015) Thromboembolic disease in pregnancy and the puerperium: acute management.

5.0 Governance

5.1 Document review history

Version number	Review date	Reviewed by	Changes made
6	**04/2020**	**Anu Rammohan**	**Full review of document**

5.2 Consultation History

Stakeholders Name/Board	Area of Expertise	Date Sent	Date Received	Comments	Endorsed Yes/No
Miss Michelle Fynes	0&G Consultant	04/05/2020	04/05/2020	No suggestions or amendments	N/A
Julie Cooper	Head of Midwifery	04/05/2020	08/05/2020	Incorporated	Yes
Sarah Davis	Consultant Haematologist	20/05/2020	14/06/2020	Incorporated	Yes
Eleanor Tyagi	Consultant Anaesthetist	20/05/2020		Incorporated	Yes
Fran Mngola	Pharmacist	20/05/2020	28/05/2020	Mostly incorporated	Yes
Anja Johansen-Bibby	O&G Consultant	26/08/2021		Changed doses of dalteparin in consultant with Haem/ pharmacy	

5.3 Audit and monitoring

Audit/Monitoring Criteria	Tool	Audit Lead	Frequency of Audit	Responsible Committee/Board
1. Documentation of risks of VTE investigations and management 2. Correct therapeutic management of suspected and proven VTE 3. 3Appopriate interval for administration of postpartum anticoagulant therapy Documentation of postpartum management plan.	Stats	Maternal medicine	Annual	Maternity CIG

5.4 Equality Impact Assessment

As part of its development, this Guideline and its impact on equality has been reviewed. The purpose of the assessment is to minimise and if possible remove any disproportionate impact on the grounds of race, gender, disability, age, sexual orientation, religion or belief, pregnancy and maternity, gender reassignment or marriage and civil partnership. No detriment was identified.

Equality Impact assessments will show any future actions required to overcome any identified barriers or discriminatory practice.

Equality Impact Assessment			
Division	Women's and Children's Health	Department	Maternity
Person completing the EqIA	Anu Rammohan	Contact No.	
Others involved:		Date of assessment:	04/2020
Existing policy/service	Yes	New policy/service	No

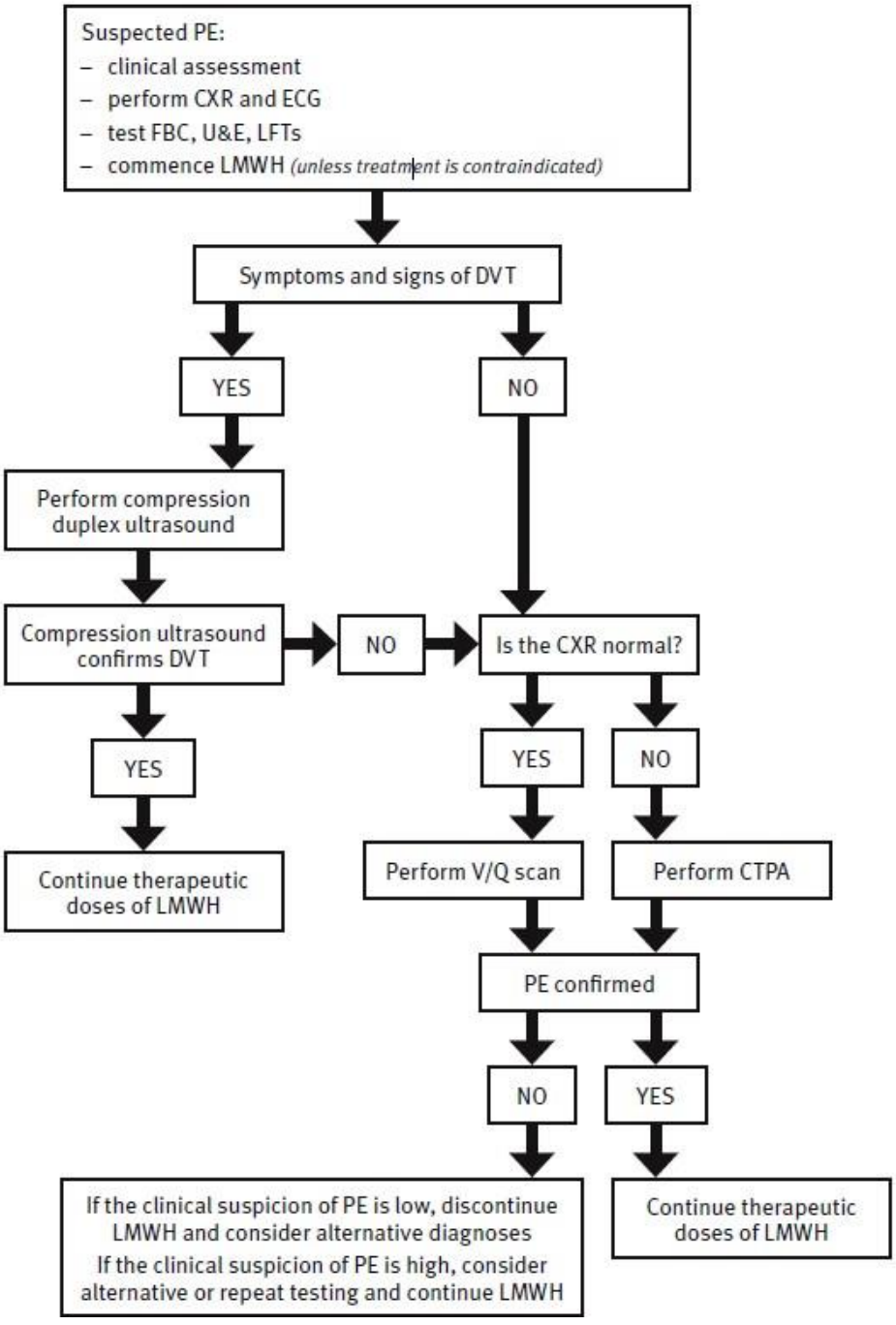
Will patients, carers, the public or staff be affected by the policy/service?	Yes
If staff, how many/which groups will be affected?	*All staff working in maternity*

Protected characteristic	Any impact?	Comments
Age	NO	Positive impact as the policy aims to recognise diversity, promote inclusion and fair treatment for patients and staff
Disability	NO	
Gender reassignment	NO	
Marriage and civil partnership	NO	
Pregnancy and maternity	NO	
Race	NO	
Religion or belief	NO	
Sex	NO	
Sexual orientation	NO	

What consultation method(s) have you carried out?
Discussion at guidelines meeting and circulation via email
How are the changes/amendments to the policies/services communicated?
Discussion at guidelines meeting and CIG, circulation via email
What future actions need to be taken to overcome any barriers or discrimination?

What?	Who will lead this?	Date of completion	Resources needed
Review date of EqIA			

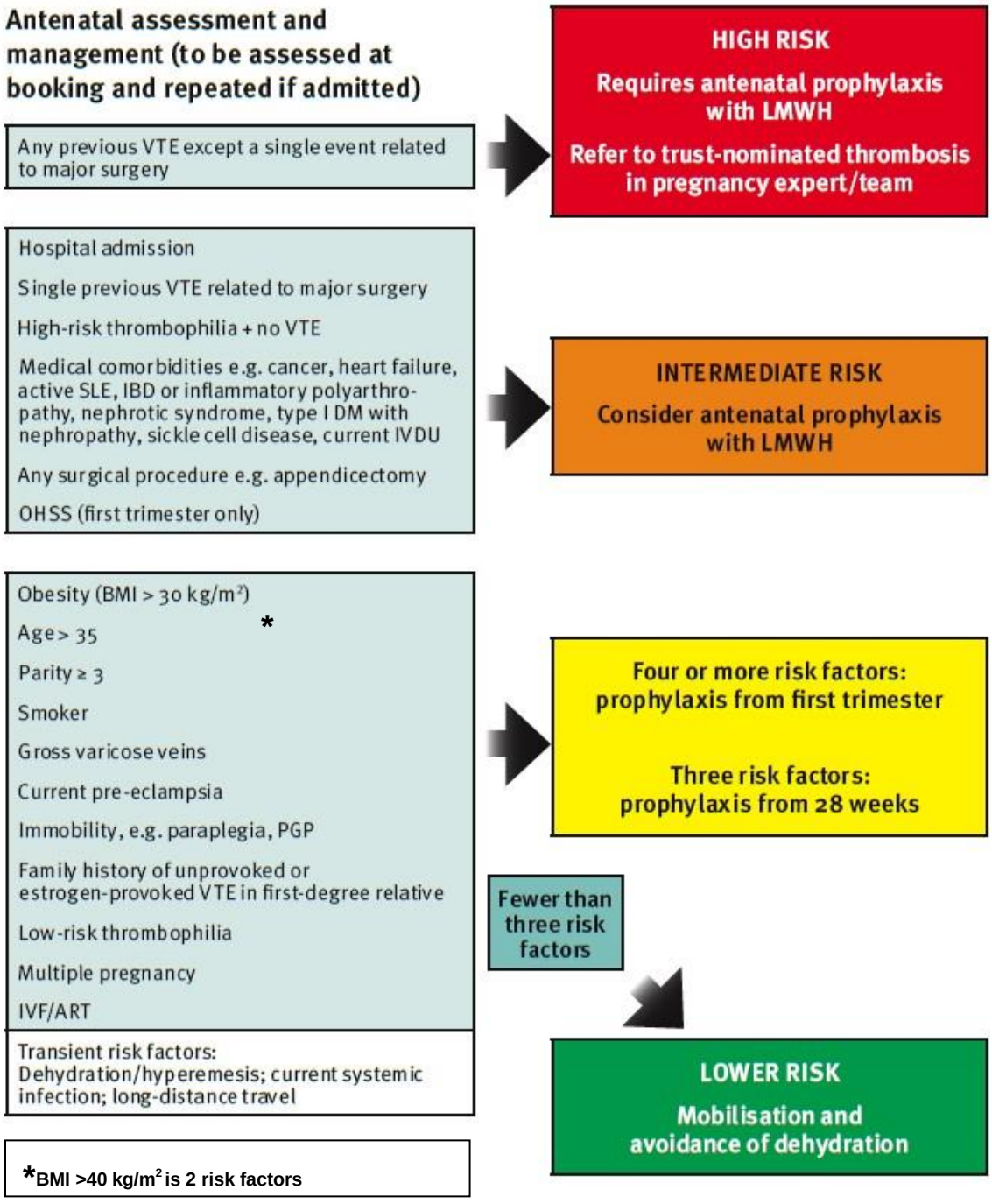
Appendix 1: Algorithm for the investigation and initial management of suspected PE in pregnancy and the puerperium



Abbreviations

CTPA computerised tomography pulmonary angiogram; **CXR** chest X-ray; **DVT** deep venous thrombosis; **ECG** electrocardiogram; **FBC** full blood count; **LFTs** liver function tests; **LMWH** low-molecular-weight heparin; **PE** pulmonary embolism; **U&Es** urea and electrolytes; **V/Q scan** ventilation/perfusion scan.

Appendix 2: Obstetric Thromboprophylaxis Risk Assessment and Management



APL = antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, β_2-glycoprotein 1 antibodies); ART = assisted reproductive technology; BMI based on booking weight; DM = diabetes mellitus; FHx = family history; gross varicose veins = symptomatic, above knee or associated with phlebitis/oedema/skin changes; high-risk thrombophilia = antithrombin deficiency, protein C or S deficiency, compound or homozygous for low-risk thrombophilias; IBD = inflammatory bowel disease; immobility = ≥ 3 days; IVDU = intravenous drug user; IVF = in vitro fertilisation; LMWH = low-molecular-weight heparin; long-distance travel = > 4 hours; low-risk thrombophilia = heterozygous for factor V Leiden or prothrombin G20210A mutations; OHSS = ovarian hyperstimulation syndrome; PGP = pelvic girdle pain with reduced mobility; PPH = postpartum haemorrhage; thrombophilia = inherited or acquired; VTE = venous thromboembolism.

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Postnatal assessment and management (to be assessed on delivery suite)

- Any previous VTE
- Anyone requiring antenatal LMWH
- High-risk thrombophilia
- Low-risk thrombophilia + FHx

→ **HIGH RISK**
At least 6 weeks' postnatal prophylactic LMWH

- Caesarean section in labour
- BMI ≥ 40 kg/m²
- Readmission or prolonged admission (≥ 3 days) in the puerperium
- Any surgical procedure in the puerperium except immediate repair of the perineum
- Medical comorbidities e.g. cancer, heart failure, active SLE, IBD or inflammatory polyarthropathy; nephrotic syndrome, type I DM with nephropathy, sickle cell disease, current IVDU

→ **INTERMEDIATE RISK**
At least 10 days' postnatal prophylactic LMWH

NB If persisting or > 3 risk factors consider extending thromboprophylaxis with LMWH

- Age > 35 years
- Obesity (BMI ≥ 30 kg/m²)
- Parity ≥ 3
- Smoker
- Elective caesarean section
- Family history of VTE
- Low-risk thrombophilia
- Gross varicose veins
- Current systemic infection
- Immobility, e.g. paraplegia, PGP, long-distance travel
- Current pre-eclampsia
- Multiple pregnancy
- Preterm delivery in this pregnancy (< 37[+0] weeks)
- Stillbirth in this pregnancy
- Mid-cavity rotational or operative delivery
- Prolonged labour (> 24 hours)
- PPH > 1 litre or blood transfusion

Two or more risk factors → INTERMEDIATE RISK

Fewer than two risk factors → **LOWER RISK**
Early mobilisation and avoidance of dehydration

Antenatal and postnatal prophylactic dose of LMWH

Weight < 50 kg = 20 mg enoxaparin/2500 units dalteparin/3500 units tinzaparin daily
Weight 50–90 kg = 40 mg enoxaparin/5000 units dalteparin/4500 units tinzaparin daily
Weight 91–130 kg = 60 mg enoxaparin/7500 units dalteparin/7000 units tinzaparin daily
Weight 131–170 kg = 80 mg enoxaparin/10 000 units dalteparin/9000 units tinzaparin daily
Weight > 170 kg = 0.6 mg/kg/day enoxaparin/ 75 u/kg/day dalteparin/ 75 u/kg/day tinzaparin

Appendix 3: Regimen for the administration of intravenous, unfractionated heparin guidance:

Guidelines on when to use and ho