

A California Toolkit to Transform Maternity Care

# Improving Health Care Response to Maternal Venous Thromboembolism: A California Quality Improvement Toolkit

*February 2018*

**THIS COLLABORATIVE PROJECT WAS DEVELOPED BY:**

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THE MATERNAL VENOUS THROMBOEMBOLISM TASK FORCE  
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CENTER FOR FAMILY HEALTH  
CALIFORNIA DEPARTMENT OF PUBLIC HEALTH

**CMQCC**  
California Maternal  
Quality Care Collaborative



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# Improving Health Care Response to Maternal VTE

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## EXECUTIVE SUMMARY

VTE is a leading cause of severe maternal morbidity and mortality. PE accounts for approximately 15% of maternal deaths in developed countries worldwide according to the World Health Organization, while accounting for 9.3% of maternal deaths in the United States. Findings from the 2002-2007 California Pregnancy-Associated Mortality Review show that VTE accounted for 9% (n=29) of all maternal deaths, with an overall pregnancy related mortality risk of 0.9 maternal deaths per 100,000 live births. Nearly all these deaths (97%) had at least some chance of preventability and more than half of them (52%) had a good-to-strong chance.

The California Toolkit to Improve Maternal Health Care Response to Maternal Venous Thromboembolism (VTE) emphasizes risk assessment throughout pregnancy to identify women who may benefit from pharmacological thromboprophylaxis. In writing the VTE Toolkit, the Task Force members have worked to maintain fundamental consistency with the National Partnership for Maternal Safety (NPMS) VTE bundle and the Safe Motherhood Initiative/American Congress of Obstetricians and Gynecologists (ACOG) District II to avoid creating disparate expert consensus and guidance. The antepartum outpatient and postpartum extended duration VTE prophylaxis strategies as presented here are not controversial and represent a consensus summary of ACOG and the American College of Chest Physicians (ACCP) guidelines.

In clinical situations where recommendations from national societies such as ACOG are non-specific, the VTE Toolkit builds upon management approaches from the National Partnership for Maternal Safety (NPMS) VTE bundle and ACOG District II's Safe Motherhood Initiative. The VTE Toolkit advocates for user-friendly guidelines that are simple enough to make real-time decisions, yet result in tailored prophylaxis recommendations appropriate for individual patient risk profiles. Each facility can individualize the specific components of this toolkit to fit its particular culture and available resources.

These VTE protocols are based upon the "three bucket model," a nationally recognized framework coined by Gregory Maynard, MD, for stratifying risk into three levels (Low, Medium, High), with appropriate thromboprophylaxis approaches for each VTE risk level. Given the lack of data validating effectiveness of any risk assessment tool, our intent is to support risk assessment with a focus on facilitating protocol adherence through simplification so that is why this model was selected.

**Teaching Slide Set:** The Toolkit includes a comprehensive slide set that outlines its key components. Providers, clinical staff, educators, hospitals and healthcare organizations can use the Toolkit and slide set for guidance in the development and implementation of strategies to improve early recognition and response to venous thromboembolism in pregnancy and postpartum.

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## INTRODUCTION

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Venous thromboembolism (VTE) includes two potentially life-threatening conditions: (i) deep vein thrombosis (DVT) which occurs when a blood clot forms in a deep vein, and (ii) pulmonary embolism (PE) which occurs when a blood clot in a vein breaks off and travels to the lungs. VTE complicates approximately 1 to 4 per thousand pregnancies.<sup>1-5</sup> The reported variance in estimates is primarily based on the population investigated, method of case identification, and duration of postpartum follow up. Eighty percent of VTE presents as DVT and 20% as PE; these events are evenly distributed between antepartum and postpartum periods.<sup>2</sup> During the antepartum period, risk is highest in the first and third trimesters. The clear majority of postpartum VTE occurs during the first 6 weeks after delivery. The relative risk of VTE events is highest during this period because the length of the postpartum period (6 weeks) is shorter than the antepartum period.<sup>6-8</sup>

*“The ultimate goal of this Toolkit is to decrease severe maternal morbidity and mortality associated with pregnancy related venous thromboembolic disease.”*

All three components of Virchow’s triad (hypercoagulability, stasis, and endothelial vascular damage) are exacerbated by the physiologic and hormonal changes associated with pregnancy resulting in a greater than 5 fold increased risk of VTE during pregnancy.<sup>9</sup> Stasis of blood flow occurs due to mechanical compression of pelvic vessels by the gravid uterus coupled with hormone- mediated venous dilation.<sup>10</sup> Additionally, hormonal changes result in a marked increase in multiple procoagulants and a decrease in fibrinolytic activity. The resultant prothrombotic state is seen as early as the first trimester.<sup>1,11,12</sup> Vascular injury and mechanical pressure/damage to the blood vessels may occur with fetal descent into the pelvis, which can be exacerbated by operative vaginal delivery and/or by cesarean delivery, the latter of which increases the risk of catastrophic pulmonary embolus.<sup>5,13</sup>

VTE is a leading cause of severe maternal morbidity and mortality. PE accounts for approximately 15% of maternal deaths in developed countries worldwide according to the World Health Organization, while accounting for 9.3% of maternal deaths in the United States.<sup>14,15</sup> Findings from the 2002-2007 CA-PAMR data show that VTE accounted for 9% (n=29) of all maternal deaths, with an overall pregnancy related mortality risk of 0.9 maternal deaths per 100,000 live births. Nearly all these deaths (97%) had at least some chance of preventability and more than half of them (52%) had a good-to-strong chance.<sup>16</sup> Non-fatal complications of PE include chronic thromboembolic pulmonary hypertension and/or cardiac compromise.<sup>17</sup> Most DVT during pregnancy is proximal in location, i.e. popliteal, deep femoral or iliac that often manifests as a large thrombus.<sup>18</sup> These characteristics are associated with an increased

risk of late term sequelae such as chronic venous insufficiency and stasis ulcers, i.e. post thrombotic syndrome.<sup>19,20</sup> Additionally, VTE events require prolonged anticoagulation and are a major risk factor for future events.

A significant proportion of pregnant women who suffer obstetric VTE and its consequences have risk factors. Preexisting risk factors such as personal or family history of VTE and thrombophilia may be readily identified at the onset of pregnancy/prenatal care. There are additional risk factors that may become more relevant during pregnancy or the postpartum period, including but not limited to prolonged bed rest, cesarean delivery, and other medical, surgical, and obstetric factors. VTE is highly amenable to prevention through mechanical and/or pharmacological thromboprophylaxis.<sup>21,22</sup> Strategies for prevention of VTE have been extensively studied and validated in non-pregnant populations.<sup>23-25</sup>

Similar thromboprophylaxis strategies can be implemented in pregnancy to reduce the risk of VTE. However, the lack of high quality data demonstrating the effectiveness of specific thromboprophylaxis approaches in the obstetric population has led to disparate national guidelines. The VTE risk assessment and thromboprophylaxis recommendations in this Toolkit are based on a critical review of guidelines from major professional organizations and societies in conjunction with consensus expert opinion where guidelines are lacking. Guidelines reviewed include: The National Partnership for Maternal Safety (NPMS), the American College of Obstetricians and Gynecologists (ACOG), the Safe Motherhood Initiative (SMI), the American College of Chest Physicians (ACCP), the Royal College of Obstetricians and Gynaecologists (RCOG), and the American Society of Regional Anesthesia and Pain Medicine (ASRA).

The proposed risk assessment and prophylaxis strategies of this Toolkit maintain fundamental consistency with major published guidelines while utilizing California specific data for guidance.<sup>26</sup> In clinical situations where recommendations from societies such as ACOG are non-specific, this bundle provides more detailed guidance by utilizing management approaches from the NPMS VTE bundle and ACOG District II's Safe Motherhood Initiative. Given that less complex protocols are more readily implementable and likely to be adhered to, the VTE Toolkit includes user-friendly guidelines that are simple enough to make real-time decisions yet result in tailored prophylaxis recommendations appropriate for individual patient risk profiles.<sup>27</sup>

The CMQCC Maternal VTE Task Force protocols are based upon the “3 bucket model,” coined by Gregory Maynard, MD, and utilized in guidelines from the American College of Chest Physicians and the Agency for Healthcare Research and Quality, among others.<sup>25</sup> This model stratifies VTE risk into three levels (Low, Medium, High), with appropriate thromboprophylaxis approaches for each level. In general, stronger pharmacological or combined mechanical and pharmacological prophylaxis is recommended for patients with greater VTE risk.<sup>25</sup>

The ultimate goal of this Toolkit is to decrease severe maternal morbidity and mortality associated with pregnancy related venous thromboembolic disease.

The major components of the California Toolkit to Improve Health Care Response to Maternal Venous Thromboembolism (VTE) include:

- 1) Risk assessment
- 2) Suggested prophylaxis and treatment regimens
- 3) Anesthesia and Analgesia considerations
- 4) Patient, provider and nursing education materials
- 5) Implementation strategies

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## ANTICOAGULATION REGIMENS

Anticoagulation in pregnancy is complex. Considerations in pregnancy include the risk of teratogenicity to the developing fetus, altered pharmacokinetics of drugs requiring dose adjustments, and the management of anticoagulation around the time of delivery and neuraxial anesthesia. Neuraxial anesthesia pertains to local anesthetics placed around the nerves of the central nervous system (spinal cord), such as spinal anesthesia (also called subarachnoid anesthesia), and epidural anesthesia. Commonly used anticoagulants outside of pregnancy include heparins and warfarin. More recently, direct oral anticoagulants (e.g., rivaroxaban, apixaban, dabigatran) are considered preferred agents in most circumstances. However, warfarin and direct oral anticoagulants have either limited or unfavorable data that may preclude their general use during pregnancy and/or the postpartum period.

### Heparins

Heparins are considered safe in pregnancy as they do not cross the placenta, are not teratogenic and do not cause anticoagulation in the fetus. The two commonly used heparins are listed in Table 1. There is consensus among multiple obstetric guidelines that low molecular weight heparin (LMWH) is the preferred pharmacologic agent over unfractionated heparin (UFH) for outpatient antepartum thromboprophylaxis for women at low risk of requiring emergent delivery anesthesia.<sup>28-31</sup>

Despite a paucity of high quality comparative data supporting the preference for LMWH, Table 1 summarizes the relative properties favoring LMWH presented in obstetric guidelines.<sup>28,29,31-42</sup>

**Table 1: Comparison of Risks and Benefits of Low Molecular Weight Heparin (LMWH) vs. Unfractionated Heparin (UFH) in Pregnancy**

	<b>Advantages/ Disadvantages</b>	<b>LMWH</b> (Low Molecular Weight Heparin)	<b>UFH</b> (Unfractionated Heparin)
1	Half life	Longer half life	Shorter half life
2	Crosses the placenta	Does not cross placenta	Does not cross placenta
3	Use during pregnancy	Preferred anticoagulant for most pregnant women	Low-dose UFH least likely to preclude neuraxial anesthesia
4	Clearance	Cleared 100% by the kidneys	Mainly cleared by reticuloendothelial system. Only 10% by the kidneys
5	Renal failure patients	Contraindicated in renal failure patients if creatinine clearance < 30 mL/min	Preferred drug of choice in renal failure patients with creatinine clearance of < 30mL/min
6	Safety of use	Indirect evidence demonstrates LMWH is associated with decreased: mortality, thrombotic complications, VTE recurrence, major bleeding. And superior thrombus size reduction	Short half-life and near complete reversal with protamine make it the preferred anticoagulant if it needs to be discontinued due to bleeding or to perform a procedure
7	HIT/HITT (Heparin induced thrombocytopenia)/(HIT and thrombosis)	Lower risk	Higher risk
8	Reversibility	Unpredictable response to protamine sulfate	Ability to reverse with protamine sulfate
9	Osteoporosis	Lower risk	Higher risk
10	Use of regional anesthesia in labor	Due to longer half-life, cannot be used for neuraxial anesthesia if most recent prophylactic dose was < 12 hours or most recent therapeutic dose was < 24 hours	Due to shorter half-life, neuraxial anesthesia can potentially be considered for patients receiving prophylactic doses of UFH (max 5,000 units bid) without a minimum time window
11	Cost of treatment	Higher cost	Lower cost
12	Frequency of dosing	Once or twice daily	Two or three times a day
13	Patient compliance and tolerance	Higher compliance and better tolerance	Lower compliance and less tolerance

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Table 2: Anticoagulation Regimen Definitions (ACOG)

Anticoagulation Regimen	Definitions
Prophylactic LMWH*	Enoxaparin, 40 mg SC once daily Dalteparin, 5,000 units SC once daily Tinzaparin, 4,5000 units SC once daily
Therapeutic LMWH <sup>†</sup>	Enoxaparin, 1mg/kg every 12 hours Dalteparin, 200 units/kg once daily Tinzaparin, 175 units/kg once daily
Minidose prophylactic UFH	UFH, 5,000 units SC every 12 hours
Prophylactic UFH	UFH, 5,000-10,000 units SC every 12 hours UFH, 5,000-7,500 units SC every 12 hours in first trimester UFH, 7,500-10,000 units SC every 12 hours in the second trimester UFH, 10,000 units SC every 12 hours in the third trimester, unless the aPTT is elevated
Therapeutic UFH <sup>†</sup>	UFH, 10,000 units or more SC every 12 hours in doses adjusted to target aPTT in the therapeutic range (1.5-2.5) 6 hours after the injection
Postpartum Anticoagulation	Prophylactic LMWH/UFH for 4-6 weeks or vitamin K antagonists for 4-6 weeks with a target INR of 2.0-3.0, with initial UFH or LMWH therapy overlap until the INR is 2.0 or more for 2 days
Surveillance	Clinical vigilance and appropriate objective investigation of women with symptoms suspicious of deep vein thrombosis or pulmonary embolism

Abbreviations: aPTT, activated partial thromboplastin time; INR, international normalized ration; LMWH, low molecular weight heparin; SC, subcutaneously; UFH, unfractionated heparin.

\*Although at extremes of body weight, modification of dose may be required.

<sup>†</sup>Also referred to as weight adjusted, full treatment dose.

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## Heparin dosing regimens and nomenclature

Heparin dosing regimens are presented in Table 2. Decisions as to dose and type of heparin are based on balancing the risk of thromboembolism against the risk of complications associated with heparin use. Heparin dosing nomenclature may be misleading given that different descriptors are associated with the same dosing regimen. For example, therapeutic dosing may be referred to as weight adjusted or full treatment dose. “Prophylactic,” “mini dose,” and “low dose” UFH all refer to UFH 5000 units subcutaneous every 12 hours. Furthermore, ACOG utilizes trimester-dependent UFH “prophylaxis,” with doses increasing up to 10,000 units subcutaneous every 12 hours as pregnancy progresses.

ACCP regimens include use of intermediate dose LMWH (e.g. enoxaparin), which is represented by a weight based dose of 0.75 mg/kg subcutaneously divided into twice daily dose or fixed dose enoxaparin 40 mg subcutaneously every 12 hours, while other guidelines consider enoxaparin 40 mg subcutaneous every 12 hours “prophylactic dosing for patients with BMI > 40 kg/m<sup>2</sup>. The CMQCC Maternal VTE Task Force encourages that a specific medication, dose, and route be specified whenever possible to minimize clinical misunderstanding.

*In this document, unless otherwise specified, prophylactic LMWH dosing is defined as fixed dose enoxaparin 40 mg subcutaneously every 24 hours and therapeutic LMWH as enoxaparin 1 mg/kg subcutaneously every 12 hours. Low-dose UFH is defined as UFH 5000 units subcutaneously every 12 hours.*

**Clinical situations favoring UFH over LMWH:** LMWH is primarily cleared by renal excretion as opposed to UFH, and therefore is relatively contraindicated in patients with significant renal impairment (GFR < 30 ml/min). In renal failure, UFH is the preferred anticoagulant in pregnancy. Additional clinical situations in which UFH may be favored over LMWH may relate to the need for rapid reversal and/or regional anesthesia concerns.

**Anti-Xa – levels:** Anti-Xa level testing is available to monitor activity of LMWH agents. While aPTT testing is helpful in determining UFH dosing, it cannot be used to evaluate LMWH activity. LMWH acts by inhibition of activated factor X (Xa) in the coagulation cascade. Anti-Xa assay is designed to measure the inactivation of coagulation factor Xa with heparin therapy. Routine Anti-Xa monitoring is not mandated by current authoritative guidelines due to cost, inconvenience, and lack of high quality data.<sup>28,29</sup> Achievement of specific Anti-Xa level for prophylaxis has not been validated to be associated with superior efficacy. Anti-Xa monitoring may be helpful at extremes of body weight (< 50 Kg or > 90 Kg), or with renal impairment, to mitigate the risk of adverse events.<sup>28,43-45</sup> Therapeutic Anti-Xa levels have not been validated in pregnancy; however anti-Xa values of 0.6-1.0 IU/mL 4- 6 hours after administration are considered therapeutic and may prove useful during acute treatment of VTE.

**Heparin Induced Thrombocytopenia (HIT):** HIT is a rare life-threatening complication seen in patients exposed to heparins with an estimated incidence less than 1/1000 in heparin naïve women during pregnancy.<sup>28,36</sup> HIT occurs due to production of an autoantibody against the endogenous platelet factor 4 heparin complex that paradoxically causes thrombosis. HIT typically manifests within 5 to 10 days of initiation of heparin in heparin naïve patients; however, in patients who had previously received any type of heparin within the preceding 100 days and are *resuming either* UFH or LMWH, HIT may occur in up to 0.8% of patients and manifest within 24 hours.<sup>46 47</sup> The risk of HIT is 14-fold higher with use of UFH compared to LMWH.<sup>48</sup> and therefore guidelines do not mandate routine platelet count monitoring for detection of HIT in pregnant patients exclusively receiving prophylactic LMWH.<sup>31,49</sup>

*Based on this information, the CMQCC Maternal VTE Task Force makes the following recommendations with regards to HIT: For patients who have received either UFH or LMWH heparin in the preceding 100 days, a baseline platelet count repeated within 24 hours of resuming therapy should be considered.<sup>31,49-51</sup> For heparin naïve patients starting UFH and anticipated to continue heparin > 1 week, it is reasonable to check a baseline CBC followed by a repeat CBC 7-10 days after initiation of therapy.*

HIT is diagnosed by the presence of one or more of the following: 50% decrease in platelet count after the start of heparin, thrombosis, skin necrosis at heparin injection site, and presence of heparin-dependent platelet-activating IgG antibodies.<sup>49</sup> If HIT is suspected, consultation with hematology must be obtained.

For patients receiving antepartum pharmacologic VTE prophylaxis along with low dose aspirin for the prevention of preeclampsia, the small theoretical risks of aspirin use past 36 weeks in combination with heparin prophylaxis justify discontinuation of aspirin at that time given unclear benefits of continuing the medication.<sup>52,53</sup>

**Warfarin:** Warfarin is a vitamin K antagonist that crosses the placenta, is teratogenic in early pregnancy resulting in “warfarin embryopathy” and causes anticoagulation in the fetus that may lead to hemorrhagic complications.<sup>54,55</sup> Warfarin embryopathy is dose related and has been described with higher doses (> 5 mg qd); however, fetal complications have been reported at doses less than 5 mg a day.<sup>56</sup> Warfarin use in pregnancy is primarily limited to select cases of mechanical heart valves only in consultation with cardiology and maternal fetal medicine and in the postpartum period. Warfarin is considered compatible with breastfeeding and therefore is a valid option for anticoagulation in the postpartum period.<sup>28</sup>

**Newer Anticoagulants:** Oral direct thrombin inhibitors (Dabigatran), oral direct factor Xa inhibitors (rivaroxaban, apixaban, edoxaban) and fondaparinux which is a heparinoid are NOT recommended for pregnant or breastfeeding mothers as they most likely cross the placenta and their effects on human fetal development are unknown.<sup>57</sup> Patients should be advised to discontinue oral anticoagulants either prior to the anticipated

pregnancy or at the time pregnancy is diagnosed. These should only be used in exceptional circumstances when no other anticoagulant option is available.<sup>28</sup>

## THROMBOPHILIAS

Inherited and acquired thrombophilias increase the risk of VTE during pregnancy and the postpartum period. Table 3 lists the commonly encountered thrombophilias (see Table 3) include the Factor V Leiden mutation, the prothrombin gene mutation, antithrombin III deficiency (< 60% of normal), Protein C deficiency (< 60% of normal), and Protein S deficiency (levels < 30% and < 24% of normal respectively during the second and third trimester). Factor V Leiden heterozygosity is the most common form of thrombophilia and confers 5- to 10-fold increased risk for VTE (5-12 per 1,000 deliveries). Risk is higher with a family or personal history of VTE. The prothrombin gene mutation is the second most common thrombophilia encountered in pregnancy and is associated with risk similar to factor V Leiden mutation. Patients who are homozygous for Factor V Leiden or the prothrombin gene mutation or are compound heterozygotes (carriers of both conditions) are at particularly high risk for VTE, with up to 10% of affected pregnancies experiencing acute VTE.

Protein C and S deficiency may be associated with a 2-7% risk of VTE in pregnancy if a personal or family history of VTE is present. While antithrombin III deficiency is a rare condition, it is associated with a very high risk for VTE, particularly in the presence of family or personal history of VTE. The CMQCC Maternal VTE Task Force recommends that all pregnant women with thrombophilias receive an individualized plan for anticoagulation during pregnancy and postpartum based on their profile.<sup>58</sup>

Antiphospholipid syndrome (APS) is an autoimmune disorder characterized by the presence of both (i) antiphospholipid antibody laboratory criteria and (ii) clinical criteria. Laboratory criteria include the presence of lupus anticoagulant or medium to high titer anticardiolipin antibodies IgG and/or IgM or anti Beta-2 glycoprotein IgG and/or IgM documentation on two or more occasions at least 12 weeks apart. Clinical criteria include vascular thrombosis or an adverse obstetric outcome (one intrauterine fetal demise > 10 weeks or three or more < 10 weeks or one premature birth < 34 weeks due to preeclampsia with severe features/eclampsia or placental insufficiency). Because of the risk of thrombosis, APS is considered an acquired form of thrombophilia that requires thromboprophylaxis based on the type of clinical criteria, i.e. vascular thrombosis vs. adverse pregnancy outcome.<sup>59</sup>

All pregnant women with thrombophilias should receive an individualized plan for anticoagulation during pregnancy and postpartum period based on their risk profile.<sup>58</sup>

Table 3: Thrombophilias

Low Risk Thrombophilia	High Risk Thrombophilia
<ul style="list-style-type: none"> <li><input type="checkbox"/> Factor V Leiden mutation (heterozygous)</li> <li><input type="checkbox"/> Prothrombin gene mutation (heterozygous)</li> <li><input type="checkbox"/> Protein S deficiency</li> <li><input type="checkbox"/> Protein C deficiency</li> </ul>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Factor V Leiden mutation (homozygous)</li> <li><input type="checkbox"/> Prothrombin gene mutation (homozygous)</li> <li><input type="checkbox"/> Compound heterozygote for Factor V and Prothrombin gene mutation</li> <li><input type="checkbox"/> Antithrombin III deficiency</li> <li><input type="checkbox"/> Antiphospholipid syndrome APS</li> </ul>

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## VENOUS THROMBOEMBOLISM (VTE) RISK ASSESSMENT

Standardized VTE risk assessment should occur throughout pregnancy, including these four important time points:

1. First prenatal visit / Outpatient prenatal care
2. Antepartum hospitalization (non-delivery)
3. Delivery hospitalization including cesarean and vaginal birth
4. Post-discharge extended duration anticoagulation

Deciding which obstetric patients should receive VTE prophylaxis (and whether pharmacologic or mechanical prophylaxis should be used if prophylaxis is indicated) is a complex clinical decision. Optimal clinical management will take a patient's individual VTE risk into consideration while weighing risks and benefits of different prophylaxis regimens. Guidelines from major societies such as the American College of Obstetrics and Gynecology, the Royal College of Obstetricians and Gynaecologists, and the American College of Chest Physicians make varying recommendations for prophylaxis and view VTE risk factors differently. To organize an approach to maternal VTE prophylaxis, pregnancy can be divided into the four time points listed above. Because of differential risk, different strategies for prophylaxis are required at each of the time points. To further simplify prophylaxis recommendations, *The CMQCC Maternal VTE Task Force stratifies patients based on their risk factors into three color-coded risk levels: **Low Risk (green)**, **Medium Risk (yellow)**, and **High Risk (red)**. With increasing VTE risk, more aggressive prophylaxis is warranted. This risk-factor-based approach to VTE prophylaxis is supported by the CMQCC Maternal VTE Task Force as well as the National Partnership for Maternal Safety (NPMS) VTE bundle.*

### First Prenatal Visit / Outpatient Prenatal Care

The relatively small number of patients who require outpatient pharmacologic prophylaxis during prenatal care can be identified based on existing risk factor guidelines from the ACCP and ACOG.<sup>58,60,61</sup> These risk factors include prior VTE events and thrombophilias (See Table 4 and Algorithm 1).

A significant proportion of pregnant women who experience maternal VTE and its consequences have preexisting VTE risk factors.<sup>21</sup> These risk factors primarily include personal or family history of VTE and/or the presence of thrombophilia. Thrombophilia is encountered in 20-50% of women who present with VTE during pregnancy.<sup>60</sup>

Table 4: First Prenatal Visit – Antepartum Outpatient VTE Prophylaxis

Clinical History	Risk Level	Management
<input type="checkbox"/> Low risk thrombophilia (isolated) <input type="checkbox"/> Low risk thrombophilia with family history of VTE <input type="checkbox"/> Prior <i>provoked</i> VTE *	LOW	No treatment
<input type="checkbox"/> Prior VTE idiopathic <input type="checkbox"/> Prior VTE with pregnancy or use of estrogen containing oral contraceptives <input type="checkbox"/> Prior VTE with low risk thrombophilia <input type="checkbox"/> Family history of VTE with high risk thrombophilia <input type="checkbox"/> High risk thrombophilia or APS	MEDIUM	Prophylactic dose LMWH or UFH
<input type="checkbox"/> Current VTE or other conditions requiring therapeutic dose of anticoagulation <input type="checkbox"/> Multiple prior VTE episodes <input type="checkbox"/> Prior VTE with high-risk thrombophilia <input type="checkbox"/> Prior VTE with APS	HIGH	Therapeutic dose LMWH or UFH <i>Recommend co-management with maternal-fetal medicine and / or hematology specialist</i>

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## DEFINITIONS

**Antiphospholipid syndrome (APS);** this diagnosis requires at least one clinical and one laboratory criteria are met

**Family History of VTE:** VTE occurring in a first-degree relative prior to age 50

**High risk thrombophilia:** Antithrombin III deficiency, Factor V Leiden or Prothrombin gene mutation homozygosity or compound heterozygosity

**Low risk thrombophilia:** Factor V Leiden or Prothrombin gene mutation heterozygosity, Protein C or S deficiency

**Mechanical prophylaxis:** Knee-length Sequential Compression Device (SCD)

**Prophylactic dose:** LMWH (Enoxaparin fixed dose 40 mg subcutaneous once a day) or UFH dosing trimester dependent.<sup>58</sup>

**Provoked VTE:** VTE associated with a temporary risk factor such as: Major/orthopedic surgery, indwelling catheter, or prolonged immobilization

**Therapeutic dose:** LMWH (Enoxaparin 1 mg/kg subcutaneous every 12 hours): Anti-factor Xa 0.6-1.0 units/mL 4-6 hours after injection with acute VTE or UFH 10,000 units subcutaneously or more every 12 hours: aPTT (1.5-2.5) 6 hours after injection.

**Note:** Dose adjustment may be considered with extremes of body weight (< 50 kg or > 90 kg). Additional detail is on page 16 in the Toolkit. Consultation and ongoing collaboration with Anesthesia is strongly recommended to individualize the choice and dose of pharmacological prophylaxis. If appropriate, low dose UFH 5000 units every 12 hours may facilitate neuraxial anesthesia.

**Management:** Consensus exists among multiple obstetric guidelines that, in general, low molecular weight heparin (LMWH) is the preferred pharmacologic agent over unfractionated heparin (UFH) for outpatient antepartum thromboprophylaxis for women at low risk of requiring emergent delivery anesthesia.<sup>28-31</sup> For women who require prophylactic or therapeutic anticoagulation during pregnancy, LMWH should be initiated as soon as intrauterine pregnancy is established, if there is no vaginal bleeding. For women requiring *therapeutic anticoagulation* during pregnancy we recommend pregnancy co-management with hematology and or maternal-fetal medicine.

**Extremely high-risk patients:** A small number of women are at extremely high risk for VTE. These include patients with Antithrombin III deficiency, mechanical heart valves, or recent/acute VTE. Specific management recommendations for these patients are beyond the scope of this Toolkit. These patients are typically on medications such as warfarin, oral anti-Xa inhibitors or direct thrombin inhibitors that are generally *contraindicated* during pregnancy. Ideally, these women should be switched to LMWH either prior to pregnancy, or at the time of confirmation of pregnancy. There are a handful of women who may still be candidates for warfarin continuation when the fetal risks of medication may be outweighed by maternal benefit. Due to the complexity of care in these situations, decisions regarding anticoagulation must be individualized and multidisciplinary consultations with maternal-fetal medicine, cardiology, and/or hematology are required. Ideally, care should start with pre-conception counseling and detailed planning for anticoagulation during pregnancy and postpartum period.<sup>57,62-66</sup>

## **Anesthesia Considerations for Anticoagulated Patients**

### ***Multidisciplinary Planning and Early Consultation***

For women who are at high risk for VTE during pregnancy such that outpatient antenatal LMWH/UFH is indicated, consultation with anesthesia should ideally occur **early** in prenatal care. *The CMQCC Maternal VTE Task Force strongly recommends that anesthesiologists, specifically an obstetric anesthesiologist if available, be involved in the multidisciplinary planning of all anticoagulated patients.* Planning should be individualized to the patient's VTE risk factors, anticoagulation risks, and anesthesia needs. A primary consideration is to balance the relative benefits of anticoagulation with the risks associated with general anesthesia if neuraxial blockade cannot be performed. This consideration is particularly important for women with medical or obstetric comorbidities, such as severe obesity or pre-existing cardiorespiratory disease. Caution is also needed when considering women with non-reassuring airways for general anesthesia. Women undergoing general anesthesia for cesarean delivery may be at increased risk of hypoxic cardiac arrest from airway complications, and prolonged postpartum immobilization from severe pain. Additionally, severe hypoxic events may occur among women exposed to high dose intravenous opioids during the postpartum period, especially after cesarean delivery.

Furthermore, patient-centric outcomes may be impacted, as some women may experience dissatisfaction or anxiety if neuraxial analgesia is unable to be administered

during labor. An optimal care plan will include full discussion of risks and benefits with each woman to facilitate full participation in shared decision making. Each patient's anticoagulation plan should be made readily available to all providers to ensure that the plan is consistently followed throughout the antepartum, intrapartum, and postpartum periods.

#### *Anesthetic Implications of LMWH vs. UFH regimens*

Because women can go into spontaneous labor or give birth unexpectedly, the time intervals between the last doses of LMWH and neuraxial blockade should be carefully considered. Because UFH has a shorter half-life than LMWH, this means that neuraxial blockade can be considered sooner after low dose prophylactic UFH compared with prophylactic LMWH. Therefore, obstetricians may consider using low dose UFH for the following clinical scenarios: (i) antepartum admissions for women where delivery is unpredictable (e.g. preterm labor, PPRM, fetal decelerations, other indications), and (ii) outpatient antepartum management from 36 weeks' gestation.

Given that an optimal care plan involves weighing the relative advantages and disadvantages of UFH and LMWH, an ideal collaborative management plan would include guidance on i) Management during potential antepartum hospitalizations, and ii) Management in the late third trimester, (including potentially switching to UFH at 36 weeks' gestation to facilitate neuraxial anesthesia.

#### ***Antenatal Thromboprophylaxis after 36 Weeks of Gestational Age***

For women requiring outpatient LMWH antepartum pharmacologic thromboprophylaxis, there are several management options after 36 weeks' gestational age.<sup>67</sup>:

1. Continuation of LMWH (Enoxaparin 40 mg subcutaneous once a day or LMWH twice daily dosing)
2. Transition to low-dose UFH (5000 units subcutaneous twice daily)
3. Transition to UFH 10,000 units subcutaneous twice daily (ACOG recommendation)
4. Therapeutic Intravenous infusion of UFH

Each of these medication regimens may have distinct **advantages** and **disadvantages**, which are discussed below.

*Low-molecular-weight heparin (prophylactic or therapeutic)*

Some obstetric providers and patients may elect to continue LMWH until delivery because of relative advantages of this class of medications. Advantages of LMWH compared to UFH include: (i) Better correlation between dose and anticoagulant response (ii) no guidelines mandating anti-Xa monitoring. The chief disadvantage of LMWH is the required time delay between last dose of medication and neuraxial anesthesia. If appropriate, some providers and patients may choose to minimize the probability of an unplanned delivery by discontinuing prophylactic or therapeutic dose LMWH, 12 or 24 hours, respectively, prior to scheduled induction of labor or cesarean (See Table 10). Should patients and providers opt to continue LMWH until planned delivery or the first signs of labor, patients should receive adequate counseling about discontinuing LMWH in the setting of labor symptoms or evidence of spontaneous rupture of membranes.

*Low-dose UFH (5000 units subcutaneous twice daily)*

The primary advantage is that low-dose UFH may be the medication regimen least likely to preclude an obstetric patient from receiving neuraxial anesthesia. Potential disadvantages of low-dose UFH include (i) expert opinion recommending higher dosage in the third trimester (ii) twice daily dosing, and (iii) significant variation in expert guidelines on the appropriate time interval (up to 6 hours) between low-dose UFH and neuraxial anesthesia. *The CMQCC Maternal VTE Task Force recommends that providers refer to the forthcoming Society for Obstetric Anesthesia and Perinatology (SOAP) guidelines that may provide more clarification about relevant time intervals between last dose of antenatal UFH and neuraxial blockade for patients receiving low dose UFH.* The revised SOAP guidelines for the anesthetic management of anticoagulated obstetric patients should also be consulted <sup>68</sup>.

*UFH (10,000 units subcutaneous twice daily)*

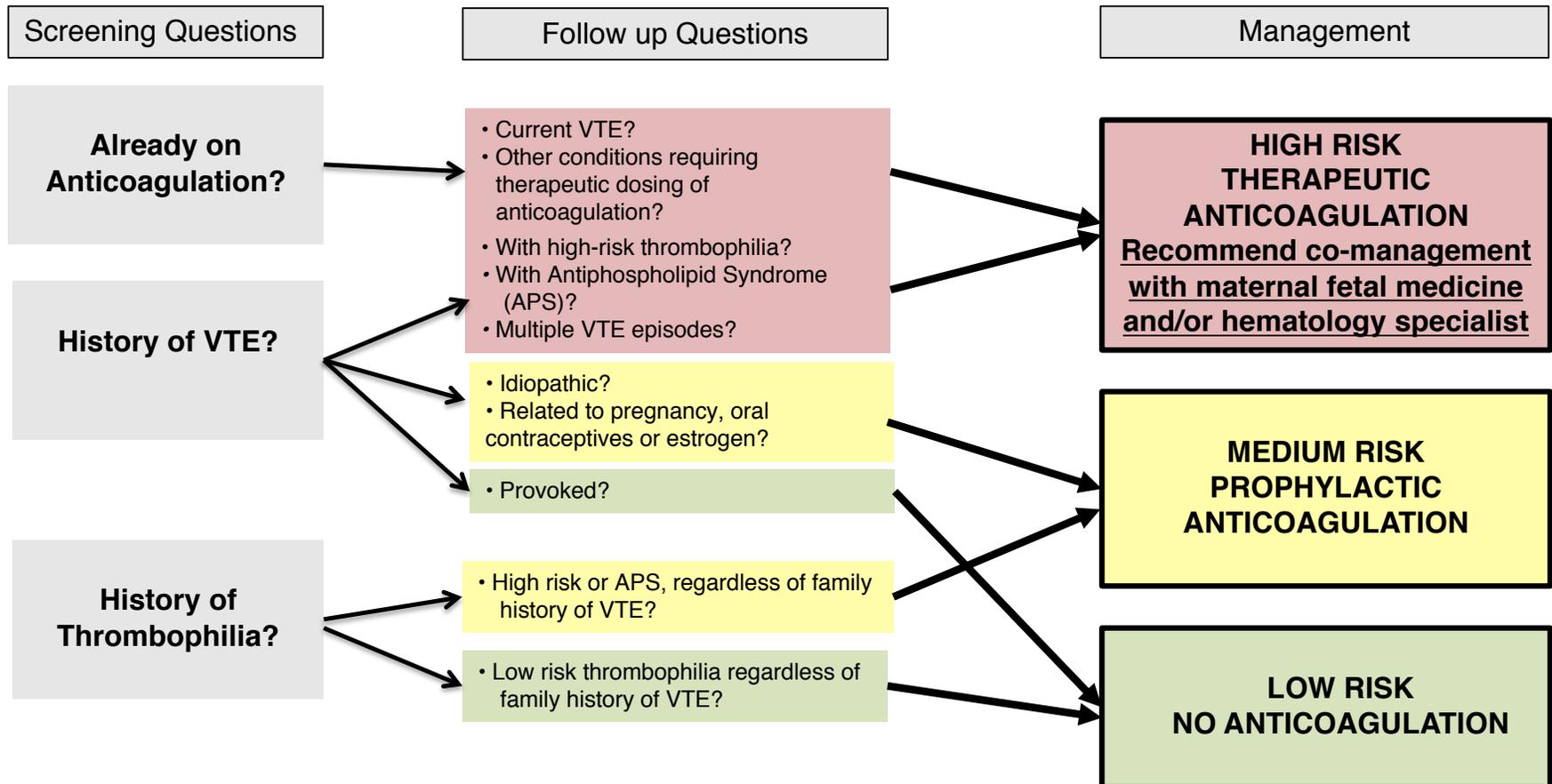
ACOG recommends use of 10,000 units UFH subcutaneously every 12 hours in the third trimester. A potential advantage of this approach is that it may provide more effective thromboprophylaxis than the lower dose UFH regimen. However, there is no high-quality research to support a definite benefit of higher dosing. Disadvantages include: (i) indeterminate time requirements between last 10,000-unit SUBCUTANEOUS dose of UFH and neuraxial anesthesia, (ii) Highly variable dose-response relationship, necessitating frequent laboratory monitoring, and (iii) twice daily dosing. *The CMQCC Maternal VTE Task Force recommends that providers refer to the forthcoming Society for Obstetric Anesthesia and Perinatology (SOAP) guidelines that may provide more clarification about relevant time intervals between last dose of antenatal UFH and neuraxial blockade for patients receiving high dose UFH.*

*Intravenous UFH infusions*

For patients at highest risk for recurrent VTE and receiving therapeutic dose of UFH or LMWH, planned delivery with conversion to an intravenous UFH infusion dose 24 hours or closer to delivery with resumption of UFH in the immediate postoperative *may be deemed appropriate for some women.* These patients require careful planning with

coordinated obstetric, hematology, and anesthesiology input. *The CMQCC Maternal VTE Task Force recommends discontinuing the UFH infusion at least 6 hours prior to the expected time of delivery.* Close monitoring of aPTT or heparin activity is needed to ensure that a therapeutic level is achieved during the period of infusion, and to assess residual UFH activity after termination of the UFH infusion. Protamine sulfate may be considered if hemorrhage occurs at delivery; however, this medication may have adverse effects such as systemic hypotension, pulmonary vasoconstriction, and allergic/anaphylactic reactions.

Algorithm 1: First Prenatal Visit: Maternal VTE Risk Assessment



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## Antepartum Hospitalization (non-delivery)

Non-pregnant, non-surgical patients admitted to the hospital are at increased risk for venous thromboembolism (VTE). This established VTE risk prompted The Joint Commission (TJC) to recommend hospitalized patients undergo VTE risk assessment within 24 hours of admission.<sup>69</sup> The obstetric population was not included in the TJC metric due to lack of data supporting specific approaches, despite the known increased risk of VTE during pregnancy.

*The CMQCC Maternal VTE Task Force recommends that upon admission to the hospital, all antepartum patients should be encouraged to (i) maintain full ambulation, (ii) ensure hydration, and (iii) utilize mechanical prophylaxis (knee length sequential compression devices) while in bed.* Emphasis on ambulation for VTE prevention and rapid deconditioning should be an integral part of the antepartum hospitalization bundle. The risks of activity restriction and bed rest are well recognized, including a significantly higher incidence of VTE.<sup>70-73</sup>, bone loss,<sup>74,75</sup> poor maternal weight gain,<sup>76</sup> and rapid deconditioning.<sup>77-79</sup> In addition, women on bed rest experience greater anxiety, and have higher rates of peri- and postpartum depression.<sup>80</sup>

Evidence suggests that there is no advantage for prolonged bed rest or activity restriction for any of the common obstetrical conditions requiring hospitalization. Studies of bed rest in multiple gestations,<sup>81</sup> preterm labor,<sup>82,83</sup> hypertensive disease of pregnancy,<sup>84,85</sup> and IUGR.<sup>86,87</sup> have failed to show evidence of benefit. A concerted educational program must be implemented to change the longstanding culture of “bed rest with bathroom privileges.” Specific activity levels should be developed for each patient, bearing in mind that there will be individual patients who will be uncomfortable with ambulation. Identifying specific goals, such as “ambulate every hour while awake,” will make implementation more successful. A recent review found that the greatest impact of early ambulation was achieved with the use of structured and standardized mobility protocols.<sup>88</sup> Technological advances in tracking activity can assist staff and encourage patients to attain activity goals.<sup>89,90</sup>

Despite efforts to improve ambulation, two recent large cohorts of pregnant patients demonstrated that non-delivery antepartum hospitalization was associated with a 12 to 18-fold higher risk of VTE.<sup>91,92</sup> VTE risk was highest for patients with length of stay  $\geq 3$  days; however, admission for  $< 3$  days was also associated with a 4-fold risk of VTE. Women with BMI  $\geq 30$  kg/m<sup>2</sup> and on bed rest combined with antepartum hospitalization may be at particularly high risk for VTE.<sup>1,8,73,93</sup> VTE risk in hospitalized pregnant women approaches that of high-risk non-pregnant patients for whom VTE thromboprophylaxis is currently recommended, such as persons with prior events and high-risk thrombophilia. *The CMQCC Maternal VTE Task Force supports NPMS and RCOG recommendations for pharmacological thromboprophylaxis for all antepartum patients hospitalized for  $\geq 72$  hours who are not at high risk for bleeding or imminent delivery.* The proposed risk assessment strategies and prophylaxis recommendations are detailed in Table 5 and

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Algorithm 2. In summary, factors to consider in assessing risk during antepartum hospital admission include: mobility, length of stay, BMI > 30 kg/m<sup>2</sup>, and pre-hospital risk.

### **Management**

Pharmacological prophylaxis may provide significant benefit for high-risk patients beyond mechanical prophylaxis or ambulation alone, given that patient, provider, and hospital factors frequently result in suboptimal protocol adherence.<sup>94-97</sup> Prior to administering pharmacologic prophylaxis, careful maternal and fetal assessment should be performed to consider risk for delivery, surgery or bleeding.

For patients at high risk for VTE, such as those already receiving outpatient anticoagulation, who may also be at risk for delivery or bleeding, mechanical prophylaxis *or* low dose UFH 5000 units subcutaneous every 12 hours may be utilized.

<sup>61</sup> If a multidisciplinary team agrees pharmacologic prophylaxis is appropriate for patients at high risk, low dose UFH 5000 units subcutaneous every 12 hours is the preferred pharmacologic agent due to the ability for rapid reversal, shorter half-life, and facilitation of regional anesthesia. Conversely, for patients at high risk for imminent delivery and/or requiring neuraxial anesthesia, hold pharmacological prophylaxis and utilize mechanical prophylaxis, given that the benefits of VTE risk reduction may be outweighed by risks of emergent general anesthesia or bleeding. These competing risks support our strong recommendation to obtain anesthesia input prior to a decision to initiate pharmacologic prophylaxis.

### **Anesthesia Collaboration**

If a multidisciplinary plan has not been created prior to hospitalization, anesthesia consultation at the time of antepartum admission is imperative for all patients who may be considered for pharmacologic prophylaxis. Obstetricians and anesthesiologists should maintain ongoing and close communication, ensuring that all providers are involved in the anticoagulation plan. An optimal, ongoing, multidisciplinary approach that includes anesthesiologists will address neuraxial anesthesia, dose adjustments of pharmacologic prophylaxis, and, if indicated, coagulation testing.

Table 5: Antepartum Hospital Admission VTE Risk Assessment

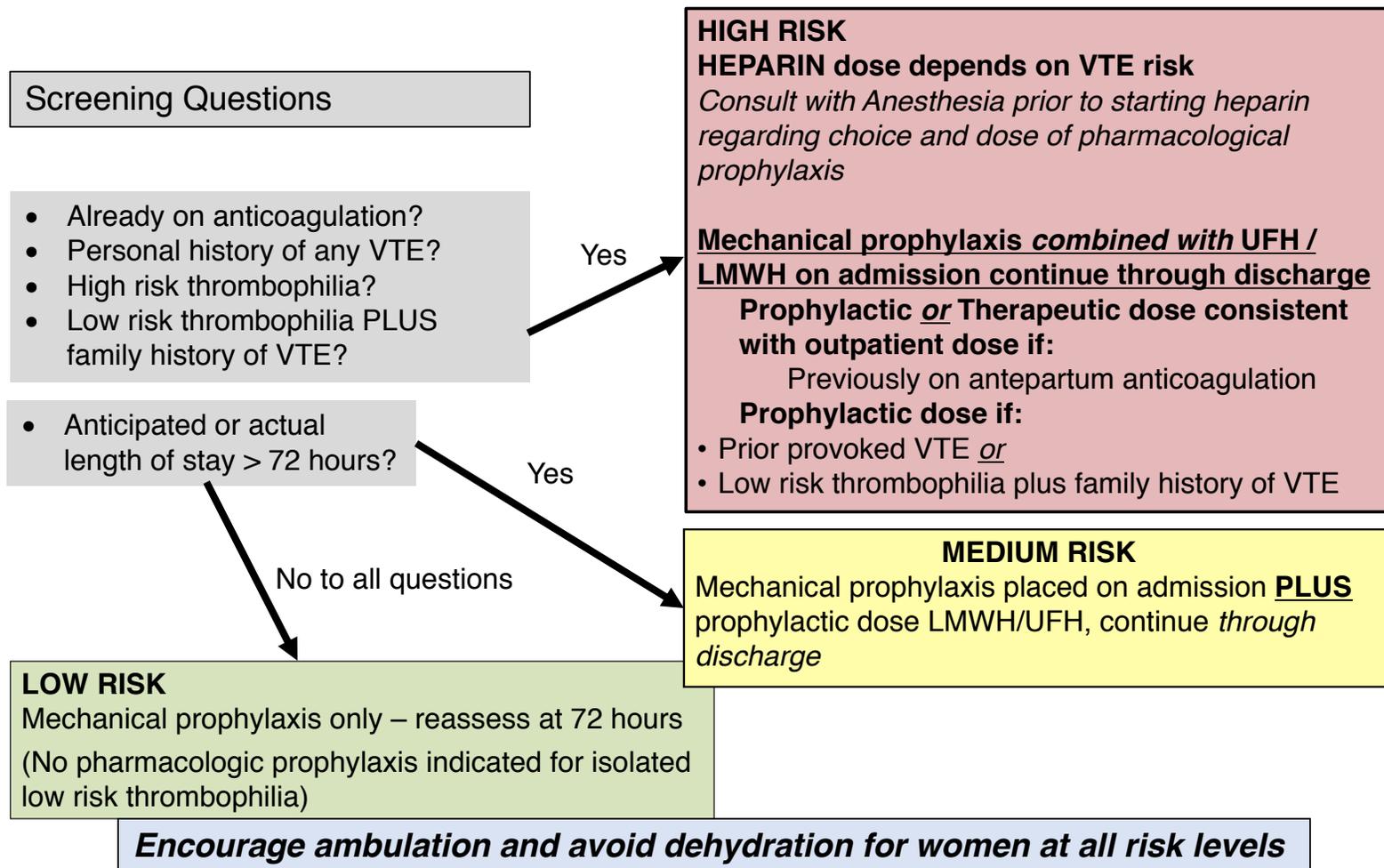
Clinical History	Risk Level	Anticoagulation
<b>Encourage ambulation and avoid dehydration at all risk levels</b>		
All patients not in high risk category with anticipated admission < 72 hours	<b>LOW</b>	Mechanical prophylaxis placed on admission continue through discharge  Reassess at 72 hours
All patients admitted not in high risk category with anticipated or actual length of stay $\geq$ 72 hours	<b>MEDIUM</b>	Mechanical prophylaxis placed on admission continue through discharge <b>PLUS</b>  Prophylactic-dose LMWH or UFH in collaboration with anesthesia
High risk or Antiphospholipid Syndrome (APS), with no prior VTE, regardless of family history Prior provoked, idiopathic, or estrogen related VTE Low risk thrombophilia <b>AND</b> family history of VTE <b>OR</b> single prior VTE  <b>OR</b>  Patients already receiving LMWH or UFH as outpatient Multiple prior VTE episodes Prior VTE <u>and</u> high risk or APS	<b>HIGH</b>	<i>Mechanical prophylaxis placed on admission continue through discharge <b>PLUS</b></i>  Prophylactic dose LMWH / UFH in collaboration with anesthesia  <b>OR</b>  <i>Mechanical prophylaxis placed on admission continue through discharge <b>PLUS</b></i>  Prophylactic <b>or</b> Therapeutic dose LMWH / UFH consistent with antepartum dosing in collaboration with anesthesia

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Please see [Definitions](#) for elaboration of key terms and dosages or page 19.

Algorithm 2: Antepartum Hospital Admission: Maternal VTE Risk Assessment

Please see [Definitions](#) for elaboration of key terms and dosages or page 19.



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## Delivery Hospitalization Including Cesarean and Vaginal Birth

Hospitals providing maternity care should implement uniform VTE prophylaxis strategies for childbearing women. Because no high-quality data has established which approach is best, hospital leaders should choose a strategy that best fits their patient population, local resources, and factors such as availability of electronic medical record (EMR) decision support.

The National Partnership for Maternal Safety (NPMS) VTE bundle provides several risk assessment strategies of varying complexity from which to choose. Significantly different rates of pharmacological prophylaxis have been shown to result, depending on which of the recommendations are applied. In a single center study of the ACOG, ACCP and RCOG recommendations applied to post-cesarean patients, approximately 1%, 35%, and 85% respectively, would have received postpartum pharmacologic prophylaxis, based on the varying recommendations.<sup>97</sup> ACOG criteria are not specific beyond recommending postpartum pharmacologic prophylaxis for patients with a personal or family history of VTE and/or thrombophilia. The RCOG guidelines, which support the most extensive prophylaxis, have been associated with decreased maternal VTE mortality risk in the United Kingdom.<sup>21,98</sup> However, beyond the highest risk patients (those with prior VTE events and high-risk thrombophilias), no high-quality evidence exists to determine which VTE risk factors, alone or in combination, place patients at such high risk that pharmacological prophylaxis is mandated.

All hospitalized pregnant women should undergo VTE risk assessment on admission, including those expected to undergo uncomplicated vaginal birth. *The CMQCC Maternal VTE Task Force recommends using simple, standardized risk assessment to stratify vaginal birth patients into Low, Medium, and High VTE-risk groups with thromboprophylaxis based upon the woman's risk level.*

Based on the best available data, including data from the California Pregnancy-Associated Mortality Review (CA-PAMR) as summarized below, the following measures should be taken for all women hospitalized for a vaginal or cesarean birth, including during admission, intrapartum, and postpartum:

- Early mobilization
- Adequate hydration
- VTE risk assessment

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## Cesarean Birth

Given the evidence gap described above, data from the CA-PAMR was analyzed to determine which factors placed women in California at highest risk for death from VTE. Data from CA-PAMR demonstrate that cesarean delivery and obesity are leading risk factors for maternal VTE death.<sup>26</sup> From 2002 to 2007, 28 post-delivery VTE-related deaths occurred in California.<sup>16</sup> Notably, only 28% of non-VTE maternal deaths had a delivery BMI of  $\geq 35$  kg/m<sup>2</sup> whereas 61% of the women who died from VTE had a delivery BMI  $\geq 35$  kg/m<sup>2</sup> (OR 3.96, CI 1.8,8.8). Of the obese women with BMI  $\geq 35$  kg/m<sup>2</sup> who died from VTE (n=17), 75% had a cesarean delivery (numbers too small for valid comparison). These CA-PAMR data suggest that postpartum obese women, particularly those who have undergone cesarean, are at high risk for death from VTE.<sup>16</sup>

### Cesarean Birth Risk Assessment

*For women undergoing cesarean birth, the CMQCC Maternal VTE Task Force recommends risk assessment and stratification into Low, Medium, and High-risk groups. Thromboprophylaxis recommendations are based upon patient risk. Given that CA-PAMR found that more than half of VTE related deaths occurred in women with delivery BMI  $\geq 35$  kg/m<sup>2</sup> who underwent cesarean birth, the CMQCC Maternal VTE Task Force recommends pharmacologic prophylaxis for this group of patients while in the hospital. Other women with a single major or two or more minor risk factors should also receive in-house post cesarean pharmacologic prophylaxis (See Tables 6 and 7). Individual risk factors are included in the assessment based on ACCP criteria and evidence from California data demonstrating risk. The simplicity of this risk assessment stratification gives any maternity unit the ability to successfully initiate a thromboprophylaxis strategy for cesarean delivery patients. This type of risk assessment is in lieu of a more complex point scoring system; however, it will still require decision support for successful implementation (See Table 10). Overall this strategy should facilitate thromboprophylaxis implementation, as it utilizes a straightforward and more discriminating approach, in contrast to the complex scoring system suggested by RCOG, which results in ~85 % of post-cesarean patients receiving postpartum pharmacologic prophylaxis.<sup>97</sup>*

**Postpartum pharmacologic dosing regimens:** Consensus is lacking regarding optimal medication, dose, or duration for postpartum VTE thromboprophylaxis in patients without personal or family history of VTE and/or thrombophilia. Most guidelines recommend either fixed dose LMWH (e.g. enoxaparin 40 mg subcutaneously every 24 hours) or UFH 5000 units subcutaneously every 12 hours continued until discharge from the hospital. In the setting of neuraxial blockade, societal anesthesia guidelines provide guidance on minimum time periods prior to first dose of postpartum pharmacologic prophylaxis (See Table 10).

Table 6: Cesarean Birth Major and Minor VTE Risk Factors

Major VTE Risk Factors	Minor VTE Risk Factors
<ul style="list-style-type: none"> <li><input type="checkbox"/> BMI &gt; 35 kg/m<sup>2</sup> @ delivery</li> <li><input type="checkbox"/> Low risk thrombophilia</li> <li><input type="checkbox"/> Postpartum hemorrhage requiring:</li> <li><input type="checkbox"/> Transfusion or further operation, (e.g. hysterectomy, D&amp;C) or Interventional Radiology procedure</li> <li><input type="checkbox"/> Infection requiring antibiotics</li> <li><input type="checkbox"/> Antepartum hospitalization ≥ 72 hours, current or within the last month</li> <li><input type="checkbox"/> Chronic medical conditions: Sickle Cell disease, Systemic Lupus Erythematosus, Significant Cardiac disease, active Inflammatory Bowel Disease, active cancer, Nephrotic syndrome</li> </ul>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Multiple gestation</li> <li><input type="checkbox"/> Age &gt; 40</li> <li><input type="checkbox"/> Postpartum hemorrhage ≥1000 ml</li> <li>but not requiring:               <ul style="list-style-type: none"> <li><input type="checkbox"/> Transfusion or further operation, (e.g. hysterectomy, D&amp;C) or Interventional Radiology procedure</li> </ul> </li> <li><input type="checkbox"/> Family history of VTE (VTE occurring in a first-degree relative prior to age 50)</li> <li><input type="checkbox"/> Smoker</li> <li><input type="checkbox"/> Preeclampsia</li> </ul>
<p>Women with <b>one major or two minor risk factors</b> should receive in-hospital post cesarean pharmacologic prophylaxis</p>	

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Table 7: Cesarean Birth VTE Risk Assessment and Suggested Prophylaxis

Clinical History	Risk Level	Prophylaxis Regimen
<p><b>Encourage ambulation and avoid dehydration at all risk levels.</b> <b>All women having cesarean birth receive mechanical prophylaxis.</b></p>		
Not meeting medium or high risk criteria	<b>LOW</b>	Mechanical prophylaxis placed prior to cesarean and continued until fully ambulatory
<b>Cesarean Delivery with 1 Major or <math>\geq 2</math> Minor Risk Factors (See Table 6)</b>	<b>MEDIUM</b>	Mechanical prophylaxis placed prior to cesarean and continued until fully ambulatory <b>PLUS</b>  Prophylactic dose LMWH / UFH postpartum, continue until discharge
<p>High risk thrombophilia (including acquired) no prior VTE, regardless of family history</p> <p>Prior provoked, idiopathic, or estrogen related VTE</p> <p>Low risk thrombophilia <b>AND</b> family history of VTE <b>OR</b> single prior VTE</p> <p>Patients already receiving LMWH or UFH as outpatient</p> <p>Multiple prior VTE</p> <p>Prior VTE with High Risk thrombophilia (including APS)</p>	<b>HIGH</b>	<p>Mechanical prophylaxis placed prior to cesarean and continued until fully ambulatory <b>PLUS</b></p> <p>Prophylactic dose LMWH / UFH in hospital and continued until 6 weeks from date of delivery</p> <p>Mechanical prophylaxis placed prior to cesarean and continued until fully ambulatory <b>PLUS</b></p> <p>Therapeutic dose LMWH / UFH postpartum (Postpartum dose <math>\geq</math> Antepartum dose) in hospital and continued until 6 weeks from delivery date after discharge</p>

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## Vaginal Birth

Risk for VTE and VTE-related maternal mortality is lower for vaginal delivery than cesarean delivery. Given the lower VTE risk associated with vaginal delivery, increased risk is required to justify administration of pharmacologic thromboprophylaxis. *The CMQCC Maternal VTE Task Force supports the ACOG recommendations that women with prior VTE events, high-risk thrombophilia, or low risk thrombophilia with family history of VTE receive postpartum pharmacologic prophylaxis.* As noted above, CA-PAMR data identified delivery BMI  $\geq 35$  kg/m<sup>2</sup> as a major risk factor for maternal death (OR 3.96, CI 1.8,8.8) due to VTE, demonstrating increasing mortality risk with increasing BMI.<sup>16</sup> Other epidemiologic data corroborate the findings from CA-PAMR and demonstrate that increasing BMI is associated with increased risk in general for VTE and in particular for PE.<sup>2,5,21,99-101</sup> The risk for VTE with increasing BMI appears to be multiplied when immobilization is present.<sup>1</sup>

Immobility risk is underscored by the Padua modified risk score for obstetrics which equates immobilization for  $> 72$  hours during hospitalization, with risk comparable to a personal history of VTE or thrombophilia, conditions for which consensus recommendations exist for pharmacological prophylaxis.<sup>1,23,61,101-103</sup>

## Vaginal Birth Risk Assessment

Given these data, our risk assessment recommends that women with BMI  $\geq 40$  kg/m<sup>2</sup> *in combination* with current, anticipated or recent (within the past month) hospitalization for  $\geq 72$  hours be considered for *intrapartum* mechanical prophylaxis and/or *postpartum* pharmacologic prophylaxis (See Table 8). These criteria will include women undergoing prolonged induction resulting in a total hospital stay of  $\geq 72$  hours. This proposed risk assessment and thromboprophylaxis criteria are specific for California, while maintaining fundamental consistency with the NPMS VTE bundle recommendations for vaginal birth thromboprophylaxis.

For high-risk women already receiving outpatient antepartum prophylaxis, or for women with preexisting risk factors warranting only *postpartum pharmacologic prophylaxis* (i.e. those with prior provoked VTE or a low risk thrombophilia *in association with either a family history of VTE or BMI  $\geq 40$  kg/m<sup>2</sup>*). *The CMQCC Maternal VTE Task Force recommends intrapartum use of intermittent sequential compression devices when a woman receives neuraxial anesthesia during labor or otherwise ceases to be fully ambulatory.* For this cohort of women with preexisting risk factors, postpartum pharmacological prophylaxis in the hospital should be continued *for six weeks after delivery* with dosage (prophylactic versus therapeutic dose) as dictated by the clinical history.<sup>28,31,58</sup>

Women at highest risk for VTE (e.g. Antithrombin III deficiency, mechanical heart valves, or recent history of VTE) or with significant persistent, chronic medical co-morbidities (e.g. sickle cell disease, systemic lupus erythematosus, significant cardiac

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disease, active inflammatory bowel disease, nephrotic syndrome, or active cancer) may benefit from consultation with maternal-fetal medicine and/or hematology for a patient-specific VTE thromboprophylaxis plan. <sup>28,31</sup>

Some providers may be concerned that women who have a vaginal birth and have multiple VTE risk factors (apart from thrombophilia, prior VTE events, immobilization, and obesity (BMI  $\geq$  40)) may be at high risk and warrant pharmacologic prophylaxis in the postpartum period. While these guidelines do not make specific recommendations for these women, this is an understandable concern. *The CMQCC Maternal VTE Task Force recommends that concerned providers consult either the concise NPMS bundle summary of RCOG criteria or review the 2015 RCOG Green-top Guideline No. 37a recommendations directly.* <sup>31</sup> *The CMQCC Maternal VTE Task Force cautions that feasible implementation of the broad risk-factor based scoring system for postpartum prophylaxis advocated by RCOG may be limited to hospital systems with robust clinical decision support.* <sup>61,104</sup> Suggested postpartum pharmacologic dosing regimens are similar to those for cesarean deliveries.

**Postpartum pharmacologic dosing regimens:** Consensus is lacking regarding optimal medication, dose, or duration for postpartum VTE thromboprophylaxis in patients without personal or family history of VTE and/or thrombophilia. Most guidelines recommend either fixed dose enoxaparin 40 mg subcutaneously every 24 hours or UFH 5000 units subcutaneously every 12 hours continued until discharge from the hospital. In the setting of neuraxial blockade, societal anesthesia guidelines provide guidance on minimum time periods prior to first dose of postpartum pharmacologic prophylaxis (See Table 10).

Table 8: Vaginal Birth VTE Risk Assessment and Suggested Prophylaxis

Clinical History	Risk Level	Anticoagulation
<b>Encourage ambulation and avoid dehydration at all risk levels</b>		
<b>Delivery BMI <math>\geq 40</math> kg/m<sup>2</sup></b>	<b>LOW</b>	Mechanical prophylaxis placed prior to delivery and continued until fully ambulatory
<b>Delivery BMI <math>\geq 40</math> kg/m<sup>2</sup></b> <b>PLUS</b> Antepartum hospitalization $\geq 72$ hours anticipated currently or within past month <b>OR</b> <b>Delivery BMI <math>\geq 40</math> kg/m<sup>2</sup> PLUS</b> Low Risk Thrombophilia	<b>MEDIUM</b>	Mechanical prophylaxis placed prior to delivery and continued until fully ambulatory <b>PLUS</b> Prophylactic dose LMWH / UFH postpartum hospitalization <b>BMI <math>\geq 40</math> kg/m<sup>2</sup> plus thrombophilia</b> (consider LMWH/UFH continuation 6 weeks postpartum)
High risk thrombophilia with no prior VTE regardless of family history Prior provoked, idiopathic, or estrogen related VTE Low risk thrombophilia <b>AND</b> family history of VTE ANY single prior VTE <b>OR</b> Patients already receiving LMWH or UFH as outpatient Multiple prior VTE Prior VTE with High Risk or Antiphospholipid Syndrome (APS)	<b>HIGH</b>	Mechanical prophylaxis placed prior to delivery and continued until fully ambulatory <b>PLUS</b> Prophylactic dose LMWH / UFH postpartum in hospital and <b>continued until 6 weeks from date of delivery after discharge</b> <b>OR</b> Mechanical prophylaxis placed prior to delivery and continued until fully ambulatory <b>PLUS</b> Therapeutic dose LMWH / UFH postpartum ( <b>Postpartum dose <math>\geq</math> Antepartum dose</b> ) in hospital and <b>continued until 6 weeks from date of delivery after discharge</b>

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Please see [Definitions](#) for elaboration of key terms and dosages or page 19.

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### **Brief Summary: Postpartum hospitalization prophylactic pharmacologic dosing**

Both prophylactic UFH (5000 units subcutaneously every 12 hours) and LMWH (e.g. enoxaparin 40mg subcutaneously every 24 hours) may provide effective postpartum VTE prophylaxis. While consensus or high quality evidence is lacking regarding which medication at which dose for how long offers the best prophylaxis, given the risk associated with hospitalization, prophylaxis should be continued until hospital discharge.

A benefit of prophylactic UFH is that this agent may be initiated much sooner in relation to neuraxial anesthesia than LMWH agents such as enoxaparin. *The CMQCC Maternal VTE Task Force supports administering the first dose of prophylactic UFH at the end of the recovery period in the patient anesthetic care unit (PACU) or upon transfer to the floor, which is typically one hour after either epidural catheter removal or spinal needle placement in patients who have undergone uncomplicated delivery.*<sup>61,104</sup> For providers opting to use prophylactic LMWH (e.g. enoxaparin 40 mg subcutaneously every 24 hours) *The CMQCC Maternal VTE Task Force recommends that a minimum 12 hours elapse between administration of medication and epidural catheter removal or spinal needle placement following uncomplicated delivery. (See Anesthesia Considerations & Table 10)*

**Therapeutic anticoagulation** is discussed below within Anesthesia Considerations and the obstetric anesthesia team should be consulted to discuss timing of onset for postpartum therapeutic anticoagulation.

For patients already receiving outpatient antepartum pharmacological prophylaxis, ACOG recommends that the postpartum treatment dosage should be greater or equal to antepartum treatment (i.e. prophylaxis or therapeutic, See Table 4) and continued until 6 weeks postpartum.

### **Special Considerations—Obesity**

Controversy exists regarding heparin dosing in obese postpartum patients. Proposed regimens seeking improved prophylaxis efficacy include weight stratified fixed dose, BMI stratified fixed dose, or weight based mg/Kg LMWH dosing.<sup>45,105</sup> Weight-based enoxaparin dosing more often achieves target anti-Xa ranges compared with BMI-stratified dosing; however, an effective anti-Xa prophylactic range has not been definitively established, and attaining target anti-Xa levels results in significantly higher amounts of enoxaparin administered.<sup>106,107</sup> Dose related complications may outweigh theoretical benefit associated with this regimen. Until data is available that demonstrates optimal thromboprophylaxis dosing for obese postpartum patients, *the CMQCC Maternal VTE Task Force suggests more conservative dosing associated with BMI stratified regimen.*<sup>108-110</sup>

The following suggested regimens in Table 9 are for women who have undergone uncomplicated neuraxial procedure and require collaboration with anesthesia to ensure

compliance with the American Society of Regional Anesthesia and Pain Medicine (ASRA) guidelines.

Table 9: Recommended Peripartum Regimen based on BMI

BMI Level	Recommended Regimen
<b>BMI <math>\leq</math> 40 kg/m<sup>2</sup></b>	Mechanical prophylaxis placed prior to delivery and continued until fully ambulatory, with initiation of pharmacological prophylaxis in accordance with anesthesia guidelines. (See Table 10).
<b>BMI <math>&gt;</math> 40 kg/m<sup>2</sup></b>	<p>Mechanical prophylaxis placed prior to delivery and combined with UFH 5000 units subcutaneously every 8-12 hours initiated on discharge from PACU, with combined mechanical and pharmacologic prophylaxis continued until discharge</p> <p style="text-align: center;"><b>OR ALTERNATIVELY</b></p> <p>Mechanical prophylaxis placed prior to delivery and combined with UFH 5000 units every 12 hours initiated on discharge from PACU, with UFH continued <i>until enoxaparin 40 mg every 12 hours</i> can be initiated <i>post neuraxial procedure</i>, with combined mechanical and pharmacologic prophylaxis continued until discharge.</p>

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## Anesthesia Considerations

Optimal implementation of an obstetric VTE prophylaxis strategy will require close collaboration between obstetric and anesthesia providers. Given that no high-quality data supports a single best approach, society guidelines make varying recommendations, and anesthesia guidelines are evolving, anesthesia and obstetric leadership for each maternity unit should work to reach consensus on a standardized approach to prophylaxis. Ideally each hospital should develop a standardized protocol that addresses prophylaxis for all patients with VTE risk. *The CMQCC Maternal VTE Task Force further recommends perioperative discussion with anesthesia (e.g. during time out) to ensure protocol adherence and patient safety.* Critical discussion points should include:

- Postpartum medication choice (LMWH versus UFH), dose, and time of first dose
- Whether neuraxial anesthesia administration involved a difficult or bloody procedure or other complication
- Whether Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) will be used in combination with postpartum anticoagulation

## Recommendations for anesthesia in relation to anticoagulation

The following recommendations are based on:

- (i) Anesthesia leadership society recommendations including ASRA and the European Society of Anaesthesiology (ESA)
- (ii) The NPMS VTE Bundle<sup>111</sup>
- (iii) Pharmacokinetic data from the anesthetic and obstetric literature
- (iv) Expert opinion from the Society for Obstetric Anesthesia and Perinatology (SOAP)

The CMQCC Maternal VTE Task Force notes that both ASRA and ESA both last published official guidelines in 2010.<sup>112, 113</sup> ASRA is currently completing a guideline revision, a preliminary version of which is available as an iPhone app.<sup>114</sup> In this Toolkit, the CMQCC Maternal VTE Task Force refers to the recommendations from the ASRA iPhone app, where applicable. In the absence of iPhone app recommendations, the CMQCC Maternal VTE Task Force refers to the 2010 ASRA and ESA guidelines. The CMQCC Maternal VTE Task Force notes that SOAP is currently developing guidelines for anticoagulated obstetric patients. The CMQCC Maternal VTE Task Force encourages using the SOAP guidelines to update hospital anesthesia and obstetric VTE protocols as appropriate.<sup>68</sup>

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## Recommendations for time-interval between the last dose of UFH/LMWH and neuraxial anesthesia

See Table 10 for summary of these recommendations.

### **Low Molecular Weight Heparin (LMWH)**

ASRA and ESA recommend a minimum of 10-12 hours after prophylactic LMWH and a minimum of 24 hours after therapeutic LMWH before performing neuraxial blockade.

### **Unfractionated Heparin (UFH)**

Low dose UFH: The NPMS bundle supports administration of low-dose UFH at any time in relation to neuraxial anesthesia based on long-standing recommendations and routine clinical practices within the United States. The preliminary 2016 ASRA app guidelines recommend a time interval of at least 4 hours (and preferably 6 hours) between a 5000 units dose of subcutaneous UFH and neuraxial blockade for women receiving a maximum of 10,000 units over a 24-hour period.

*The CMQCC Maternal VTE Task Force notes that ASRA recommendations do not account for the pharmacokinetic differences of UFH between pregnant and non-pregnant women. The Society for Obstetric Anesthesia and Perinatology (SOAP) have issued consensus recommendations that support decision-making incorporating the competing risks/benefits of neuraxial versus general anesthesia, obstetric pharmacokinetic data, and relevant data on complications.<sup>68</sup>*

### **High dose UFH**

Recommendations for neuraxial anesthesia in relation to higher doses of UFH are unclear. The 2016 ASRA app guideline does not classify what constitutes a “therapeutic” dose of UFH. The 2010 ASRA guideline states that the safety of neuraxial blockade is not established for patients receiving more than twice daily dosing or > 10,000 units of UFH daily; anesthesia recommendations for women receiving these doses are not provided. ESA guidelines define “prophylactic” UFH as  $\leq 15,000$  units per day. For women receiving “treatment” dose UFH (which the CMQCC Maternal VTE Task Force interprets as > 15,000 units per day), ESA recommends that 8-12 hours between last UFH dose and neuraxial blockade. *The CMQCC Maternal VTE Task Force recommends waiting 6 hours after the last dose of UFH prior to neuraxial blockade then check aPTT. If aPTT is within normal limits, block may be considered. If aPTT is elevated, delay block 1 hour then recheck aPTT. Given the inconsistency in society recommendations, the CMQCC Maternal VTE Task Force recommends that obstetric providers create local protocols with input for hematologists as necessary.*

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## Recommendations for First Postpartum Anticoagulation Dose After Neuraxial Blockade or Epidural Catheter Withdrawal

See Table 10 for detailed summary about these recommendations.

- i. LMWH 24-hour dosing (e.g., Enoxaparin 40 mg every 24 hours): According to 2016 app guidelines, ASRA recommends a minimum of 12 hours after uncomplicated neuraxial block before administering LMWH. For patients receiving post-cesarean epidural analgesia, ASRA recommends that waiting at least 4 hours after epidural catheter withdrawal and 12 hours after surgery before initiating prophylactic LMWH.
- ii. LMWH 12-hour dosing (e.g., Enoxaparin 40 mg every 12 hours): According to 2016 app guidelines, ASRA recommend a minimum of 12 hours after uncomplicated neuraxial block before initiating LMWH. For patients receiving post-cesarean epidural analgesia, ASRA recommends that waiting at least 4 hours after epidural catheter withdrawal and 12 hours after surgery before initiating prophylactic LMWH. ASRA recommends removal of indwelling catheters before the first dose of 12-hour dosing of prophylactic LMWH.
- iii. Therapeutic postpartum LMWH: *The CMQCC Maternal VTE Task Force recommends waiting 24 hours after neuraxial block or epidural catheter removal before initiating therapeutic LMWH (e.g. enoxaparin 1mg/kg every 12 hours or 1.5mg/kg every 24 hours).<sup>115</sup> The CMQCC Maternal VTE Task Force also recommends avoiding concomitant NSAIDs for patients receiving therapeutic dose LMWH or therapeutic dose IV UFH.<sup>115</sup> These recommendations are consistent with the 2010 ASRA guidelines. Of relevance to patients who require post-cesarean epidural analgesia, ASRA also recommends indwelling catheters be removed before the first dose of therapeutic LMWH.*

**UFH:** The 2016 ASRA app supports administration of heparin 5,000 units every 12 hours immediately after neuraxial block or epidural catheter removal. Given special considerations for postpartum obstetric patients, The CMQCC Maternal VTE Task Force recommends that the first dose of prophylactic UFH be administered at the end of the recovery period in the postop anesthetic care unit (PACU) or on discharge to the postpartum floor.<sup>61,104</sup> For the vast majority of patients, at least one hour will have elapsed between the time of neuraxial blockade or epidural catheter removal (at the end of surgery or after delivery) and PACU discharge or transfer (See Table 10).

Table 10: CMQCC Maternal VTE Task Force Recommendations for the Minimum Time Intervals between Neuraxial Blockade and Peripartum Anticoagulation

<b>Antepartum/Intrapartum</b>	
Minimum time periods between discontinuing antepartum anticoagulation and performing neuraxial blockade, defined here as any of the following: single shot spinal, epidural, or combined spinal-epidural	
<b>Anticoagulation Dose</b>	<b>Minimum Timeframe</b>
UFH dose $\leq$ 10,000 units/day	No contraindications to timing of heparin dose and performance of neuraxial blockade
UFH dose $>$ 10,000 units/day	Wait 6 hours after the last dose of UFH prior to neuraxial blockade then check aPTT. If aPTT within normal limits – block may be considered. IF aPTT elevated, delay block 1 hour then recheck aPTT
LMWH prophylactic dose	Wait $\geq$ 12 hours post last dose prior to neuraxial blockade
LMWH therapeutic dose	Wait $\geq$ 24 hours post last dose prior to neuraxial blockade
<b>Postpartum</b>	
Minimum time periods between neuraxial block or epidural catheter removal and first postpartum dose of anticoagulant	
<b>Anticoagulation Dose</b>	<b>Minimum Timeframe</b>
UFH prophylactic dose $\leq$ 10,000 units/day	Wait $\geq$ 1 hour after epidural catheter removal or spinal procedure
UFH therapeutic dose $>$ 10,000 units/day	Wait $\geq$ 1 hour after epidural catheter removal or spinal procedure
<b>LMWH prophylactic dose</b> e.g. Enoxaparin 40 mg every 24 <i>or</i> every 12 hours	<b>After neuraxial blockade: wait <math>\geq</math> 12 hours before first dose of LMWH</b> For patients receiving post-cesarean epidural analgesia: wait $\geq$ 4 hours after epidural catheter removal (provided that 12 hours has elapsed since cesarean section)
<b>LMWH therapeutic dose</b> e.g. Enoxaparin 1mg / kg every 12 hours <i>or</i> 1.5 mg /kg every 24 hours	<b>After neuraxial blockade: wait <math>\geq</math> 24 hours before first dose of LMWH.</b> Indwelling catheters should be removed before initiation of therapeutic LMWH. For patients receiving post-cesarean epidural analgesia: wait $\geq$ 24 hours after epidural catheter removal before first dose of LMWH

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## NSAIDs and Heparin

*The CMQCC Maternal VTE Task Force supports the concurrent use of oral non-steroidal anti-inflammatory drugs (NSAIDs) and prophylactic heparin (UFH 5000 units twice daily or prophylactic enoxaparin 40mg once daily) after uncomplicated neuraxial anesthesia. The NPMS VTE bundle and SOAP also support this approach.*<sup>61,104</sup>

Support for this management is based on clinical experience and the expert opinions of NPMS and SOAP committees. Given that high-quality research safety data on high dose NSAIDs in this clinical setting is not available, it may be reasonable to restrict regimens such as concurrent intravenous ketorolac and oral NSAIDs in the first 18 hours after neuraxial anesthesia in the setting of LMWH or UFH use.

*The CMQCC Maternal VTE Task Force recommends **avoidance** of concomitant use of NSAIDs for patients receiving therapeutic dose LMWH or therapeutic dose intravenous UFH. The Task Force recommends the adoption of standardized approaches in each maternity unit in collaboration with anesthesia to address use of NSAIDs with UFH/LMWH after neuraxial anesthesia. SOAP is preparing an expert statement that will provide critical guidance on this subject.*

### *Bloody or Difficult Neuraxial Procedures*

Delayed initiation of LMWH for 24 hours is recommended for patients with bloody or complicated neuraxial procedure. The CMQCC Maternal VTE Task Force recommends that anesthesia providers discuss with obstetric providers whether the plan for anticoagulation requires modification. Once postpartum anticoagulation is initiated, the *CMQCC Maternal VTE Task Force recommends close neurological monitoring so that symptoms and signs of epidural hematoma are detected early such as progression of sensory or motor block, or bowel/bladder dysfunction.*

### ***Evolving Anesthesia Guidelines***

At the time of this publication, SOAP expert consensus opinion on antithrombotic therapy in the setting of neuraxial anesthesia are forthcoming. Until this information is available, *the CMQCC Maternal VTE Task Force recommends that obstetric providers in each institution develop local, standardized approaches, in collaboration with anesthesia providers.*<sup>52,61,114,115</sup>

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## Post-Discharge Extended Duration Anticoagulation

A subset of women who are at high risk for postpartum VTE will require extended duration anticoagulation for a total of 6 weeks from the date of delivery (e.g. women who are discharged at one week postpartum would then receive extended duration anticoagulation for five weeks). These include patients with a high-risk thrombophilia, personal history of VTE, or a low-risk thrombophilia with family history of VTE. Moreover, while pharmacologic prophylaxis for patients with a single prior provoked PE or a low risk thrombophilia in the setting of a positive family history for VTE is not recommended on an *antepartum* basis, higher postpartum risk supports outpatient prophylaxis for 6 weeks after delivery (see Table 11). Epidemiologic data, ACCP, RCOG, and NPMS VTE bundle supports our recommendation for continuation of postpartum pharmacologic prophylaxis until 6 weeks postpartum, with dosing dependent upon VTE risk.<sup>6-8,28,31</sup> These recommendations are similar to those from ACOG; however, ACOG allows a minimum of 4 prophylaxis weeks postpartum.

For women at very high risk for VTE events (e.g. Antithrombin III deficiency, mechanical heart valves, or a recent history of VTE), consultation with maternal fetal medicine or hematology for a patient-specific VTE thromboprophylaxis plan is required. Patients with risk factors and significant persistent chronic medical co-morbidities (sickle cell disease, systemic lupus erythematosus, clinically significant cardiac disease, active Inflammatory bowel disease, nephrotic syndrome, active cancer) may also benefit from maternal-fetal and/or hematology consultation.

*For the very rare patient who requires more than six weeks' postpartum anticoagulation, the CMQCC Maternal VTE Task Force does not recommend bridging to warfarin sooner than two weeks postpartum, which may be associated with delayed postpartum hemorrhage.*<sup>60,116</sup> Bridging to warfarin typically requires 7 to 14 days of simultaneous administration of warfarin with heparin. The use of two concurrent anticoagulants increase the risk of bleeding and bridging to warfarin requires frequent laboratory monitoring. Consequently, many women for whom less than six weeks' postpartum anticoagulation is recommended choose to remain on low molecular weight heparin in lieu of bridging to warfarin. Neither LMWH nor warfarin is contraindicated with breastfeeding. The new oral anticoagulants are currently not recommended with breastfeeding due to insufficient data.

Table 11: Post-Discharge Extended Duration Anticoagulation

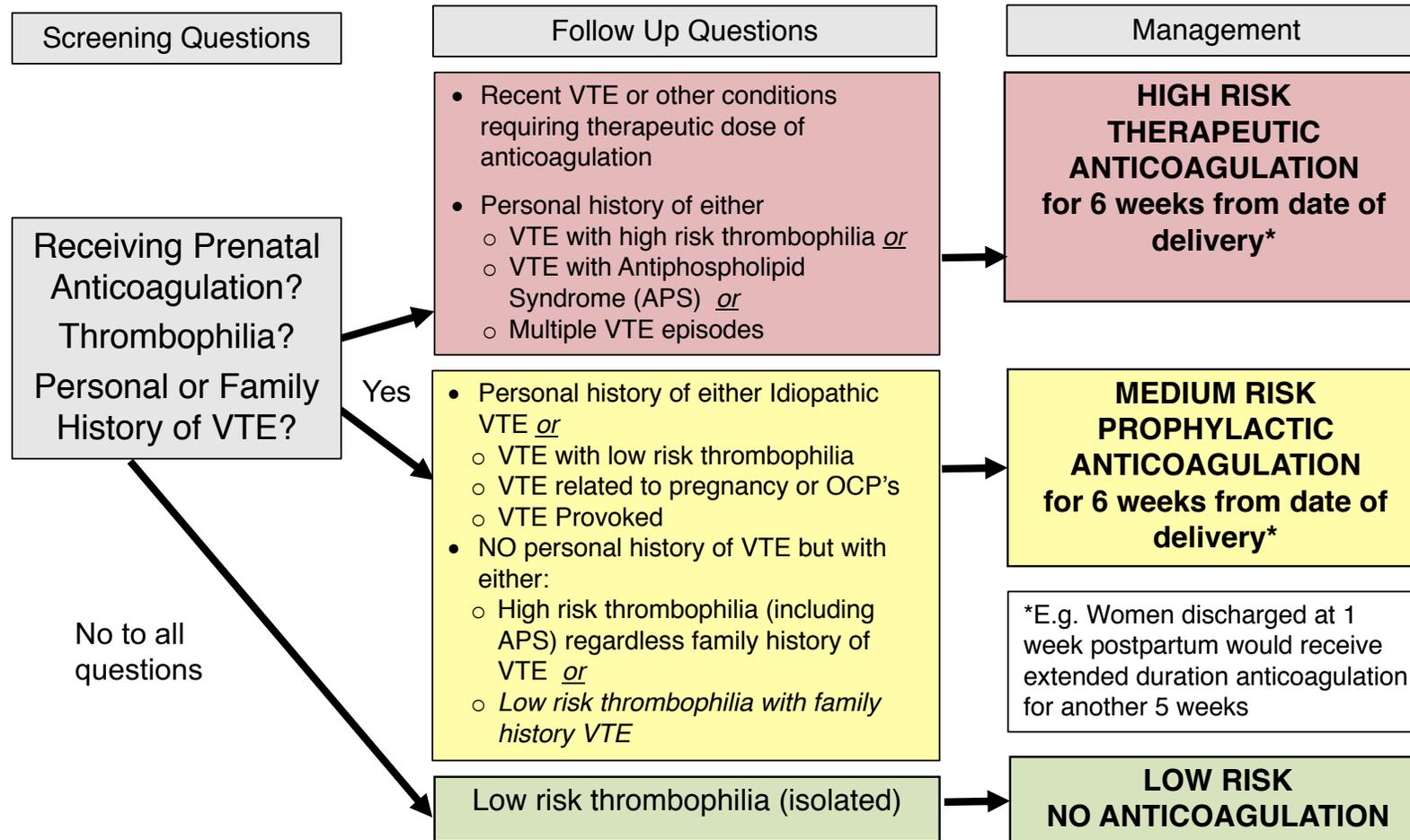
Clinical History	Risk Level	Anticoagulation
<input type="checkbox"/> Low risk thrombophilia	<b>LOW</b>	<b>No treatment</b>
<input type="checkbox"/> Prior idiopathic VTE <input type="checkbox"/> Prior provoked VTE <input type="checkbox"/> Prior VTE with pregnancy or oral contraceptive <input type="checkbox"/> Prior VTE with low risk thrombophilia <input type="checkbox"/> Family history of VTE with high risk thrombophilia <input type="checkbox"/> High risk or APS regardless of family history of VTE <input type="checkbox"/> Low risk thrombophilia and family history of VTE	<b>MEDIUM</b>	<b>Prophylactic dose LMWH or UFH for 6 weeks postpartum</b>
<input type="checkbox"/> Already on long term anticoagulation prior to pregnancy for VTE or any other reason <input type="checkbox"/> Multiple prior VTE episodes <input type="checkbox"/> Prior VTE with high-risk or APS	<b>HIGH</b>	<b>Therapeutic dose LMWH or UFH for 6 weeks postpartum (PP dose ≥ AP dose)</b>

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Please see [Definitions](#) for elaboration of key terms and dosages and page 19.

Algorithm 3: Post-Discharge Extended Duration Anticoagulation: Maternal VTE Risk Assessment

Please see [Definitions](#) for elaboration of key terms and dosages.



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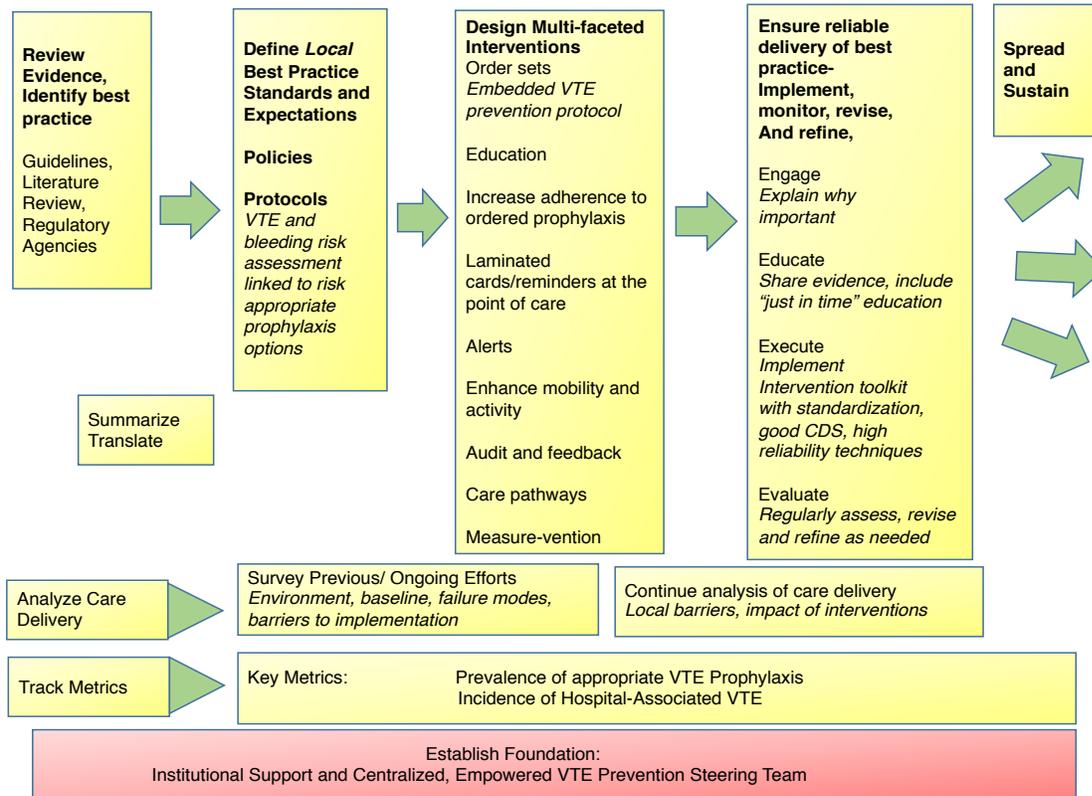
## IMPLEMENTATION STRATEGIES FOR VTE PREVENTION DURING PREGNANCY AND POSTPARTUM

### PART 1: Principles

Thus far, the CMQCC Maternal VTE Task Force have attempted to succinctly review guidelines and other literature, and summarized this material into tables and algorithms that highlight VTE risk stratification and risk appropriate prophylaxis for the pregnant woman at several phases throughout her pregnancy. In this section, The CMQCC Maternal VTE Task Force focuses on methods to translate these tables and algorithms into actual practice in a reliable manner in the clinical setting. These methods represent the art and science of implementation and quality improvement.

Using a Quality Improvement (QI) framework, principles of effective implementation and clinical decision support (CDS) can dramatically improve the chances of success. Figure 1 depicts a QI framework that has proven effective in VTE prevention and other QI efforts. This framework, drawn from common elements of QI models, is presented here in its current ARHQ format.<sup>25,117-120</sup>

Figure 1: Framework for Quality Improvement Focused on VTE Prevention



Source: Agency for HealthCare Research and Quality (AHRQ). This document is in the public domain and may be used and reprinted without special permission.<sup>25</sup>

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## Steps for Effective Implementation of VTE Prevention Strategies

### ***Step 1. Ensure support from the institution or practice***

Sponsorship and support from the administration and key leaders is essential. True support is reflected by prioritization of the VTE prevention effort, enforcing and enabling standardization of practice and order sets, and resources to build protocol driven order sets, documentation tools, and track measures of VTE prophylaxis and VTE rates.

### ***Step 2. Assemble an effective team***

In a clinic setting, the team might be quite small, but teams in a more complex hospital setting require broader representation. For multi-hospital systems, a VTE prevention steering team might devise protocols and order sets centrally, but each hospital still requires a team to address local implementation issues, barriers, education, and unique local circumstances. Interdisciplinary teams are essential:

- Physicians, nursing, and pharmacy professional are all essential members of the team.. Anesthesiologists must be involved to effectively address the use of anticoagulant prophylaxis around delivery, and to address safe use of anticoagulant prophylaxis with neuraxial analgesia.
- Additional desirable team members to be involved from the beginning include those with analytic and EMR expertise. An executive sponsor should be involved, if not present at every meeting, to keep hospital leadership engaged and supportive, and to help address barriers as they arise.
- QI facilitators / project managers can be very helpful in organizing, communication, and introducing QI tools at appropriate times as needed.
- Finally, consider including a patient representative. Hospitals are increasingly seeking input from patient and family advisory councils. This input can be especially valuable for many aspects of VTE prevention, for example, in developing patient educational materials and addressing adherence to mechanical prophylaxis.

The key dynamic for an effective team is the removal of authority gradients. Because the perspective of every team member is potentially critical, every perspective must be heard and each team member must be comfortable expressing his or her viewpoint.

### ***Step 3. Analyze care delivery, environment, facilitators and barriers***

In this step, team members survey the landscape for pre-existing order sets, protocols and policies, and identify cultural or structural barriers to improvement (e.g. lack of ability to measure prophylaxis, multiple OB groups with highly varied practices toward VTE prevention, etc.).

- Were there past attempts to address VTE prevention?

- What worked and what didn't work?
- What is the current work flow for ordering prophylaxis on admission, post-delivery, and at discharge?
- How does communication and coordination occur to avoid anticoagulant exposure at critical time periods with higher bleeding risk, such as initiation and cessation of epidural analgesia?

Mapping out the process and identifying the steps that are most likely to fail is a great way to focus improvement efforts. Having a good understanding of committee structure and the steps for changing policies and protocols fosters better communication and averts non-productive duplication of effort.

***Step 4. Define the scope of efforts, set realistic goals, specific (SMART) objectives, and timelines***

Prioritize and focus efforts by being specific about which population or problems are within the scope of your efforts.

- Will the team be tackling all the different phases of pregnancy, just the clinic, or just the hospitalization phases?
- Will the team work first on C-section, or try to address vaginal deliveries and admissions before delivery as well?

When setting goals for reducing VTE rates and reliably delivering protocol-driven prophylaxis, clinical leaders should identify specific aims that define the necessary steps that need to be completed along the way to attain the larger goals. For example, specific aims might include completing a literature search, designing an evidence-based algorithm, and designing and implementing a protocol driven order set for maternity patients delivering in the hospital, each with different timelines and accountable team members.

***Step 5. Review the evidence, distill into most important aspects, and translate into local best practice standards, policies, and protocols***

The CMQCC Maternal VTE Task Force has attempted to assist improvement teams by pre-digesting this complex literature and creating tables and algorithms that will furnish a great starting point, but much more work remains to attain the granular detail needed for local implementation. In this document the “protocol” refers to local definitions of best practice, operational definitions, and details that assign responsibility.

For example, whereas guidelines and the literature may say that mechanical prophylaxis (sequential compression devices or SCDs) is needed, a protocol will spell out who needs SCDs, who is responsible for putting SCDs on the patient, at what point in the process SCDs are recommended, and when it is acceptable to take them off, etc. Preferred anticoagulant prophylaxis for different situations should be specifically

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delineated. For prophylaxis before delivery or cesarean, for example, UFH 5000 units subcutaneous every 12 hours can be called out as the preferred prophylaxis, to allow a quicker diminution of anticoagulant effect, whereas for extended duration post-partum prophylaxis or prolonged prenatal prophylaxis, LMWH is likely preferred. In another example, anesthesiology and other services need to develop specific and reliable methods to minimize bleeding risks around neuraxial analgesia and procedures.

The protocol will be used to create educational material, measurement and documentation tools, and the design of order sets. Trying to design order sets before spending the time to create a thorough and thoughtful protocol is a recipe for mediocre results, and the importance of this step cannot be overstated.

Medical center policies add another layer of definition and reinforcement to local standards. Policies often require medical center committee or medical staff votes to alter them. These policies have a longer review and revision cycle. Policies will ideally state acceptable standards in more general terms, while protocols are more specific and easier to revise.

***Step 6. Design multi-faceted interventions to reinforce and integrate the protocol into practice.***

Creating a protocol is an important step, but all the work that goes into that task can largely go to waste, unless protocol guidance can be integrated into routine clinical care of the patient. Integrating VTE risk assessment into admission and post-delivery order sets is a key intervention in the inpatient setting, but this alone will not allow you to reach the high degree of performance required to optimize prophylaxis and reduce hospital associated VTE. Additional interventions reinforcing your protocol, layered on top of the essential VTE prevention order sets, are the key to success. Multiple active interventions (like alerts, active surveillance to correct lapses in care, checklists) are more effective than passive interventions (mass e-mail reminders, posters, etc.).<sup>121-126</sup> Design and implementation of protocol driven order sets is of such key importance that the CMQCC Maternal VTE Task Force will go into more depth on this later in this section.

***Step 7. Implement protocol, ensure reliable and valid delivery of best practice.***

While launching order sets is a key step, effective implementation requires engagement of stakeholders, education, ongoing evaluation, and other techniques to optimize prophylaxis.

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**Step 8. Monitor and track performance with well-defined metrics.**

Set up regular data collection and charting that is reliable, inexpensive, and directly relevant to the aims whenever possible. Key metrics include the prevalence of appropriate VTE prophylaxis, adherence to ordered prophylaxis, and the incidence of hospital associated – VTE. Measurement helps assess baseline performance, but should inform improvement efforts longitudinally.

**Step 9. Continue analysis of care delivery, address failures in process, redesign and tweak processes as needed.**

Monitoring must be ongoing to identify failures to deliver prophylaxis per protocol. It is also important to realize that the protocol may not serve all patients well, offering an opportunity to revise the protocol.

**Step 10. Develop a plan for continuous quality improvement (CQI) to achieve sustainability, maintenance and expansion.**

Spread efforts to other patients, hospitals, or clinics, and sustain ongoing VTE prevention efforts. Some monitoring is generally required to make sure earlier gains are being maintained, albeit perhaps on a less intense basis. If order sets, metrics, and documentation tools have been built thoughtfully, spread and sustainability are easier to achieve, particularly when a common electronic health record (HER) is in place. Spreading interventions and protocols should not consist of simply “turning on the switch” for EHR tools, however, as local factors, barriers, and different processes should be addressed in each new setting.

## **Introduction to the Hierarchy of Reliability**

The CMQCC Maternal VTE Task Force have already shared a working conceptual framework consisting of a multi-faceted intervention to achieve optimal VTE prophylaxis in Figure 1. The hierarchy of reliability is another construct that depicts different stages of the QI effort and the results the team can expect to have at each stage (See Table 12).<sup>25,27,123</sup> While the estimates of predicted performance may vary, the hierarchy of reliability has proven useful in glycemic control and anticoagulation improvement efforts.<sup>127-129</sup>

Within the Hierarchy, teams move away from Level 1 “State of Nature” by developing consensus on the definition of best care, embedding that definition as a protocol for standard work, and then monitoring and learning from variation from that protocol. Level 2 exists when protocol guidance exists, but is not present at the right time or place to influence VTE prevention orders, or when there is a simple listing of options for prophylaxis in order sets without guidance about preferred options.

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In the Hierarchy, the first real big “bang for the buck” comes at Level 3. At Level 3, a best-practice protocol is standardized through integration into the clinical workflow, most commonly by embedding the protocol within pre-printed or electronic order set. This integration with clinical workflow gives providers the information they need, when and where they need it, to make an appropriate choice. The order set must earn high utilization by being easy to use, concise, and clear.

Unfortunately, even the best order set will fail to achieve near perfect appropriate prophylaxis. Level 4 in the Hierarchy is achieved when the presence of Level 3 is augmented by additional strategies, such as traditional delayed audit-and-feedback to care teams about protocol use, integration of the protocol(s) into care pathways or checklists, automated alerts, and addressing factors that contribute to VTE such as failure to mobilize patients and poor adherence to mechanical prophylaxis.

The level achieved on the hierarchy of reliability is generally predictive of performance regarding the level of appropriate VTE prophylaxis. A protocol available at the point-of-care (Level 3), essential to embedding best-practice in the clinical workflow, establishes a foundation for other interventions (Level 4) and measure-vention (Level 5).

At Level 5, an improvement team uses measure-vention, a profound leap in reliability. Measure-vention is a form of active surveillance that identifies and *measures* patients on suboptimal prophylaxis on a regular basis and *intervenes* to correct lapses in care concurrently. Measure-vention creates improvement interventions directly from performance measurement. In other words, measure-vention introduces the variable of time to measurement systems: real time measurement can highlight today’s potential missed opportunities, creating an opportunity to address them immediately. As opposed to retrospective data collection commonly used to populate static dashboards, measure-vention techniques call for a regular measurement of performance on every pertinent patient at daily or more frequent intervals. Especially when outliers are identified electronically, measure-vention lends itself to automated data capture and display in run charts. Many examples of measure-vention are available.<sup>25,127</sup>

Table 12: Hierarchy of Reliability

Level	Characteristics	Predicted Performance
1	No protocol (“State of Nature”)	40%
2	Pseudo-protocol: Decision support exists but not linked to order writing, or prompts within orders but no decision support	50%
3	<b>Protocol:</b> Standardized decision support well integrated into orders at point of care	65-85%
4	Enhanced protocol: Complementary strategies increase use of protocol	90%
5	Measure-vention: Oversights identified and addressed in real time	90+%

Source: Agency for HealthCare Research and Quality (AHRQ). This document is in the public domain and may be used and reprinted without special permission.<sup>25</sup>

## Five Key Principles for Effective Implementation and Clinical Decision Support

Reaching Level 3 on the Hierarchy of Reliability (Table 12) is such an important step; the CMQCC Maternal VTE Task Force now reviews in more depth the principles for effective clinical decision support that make protocol integration into order sets more seamless and effective.

### ***Principle 1. Keep it simple for the end user.***

It is not practical to provide comprehensive guidance for the entire spectrum of patients and situations at the point of care. Improvement teams must strike a fine balance between providing a good risk assessment for most of the targeted population, yet keep the process simple and efficient for the end user. Almost always, simpler is better, and ease of use is more important than providing comprehensive guidance. Having links to comprehensive guidance within the order set is simple to do, but rarely effective, as clinicians rarely click on those links.

It is far more effective to provide less guidance in the same time and space where prophylaxis is ordered. Minimize calculations and data entry the end users must make, or automate that process for them. Ordering the correct VTE prophylaxis also becomes simpler and more reliable when options for prophylaxis are standardized to limit choices to a preferred few options, rather than including all options that might be acceptable by guideline.

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***Principle 2. Do not interrupt workflow.***

Ordering clinicians will have multiple demands competing for attention and time. In general, if an intervention interrupts workflow, it will be rejected. There are several implications for design and implementation of VTE prevention order sets. VTE prevention order sets enjoy the highest utilization when they simply appear as a module that is fully integrated into admission and post-procedural order sets that are already being used, rather than a stand-alone order set the clinician must go out of their way to identify and choose.

Ideally, the VTE risk assessment and bleeding risk assessment are performed quickly and concurrently, and the choices for that combination are directly presented to the provider, without interruption by intervals in time or space. For example, VTE risk levels described by simple text are offered in the order set. Once the VTE risk level is chosen, the appropriate prophylaxis options for that level of VTE risk emerges from their nested position under the risk designation, or the risk assessment data entered on the first Computerized Physician (or Provider) Order Entry (CPOE) screen triggers the appearance of a second screen that contains only the choices appropriate for that level of risk in an algorithmic fashion. The ordering provider is not asked to remember the risk designation from a previous screen, add up points, etc. These tasks are either done for them or eliminated from the process to provide a smooth and uninterrupted workflow.

***Principle 3. Design reliability into the process (inputs, results and outcomes are the same for all providers following the same policy and protocols).***

Do not expect humans to be perfect, especially in the complicated health care setting. Part of the team's job is to engineer higher reliability into the process of preventing hospital-acquired VTE. If the VTE protocol relies solely on traditional methods -- personal checklists, working harder next time, and education -- the team will be disappointed with the results. These traditional methods are not sufficient to achieve breakthrough improvement. The team should design order sets and reinforcing interventions that use some of the following high reliability strategies:

- Use a ***forcing function***. Completion of a VTE prevention order set can be made mandatory by a forcing function. Forcing functions should be used sparingly, but for enforcing VTE prevention, forcing functions are often justifiable and recommended.
- Make the desired action the ***default*** action (i.e., not doing the desired action requires opting out). Examples would include default selection of mechanical prophylaxis for all cesarean patients, along with further risk assessment to determine if anticoagulant prophylaxis was also warranted. In another example, as described above, only the protocol-preferred choices can be presented to the ordering provider after the VTE risk level has been selected. Progressive ambulation / mobility can be made the default mode, unless the physician provides guidance and opts out of that pathway.

- **Standardize** choices and care whenever feasible to do so, and **schedule** desired actions that are important. For example, an order to schedule a reassessment of VTE risk after the first 2-3 days in the hospital could prevent potential lapses in care.
- **Prompting** by use of human or electronic reminders can improve reliable care. For example, for patients with orders for mechanical prophylaxis but no documentation of mechanical prophylaxis being on and in place in the last shift, a prompt could remind nursing to place sequential compression devices (SCDs) or document why they are contraindicated.
- **Redundancy** for key steps should be used judiciously, but a redundant check to make sure proper prophylaxis is ordered and in place by pharmacy or nursing can insure physician errors or omissions are addressed.

***Principle 4. Pilot interventions on a small scale before attempting wide implementation.***

No plan survives its first contact with reality. Inevitably there will be glitches with a first pass at anything new. Piloting on a small scale creates opportunities to iron out glitches before implementing more broadly. Piloting in a live version of CPOE, limiting the order set to one ward or service, can be difficult or impossible in some centers. However, small-scale pilots can be as simple as a 5-minute focus group where five physicians give feedback on several versions of the protocol.

***Principle 5. Monitor use of the protocol (and the plan for measurement / monitoring).***

Rolling out the protocol is only a beginning. Monitoring can detect justifiable variations from the protocol that may instruct refinement, or detect variation that stems from lack of physician buy-in or lapses in process or education. Improvement teams should strive to make measurement an integral part of the process of patient care, by designing order sets and documentation in such a way that they can capture VTE risk, ordered prophylaxis, contraindications to prophylaxis, mobility, and whether mechanical prophylaxis is on or not. Information stored as discrete data elements can be recalled and organized into meaningful reports more easily than free text. Automating measures is easier if planned into the process at inception.

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## PART 2: Example Order Sets and Workflows

In this part, The CMQCC Maternal VTE Task Force walks through example order sets that fit the recommendations in this Toolkit and illustrate how they can be implemented into routine care. The CMQCC Maternal VTE Task Force concentrates on three key areas for our examples:

- Onset of Prenatal Care
- Antepartum Admission
- Post-cesarean delivery

### Workflow for Onset of Prenatal Care

**1. Laminate Algorithm 1: First Prenatal Visit: Maternal VTE Risk Assessment** and keep available in the office; educate office staff to the guidelines; ask them to highlight three screening questions (these are all you need!):

- Personal or Family History of VTE?
- Personal History of Thrombophilia?
- Current anticoagulant use?

**2. Integrate into the typical workflow:** In prenatal care the typical workflow includes starting with a detailed history and then creating a pregnancy management plan based on the positive responses. The algorithm works well for that.

**3. Use Algorithm 1: First Prenatal Visit: Maternal VTE Risk Assessment as the template for your Electronic Health Record.** It was designed fit the sequence of questions with three screening questions and nested follow-up questions leading to a recommended approach.

### Workflow for Antepartum Admissions

The CMQCC Maternal VTE Task Force have provided a conversion of Algorithm 2: Maternal VTE Assessment: Antepartum Hospital Admission Antepartum Algorithm into a sample Standard Order set. The CMQCC Maternal VTE Task Force kept it to a one level hierarchy that is the limit of many EHRs. One issue is the need to reevaluate status at 72 hours; recommend a specific order to remind the team. Each hospital will determine the choices for prophylactic and therapeutic doses to be displayed. A sample of such an order set is below (See Table 13).

Table 13: Order Set Example, Antepartum Admission for Maternal VTE Prevention

<b>DVT/PE Risk Level and Prophylaxis Orders: Antepartum Admission</b>		
	<b>Risk Criteria</b>	<b>Orders</b>
<b>Low Risk</b>	All patients without history of VTE, thrombophilia or current anticoagulant use admitted with <b>anticipated admission length of stay duration <math>\leq</math> 72 hours</b>	<p><input checked="" type="checkbox"/> Continuous use of knee-length Sequential Compression Device, per protocol, while not ambulating</p> <p><b>PLUS</b></p> <p><input checked="" type="checkbox"/> Nursing reminder to reassess need for chemoprophylaxis at 72 hours following admission (see Medium Risk below)</p>
<b>Medium Risk</b>	All patients without history of VTE, thrombophilia or current anticoagulant use admitted with <b>anticipated or actual length of stay <math>\geq</math> 72 hours</b>	<p>SAME ORDERS FOR BOTH MEDIUM AND HIGH RISK</p> <p><input checked="" type="checkbox"/> Continuous use of knee-length Sequential Compression Device, per protocol, while not ambulating</p> <p><b>PLUS PROPHYLACTIC DOSE PHARMACOPROPHYLAXIS</b></p> <p><input checked="" type="checkbox"/> UFH 5,000 units subcutaneous every 12 hours <i>Note: the anesthesia guidelines for this dosage call for NO DELAY if emergency neuraxial block required for delivery.</i></p> <p>OR, IF EMERGENT DELIVERY NOT ANTICIPATED</p> <p><input checked="" type="checkbox"/> Enoxaparin 40 mg subcutaneous once a day <i>Note: the ASRA 2010 anesthesia guidelines for this dosage call for a 12 HOUR DELAY if emergency neuraxial block required for delivery.</i></p>
<b>High Risk</b>	<p>Patients already receiving LMH or UFH as outpatients: At <b>prophylactic</b> dosing levels</p> <p>High risk thrombophilia, (including acquired) no prior VTE, regardless of family history</p> <p>Personal history of any VTE (Provoked, idiopathic, or estrogen related VTE)</p> <p>Low risk thrombophilia <b>WITH</b> family history of VTE <b>OR</b> single prior VTE</p>	<p>Continuous use of knee-length Sequential Compression Device, per protocol, while not ambulating</p> <p><b>PLUS THERAPEUTIC DOSE CHEMOPROPHYLAXIS</b></p> <p>UFH 10,000 units subcutaneous every 12 hours (Adjusted by Pharmacy to therapeutic range)</p> <p><input checked="" type="checkbox"/> Enoxaparin 40 mg subcutaneous every 12 hours (Adjusted by Pharmacy to therapeutic range)</p> <p><i>Note the ASRA 2010 anesthesia guidelines for these dosages call for a 6 HOUR DELAY (heparin) and a 24 HOUR DELAY (Enoxaparin/ Lovenox) if emergency neuraxial block required for delivery.</i></p>
<b>Highest Risk</b>	<p>Patients already receiving LMH or Unfractionated Heparin as outpatients:</p> <p><b>AT THERAPEUTIC DOSING LEVELS</b></p>	<p>Continuous use of knee-length Sequential Compression Device, per protocol, while not ambulating</p> <p><b>PLUS THERAPEUTIC DOSE CHEMOPROPHYLAXIS</b></p> <p>UFH 10,000 units subcutaneous every 12 hours (Adjusted by Pharmacy to therapeutic range)</p> <p><input checked="" type="checkbox"/> Enoxaparin 40 mg subcutaneous every 12 hours (Adjusted by Pharmacy to therapeutic range)</p> <p><i>Note the ASRA 2010 anesthesia guidelines for these dosages call for a 6 HOUR DELAY (heparin) and a 24 HOUR DELAY (Enoxaparin/ Lovenox) if emergency neuraxial block required for delivery.</i></p>

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## Workflow for Cesarean Birth

At the time of admission for labor, chemoprophylaxis is held until delivery. Use of Sequential Compression Devices can be considered for the highest risk patients but no guidelines exist. The most important decision points are prior to cesarean delivery, the postpartum orders and discharge.

### Recommendations

- Integrate into the pre-operative surgical checklist for cesarean birth: Sequential Compression Devices activated pre-operatively and a reminder to perform risk assessment for the post-operative order sets.
- Integrate VTE risk screening as part of the standard post-vaginal birth and post cesarean birth order sets. These order sets would need to be one-level hierarchy (the limit of many EHRs).
- Ideally the EHR could automatically add up the major and minor factors and lead the user to the right level of prophylaxis, but many EHRs cannot do that, so the example order set is designed as simply as possible to allow ease of use.
- Involve the anesthesia and pharmacy departments in the creation of the EHR algorithms for post-delivery prophylaxis.
- A sample of such an order set for cesarean delivery is provided below (See Table 13). It also provides a reminder order for discharge prophylaxis where appropriate.
- Each hospital will determine the choices for prophylactic and therapeutic doses to be displayed.

Table 14: Order Set Example, Post Cesarean Delivery for Maternal VTE Prevention

DVT/PE Prophylaxis Orders: POST CESAREAN DELIVERY																		
	Risk Criteria	Orders																
<b>Low Risk</b>	All patients without history of VTE, high risk thrombophilia or current anticoagulant use and not meeting moderate risk criteria (below)	<ul style="list-style-type: none"> <li>▲ For Cesarean delivery, knee-length Sequential Compression Device, per protocol, until fully ambulatory</li> </ul> <p><i>Note: VTE pharmacologic prophylaxis not indicated</i></p>																
<b>Medium Risk</b>	All patients without history of VTE, high risk thrombophilia or current anticoagulant use and who have <b>2 MAJOR OR 1 MAJOR AND 2 MINOR RISK FACTORS</b> from the table below: <table border="1" style="width: 100%; margin-top: 10px;"> <thead> <tr> <th style="width: 50%;">MAJOR VTE RISK FACTORS</th> <th style="width: 50%;">MINOR VTE RISK FACTORS</th> </tr> </thead> <tbody> <tr> <td>Any Cesarean Delivery</td> <td>Multiple gestation</td> </tr> <tr> <td>BMI <math>\geq 35</math> kg/m<sup>2</sup> at delivery</td> <td>Age <math>\geq 40</math></td> </tr> <tr> <td>Low risk thrombophilia</td> <td>VTE occurring in a first-degree relative before age 50</td> </tr> <tr> <td>Postpartum hemorrhage <i>requiring</i>: Transfusion or further operation, (e.g. hysterectomy, D&amp;C) or Interventional Radiologic procedure</td> <td>Postpartum hemorrhage <math>\geq 1000</math> ml but <i>not requiring</i>: Transfusion or further operation, (e.g. hysterectomy, D&amp;C) or Interventional Radiologic procedure</td> </tr> <tr> <td>Infection requiring antibiotics</td> <td>Smoker</td> </tr> <tr> <td>Antepartum hospitalization <math>\geq 3</math> days, current or within the last month</td> <td>Preeclampsia</td> </tr> <tr> <td>Chronic medical conditions</td> <td></td> </tr> </tbody> </table>	MAJOR VTE RISK FACTORS	MINOR VTE RISK FACTORS	Any Cesarean Delivery	Multiple gestation	BMI $\geq 35$ kg/m <sup>2</sup> at delivery	Age $\geq 40$	Low risk thrombophilia	VTE occurring in a first-degree relative before age 50	Postpartum hemorrhage <i>requiring</i> : Transfusion or further operation, (e.g. hysterectomy, D&C) or Interventional Radiologic procedure	Postpartum hemorrhage $\geq 1000$ ml but <i>not requiring</i> : Transfusion or further operation, (e.g. hysterectomy, D&C) or Interventional Radiologic procedure	Infection requiring antibiotics	Smoker	Antepartum hospitalization $\geq 3$ days, current or within the last month	Preeclampsia	Chronic medical conditions		<ul style="list-style-type: none"> <li>▲ Continuous use of knee-length Sequential Compression Device, per protocol, until fully ambulatory</li> </ul> <p><b>PLUS ANTICOAGULANT PROPHYLACTIC DOSING:</b></p> <ul style="list-style-type: none"> <li>▲ Heparin 5,000 units subcutaneous every 12 hours</li> </ul> <p style="text-align: center;"><b>OR</b></p> <ul style="list-style-type: none"> <li>▲ Enoxaparin 40 mg subcutaneous once a day</li> </ul> <p><b>For BMI &gt; 40 kg/m<sup>2</sup></b></p> <ul style="list-style-type: none"> <li>▲ Heparin 5,000 units subcutaneous every 8 hours</li> </ul> <p><i>Note: anesthesia guidelines for heparin call for a <math>\geq 1</math> HOUR WAIT TIME after spinal placement or epidural catheter removal.</i></p> <p style="text-align: center;"><b>OR</b></p> <ul style="list-style-type: none"> <li>▲ Enoxaparin 40 mg subcutaneous every 12 hours</li> </ul> <p><i>Notes:</i> ASRA 2016 unofficial anesthesia guidelines for enoxaparin/Lovenox call for a <math>\geq 12</math> HOUR WAIT after spinal placement or epidural catheter removal prior to first dose of enoxaparin</p> <p><i>Postpartum hemorrhage should be well controlled before anticoagulants administered.</i></p> <p><i>Post discharge VTE prophylaxis NOT INDICATED</i></p>
MAJOR VTE RISK FACTORS	MINOR VTE RISK FACTORS																	
Any Cesarean Delivery	Multiple gestation																	
BMI $\geq 35$ kg/m <sup>2</sup> at delivery	Age $\geq 40$																	
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Infection requiring antibiotics	Smoker																	
Antepartum hospitalization $\geq 3$ days, current or within the last month	Preeclampsia																	
Chronic medical conditions																		

(Table 14 continued on next page)

Table 14: Order Set Example, Post Delivery for Maternal VTE Prevention (*continued from previous page*)

<b>DVT/PE Prophylaxis Orders: POST CESAREAN DELIVERY (continued)</b>		
	<b>Risk Criteria</b>	<b>Orders</b>
<b>High Risk</b>	<p>Patients already receiving <b>prophylactic</b> dosing of LMWH or UFH as an outpatient</p> <p>High risk thrombophilia including antiphospholipid syndrome (APS) no prior VTE, regardless of family history</p> <p>Personal history of any VTE (provoked, idiopathic, or estrogen related)</p> <p>Low risk thrombophilia <b>WITH</b> family history of VTE <b>OR</b> single prior VTE</p>	<p>COMPRESSION DEVICE, AND HEPARIN OR ENOXAPARIN EXACTLY AS FOR MEDIUM RISK ABOVE</p> <p><b>PLUS (for all BMIs)</b></p> <p>▶ Discharge reminder for 6 weeks of PROPHYLACTIC dose anticoagulation</p>
<b>Highest Risk</b>	<p>Patients already receiving LMWH or UFH as outpatients: at <b>therapeutic</b> dosing levels</p> <p>Multiple Prior VTE</p> <p>Prior VTE <b>WITH</b> High Risk or APS</p>	<p>▶ Continuous use of Knee-length Sequential Compression Device, per protocol, until fully ambulating</p> <p><b>PLUS</b></p> <p>THERAPEUTIC DOSE ANTICOAGULATION</p> <p>▶ UFH 10,000 units subcutaneous every 12 hours (Adjusted by Pharmacy to therapeutic range) <i>Note: SOAP anesthesia guidelines for heparin call for a ≥ 1 HOUR WAIT after spinal placement or epidural catheter removal.</i></p> <p>▶ Enoxaparin 40 mg subcutaneous every 12 hours (Adjusted by Pharmacy to therapeutic range) <i>Note: ASRA 2010 anesthesia guidelines for enoxaparin/Lovenox call for a ≥24 HOUR WAIT after spinal placement or epidural catheter removal.</i></p> <p><b>PLUS</b></p> <p>▶ Discharge reminder for 6 weeks of THERAPEUTIC dose anticoagulation</p>

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### Part 3: Nursing Implications in VTE Assessment and Management

It is critically important that nurses working in the perinatal area be knowledgeable and proficient in the assessment of risk factors and use of prevention interventions to reduce the VTE risk in pregnancy and postpartum. To accomplish these tasks, the nurse needs to take a standardized approach to assessing each patient in the following manner as appropriate for the practice setting:

- Perform a standardized VTE risk assessment at the following times:
  - During the first prenatal visit
  - During any antepartum hospital admission including birth hospitalization
  - During the immediate postpartum period (just after the birth)
  - Upon discharge home after the birth
- Classify a woman’s VTE risk accordingly into Low, Medium or High VTE risk to determine treatment strategies. (See appropriate Risk Table depending on your practice setting)
- Assess for signs and symptoms of Deep Vein Thrombosis (DVT) or Pulmonary Embolus (PE)

Nurses should acquaint themselves with the risk factors for development of DVT such as prior deep vein injury (accident or surgery), increased estrogen exposure, prolonged bedrest during pregnancy, or the presence of other chronic medical conditions or risk factors previously mentioned in this toolkit.

Table 15: Signs and Symptoms of Deep Vein Thrombosis and Pulmonary Embolus

Deep Vein Thrombosis (DVT)	Pulmonary Embolism (PE)
<ul style="list-style-type: none"> <li>• Pain and/or tenderness of vein</li> <li>• Unilateral leg swelling</li> <li>• Warmth in skin of affected limb</li> <li>• Redness and/or discoloration</li> </ul>	<ul style="list-style-type: none"> <li>• Apprehension, feelings of “impending doom”</li> <li>• Sudden onset of dyspnea, tachypnea</li> <li>• Chest/pleuritic pain, neck vein distension</li> <li>• Dry cough, hemoptysis</li> <li>• Tachycardia</li> <li>• Hypoxia</li> <li>• Cyanosis</li> <li>• Syncope, hypotension</li> <li>• Sudden Collapse</li> </ul>

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Pulmonary embolism and DVT are often underdiagnosed. Therefore, nurses should be hyper-vigilant for signs and symptoms of DVT/PE to prevent delay in diagnosis and treatment. It is important to remember that women may be asymptomatic or have symptoms that mimic common conditions of pregnancy, such as swelling, tenderness and pain in the lower extremities, all of which are common in the second and third

trimesters. When examining a lower extremity for DVT diagnosis, a 2 cm discrepancy between calf measurements in the affected and unaffected leg is considered significant. DVTs most often develop in the lower legs, thigh, or pelvic region; however, they can also occur in the upper arm.

Pulmonary emboli from DVTs often present with a sudden onset of symptoms; dyspnea and tachycardia are the predominant presenting signs. (See Table 15) Because PE can be life threatening, any patient with a suspected or confirmed DVT should be monitored for PE. It is important to note that a PE can also be present without the signs and symptoms of a DVT.

### **Nursing Practices to Identify and Minimize VTE Risk in all Women**

- All hospitalized antepartum patients should be encouraged on admission to maintain full ambulation, adequate hydration and utilize mechanical prophylaxis (knee-length sequential compression devices) while in bed.
- Sequential compression devices should be used until 24 hours after the cesarean birth or until fully ambulatory.
- Administer anticoagulants as indicated by risk assessment and providers' orders 12-24 hours after cesarean birth.
- If a woman is on anticoagulants, monitor for bleeding and instruct her (and her significant others) to notify the health care team if she experiences any of the following: nose or gum bleeding, excessive bruising or hematuria.
- Provide women and their families with information on oral anticoagulants, including their impact on breastfeeding and the effect of other medications and foods that affect INR, including over the counter medications, prescriptions, and foods rich in Vitamin K (broccoli, lettuce, and spinach). In addition, advise women to notify their provider if they become pregnant or plan to conceive while on anticoagulant medications.
- Warfarin, LMWH, UFH are all compatible with breastfeeding.<sup>59,60</sup>
- Discharge instructions should be provided to the woman and her family which should include signs & symptoms of DVT/PE, when to notify her provider or seek urgent care as well as lifestyle changes and preventable risk factors (smoking, obesity). See [Maternal VTE Patient Education Handout](#).

Nurses play a pivotal role in the prevention of both DVT and PE among pregnant and postpartum women. Prevention strategies, inclusive of, but not limited to timely and appropriate recognition, early diagnosis and treatment, and education can save lives and have long-term effects on women's health. A long-term benefit of early diagnosis and treatment is a decrease in the risk of post-thrombotic syndrome as a complication that may lead to long term pain and venous insufficiency.

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## **Part 4: Maternal VTE Patient Education Handout**

### **BE AWARE!**

#### **Do you know the signs and symptoms of Blood Clots in Pregnancy or After Having a Baby?**

All pregnant and postpartum women are at higher risk for blood clots.

Blood clots in pregnant women usually form in the deep veins of the legs or in the pelvic area. This condition is known as deep vein thrombosis (DVT). These blood clots can break off and move to different parts of your body like the lungs or brain, and be life-threatening to you or your baby.

#### **What symptoms do I need to watch for during my pregnancy and up to six weeks after my baby is born?**

- Extreme swelling in your leg (or arm), especially in your calf and thigh
- Leg pain, tenderness, or persistent cramping
- Leg (or arm) warmer to the touch than other parts of the body
- Redness or bluish skin discoloration
- Severe shortness of breath
- Persistent or increasing headache and/or vision problems
- Irregular heartbeat or chest pains
- Fainting or feeling anxious
- Coughing up blood

#### **What should I do if I have any of these symptoms and they don't go away?**

**IMMEDIATELY** contact your obstetrician, midwife, family medicine doctor or your primary care provider

- Describe your symptoms clearly and explain how sick you feel, including any feelings of anxiety or dread
- If your symptoms occur postpartum, be sure to tell the provider you recently had a baby
- If your provider says your symptoms are normal, ask what symptoms should cause you to call or come back

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## When should I seek EMERGENCY MEDICAL CARE?

- If you have severe shortness of breath or feel extremely sick.
- If you are very sick and there isn't someone to drive you, call 9-1-1.
- If you are pregnant, make every effort to go to a hospital where there is obstetric (OB) care.

## What are my risk factors for developing a blood clot in pregnancy or after having a baby?

### ANY WOMAN CAN DEVELOP BLOOD CLOTS IN PREGNANCY OR POSTPARTUM BUT YOU ARE AT HIGHER RISK IF YOU:

- Have a personal or family history of blood clots
- Have a thrombophilia (blood clotting disorder)
- Smoke
- Are overweight
- Sit or lie still for long periods of time due to bed rest or long car or air travel
- Are over 35 years old
- Have a cesarean delivery of your baby
- Take estrogen containing oral contraceptives
- Have any combination of the above risk factors

### BOTTOM LINE: LISTEN TO YOUR BODY

- Trust your instincts when you feel something is wrong
- When you see a health care provider, bring your partner, friend or family member who can support you and help explain that these symptoms are not normal for you
- It's ok to get a second opinion if you don't feel listened to or your symptoms are not taken seriously

### Get online support and information

- The Shane Foundation
  - <http://www.shanefoundation.org/>
- National Blood Clot Alliance (NBCA)
  - <https://www.stopthecлот.org/>
  - <https://womenandbloodclots.org/pregnancy-and-post-childbirth/>
- American Society of Hematology
  - [www.hematology.org/patients/clots/pregnancy.aspx](http://www.hematology.org/patients/clots/pregnancy.aspx)
- Foundation of Women and Girls with Blood Disorders
  - <http://www.fwgbd.org/>

## **SLIDASET FOR PROFESSIONAL EDUCATION**

Attached separately

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## DEFINITIONS

<b>Antiphospholipid syndrome</b>	(APS); this diagnosis requires at least one clinical and one laboratory criteria are met
<b>Family History of VTE</b>	VTE occurring in a first-degree relative prior to age 50
<b>High risk thrombophilia</b>	Antithrombin III deficiency, Factor V Leiden or Prothrombin gene mutation homozygosity or compound heterozygosity
<b>Low risk thrombophilia</b>	Factor V Leiden or Prothrombin gene mutation heterozygosity, Protein C or S deficiency
<b>Mechanical prophylaxis</b>	Knee-length Sequential Compression Device (SCD)
<b>Prophylactic dose</b>	LMWH (Enoxaparin fixed dose 40 mg subcutaneous once a day) or <b>UFH</b> dosing trimester dependent. <sup>58</sup>
<b>Provoked VTE</b>	VTE associated with a temporary risk factor such as: Major/orthopedic surgery, indwelling catheter, or prolonged immobilization
<b>Therapeutic dose</b>	LMWH (Enoxaparin 1 mg/kg subcutaneous every 12 hours): Anti-factor Xa 0.6-1.0 units/mL 4-6 hours after injection with acute VTE or UFH 10,000 units subcutaneously or more every 12 hours: aPTT (1.5-2.5) 6 hours after injection.

**Note:** Dose adjustment may be considered with extremes of body weight (< 50 kg or > 90 kg). Additional detail is on page 16 in the Toolkit. Consultation and ongoing collaboration with Anesthesia is strongly recommended to individualize the choice and dose of pharmacological prophylaxis. If appropriate, low dose UFH 5000 units every 12 hours may facilitate neuraxial anesthesia.

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