

Queensland Clinical Guidelines

Translating evidence into best clinical practice

Maternity and Neonatal **Clinical Guideline**

Venous thromboembolism (VTE) prophylaxis in pregnancy and the puerperium

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Cultural acknowledgement

We acknowledge the Traditional Custodians of the land on which we work and pay our respect to the Aboriginal and Torres Strait Islander elders past, present and emerging.

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- Applying standard precautions, and additional precautions as necessary, when delivering care
- Documenting all care in accordance with mandatory and local requirements

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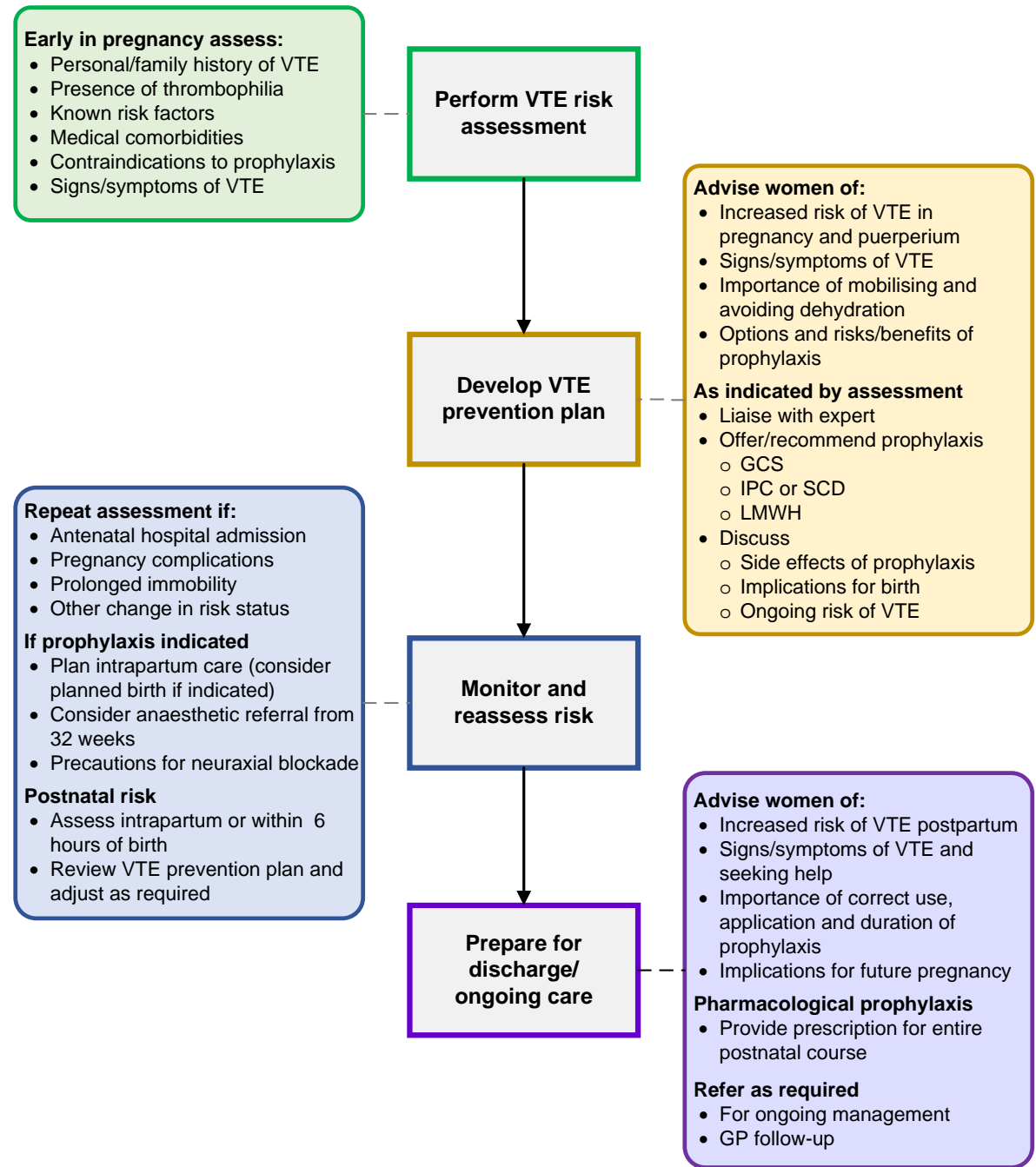


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Flow Chart: VTE assessment for pregnant and postpartum women

**Assess women on an individual basis.
Liaise with a team experienced in prophylactic assessment and management as required**



Signs and symptoms VTE

PE: dyspnoea, palpitations/tachycardia, chest pain, haemoptysis, tachypnoea, hypotension, collapse

DVT: unilateral leg pain, swelling in extremity, increase in calf circumference (more than 2 cm), increased temperature, prominent superficial veins, pitting edema

DVT: deep vein thrombosis, **GCS:** graduated compression stockings, **GP:** general practitioner, **IPC:** intermittent pneumatic compressions, **LMWH:** low molecular weight heparin, **PE:** pulmonary embolism, **SCD:** sequential compression device, **VTE:** venous thromboembolism,

Flowchart: Antenatal and postnatal thromboprophylaxis according to risk

High risk	1	ANY ONE OF <input type="checkbox"/> Pre-pregnancy therapeutic anticoagulation (any reason) <input type="checkbox"/> Any previous VTE plus high risk thrombophilia** <input type="checkbox"/> Recurrent unprovoked VTE (2 or more) <input type="checkbox"/> VTE in current pregnancy (seek expert advice)	Therapeutic anticoagulation <ul style="list-style-type: none"> Continue/commence antenatal Continue 6 weeks postpartum <i># High prophylactic dose may be appropriate</i>																																																														
	2	ANY ONE OF <input type="checkbox"/> Any single previous VTE not provoked by surgery <input type="checkbox"/> Recurrent provoked VTE (2 or more) <input type="checkbox"/> Active autoimmune or inflammatory disorder <input type="checkbox"/> Medical co-morbidity: (e.g. cancer, nephrotic syndrome, heart failure, sickle cell, type I diabetes with nephropathy)	LMWH standard prophylaxis <ul style="list-style-type: none"> From first trimester Continue 6 weeks postpartum 																																																														
	3	IF THROMBOPHILIA <input type="checkbox"/> High or low risk thrombophilia* (no personal history VTE)	Refer to Flowchart: <i>VTE prophylaxis if thrombophilia</i>																																																														
	4	ANY ONE OF <input type="checkbox"/> Antenatal hospital admission <input type="checkbox"/> Ovarian hyperstimulation syndrome (first trimester only) <input type="checkbox"/> Any surgery (pregnancy or postpartum) <input type="checkbox"/> Severe hyperemesis or dehydration requiring IV fluid	LMWH Standard prophylaxis <ul style="list-style-type: none"> While in hospital or until resolves 																																																														
All risk	5	SELECT ALL THAT APPLY Risk Score <i>at every assessment (antenatal or postnatal)</i> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr><td><input type="checkbox"/> Family history (1st degree relative) of unprovoked or estrogen provoked VTE</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Single VTE provoked by surgery</td><td style="text-align: right;">3</td></tr> <tr><td><input type="checkbox"/> Age > 35 years</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Parity ≥ 3</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Smoking (any amount)</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Gross varicose veins</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Current BMI 30–39 kg/m²</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Current BMI ≥ 40 kg/m²</td><td style="text-align: right;">2</td></tr> <tr><td><input type="checkbox"/> IVF/ART</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Multiple pregnancy</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Pre-eclampsia in current pregnancy</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Immobility</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Current systemic infection</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Pre-existing diabetes</td><td style="text-align: right;">1</td></tr> <tr><td colspan="2"><hr/></td></tr> <tr><td><input type="checkbox"/> Caesarean section in labour</td><td style="text-align: right;">3</td></tr> <tr><td><input type="checkbox"/> Elective caesarean section</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Prolonged labour > 24 hours</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Operative vaginal birth</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Preterm birth (< 37+0 weeks)</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> PPH > 1 L or transfusion</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Stillbirth in current pregnancy</td><td style="text-align: right;">1</td></tr> <tr><td><input type="checkbox"/> Caesarean hysterectomy</td><td style="text-align: right;">3</td></tr> </table>	<input type="checkbox"/> Family history (1st degree relative) of unprovoked or estrogen provoked VTE	1	<input type="checkbox"/> Single VTE provoked by surgery	3	<input type="checkbox"/> Age > 35 years	1	<input type="checkbox"/> Parity ≥ 3	1	<input type="checkbox"/> Smoking (any amount)	1	<input type="checkbox"/> Gross varicose veins	1	<input type="checkbox"/> Current BMI 30–39 kg/m ²	1	<input type="checkbox"/> Current BMI ≥ 40 kg/m ²	2	<input type="checkbox"/> IVF/ART	1	<input type="checkbox"/> Multiple pregnancy	1	<input type="checkbox"/> Pre-eclampsia in current pregnancy	1	<input type="checkbox"/> Immobility	1	<input type="checkbox"/> Current systemic infection	1	<input type="checkbox"/> Pre-existing diabetes	1	<hr/>		<input type="checkbox"/> Caesarean section in labour	3	<input type="checkbox"/> Elective caesarean section	1	<input type="checkbox"/> Prolonged labour > 24 hours	1	<input type="checkbox"/> Operative vaginal birth	1	<input type="checkbox"/> Preterm birth (< 37+0 weeks)	1	<input type="checkbox"/> PPH > 1 L or transfusion	1	<input type="checkbox"/> Stillbirth in current pregnancy	1	<input type="checkbox"/> Caesarean hysterectomy	3	<div style="background-color: #4a7ebb; 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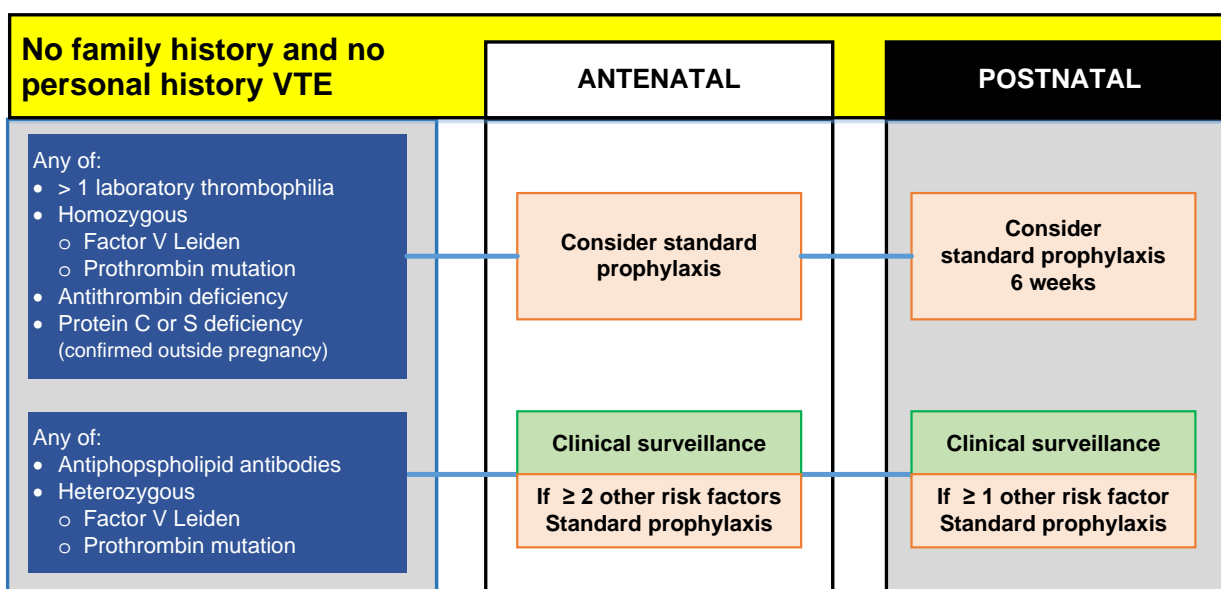
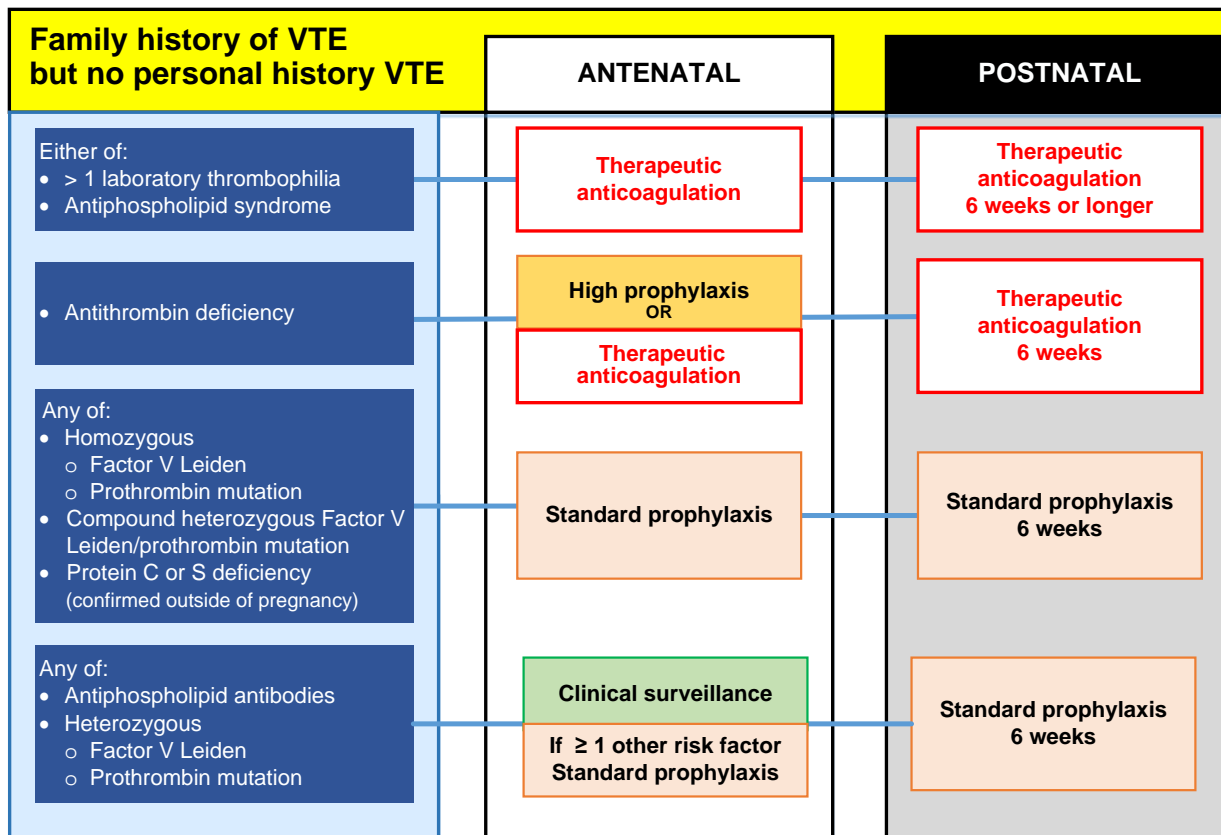
* **High risk thrombophilia:** > 1 laboratory thrombophilia, APS, antithrombin deficiency, protein C deficiency, protein S deficiency, homozygous FVL, homozygous prothrombin mutation, compound heterozygous FVL/prothrombin mutation

Low risk thrombophilia: heterozygous FVL, heterozygous prothrombin mutation, antiphospholipid antibodies

APS: antiphospholipid syndrome, **ART:** artificial reproductive technology, **BMI:** body mass index, **FVL:** factor V Leiden, **GCS:** graduated compression stockings, **IPC:** intermittent pneumatic compressions, **IVF:** in-vitro fertilisation, **LMWH:** low molecular weight heparin, **PE:** pulmonary embolism, **PPH:** Primary postpartum haemorrhage, **SCD:** sequential compression device, **SLE:** systemic lupus erythematosus, **TEDS:** thromboembolic deterrent stockings **VTE:** venous thromboembolism, **≥:** greater than or equal to, **>:** greater than

Flowchart: Thromboprophylaxis if thrombophilia

Assess women on an individual basis
Consult with or refer to an experienced physician as required



Enoxaparin: standard prophylaxis (subcut)

- 50–90 kg 40 mg daily
- 131–170 kg 80 mg daily
- 91–130 kg 60 mg daily
- > 171 kg 0.5 mg/kg

Enoxaparin: high prophylaxis (subcut)

- 50–130 kg 80 mg daily
- > 131 kg 60 mg BD

Enoxaparin: therapeutic anticoagulation (subcut)

- Antenatal: 1 mg/kg BD
- Postnatal 1.5 mg/kg daily

High risk thrombophilia: > 1 laboratory thrombophilia, APS, antithrombin deficiency, protein C deficiency, protein S deficiency, homozygous FVL, homozygous prothrombin mutation, compound heterozygous FVL/prothrombin mutation
Low risk thrombophilia: heterozygous FVL, heterozygous prothrombin mutation, antiphospholipid antibodies

APS: antiphospholipid syndrome, **BD:** twice daily, **>:** greater than **≥:** greater than or equal to

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Abbreviations

AOR	Adjusted odds ratio
BMI	Body mass index
CI	Confidence interval
COCP	Combined oral contraceptive pill
DVT	Deep vein thrombosis
GCS	Graduated compression stockings
HIT	Heparin induced thrombocytopenia
INR	International normalised ratio
IPC	Intermittent pneumatic compression
IV	Intravenous
LMWH	Low molecular weight heparin
PE	Pulmonary embolism
PPH	Postpartum haemorrhage
VTE	Venous thromboembolism

Definition of terms

Family history of VTE	Family history is considered positive if one or more first degree relatives are affected.
Immobility	Includes: <ul style="list-style-type: none"> • Long distance travel (rail, road or air) of four hours or more¹ • Majority of time on bedrest—24 hours or more • Other issue significantly affecting mobility (e.g. paralysis)
Neuraxial blockade	Term that includes both spinal and epidural procedures
Obstetrician	Local facilities may as required, differentiate the roles and responsibilities assigned in this document to an 'Obstetrician' according to their specific practitioner group requirements; for example, to General Practitioner Obstetricians, Specialist Obstetricians, Consultants, Senior Registrars and Obstetric Fellows.
Provoked VTE ²	Major transient risk factors (during 3 months before diagnosis of VTE): <ul style="list-style-type: none"> • Surgery with general anaesthesia over 30 minutes duration • Confined to hospital bedrest (bathroom privileges only) for at least 3 days with an acute illness • Caesarean section
	Minor transient risk factors (during 2 months before diagnosis of VTE): <ul style="list-style-type: none"> • Surgery with general anaesthesia less than 30 minutes • Hospital admission for less than 3 days with acute illness • Oestrogen therapy • Pregnancy or puerperium • Confined to bed out of hospital for 3 or more days with acute illness • Leg injury associated with reduced mobility for 3 or more days
	Persistent risk factor <ul style="list-style-type: none"> • Active cancer, inflammatory bowel disease
Unprovoked VTE ²	VTE occurring where there are no identified risk factors (transient or persistent).
Recurrent VTE	Two or more VTE.
Thromboprophylaxis	In this guideline: <ul style="list-style-type: none"> • Standard prophylaxis refers to pharmacological management with the lowest recommended dose • High prophylaxis refers to pharmacological management at doses between standard prophylaxis and therapeutic anticoagulation
Thrombophilia	High risk thrombophilia (any of) <ul style="list-style-type: none"> • Presence of more than one laboratory thrombophilia, antithrombin deficiency, antiphospholipid syndrome, protein C deficiency, protein S deficiency, homozygous factor V Leiden, homozygous prothrombin mutation, compound heterozygous factor V Leiden/prothrombin mutation
	Low risk thrombophilia (any of) <ul style="list-style-type: none"> • Heterozygous factor V Leiden, heterozygous prothrombin mutation, antiphospholipid antibodies

1 Introduction

Pulmonary embolism (PE) and deep vein thrombosis (DVT) are two components of a single disease called venous thromboembolism (VTE).³ VTE was the leading cause of direct maternal death in Australia 2006–2016.⁴ World-wide there has been no consistent decrease in mortality over the past 20 years.⁵ This may be due to deficiencies in standard risk assessment tools and care recommendations, or to changes in the characteristics of women giving birth (e.g. increasing age and obesity).

1.1 Burden of disease

Failure to recognise and/or treat personal or pregnancy specific risk factors has been identified as a significant contributing factor to maternal mortality and morbidity arising from VTE in pregnancy.⁵

Table 1. Burden of disease

Aspect	Consideration
Increased risk in pregnancy³	<ul style="list-style-type: none"> • 4 to 5-fold increased risk of developing a VTE in pregnancy due to^{3,6,7} <ul style="list-style-type: none"> ○ Hypercoagulability ○ Increased venous stasis ○ Decreased venous outflow ○ Compression of the inferior vena cava and pelvic veins by the gravid uterus ○ Decreased mobility ○ Altered levels of coagulation factors responsible for haemostasis
Prevalence	<ul style="list-style-type: none"> • VTE complicates approximately 1.2 of every 1000 births^{3,8} • Risk higher in third trimester compared with first and second trimester^{3,7,9} • Greatest risk in the weeks immediately after birth^{3,7} <ul style="list-style-type: none"> ○ Risk declines to that of general population by about 13 to 18 weeks postpartum¹⁰ • Recurrence rate 2–11%¹¹
Aetiology	<ul style="list-style-type: none"> • 75–80% caused by DVT³ <ul style="list-style-type: none"> ○ Higher frequency of iliofemoral (64%) and iliac vein involvement (17%) ○ DVT more common in left lower extremity ○ Proximal VTE more common in pregnant than non-pregnant population • 20–25% caused by PE³
Morbidity	<ul style="list-style-type: none"> • One third of the general population with DVT develop post-thrombotic syndrome (PTS) within five years¹² <ul style="list-style-type: none"> ○ Characterised by chronic pain, swelling, skin changes in the affected limb, paraesthesia, venous leg ulceration⁹ and lower quality of life⁷
Mortality	<ul style="list-style-type: none"> • Most maternal deaths result from PE⁵ • In Australia 2006–2016, VTE was responsible for 10.6% of maternal deaths⁴ • In the United States, 2011–2013, PE was responsible for 9.2% of maternal deaths¹³ • In the United Kingdom, 2014–2016 VTE was responsible for 14% of maternal deaths⁵ <ul style="list-style-type: none"> ○ The same maternal mortality rate (1.4 per 100,000) as in 1985–87⁵ • In the United Kingdom, 2006–2008, 89% of maternal deaths from PE had identifiable risk factors <ul style="list-style-type: none"> ○ Obesity (body mass index (BMI) greater than or equal to 30 kg/m²) was identified in 57% of these⁵

1.2 Signs and symptoms of VTE

Inform women about the signs and symptoms of VTE. Refer to Section 3.1 Communicating risk and benefit.

Table 2. Signs and symptoms of VTE

Aspect	Consideration
Pulmonary embolism	<ul style="list-style-type: none"> • Dyspnoea (most common symptom of PE) • Palpitations/tachycardia • Chest pain • Haemoptysis • Hypoxia/cyanosis • Tachypnoea • Hypotension • Collapse
Deep vein thrombosis	<ul style="list-style-type: none"> • In pregnancy is often proximal and may not present with usual features of distal DVT³ • Unilateral leg pain³ • Swelling in an extremity³ with pitting oedema • Increase in calf/thigh circumference particularly of 2 cm or more³ • Increased temperature • Prominent superficial veins • Pitting oedema

1.3 Clinical standards

Provide care in accordance with the Australian Commission on Safety and Quality in Health Care (ACSQHC): Venous Thromboembolism Prevention Clinical Care Standard.¹⁴

Table 3. Clinical standards

Aspect	Consideration
ACSQHC clinical care standards	<ul style="list-style-type: none"> • The VTE prevention clinical care standard includes¹⁴: <ul style="list-style-type: none"> ○ Assess and document VTE risk ○ Develop a VTE prevention plan, balancing the risk of VTE against bleeding ○ Inform and partner with the woman ○ Document and communicate the VTE prevention plan ○ Use approved VTE prevention methods ○ Reassess risk and monitor for VTE related complications ○ Transition from hospital and ongoing care
Standard documentation	<ul style="list-style-type: none"> • Use an agreed risk assessment tool³ <ul style="list-style-type: none"> ○ No widely accepted scoring system has been prospectively validated in the obstetric population³ ○ There is evidence that clinicians find existing risk scoring systems difficult to apply consistently in practice⁵ • Document completion of the inpatient risk assessment • Use standard administration forms for prophylactic and therapeutic medications (e.g. heparin intravenous infusion order and administration form¹⁵)
Clinician education	<ul style="list-style-type: none"> • Inconsistency of risk assessment is identified as a major contributor to maternal mortality from VTE⁵ • Provide opportunities to increase competency and consistency of risk assessment (e.g. team review/discussion of complex cases, disseminate results of clinical audit)
Clinical audit	<ul style="list-style-type: none"> • Undertake regular audit to assess whether⁵: <ul style="list-style-type: none"> ○ Thromboembolism risk assessment was performed ○ Risk assessment was correct
Transfer of care	<ul style="list-style-type: none"> • Provide care in accordance with local service capabilities • Consult with, refer or transfer care to higher level services as appropriate¹⁶ • Document processes for referral and transfer appropriate to local facility

2 Risk factors

The evidence correlating risk factors and the occurrence of VTE is imprecise with wide and sometimes contradictory estimates of risk.¹⁷ The presence of multiple risk factors may have additive or synergistic effects^{11,17,18} but the combinations with the greatest risk are unknown.

2.1 Personal history of VTE

The strongest personal risk factor for VTE in pregnancy is a history of VTE. 15–25% of VTE in pregnancy are recurrent events.¹⁹ A history of unprovoked VTE (no identifiable associated risk factor) carries a greater risk than a history of provoked VTE (associated risk factor can be identified).

2.2 Thrombophilia and risk of VTE

Thrombophilia is present in 20–50% of women who experience VTE during pregnancy and postpartum.¹⁹ For women with thrombophilia, who have no *personal* history of VTE but do have a *family* history of VTE, the risk of VTE is increased two to four-fold, depending on the number and age of affected relatives.²⁰ Seek expert advice about individual thromboprophylaxis requirements for women with thrombophilia, especially in the presence of additional risk factors. Refer to Flowchart: Pharmacological thromboprophylaxis if thrombophilia

2.2.1 Absolute risk of pregnancy associated VTE with hereditary thrombophilia

Table 4. Estimated absolute risk of pregnancy associated VTE with hereditary thrombophilia

Hereditary thrombophilia	Non-family studies	With family history
High risk		
Antithrombin deficiency ¹⁷	0.3–4%	3.0–18.0%
Homozygous factor V Leiden mutation ¹⁷	1.3–2.3%	9.0–17.0%
Homozygous prothrombin mutation ²⁰	3.7%	–
Compound heterozygous factor V Leiden/prothrombin mutation ¹⁷	5.2% (single study)	1.8–5.5%
Protein C deficiency ¹⁷	0.5–1.8%	1.7–5.0%
Protein S deficiency ¹⁷	0.1%–1.0%	2.0–6.6%
Low risk		
Heterozygous factor V Leiden mutation ¹⁷	0.2–0.5%	1.5–3.9%
Heterozygous prothrombin mutation ¹⁷	0.2–0.4%	1.0–2.8%
Family history of VTE with thrombophilia unaffected controls ¹⁷	–	0.4–1.4%

2.3 Obesity and risk of VTE

Obesity is increasingly recognised as a major risk factor for the development of VTE in pregnancy and the puerperium.²¹ Increasing BMI is associated with increasing risk.²¹

Table 5. Adjusted Odds ratio between maternal BMI and VTE

BMI (kg/m ²)	Antepartum		Postpartum	
	n/N	*AOR (95%CI) ²¹	n/N	*AOR (95%CI) ²¹
Underweight (less than 18.5)	21/91,115	0.86 (0.5–1.49) [#]	18/91,090	0.7 (0.45–1.11) [#]
Normal BMI (18.5–24.9)	339/1,120,417	reference	346/1,120,025	reference
Overweight (25.0–29.9)	224/589,507	1.27 (1.04–1.54)	229/589,252	1.21 (1.02–1.43)
Obesity Class I (30.0–34.9)	122/288,939	1.37 (1.11–1.68)	161/288,799	1.74 (1.43–2.12)
Obesity Class II (35.0–39.9)	56/118,368	1.4 (1.01–1.93)	107/118,302	2.70 (2.16–3.36)
Obesity Class III (40 or more)	73/69,160	2.89 (2.3–3.81)	91/69,080	3.64 (2.92–4.55)

n=number of events; N=total number of women in each body mass index class

*adjusted for maternal age, race/ethnicity, education, insurance, smoking and parity

[#] result not significant

2.4 Other known risk factors

It is unclear for most risk factors whether they are more likely to be associated with antenatal or postnatal VTE (or both). For risk factor assessment in pregnancy and the puerperium, refer to:

- Appendix A: Odds ratios for VTE risk factors (where these are known)

3 Risk assessment

No widely accepted scoring system has been prospectively validated in the obstetric population and most have made extrapolations based on relative risk of VTE.³

Table 6. Risk assessment

Aspect	Consideration
Timing of assessment	<ul style="list-style-type: none"> • Initial assessment in early pregnancy³ or before conception⁵ • Repeat assessment if⁵: <ul style="list-style-type: none"> ○ Antenatal admission to hospital ○ Pregnancy complication develops (e.g. pre-eclampsia) ○ Prolonged immobility ○ Intrapartum or within 6 hours of birth • Commencing thromboprophylaxis at times of additional VTE risk is clinically important and appropriate
Assess for:	<ul style="list-style-type: none"> • Personal and family history for VTE • High risk and other known risk factors for VTE • Ask about VTE symptoms • Contraindications and cautions for prophylactic options including risk of bleeding
If previous VTE:	<ul style="list-style-type: none"> • Before commencing prophylaxis, recommend a full thrombophilia screen including: <ul style="list-style-type: none"> ○ Activated protein C resistance (APCR) <ul style="list-style-type: none"> ▪ Factor V Leiden mutation is included if APCR detected ○ Prothrombin gene mutation ○ Antithrombin deficiency ○ Protein C deficiency (before pregnancy) ○ Protein S deficiency (before pregnancy) ○ Antiphospholipid antibodies: <ul style="list-style-type: none"> ▪ Lupus anticoagulant ▪ Anticardiolipin antibodies ▪ Anti-beta 2 Glycoprotein 1 antibodies (B2GP1)
If pre-existing medical conditions	<ul style="list-style-type: none"> • Recommend counselling and advice from a medical specialist as risk of maternal mortality increased with: <ul style="list-style-type: none"> ○ Cerebral haemorrhage ○ Gastrointestinal haemorrhage ○ Heparin induced thrombocytopenia (HIT)/thrombocytopenia ○ Renal insufficiency ○ Mechanical heart valves ○ Chronic thromboembolic pulmonary hypertension ○ History of myocardial infarction ○ Permanent occlusion of a major vessel ○ History of recurrent thrombosis while fully anticoagulated
Plan care¹⁴	<ul style="list-style-type: none"> • Discuss options for VTE thromboprophylaxis with the woman • Document a plan of care • Liaise with a team experienced in prophylactic assessment and management as required
Referral	<ul style="list-style-type: none"> • If there are high risk circumstances: <ul style="list-style-type: none"> ○ Refer to an obstetrician or physician experienced in VTE thromboprophylaxis¹¹ ○ Use a multidisciplinary approach to care ○ Individualise thromboprophylaxis as required ○ Refer to anaesthetics team to discuss management plan peripartum

3.1 Communicating risk and benefit

Discuss with the woman her individual risk of VTE in pregnancy and the puerperium, as well as the risks and benefits of VTE prophylaxis appropriate to the circumstances.

Table 7. Communicating risk and benefit

Aspect	Consideration
Individual preferences	<ul style="list-style-type: none"> When making recommendations, consider a woman's values and preferences related to²⁰: <ul style="list-style-type: none"> Tolerance for risk Burden associated with use Medicalisation of pregnancy
Advise women	<ul style="list-style-type: none"> Pregnancy alone increases the risk of VTE <ul style="list-style-type: none"> Refer to Section 1.1 Burden of disease About symptoms of VTE and the importance of seeking urgent medical assistance if symptoms develop^{5,20} <ul style="list-style-type: none"> Refer to Section 1.2 Signs and symptoms of VTE About the importance of mobilisation and hydration in preventing VTE in pregnancy and after birth Limitations in the evidence about risk factors and about prevention strategies in pregnancy
Risks and benefits	<ul style="list-style-type: none"> Discuss risk of VTE in pregnancy to immediate and longer-term health Discuss the risks, benefits and side effects associated with recommendations for VTE prophylaxis Discuss: <ul style="list-style-type: none"> Ongoing risk of VTE despite thromboprophylaxis Burden of prolonged compliance with treatment option Risk of antenatal and postnatal bleeding with pharmacological thromboprophylaxis and potential management [refer to Queensland Clinical Guidelines: <i>Primary postpartum haemorrhage</i>²²] Implications for epidural management and/or the need for general anaesthesia

4 Thromboprophylaxis according to risk assessment

There is limited high-level evidence to guide decisions about which women will benefit most from thromboprophylaxis. The optimal strategy is unknown²⁰ and varies significantly between professional organisations.²³ The recommendations in the following sections are based on evidence, expert opinion and consensus. Refer to:

- Flowchart: Antenatal and postnatal pharmacological thromboprophylaxis according to risk
- Flowchart: Pharmacological thromboprophylaxis if thrombophilia

4.1 Intrapartum thromboprophylaxis

Table 8. Intrapartum thromboprophylaxis

Aspect	Consideration
Plan care	<ul style="list-style-type: none"> Involve the woman in developing a documented plan of care prior to the onset of labour/planned birth that considers her individual preferences, risk factors and clinical circumstances Consider anaesthetic referral from 32 weeks gestation for women with multiple co-morbidities²⁴
Ceasing/recommencing anticoagulants	<ul style="list-style-type: none"> Liaise with a multidisciplinary team regarding timing of: <ul style="list-style-type: none"> Conversion of therapeutic or prophylactic antenatal low molecular weight heparin (LMWH) to unfractionated heparin (UFH) Cessation of UFH prior to established labour/planned birth Recommencement of therapeutic anticoagulation following birth Commence standard prophylaxis within six hours of birth (where haemostasis is assured) following¹¹: <ul style="list-style-type: none"> Vaginal birth Caesarean section under general anaesthetic

4.2 Neuraxial blockade

Table 9. Neuraxial blockade

Aspect	Consideration
Clinical surveillance	<ul style="list-style-type: none"> Refer/discuss with the anaesthetic team prior to labour/planned birth²⁴ Monitor for neuraxial haematoma for 24 hours after commencement of neuraxial blockade or removal of catheter <ul style="list-style-type: none"> Spinal haematoma is a clinical emergency more likely to occur at insertion or removal of catheter If thromboprophylaxis for 4 days or more (LMWH or UFH) consider platelet count before onset of labour²⁴
Commencement of neuraxial blockade and interval to next dose LMWH	<ul style="list-style-type: none"> There is limited high-level evidence and significant variation among international professional organisations²⁴⁻³⁰ Consensus expert opinion in Queensland supports the recommendations of the Association of Anaesthetists of Great Britain and Ireland, Obstetric Anaesthetists' Association and Regional Anaesthesia UK²⁸ and the Royal College of Obstetricians and Gynaecologists¹¹ In this guideline, the recommended interval from commencement of neuraxial blockade to next dose of LMWH is 4 hours²⁸
Neuraxial blockade and high-risk circumstances	<ul style="list-style-type: none"> Consider individual circumstances and seek expert advice²⁹ If abnormal coagulation, abnormal renal function or in the presence of medications affecting coagulation (e.g. aspirin or non-steroidal), consider more conservative time-frames Commence UFH in preference to LMWH: <ul style="list-style-type: none"> If increased risk of post-partum haemorrhage following caesarean section As indicated by other clinical circumstances
Newer agents	<ul style="list-style-type: none"> Limited safety data about newer drugs (e.g. fondaparinux) Not recommended in conjunction with neuraxial blockade²⁸

4.2.1 Neuraxial blockade and dose intervals

Table 10. Neuraxial blockade interval timings

Last dose to neuraxial block	Hours to wait after last dose	
	<i>Prophylactic</i>	<i>Therapeutic</i>
LMWH	12 hours	24 hours
UFH*	4 hours	#4 hours
Neuraxial block to next dose	Hours to wait after neuraxial block	
	<i>Prophylactic</i>	<i>Therapeutic</i>
LMWH	4 hours	Avoid with catheter in situ
UFH*	1 hour	1 hour
Last dose to catheter removal	Hours to wait after last dose	
	<i>Prophylactic</i>	<i>Therapeutic</i>
LMWH	12 hours	24 hours
UFH*	4 hours	4 hours
Catheter removal to next dose	Hours to wait after catheter removal	
	<i>Prophylactic</i>	<i>Therapeutic</i>
LMWH	4 hours	4 hours
UFH*	1 hour	1 hour
*Seek anaesthetic advice for UFH dosages higher than 5000 units BD or TDS. Therapeutic UFH is via IV infusion # Perform APTT 3–4 hours after ceasing UFH infusion		

5 Methods of thromboprophylaxis

5.1 Hydration and mobilisation

Routinely advise pregnant and postnatal women about the risk of VTE in pregnancy and the importance of mobilisation and avoiding dehydration as universal VTE prevention strategies.

Table 11. Hydration and mobilisation

Aspect	Consideration
Fluid intake	<ul style="list-style-type: none"> Requirements vary according to environmental conditions, physical activity and individual metabolism³¹ Recommended average daily fluid intake (including plain water, milk and other drinks)³¹ <ul style="list-style-type: none"> For pregnant women is 2.3 L per day For breastfeeding women 2.6 L per day
Exercise	<ul style="list-style-type: none"> For women without complications, recommend activity in accordance with Australian Physical Activity Guidelines as part of a healthy lifestyle³² When recommending exercise, take into account, frequency, intensity, duration and mode of exercise as well as baseline fitness level and exercise experience³³ Deep tissue massage is not recommended in the presence of VTE or pharmacological thromboprophylaxis³⁴

5.2 Mechanical

In combination with other prophylactic modalities, graduated compression stockings (GCS), thromboembolic deterrent stockings (TED stockings) and intermittent pneumatic compression (IPC) or sequential compression devices (SCD) have been shown to reduce the incidence of DVT in high-risk non-pregnant patients.³⁵ There is limited evidence that specifically relates to pregnancy and postpartum.

Table 12. Contraindications to mechanical methods

Aspect	Consideration
Contraindications all mechanical methods³⁶	<ul style="list-style-type: none"> Severe peripheral arterial disease or ulcers Recent skin graft Peripheral arterial bypass grafting Severe leg oedema or pulmonary oedema from congestive heart failure Known allergy to material of manufacture Severe local problems on legs (e.g. gangrene, dermatitis, untreated infected wounds, fragile 'tissue paper' skin)
Contraindications stockings³⁶	<ul style="list-style-type: none"> Admission for stroke Severe leg deformity or morbid obesity preventing correct fit Severe peripheral neuropathy

5.2.1 Intermittent pneumatic compression or sequential compression devices

Table 13. Compression devices

Aspect	Consideration
Context	<ul style="list-style-type: none"> Improves blood flow and prevents venous stasis³⁷ In non-obstetric patients IPC device in combination with pharmacologic agents shown to be superior to IPC alone³⁷ Weak evidence from surgical patients suggests IPC may be more effective than GCS³⁸ May cover whole leg, calf only or foot only
Application³⁶	<ul style="list-style-type: none"> Measure and fit for each woman Position inflation pad over calf for maximum effectiveness Can be applied over bare legs, pyjama pants or socks Check skin integrity regularly
Recommendation	<ul style="list-style-type: none"> Recommend use after CS at least until the following day If risk factors for VTE and hospitalised or immobile (antenatal or postnatal), offer use of compression device Consider overnight use for inpatient postnatal women considered unsuitable for stockings (e.g. morbid obesity)

5.2.2 Lower extremity stockings

Table 14. Lower extremity stockings

Aspect	Consideration
Graduated compression stockings	<ul style="list-style-type: none"> • Primarily for ambulatory patients • Compression levels range from 15–60 mmHg <ul style="list-style-type: none"> ○ Above 20 mmHg generally considered prescription strength (usually those requiring increased compression for conditions such as venous insufficiency, lymphedema and varicose veins) ○ Greatest degree of compression at the ankle where the effect of gravity is greatest on the veins while standing³⁶ • Reduction in postpartum VTE from 4.3% to 0.9% reported when GCS used in conjunction with LMWH in high risk women³⁹ • Conflicting evidence about the role of GCS in reducing incidence of PTS after DVT^{12,40} • Limited evidence for duration of application postpartum⁴¹ <ul style="list-style-type: none"> ○ Most studies (primarily surgical patients) report use until discharge or full ambulation³⁵
TED stockings	<ul style="list-style-type: none"> • Primarily for non-ambulatory patients or immediately post-surgery to prevent pooling of the blood in the legs • Compression level <ul style="list-style-type: none"> ○ At or below 20 mmHg ○ Greatest degree of compression at the calf where blood tends to pool when in bed
Knee versus thigh length	<ul style="list-style-type: none"> • Insufficient quality evidence to determine whether knee or thigh length stockings differ in effectiveness for reducing incidence of DVT^{42,43} • Consider comfort, compliance and physical characteristics of the woman when recommending length
Application	<ul style="list-style-type: none"> • Measure and fit for each woman⁴⁴ <ul style="list-style-type: none"> ○ Refer to the manufacturer's instructions on measuring ○ Seek assistance from a health professional trained in garment sizing and application ○ Provide instruction for washing and reuse⁴⁴ • Compliance is essential—encourage⁴⁴: <ul style="list-style-type: none"> ○ Continuous wearing ○ Not to roll stocking down ○ To wear footwear to minimise risk of slipping ○ Correctly fitted knee length stockings finish 3 cm below the popliteal fossa • Check skin integrity regularly • Most frequently reported adverse effects are itching, erythema and rash
Recommendation	<ul style="list-style-type: none"> • Provide information about potential benefit and adverse effects of use • Recommend if receiving pharmacological thromboprophylaxis (antenatal or postnatal) • Consider for postnatal women until fully mobile • Discuss ongoing requirement on an individual basis according to risk assessment

5.3 Pharmacological

Table 15. Pharmacological prophylaxis

Aspect	Consideration
Context	<ul style="list-style-type: none"> Limited evidence upon which to base recommendations for thromboprophylaxis during pregnancy and the early postnatal period⁴⁵ Individualise according to assessment of risk factors and clinical circumstances Contradictory and varied evidence about creatine clearance levels and LMWH accumulation^{46,47} Seek expert advice as required
Animal origins of heparin sodium	<ul style="list-style-type: none"> Heparin sodium and other LMWH commonly used in pregnancy are porcine derived⁴⁸ If unacceptable for religious/cultural reasons, seek expert advice about the use of clinical alternatives that may be suitable for use in pregnancy Fondaparinux is a synthetic antithrombotic agent that <i>may be</i> suitable as a clinical alternative⁴⁹
Contraindications	<ul style="list-style-type: none"> Known hypersensitivity⁵⁰ History of or current HIT^{50,51} Creatinine clearance less than 15 mL/minute associated with significant platelet dysfunction—seek expert advice before use
Cautions	<ul style="list-style-type: none"> Renal impairment⁵¹ (creatinine clearance less than 30 mL/minute) <ul style="list-style-type: none"> Consider heparin sodium (UFH) in preference to LMWH⁵⁰ Hepatic impairment⁵⁰ Thrombocytopenia⁵⁰ (platelets less than $100 \times 10^9/L$ or trending down) <ul style="list-style-type: none"> May increase bleeding risk but does not protect against VTE⁵²
Risk factors for bleeding³⁶	<ul style="list-style-type: none"> Active antenatal or postpartum bleeding (requiring at least two units of blood or blood products to be transfused in 24 hours, or primary postpartum haemorrhage (PPH) greater than 1 L) Chronic, clinically significant and measurable bleeding over 48 hours Women at risk of major haemorrhage (e.g. placenta praevia) Acquired or inherited bleeding disorders (e.g. acute liver failure, Von Willebrand's disease) Recent central nervous system bleeding Intracranial or spinal lesion Abnormal blood coagulation Thrombocytopenia Severe platelet dysfunction (e.g. Bernard Soulier, Glanzmann's thrombasthenia) or antiplatelet drug use Active peptic ulcer or active ulcerative gastrointestinal disease Obstructive jaundice or cholestasis Recent major surgical procedure of high bleeding risk Concomitant use of medications that may affect the clotting process Neuraxial analgesia (epidural in labour ward) or anaesthesia (spinal or epidural for operative procedure) or diagnostic lumbar puncture

5.3.1 Low molecular weight heparin

Class of drug that includes dalteparin, enoxaparin and nadroparin (as well as others less commonly used in pregnancy). Low molecular weight heparin products are not clinically interchangeable.⁵³ Seek expert advice as required.

Table 16. Low molecular weight heparin

Aspect	Consideration
Fetus/newborn	<ul style="list-style-type: none"> • Does not cross placenta³ • No evidence of teratogenicity or increased risk of fetal bleeding⁵³ • Safe while breastfeeding²⁰
Safety profile	<ul style="list-style-type: none"> • A systematic review (n=2603 pregnancies) with thromboprophylaxis or adverse pregnancy outcome as the indication for LMWH (enoxaparin, dalteparin or nadroparin) reported⁵⁴: <ul style="list-style-type: none"> ○ No maternal deaths or HIT ○ VTE 0.84 % ○ Significant maternal bleeding 2% (11/52 antenatal bleeding, 24/52 primary obstetric cause at birth, 17/52 wound haematoma) ○ Thrombocytopenia 0.08% ○ Allergic skin reactions 1.84% (3/48 with enoxaparin) • Compared to UFH, LMWH associated with⁵⁵: <ul style="list-style-type: none"> ○ Fewer bleeding episodes ○ Lower risk of HIT ○ Lower risk of heparin induced osteoporosis
Monitoring	<ul style="list-style-type: none"> • Consider baseline platelet count, serum creatinine • Routine monitoring of anti-Xa levels not recommended²⁰ • Consider periodic platelet count as indicated
Recommendation	<ul style="list-style-type: none"> • LMWH is safe and effective for prevention of VTE in pregnancy⁵⁴ • Agent of choice for antenatal and postnatal thromboprophylaxis³ • Reduce dose if renal impairment⁵⁶ or consider UFH • Consider increased dose if antithrombin deficiency

5.3.2 Unfractionated heparin

Table 17. Unfractionated heparin

Agent	Consideration
Fetus/newborn	<ul style="list-style-type: none"> • Does not cross the placenta⁵⁵ • No evidence of teratogenicity⁵⁵ • Safe while breastfeeding²⁰
Safety profile	<ul style="list-style-type: none"> • Associated with increased bruising at the injection site³ • May be preferred²⁰: <ul style="list-style-type: none"> ○ If significant renal dysfunction²⁰ ○ When rapid reversal of anticoagulation may be required²⁰ ○ If high risk of VTE and neuraxial blockade recommendations for LMWH limit early commencement • Associated with higher risk of bleeding, HIT and heparin induced osteoporosis than LMWH
Monitoring	<ul style="list-style-type: none"> • Consider baseline platelet count and monitor for HIT
Recommendation	<ul style="list-style-type: none"> • Not routinely recommended as first line thromboprophylaxis in pregnancy • Consider switching from LMWH to UFH prior to onset of labour/planned birth

5.3.3 Other anticoagulants

Table 18. Other anticoagulants

Agent	Consideration
Warfarin	<ul style="list-style-type: none"> • Vitamin K antagonist that is teratogenic especially in the first trimester³ • Crosses placenta and may cause fetal haemorrhage • Seek specialist advice before use during pregnancy • For women with mechanical heart valves <ul style="list-style-type: none"> ○ May be indicated based on individual assessment of risk and benefit ○ Recommendation incorporates the woman's values and preferences⁵⁷ ○ Seek specialist advice • Safe while breastfeeding⁵⁸ • Consider postnatal only if prolonged thromboprophylaxis/treatment indicated²⁰
Fondaparinux	<ul style="list-style-type: none"> • Discuss with a team experienced in their use before commencement • Limit fondaparinux to women with severe allergic reactions to heparin who cannot receive danaparoid⁵⁹ • Withhold for 5 days prior to birth (due to long half-life)
Other direct thrombin and factor Xa inhibitors	<ul style="list-style-type: none"> • Includes: rivaroxaban, apixaban, edoxaban, dabigatran • Avoid use in pregnancy including while breastfeeding⁵⁹ <ul style="list-style-type: none"> ○ Limited information about use in pregnancy and while breastfeeding^{3,20} • Not recommended in conjunction with neuraxial blockade²⁸
Aspirin	<ul style="list-style-type: none"> • No controlled trials on the use of aspirin for thromboprophylaxis in pregnancy • The American College of Physicians recommend against the use of aspirin as sole agent for VTE prophylaxis in any pregnancy⁵⁹ • No adverse fetal or maternal outcomes were reported in a meta-analysis of large randomised controlled trials of low-dose aspirin for the prevention of pre-eclampsia in pregnancy⁶⁰ • Insufficient evidence to recommend routine use of aspirin for thromboprophylaxis in the antenatal or postnatal period

5.4 Dosage

There is limited data about the optimal dosage regimen and a variety of regimens are used. Use clinical judgement and consult with an expert as required. Recommended dosage based on actual (current or last recorded) weight in kilograms, including current postnatal weight.¹¹

5.4.1 Standard prophylactic dosage

Twice daily dosing may be more effective than once daily dosing in obese women.⁵⁶

Table 19. Standard prophylactic dosage

Current weight (kg)	Administer via subcutaneous route		
	Dalteparin ^{11,20} (LMWH)	Enoxaparin ^{11,20} (LMWH)	Heparin Sodium (UFH) ^{3,51}
Less than 50	• 2,500 units daily	• 20 mg daily	• Consider reduced dose
50–90	• 5,000 units daily	• 40 mg daily	• 5,000 units twice per day
91–130	• 7,500 units daily	• 60 mg daily*	• 7,500 units twice per day
131–170	• 10,000 units daily	• 80 mg daily*	
171 or more	• 75 units/kg/day	• 0.5 mg/kg/day*	

* may be administered in divided dose

5.4.2 High prophylactic dosage

Consider for women with multiple significant risk factors (e.g. previous DVT while on standard prophylactic dose, antiphospholipid syndrome and history of DVT and in women at increased risk of arterial thrombosis (e.g. homocysteinaemia)). High prophylactic dosage is usually between the prophylactic and the therapeutic dose. Seek advice from an experienced team.

Table 20. High prophylactic dosage

Current weight (kg)	Administer via subcutaneous route		
	Dalteparin ^{11,20} (LMWH)	Enoxaparin ^{11,20} (LMWH)	Heparin Sodium (UFH) ³
Less than 50*	<ul style="list-style-type: none"> 2,500 units twice per day 	<ul style="list-style-type: none"> 40 mg daily 	<ul style="list-style-type: none"> Consider reduced dose (5,000 units twice per day)
50–130	<ul style="list-style-type: none"> 5,000 units twice per day 	<ul style="list-style-type: none"> 80 mg daily 	<ul style="list-style-type: none"> 7,500 units twice per day
131 or more*	<ul style="list-style-type: none"> 7,500 units twice per day 	<ul style="list-style-type: none"> 60 mg twice per day* 	<ul style="list-style-type: none"> 7,500 units three times per day

*Suggested regimen is not evidence based. If body weight less than 50 kg or 130 kg or more, seek expert advice

5.4.3 Therapeutic anticoagulation

If weight greater than 100 kg, liaise with an experienced physician regarding dose. If the woman has antithrombin deficiency, consider increased dose and monitoring of anti-Xa levels.

Table 21. Therapeutic anticoagulation

Medicine	Dosage
Dalteparin	<ul style="list-style-type: none"> 100 units/kg twice per day⁶¹
Enoxaparin	<ul style="list-style-type: none"> Antenatal: <ul style="list-style-type: none"> 1 mg/kg subcutaneous twice per day⁶¹ Postnatal: <ul style="list-style-type: none"> 1.5 mg/kg subcutaneous daily⁶¹
Heparin sodium (UFH)	<ul style="list-style-type: none"> Loading Dose⁶¹: <ul style="list-style-type: none"> 80 units/kg IV stat Infusion⁶¹: <ul style="list-style-type: none"> 18 units/kg/hour IV infusion Monitor APTT⁶¹ as per Queensland Health form: Heparin intravenous infusion order and administration—adult¹⁵
Warfarin	<ul style="list-style-type: none"> Variable oral dose <ul style="list-style-type: none"> Aim for INR 2–3 unless specified otherwise Refer to Queensland Health's guidelines for anticoagulation using warfarin^{62,63}

6 Discharge

Table 22. Discharge

Aspect	Considerations
VTE risk	<ul style="list-style-type: none"> • Offer postnatal women and their families verbal and written information on <ul style="list-style-type: none"> ○ Signs and symptoms of VTE ○ How to reduce the risk of VTE ○ Risk associated with prolonged immobility (e.g. long-distance travel, cultural practices associated with 'lying in'⁶⁴)
Prophylaxis continuation	<ul style="list-style-type: none"> • If prophylaxis to continue beyond discharge, advise about: <ul style="list-style-type: none"> ○ Importance of compliance with VTE prophylaxis ○ Correct use/application and duration of recommended treatment including onset of action, monitoring requirements and side effects of recommended treatment ○ The importance of seeking help and who to contact if concerned ○ Provide prescriptions for pharmacological thromboprophylaxis for the entire postnatal course⁵
Subsequent pregnancy	<ul style="list-style-type: none"> • Discuss future anti-coagulation needs for subsequent pregnancies • Advise pre-conception consultation with health care provider
Ongoing care	<ul style="list-style-type: none"> • If required, recommend pain relief to facilitate mobility • Refer as required to medical physician or other specialist for ongoing management • Communicate to GP advice for ongoing thromboprophylaxis (e.g. type, dose, duration, recommendation for contraceptive choice, plan for next pregnancy)

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Appendix A: Odds ratios for VTE risk factors

Risk Factor	AOR (*OR)	95%CI	Comment
Previous VTE	24.8	17.1–36	n=603
Age 35 years or more	1.3	1.0–1.7	pn=256
	1.4	1.0–2.0	n=143 an PE
	2.65	1.09–6.45	n=129
BMI 30 mg/kg ² or more	5.3	2.1–13.5	
	4.4	3.4–5.7	
	1.7	1.2–2.4	pn=256
BMI 25 mg/kg ² or more	1.8	1.3–2.4	an=268
	2.4	1.7–3.3	pn=291
	1.7	1.2–2.4	pn=256
Parity 1	4.03	1.6–9.84	n=143 an PE
Parity 2	1.5	1.1–1.9	n=603
Parity 3	2.4	1.8–3.1	n=603
Smoking	2.1	1.3–3.4	an=268
	3.4	2.0–5.5	pn=291
Smoking 10–30 per day	1.4	1.1–1.9	n=603
	2.5	1.3–4.7	n=90
Current smoker	2.7	1.5–4.9	n=129
	6.7	4.4–10.1	
Sickle cell	2.5	1.5–4.1	DVT
	1.7	0.9–3.1	PE
Heart disease	7.1	6.2–8.3	
	5.4	2.6–11.3	pn=256
Systemic lupus erythematosus (SLE)	8.7	5.8–13	
Anaemia	2.6	2.2–2.9	
Varicose veins	2.4	1.04–5.4	
Immobility	7.7	3.2–19	an
	10.8	4.0–28.8	pn
Preeclampsia	2.9	2.1–3.9	
	3.1	1.8–5.3	
Preeclampsia and fetal growth restriction	5.8	2.1–16	
Hyperemesis	2.5	2–3.2	
Assisted reproductive technology	4.3	2.0–9.4	an
Twins	2.6	1.1–6.2	an
Multiple pregnancy	4.2	1.8–9.7	n=603
Preterm delivery less than 36 weeks	2.4	1.6–3.5	an=109
Antepartum haemorrhage	2.3	1.8–2.8	pn=256
Caesarean section (emergency)	2.7	1.8–4.1	
Caesarean section (elective)	*2.30	1.72 to 3.07	
Caesarean section (any)	3.6	3.0–4.3	pn=256
Postpartum haemorrhage 1000 mL or more	4.1	2.3–7.3	
Postpartum haemorrhage and surgery	12	3.9–36.9	
Obstetric haemorrhage	9	1.1–71	
Postpartum infection	4.1	2.9–5.7	
Postpartum infection and caesarean section	6.2	2.4–16.2	
Transfusion	7.6	6.2–9.4	

AOR: adjusted odds ratio; an=antenatal; pn=postnatal; n=number of cases in case-control study; OR: odds ratio

Source: Royal College of Obstetricians and Gynaecologists. Reducing the risk of thrombosis and embolism during pregnancy and the puerperium. Green-top Guideline No.37a. 2009.

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