Thromboprophylaxis in Pregnancy and Puerperium

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Disclaimer -

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Index
Guideline Statement
Executive Summary
1.0 Roles and Responsibilities:
2.0 Implementation and dissemination of document
3.0 Processes and procedures
Thrombophilias
Bone fracture
New onset/transient
3.1 Pre-pregnancy, antenatal & postnatal risk assessment
3.2 Thromboprophylaxis for service users with risk factors in pregnancy
3.3 Timing of initiation of antenatal thromboprophylaxis
3.4 Advice to service users receiving antenatal thromboprophylaxis regarding
labour/undergoing planned caesarean section /Induction of labour7
3.5 Guidance on Use of regional analgesia in service users on antenatal8
thromboprophylaxis
3.6 Thromboprophylaxis immediately after delivery8
3.7 Postnatal thromboprophylaxis8
3.8 Recommended agents for thromboprophylaxis
3.8.1 Low molecular weight heparins (LMWH)9
3.8.2 Unfractionated heparin
3.8.3 Warfarin
3.8.4 Non-vitamin K antagonist oral anticoagulants(NOACS)
3.9 Thromboprophylaxis for service users with DIC/massive obstetric
haemorrhage with thrombocytopenia
3.10.1 Suggested thromboprophylactic doses for antenatal and postnatal
LMWH 11
3.11 Rationale for main recommendations
4.0 Statement of evidence/references
References:12
5.0 Governance
5.1 Document review history
5.2 Consultation History
5.3 Audit and monitoring
5.4 Equality Impact Assessment
Appendix 1 Antenatal Booking risk assessment
Appendix 2 Antenatal admission risk assessment
Appendix 3 Postnatal risk assessment (To be assessed on Labour Ward)



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Guideline Statement

The aim of this guideline is to provide information, based on clinical evidence where available, to support the risk assessment and management of thromboprophylaxis during pregnancy or 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. This is despite detailed guidance for both prevention and treatment of thromboembolic disease from the Royal College of Obstetricians and Gynaecologists, most recently updated in 2015, and the Institute of Obstetricians and Gynaecologists, updated in 2016, leading to the wider use of thromboprophylaxis (Royal College of Obstetricians and Gynaecologists 2015b, Institute of Obstetricians and Gynaecologists Royal College of Physicians of Ireland, HSE Clinical Care Programme in Obstetrics and Gynaecology et al. 2016). Alongside the changes in guidelines, the maternity population as well as interventions are changing. Service users giving birth are now older, with more risk factors for thromboembolic disease such as obesity. More interventions such as caesarean section are undertaken, also placing service users at higher risk of VTE. Thus it is likely that VTE in association with pregnancy will become an even greater problem without careful attention to prevention

Many pulmonary emboli are preventable with appropriate thromboprophylaxis. National Institute of Health and Clinical Excellence (NICE) estimates that Low molecular weight heparin (LMWH) reduces VTE risk in medical and surgical patients by 60% and 70%, respectively.

There were 39 service users who died from venous thromboembolism in the UK and Ireland between 2014 and 2016. Thirty service users died from pulmonary embolism and two service users died from venous sinus thrombosis during pregnancy or up to 6 weeks after pregnancy

Many fatal antenatal VTE events occur in the first trimester and therefore prophylaxis for service users with previous VTE should begin early in pregnancy.

1.0 Roles and Responsibilities:

Midwives are responsible for ensuring that all service users have risk assessments at booking, during any antenatal admission and following delivery.

Medical staff are responsible for undertaking risk assessments and for acting on the results of risk assessments where appropriate.

2.0 Implementation and dissemination of document

This guideline is available on the Trust intranet.

3.0 **Processes and procedures**

Risk factors for venous thromboembolism in pregnancy and the puerperium are shown in table below:



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Pre-existing	Previous VTE						
	Thrombophilia's						
	Heritable						
	Antithrombin deficiency						
	Protein C deficiency						
	Protein S deficiency						
	Factor V Leiden						
	Prothrombin gene mutation						
	Acquired Antiphospholipid antibodies						
	Persistent lupus anticoagulant and/or persistent moderate/high titre						
	anticardiolipin antibodies and/or β_2 -glycoprotein 1 antibodies						
	Medical comorbidities e.g. cancer; heart failure; active SLE,						
	inflammatory polyarthropathy or IBD; nephrotic syndrome; type I						
l	diabetes mellitus with nephropathy; sickle cell disease; current						
	intravenous drug user						
	Age > 35 years						
	Obesity (BMI \geq 30 kg/m ²) either pre-pregnancy or in early pregnancy						
	Parity ≥ 3						
	Smoking/Vaping						
	Paraplegia						
	Significant family history/first degree relative with VTE						
	Gross varicose veins (symptomatic or above knee or with associated						
	phlebitis, oedema/skin changes)						
Obstetric risk factors	Multiple pregnancy						
	Current pre-eclampsia						
	Caesarean section						
	Prolonged labour (> 24 hours)						
	Mid-cavity or rotational operative delivery						
	Stillbirth						
	Preterm birth						
	Postpartum haemorrhage (> 1 litre/requiring transfusion)						
New onset/transient	Any surgical procedure in pregnancy or puerperium except immediate						
	repair of the perineum, e.g. appendicectomy, postpartum sterilisation						
	Bone fracture						
New onset/transient	Hyperemesis, dehydration						
	Ovarian hyperstimulation Assisted reproductive technology						
	syndrome (first trimester only) (ART), in vitro fertilisation (IVF)						
	Admission or immobility (≥ 3 days' e.g. pelvic girdle pain restricting						
	bed rest) mobility (2.5 days e.g. period grade pain restricting						
	Current systemic infection (requiring e.g. pneumonia,						
	intravenous antibiotics or admission pyelonephritis, postpartum						
	to hospital) wound infection						

3.1 Pre-pregnancy, antenatal & postnatal risk assessment

- All service users should undergo a documented assessment of risk factors for venous thromboembolism (VTE) in early pregnancy or pre-pregnancy. To remain as this sentencee (See Appendix 1).
- VTE assessment should be undertaken for all service users at every admission to hospital for any reason or if they develop other problems, (See Appendix 2).
- VTE assessment should be undertaken for all service users using the Antenatal booking assessment (Appendix 1) Antenatal Admission Risk Assessment and Management for (Appendix 2) and Postnatal Risk Assessment and Management (To be completed on delivery suite) (Appendix 3)
- Risk assessment should be repeated again intrapartum or immediately postpartum(see appendix 3)
- Any service user with **four or more** current risk factors shown in (other than previous VTE or thrombophilia) should be considered for prophylactic low-molecular-weight heparin (LMWH) throughout the antenatal period and will usually require prophylactic LMWH for 6 weeks postnatally but a postnatal risk reassessment should be made.
- Any service user with **three current risk factors** (other than previous VTE or thrombophilia) should be considered for prophylactic LMWH from 28 weeks and will usually require prophylactic LMWH for 6 weeks postnatally but a postnatal risk reassessment should be made.
- Any service user with **two current risk factors** (other than previous VTE or thrombophilia) should be considered for prophylactic LMWH for at least 10 days postpartum.
- Service users admitted to hospital when pregnant (including to the gynaecology ward with hyperemesis gravidarum or ovarian hyperstimulation syndrome) should usually be offered thromboprophylaxis with LMWH unless there is a specific contraindication such as risk of labour or active bleeding.

3.2 Thromboprophylaxis for service users with risk factors in pregnancy

- Service users with previous VTE should have a careful history documented.
- All service users with single previous VTE should be offered pre-pregnancy or early
 pregnancy counselling with a prospective management plan for thromboprophylaxis in
 pregnancy and made a referral to the joint Obstetric and Haematology clinic.
 Referral to hematology is not routinely required in the absence of complicating
 factors.
- Service users with previous VTE (except those with a single previous VTE related to major surgery and no other risk factors) should be offered thromboprophylaxis with LMWH throughout the antenatal period.

• In service users in whom the original VTE was provoked by major surgery from which they have recovered and who have no other risk factors, thromboprophylaxis with LMWH can be withheld antenatally until 28 weeks provided no additional risk factors are present (in which case they should be offered LMWH). They require close surveillance for the development of other risk factors

Where objective documentation is not available, the previous diagnosis of VTE can be assumed in cases where the service user gives a good history and received prolonged (greater than 6 weeks) therapeutic anticoagulation

- Service users with previous VTE associated with Antithrombin deficiency & Antiphosphilipid syndrome (APS) should be referred directly to the joint Obstetric and Haematology clinic. They should be offered thromboprophylaxis with higher dose LMWH (either 50%, 75% or full treatment dose) antenatally and for 6 weeks postpartum or until returned to oral anticoagulant therapy after delivery.
- Management should be undertaken in **collaboration with the joint Obstetric and Haematology clinic** with expertise in thrombosis in pregnancy and consideration given to antenatal anti-Xa monitoring and the potential for antithrombin replacement at initiation of labour or prior to caesarean section.
- For service users on treatment dose of LMWH, Anti-Xa levels are measured 4-hours after dose & peak levels of 0.5–1.0 iu/ml aimed for.
- Heritable thrombophilic defects other than Antithrombin deficiency are lower risk and can be managed with standard doses of thromboprophylaxis. Routine referral to hematology is not required.
- Service users with previous recurrent VTE not on warfarin or other oral anticoagulants should be advised to start LMWH as soon as they have a positive pregnancy test. **Refer to Obstetric and Haematology clinic.**
- Service users on long-term warfarin or other oral anticoagulants should be counselled about the risks of these agents to the fetus and advised to stop their oral anticoagulant therapy and change to LMWH as soon as pregnancy is confirmed, ideally within 2 weeks of the missed period and before the sixth week of pregnancy
- Service users with previous VTE and a family history of VTE, (please refer to **Obstetric and Haematology clinic**) and either antithrombin deficiency or where the specific thrombophilia has not been detected should be tested for antithrombin deficiency.
- Service users with an unprovoked VTE should be tested for the presence of antiphospholipid antibodies.
- Service users with asymptomatic antithrombin, protein C or S deficiency or those with more than one thrombophilic defect (including homozygous factor V Leiden, homozygous prothrombin gene mutation and compound heterozygotes) should be referred to Obstetric and Haematology clinic and antenatal prophylaxis considered. They should be recommended for six weeks' postnatal prophylaxis even in the absence of additional risk factors

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- Service users with heterozygosity for factor V Leiden or prothrombin gene mutation or antiphospholipid antibodies may be considered for antenatal thromboprophylaxis in the presence of 3 other risk factors, if there are two other risk factors thromboprophylaxis should be considered from 28 weeks and if there is one other risk factor postnatal thromboprophylaxis for 10 days should be considered(see appendix 1)
- Homozygosity for methylene tetrohydrofolate reductase (MTHFR) does not predispose to an increased risk of VTE in pregnancy and should be ignored
- Service users with no personal history or risk factors for VTE but who have a family history of an unprovoked or estrogen-provoked VTE in a first-degree relative when aged under 50 years should be considered for thrombophilia testing. This will be more informative if the relative has a known thrombophilia. Please refer to Obstetric and Haematology clinic

3.3 Timing of initiation of antenatal thromboprophylaxis

- Antenatal thromboprophylaxis for those with previous VTE should begin as early in pregnancy as practical
- Service users without previous VTE and without particular first trimester risk factors or admission to hospital, but with four other risk factors, should be considered for antenatal prophylaxis throughout pregnancy.
- Service users without previous VTE and without particular first trimester risk factors or admission to hospital, but with three other risk factors, can start antenatal prophylaxis at 28 weeks of gestation
- Service users admitted with hyperemesis should be considered for thromboprophylaxis with LMWH and can discontinue thromboprophylaxis when the hyperemesis resolves. Service users should be discharged with 10 days of LMWH.
- Service users with ovarian hyperstimulation syndrome should be considered for thromboprophylaxis with LMWH in the first trimester.

3.4 Advice to service users receiving antenatal thromboprophylaxis regarding labour/undergoing planned caesarean section /Induction of labour

- Some women may have a bespoke plan for dalteparin use around induction. Please check birth plan from Joint Obstetric Haematology clinic
- Service users receiving antenatal LMWH should be advised that if they have any vaginal bleeding or once labour begins, they should not inject any further LMWH. Assessment should be made on admission and further doses should be prescribed by medical staff.
- Service users receiving antenatal LMWH having an elective caesarean section should receive a thromboprophylactic dose of LMWH on the day prior to delivery and, on the day of delivery, any morning dose should be omitted, and the operation performed that morning. Service users should be advised that as long as the prophylactic dose is taken 12 hrs before their planned CS and treatment dose of LMWH is taken 24 hrs

before their planned CS, they can continue with the LMWH on the day prior to the planned CS.

On the day prior to admission for IOL, service users should be, advised that they can take the LMWH as long as the last prophylactic dose is at least 12hr and treatment dose is at least 24 hrs from the start of induction process.

• Service users on high prophylactic or therapeutic doses of LMWH can continue to have their full dose on day prior to admission for IOL, unless they are at high risk of bleeding., as long as the last dose is taken at least 24 hrs before the start of IOL process.

3.5 Guidance on Use of regional analgesia in service users on antenatal thromboprophylaxis

- Obstetric anaesthetist should be informed once patient is admitted in labour.
- Regional techniques should be avoided until at least 12 hours after the previous prophylactic dose of LMWH
- Regional techniques should be avoided for 24 hours after the last therapeutic dose of LMWH
- LMWH should not be given for 4 hours after use of spinal anaesthesia or after the epidural catheter has been removed.
- Epidural catheter should not be removed within 12 hours of the most recent injection of prophylactic dose LMWH.

3.6 Thromboprophylaxis immediately after delivery

- The first thromboprophylactic dose of LMWH should be given as soon as possible after delivery, usually between 4-6 hrs, if there is no postpartum haemorrhage and regional analgesia has not been used.
- Service users at high risk of haemorrhage with risk factors including major antepartum haemorrhage, coagulopathy, progressive wound haematoma, suspected intra-abdominal bleeding and postpartum haemorrhage may be managed with anti-embolism stockings (AES), foot impulse devices or intermittent pneumatic compression devices. Unfractionated heparin (UFT) may also be considered.
- If a service user develops a haemorrhagic problem, while on LMWH the treatment should be stopped and expert haematological advice sought.
- Thromboprophylaxis should be started or reinstituted as soon as the immediate risk of haemorrhage is reduced.

3.7 Postnatal thromboprophylaxis

• All service users should have a postnatal risk assessment immediately after delivery.

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- Thromboprophylaxis should be continued for 6 weeks in high-risk service users and for 10 days in intermediate-risk service users. High risk service users may have additional plans from the Joint Obstetric Haematology to follow.
- Service users with two or more persisting risk factors (see appendix 3) should be considered for LMWH in prophylactic doses appropriate for their weight for 10 days after delivery.
- In service users who have additional persistent (lasting more than 10 days postpartum) risk factors, such as prolonged admission, wound infection or surgery in the puerperium, thromboprophylaxis should be extended for up to 6 weeks or until the additional risk factor/s is/are no longer present.
- All service users with class 3 obesity (BMI greater than or equal to 40 kg/m²) should be considered for prophylactic LMWH in doses appropriate for their weight for 10 days after delivery.
- All service users with a previous history of confirmed VTE should be offered thromboprophylaxis with LMWH or warfarin for at least 6 weeks postpartum regardless of the mode of delivery
- Service users with thrombophilia without previous VTE should be stratified according to both the level of risk associated with their thrombophilia and the presence or absence of a family history or other risk factors.
- Service users with a family history of VTE and an identified thrombophilia should be considered for 6 weeks' postnatal thromboprophylaxis
- All service users who have had caesarean sections should be considered for thromboprophylaxis with LMWH for 10 days after delivery apart from those having an elective caesarean section who should be considered for thromboprophylaxis with LMWH for 10 days after delivery if they have any additional risk factors.
- Risk assessment should be performed on each service user at least once following delivery, (within 6 hours) completed by the delivering midwife or obstetric team/anaesthatist on labour ward before before transfer to the ward or discharge and arrangements made for LMWH prescription and administration (usually by the service user themselves) in the community where necessary.
- Prolonged postnatal admission >3 days or readmission in the puerperium is a trigger for intermediate risk and will need reassessment at day 3.

3.8 Recommended agents for thromboprophylaxis

3.8.1 Low molecular weight heparins (LMWH)

- LMWHs are the agents of choice for antenatal and postnatal thromboprophylaxis.
- Doses of LMWH are based on weight. For thromboprophylaxis the booking or most recent weight can be used to guide dosing.



- It is only necessary to monitor the platelet count if the service user has had prior exposure to unfractionated heparin (UFH).
- Monitoring of anti-Xa levels is not required when LMWH is used for thromboprophylaxis.
- Doses of LMWH should be reduced in service users with renal impairment.
- LMWH is safe in breastfeeding.

3.8.2 Unfractionated heparin

- In service users at very high risk of thrombosis (previous VTE on long-term oral anticoagulant therapy
- Antithrombin deficiency, Antiphospholipid syndrome with previous VTE), UFH may be used peripartum in preference to LMWH where there is an increased risk of haemorrhage or where regional anaesthetic techniques may be required.
- If UFH is used after caesarean section (or other surgery), the platelet count should be monitored every 2–3 days from days 4–14 or until heparin is stopped.
- Aspirin is not recommended for thromboprophylaxis in obstetric patients.

3.8.3 Warfarin

- Warfarin is teratogenic, especially between 6 and 12 weeks of gestation.
- Warfarin use in pregnancy should be avoided and is restricted to the few situations where heparin is considered unsuitable, e.g. some service users with mechanical heart valves.
- Service users receiving long-term anticoagulation with warfarin can be converted from LMWH to warfarin postpartum when the risk of haemorrhage is reduced, usually 5–7 days after delivery.
- Warfarin is safe in breastfeeding.

3.8.4 Non-vitamin K antagonist oral anticoagulants(NOACS)

- Non-vitamin K antagonist oral anticoagulants (NOACs) should be avoided in pregnant service users.
- Use of NOACs is not currently recommended in service users who are breastfeeding.

3.9 Thromboprophylaxis for service users with DIC/massive obstetric haemorrhage with thrombocytopenia

- Discuss management with consultant haematologist on call
- Risk assess the patient for VTE prophylaxis and risk of bleeding.





• LMWH can be safely given if platelet count is more than 50 and clotting is normal.

3.10 Guidance about use of LMWH

- Booking weight of the service users is used for calculating the dose.
- •
- Monitoring anti factor Xa levels is not required if there is good renal function
- Lower dose Dalteparin should be used if the creatinine clearance is less than 30ml/minute.
- Very low risk of thrombocytopenia, hence no need for repeated platelet testing.
- Risk of osteoporosis is 0.04%
- Allergic skin reactions is 1.8%
- Risk of bleeding is less than 2 %
- Wound haematoma is 2% (hence, undergoing LSCS who are on treatment dose of LMWH needs drain in fatty tissue).

3.10.1 Suggested thromboprophylactic doses for antenatal and postnatal LMWH

Weight (kg)	Daltaparin
<50	2500 units daily
50-90	5000 units daily
91-130	7500 units daily
131-170	10000 units daily
>170	75 units/kg/day

3.10.2 Heparin Intolerance/Allergy

In case of Heparin induced thrombocytopenia (HIT) or skin allergy to heparin, expert advice should be sought from Consultant hematologist.

Potential use of Danaparoid or Fondaparinux should be in conjunction with a consultant hematologist with expertise in hemostasis and pregnancy.

3.11 Rationale for main recommendations



The recommendations of this guideline will ensure that all service users have appropriate risk assessments during pregnancy and the postnatal period in line with national guidance. Additionally, the guideline indicates where treatment is appropriate and what treatment should be prescribed.

4.0 Statement of evidence/references

References:

MBRRACE-UK - Saving Lives, Improving Mothers' Care November 2020

Royal College of Obstetricians and Gynaecologists (April 2015) Thrombosis and Embolism during Pregnancy and the Puerperium, Reducing the Risk (Green-top Guideline No. 37a)

National Institute for Health and Clinical Excellence. *Venous thromboembolism: reducing the risk. Reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital.* NICE clinical guideline 92. London: NICE; 2010.



5.0 Governance

5.1 Document review history

Version number	Review date	Reviewed by	Changes made
5	Jan 2023	Bethan Percival, Lorraine Hawkins, Erum Khan, Dr Sarah Davis	Reviewed and updated
4 and 4.1	Apr 2019	Davis Faryal Nizami, Erum Khan and Dr Sarah Davis	Addition of BMI 40 to all risk assessments forms Addition of table of risk factors for venous thromboembolism in pregnancy and the puerperium Executive summary Changes to section 3.2 , to include indications for referral to hematology.Routine referral to hematology is not required in all cases. Changes to section 3.4 relating to LMWH & planned CS/IOL Changes to Section 3.6 relating to first dose of LMWH following delivery Changes to section 3.8.3 relating to Warfarin use in pregnancy Changes to section 3.10.1 table
	1	1	





5.2 Consultation History

Stakeholders Name/Board	Area of Expertise	Date Sent	Date Received	Comments	Endorsed Yes/No
Circulated to all Maternity staff on the 3/2/16					
Steph Smith	Pharmacist	3/2/16	25/2/16	Yes	Yes
Circulated to staff in Maternity		30/04/2019			
Fran Mngola	Pharmacist	30/04/2019			
Anja Johansen- Bibby	Consultant Obstetrician				

5.3 Audit and monitoring

Audit/Monitoring	ΤοοΙ	Audit	Frequency	Responsible
Criteria		Lead	of Audit	Committee/Board
 a) Monitor the implementation of antenatal risk assessments b) Monitor the implementation of antenatal admission risk assessments c) Monitor the implementation of postnatal risk assessments d) Monitor the use of antenatal LMWH e) Monitor care in labour for service users who have received antenatal LMWH f) Monitor the use of postnatal LMWH 	Audit	Clinical Staff	12 months	Maternity Clinical Improvement Group



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	Wor	Women's Health			Department	Maternity	
Person completing the E	qIA B P	B Percival, L Hawkins			Contact No.		
Others involved:					Date of assessment:	Jan 2023	
Existing policy/service			yes		New policy/service		
			Γ				
Will patients, carers, the be affected by the policy	•	staff	aff Yes				
If staff, how many/which affected?	groups wi	ll be	be Maternity, pharmacy				
Protected characteristic		Any ir	mpact?	Comme	nts		
Age			NO		impact as the policy ai		
Disability			NO	-	recognise diversity, promote inclus		
Gender reassignment		NO			ment for patients and s	stall	
Marriage and civil part	nership	NO					
Pregnancy and materr	nity	YES					
Race		NO					
Religion or belief		NO					
Sex		NO					
Sexual orientation		NO					
What consultation metho	()	•					
Email consultation and C			-				
How are the changes/an			·				
Guideline review group r			-		-		
What future actions need to be taken to overcome any barriers or discrimination?							
What?	Who will lead this? D		? Date of o	completion	Resources nee	eded	
Review date of EqIA	Jan 2026						



Appendix 1 Antenatal Booking risk assessment





Appendix 2 Antenatal admission risk assessment

Antenatal Admission Risk Surname: Assessment and Management Forename: DOB: Hospital No: Or affix Patient Label Risks Tick Risk assessment HIGH RISK at booking Requires antenatal prophylaxis with Low Any previous VTE except a single event related Molecular Weight Heparin to major surgery (LMWH) Hospital admission Refer to Maternal Medicine Single previous VTE related to major surgery Obstetrician High risk thrombophilia and no VTE Medical comorbidities e.g. cancer, heart failure, INTERMEDIATE RISK active SLE. IBD or inflammatory polyarthro-Consider antenatal pathy, nephrotic syndrome, type I DM with prophylaxis with LMWH nephropathy, sickle cell disease, current IVDU Any surgical procedure e.g. appendicectomy OHSS (first trimester only) Four or more risk COVID Infection add addition 1 factors: Prophylaxis from first Obesity (BMI > 30 kg/m2) trimester (BMI ≥40kg/m_{2i} score 2 points) Three risk factors: Age > 35 Prophylaxis from 28 Parity ≥ 3 weeks Smoker/ Vaping Gross varicose veins Current pre-eclampsia Immobility e a paraplegia PGP Fewer than three risk Family history of unprovoked or estrogenfactors provoked VTE in first-degree relative Low-risk thrombophilia LOWER RISK Multiple pregnancy Mobilisation and avoidance of IVF/ART dehydration Transient risk factors: Dehydration/hyperemesis; current systemic infection; long-distance travel, COVID

Date	Time	Risk Assessment Score	Action	Sign and Print

* Daily risk assessment to be undertaken



Appendix 3 Postnatal risk assessment (To be assessed on Labour Ward)



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