



Venous Thromboembolism Diagnosis and Treatment – Adult – Inpatient/Ambulatory/Emergency Department-Clinical Practice Guideline

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Executive Summary

Guideline Overview

This guideline provides recommendations and guidance for the diagnosis and treatment of venous thromboembolism (VTE) in the inpatient, ambulatory and emergency department/urgent care settings.

Key Practice Recommendations

Treatment of venous thromboembolism (VTE) can be done with a variety of modalities including; anticoagulants, thrombolysis, surgical interventions or a combination of these treatment options. While there are a variety of options available there is limited data that directly compares the outcomes for these therapies. The selection of treatment options should be directed based on severity of clot burden and patient specific factors.

Companion Documents

Hyperlink any companion documents (algorithms, tables, forms, etc.) here.

1. [Diagnostic algorithm for DVT](#)
2. [Diagnostic algorithm for PE](#)
3. [Treatment algorithm for PE](#)
4. [Pulmonary embolism severity index scoring table](#)
5. [Anticoagulation treatment algorithm](#)
6. [Warfarin Management - CPG - Adult - Ambulatory](#)
7. [Warfarin Management - CPG - Adult - Inpatient](#)
8. [Therapeutic Dosing of Unfractionated Heparin - CPG - Adult](#)

Scope

Disease/Condition(s): VTE which most commonly consists of deep vein thrombosis (DVT) and pulmonary embolism (PE), but may also include other types of thrombosis.

Clinical Specialty: Primary Care Providers, Emergency Department Providers, Urgent Care Providers, Hospitalists, Cardiology, Surgical Specialities, Nursing, and Pharmacy

Intended Users: Physicians, Advanced Practice Providers, Nurses, and Pharmacists.

Objective(s): To assist clinicians in the diagnosis and treatment of venous thromboembolism

Target Population: Adult patients diagnosed with VTE in the ambulatory, inpatient, and/or emergency department/urgent care setting.

Interventions and Practices Considered: This guideline contains recommendations designed to assist clinicians in the diagnosis and treatment of patients with VTE:

- Utilization of probability score for diagnosis
- Diagnosis algorithms for DVT and PE
- Utilizing severity scores for outpatient treatment
- Selection of therapeutic treatment options based on patient specific risk factors

Major Outcomes Considered: Specific outcomes/performance measures considered for this guideline will include:

- Evaluation of treatment setting for VTE (i.e. inpatient, outpatient)
- Evaluation of treatment selection for VTE (i.e. anticoagulation, interventional procedure)
- Number of readmissions or complications post VTE Treatment

Methodology

Methods Used to Collect/Select the Evidence:

Electronic database searches (e.g., PUBMED) were conducted by the guideline author(s) and workgroup members to collect evidence for review. Expert opinion and clinical experience were also considered during discussions of the evidence.

Methods Used to Formulate the Recommendations:

The workgroup members agreed to adopt recommendations developed by external organizations and/or arrived at a consensus through discussion of the literature and expert experience. All recommendations endorsed or developed by the guideline workgroup were reviewed and approved by other stakeholders or committees (as appropriate).

Methods Used to Assess the Quality of the Evidence/Strength of the Recommendations:

Recommendations developed by external organizations maintained the evidence grade assigned within the original source document and were adopted for use at UW Health.

Internally developed recommendations, or those adopted from external sources without an assigned evidence grade, were evaluated by the guideline workgroup using an algorithm adapted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (see **Figure 1** in [Appendix A](#)).

Rating Scheme for the Strength of the Evidence/Recommendations:

See [Appendix A](#) for the rating scheme(s) used within this document.

Cost Analysis: \$ = \$0.01-\$1.00, \$\$ = \$1.01-\$10.00, \$\$\$ = \$10.01-\$50, \$\$\$\$ = > \$50

Table 1. Cost analysis – reflects cash pricing

Medication*	Price Per Dose (\$)	Price Per Month (\$)
Apixaban 10 mg	\$\$	----
Apixaban 5 mg	\$\$	\$\$\$\$
Dabigatran 150 mg	\$\$	\$\$\$\$
Edoxaban 60 mg	\$\$	\$\$\$\$
Enoxaparin 80 mg	\$\$	\$\$\$\$
Enoxaparin 100 mg	\$\$	\$\$\$\$
Enoxaparin 120 mg	\$\$\$	\$\$\$\$
Rivaroxaban 15 mg	\$\$	\$\$\$\$
Rivaroxaban 20 mg	\$\$	\$\$\$\$
Warfarin 5 mg	\$	\$\$

*Some of these agents may have patient assistance programs/vouchers that provide medications at low or no cost to the patient.

Introduction

Treatment of venous thromboembolism (VTE), which includes pulmonary embolism (PE) and deep vein thrombosis (DVT), can be done with a variety of modalities including; anticoagulants, thrombolysis, surgical interventions or a combination of these treatment options.^{1,2} While there are a variety of options available for VTE treatment there is limited data that directly compares the outcomes for these therapies. The selection of treatment options should be directed based on severity of clot burden and patient specific factors.¹ This guideline is intended to provide recommendations for diagnosis of VTE, selection of therapy and length of therapy.

Recommendations

Diagnosis of VTE

1. The diagnosis of VTE should be based on both clinical findings and diagnostic testing^{1,3,4} (*UW Health GRADE High quality evidence, strong recommendation*)
2. Clinical presentation for both PE and DVT are listed in Table 2.

Table 2 Common signs and symptoms of DVT and PE^{1,2}

DVT (uni-lateral)	PE
Swelling	Shortness of breath
Pain or tenderness	Pleuritic chest pain
Redness	Accelerated heart rate
Warmth	Temperature (low grade)
	Cough

3. In addition to symptoms, clinical probability scores and algorithms can identify patients who need further diagnostic testing to confirm the diagnosis of VTE^{1,3,4} (*UW Health GRADE High quality evidence, strong recommendation*)
 - 3.1 The Wells Prediction Score is one of the most widely used scoring tools for determining probability of DVT (Table 3) or PE (Table 4). Risk factors are given points which are additive.^{3,4}

Table 3 Wells score for predicting the probability of DVT – adapted³

Risk Criteria	Points
Recent treatment for cancer: (within previous 6 months) or palliative	1
Calf swelling: (≥ 3 cm compared to asymptomatic calf)	1
Swollen superficial veins in symptomatic leg: (unilateral)	1
Pitting edema in symptomatic leg (unilateral)	1
History of DVT	1
Entire leg swelling	1
Localized pain/tenderness	1
Recent surgery in previous 12 weeks or bedridden for ≥ 3 days	1
Paralysis, paresis or recent casting of lower extremities	1
Alternative diagnosis more probable than DVT: Baker's cyst, cellulitis, superficial venous thrombosis, post phlebotic syndrome or lymphadenopathy	-2

Score < 1: low probability and unlikely DVT

Score 1-2: moderate probability

Score >2: high probability

Table 4 Wells score for predicting the probability of PE – adapted⁴

Risk Criteria	Points
Clinical signs and/or symptoms of DVT	3
PE most likely diagnosis	3
Heart rate > 100 BPM	1.5
Recent surgery (previous 4 weeks) or immobilization (\geq 3 days)	1.5
Previous history of VTE	1.5
Hemoptysis	1
Recent treatment for cancer (within previous 6 months) or palliative	1

Score < 2: low probability
 Score 2-6: moderate probability
 Score > 6: high probability

3.2 For additional assistance to further rule out PE is the pulmonary embolism rule-out criterion (PERC). PERC is a decision support tool to assist with the decision for further diagnostic testing in patients with low clinical suspicion for PE⁵⁻⁸. The PERC criteria is listed in Table 5. Any answer of “Yes” warrants further diagnostic testing.

Table 5. Pulmonary embolism rule-out criteria (PERC) score – adapted⁵

PERC Criteria	
Age > 49 years	Yes/No
HR > 99 BPM	Yes/No
Pulse Oximetry < 95% on room air	Yes/No
Hemoptysis present	Yes/No
Taking exogenous estrogen	Yes/No
History of VTE	Yes/No
Recent surgery or trauma (<i>requiring intubation or hospitalization in previous 4 weeks</i>)	Yes/No
Unilateral leg swelling	Yes/No

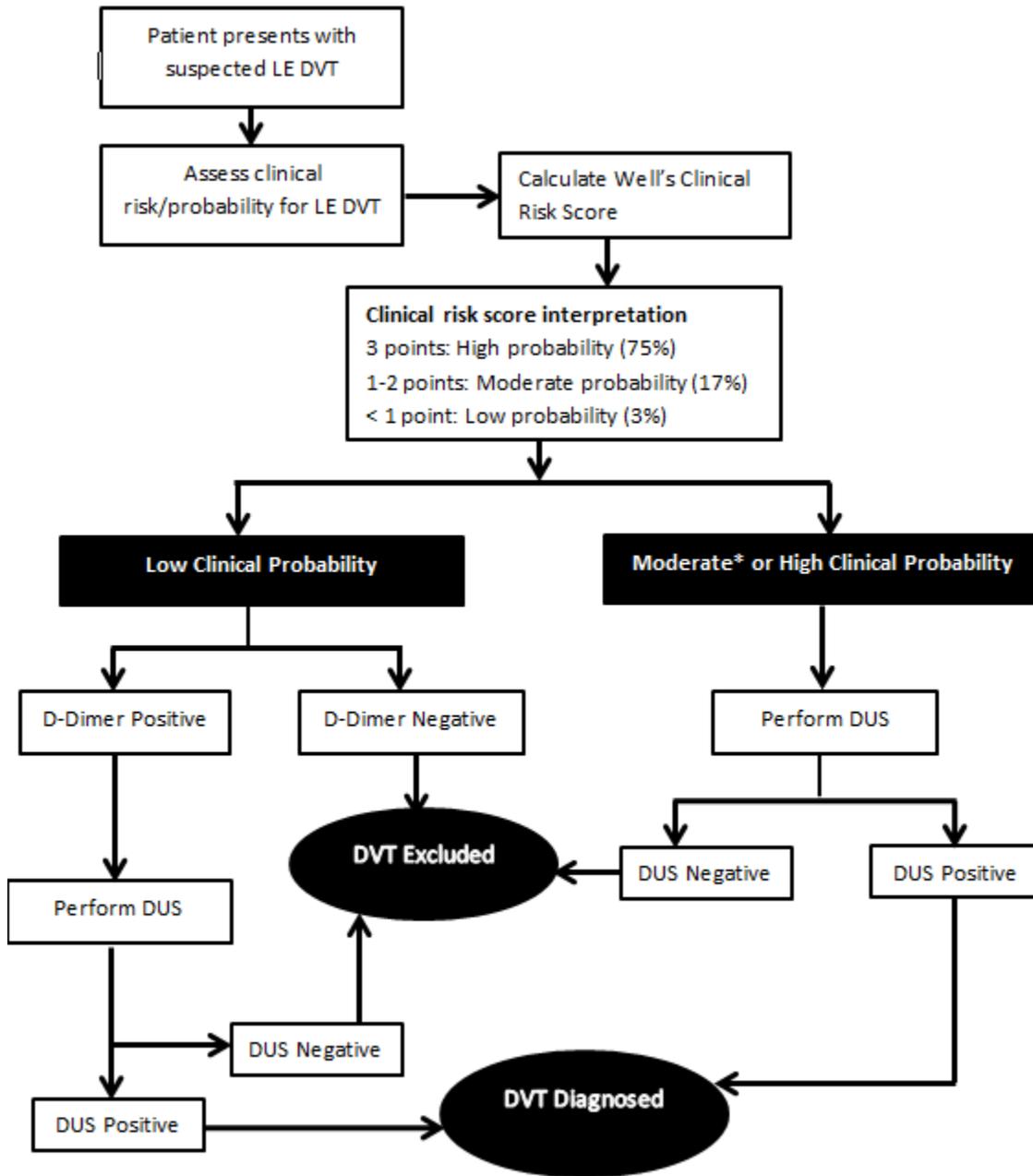
If “yes” to any of the above question than further diagnostic testing required

3.3 PERC has been studied for its ability to identify low risk VTE patients. Identifying low risk VTE patients using both clinical gestalt and a PERC negative score have demonstrated a false negative rate of 1-2.4%⁵⁻⁸.

4. Diagnostic algorithms for DVT and PE assist with standardizing the diagnostic approach using a combination of clinical presentation, probability scoring and laboratory testing¹.
(UW Health Moderate quality evidence, strong recommendation)

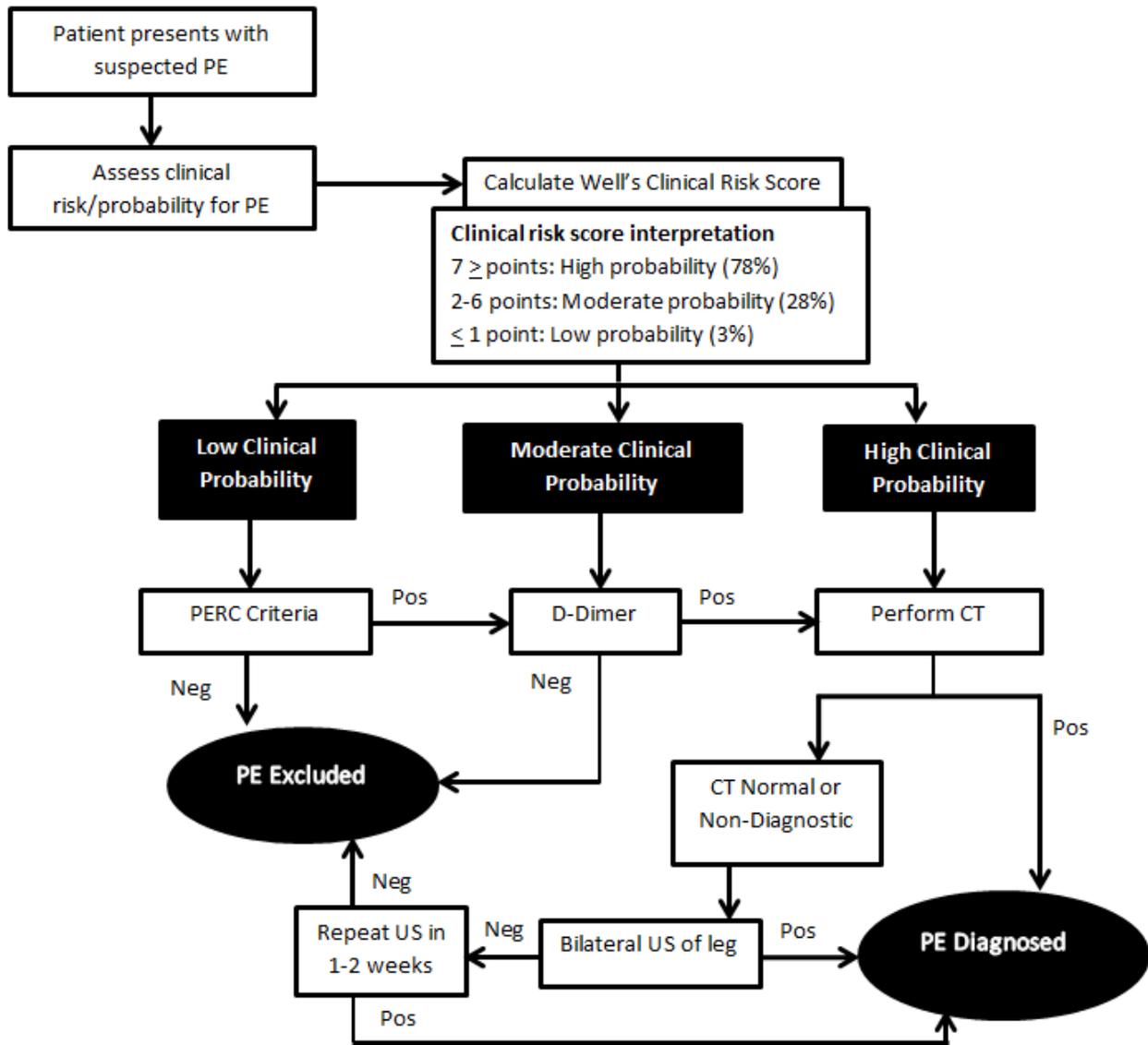
4.1 Figure 2 outlines the diagnostic algorithm for DVT and Figure 3 outlines the diagnostic algorithm for PE

Figure 2. Diagnostic algorithm for DVT¹



*Moderate Clinical Probability – if DUS not readily available a D-Dimer can be used to help rule out a DVT. If D-Dimer negative then DVT excluded. If D-Dimer positive then send for DUS.

Figure 3. Diagnostic algorithm for PE¹

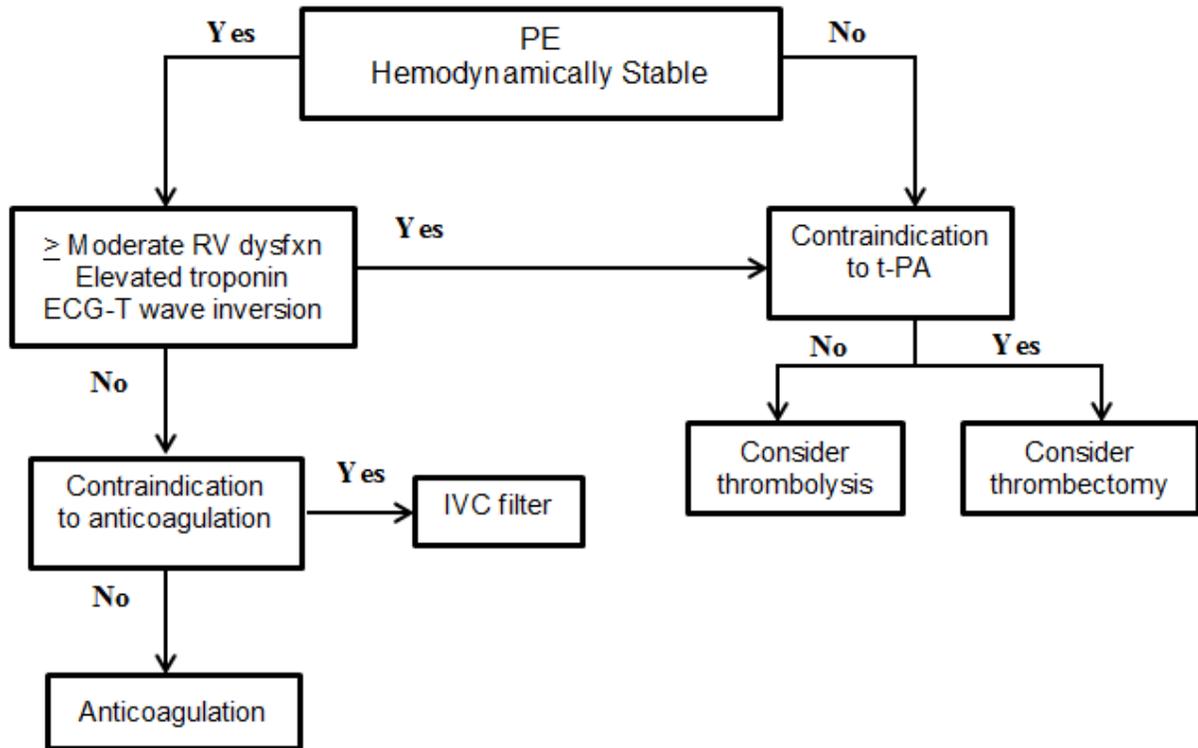


Treatment of VTE

When diagnosis of VTE has been confirmed treatment must be selected. There are many options available in addition to anticoagulation treatment including; surgical intervention, thrombolytic intervention or mechanical intervention.^{1,2,9} Considerations for each option should be weighed based on the severity of the clot, presentation of the patient and patient specific risk factors to select the best treatment for the patient.

5. Treatment algorithms can assist with identifying optimal strategies for treating VTE.^{1,2} (UW Health Moderate quality of evidence, weak/conditional recommendation)
Figure 4 outlines a treatment algorithm for PE

Figure 4. Treatment algorithm for PE



6. Treatment Settings

The majority of patients with DVT and low risk PE can be successfully treated in the outpatient setting. Outpatient management of acute DVT has not been associated with increased mortality, recurrent VTE or increases in major bleeding events and generally has been accepted as a standard of care.^{1,2} Outpatient management of PE, while not as well documented, has started gaining favor in the medical community. Two randomized trials and several observational studies have suggested that management of acute PE, in low risk patients, in the ambulatory setting did not increase mortality, recurrent VTE or major bleeding events.^{10-14.}

6.1 Eligibility criteria for outpatient PE management^{2,10-16} (UW Health Moderate quality evidence, strong recommendation)

- 6.1.1 ≥ 18 years of age
- 6.1.2 Diagnosis of acute pulmonary embolism
- 6.1.3 Able and willing to comply with home care
- 6.1.4 Able to obtain necessary medications

6.2 If patient meets the eligibility criteria, calculate the Pulmonary Embolism Severity Index (PESI) score as described in Table 6.^{15,16} (UW Health Moderate quality evidence, strong recommendation)

Table 6. Pulmonary Embolism Severity Index Scoring Tool^{15,16}

Age	+ 1 per year
Male	+ 10
Recent history of malignancy*	+ 30
Any history of Heart Failure	+ 10
Any history of Chronic Lung Disease	+ 10
Triage HR > 110	+ 20
Triage SBP < 100	+ 30
Triage Temp < 36C	+ 20
Triage RR > 29	+ 20
Triage Oxygen sat < 90%	+ 20
Altered Mental Status	+ 60

* Any diagnosis of cancer other than basal-cell or squamous-cell carcinoma of the skin, within the prior 6 months, any treatment for cancer in the previous 6 months, or recurrent or metastatic cancer¹⁵

- 6.2.1 If PESI score is ≥ 86 , hospitalize the patient^{15,16} (*UW Health Moderate quality evidence, strong recommendation*)
- 6.2.2 If PESI score is ≤ 85 , continue to the exclusion criteria^{15,16} (*UW Health Moderate quality evidence, strong recommendation*)

6.3 Additional exclusion criteria^{2, 15,16} (*UW Health moderate quality evidence, weak/conditional recommendation*)

- 6.3.1 Intracardiac or central vein thrombus
- 6.3.2 Central PE (main pulmonary artery)
- 6.3.3 Requires admission for reasons other than acute PE/DVT
- 6.3.4 Not appropriate for long term anticoagulation (unreliable, or unable to comply with follow up)
- 6.3.5 Any stroke in the last 6 weeks
- 6.3.6 Brain, spinal, or ophthy surgery (excludes cataract) in the last 6 weeks
- 6.3.7 Non-cutaneous surgery in the last 2 weeks
- 6.3.8 GI bleed in the last 2 weeks
- 6.3.9 Active major bleeding
- 6.3.10 Therapeutic anticoagulation at the time of diagnosis (e.g. INR ≥ 2)
- 6.3.11 Thrombocytopenia (Plt < 75,000 K/uL)
- 6.3.12 Bleeding disorder (e.g. Von Willebrand Disease)
- 6.3.13 Creatinine clearance ≤ 30 mL/min
- 6.3.14 Hypoxia (< 90% at any time in the ED)
- 6.3.15 Hypotension (SBP < 100mmHg at any time in the ED)
- 6.3.16 Evidence of RV strain on ECHO or CT (if obtained)
- 6.3.17 Treated with thrombolytics in the ED
- 6.3.18 Pregnant (verified by positive pregnancy test in woman of childbearing age)
- 6.3.19 > 150 kg
- 6.3.20 Elevated biomarkers (i.e. troponin, BNP)

- 6.4 If no to all exclusion criteria, then the patient may be managed with anticoagulant therapy in the outpatient setting with proper home instructions. See section 7 for treatment options. (*UW Health Moderate quality evidence, weak/conditional recommendation*)
- 6.5 Eligibility criteria for outpatient DVT management (*UW Health Moderate quality evidence, strong recommendation*)
- 6.5.1 ≥ 18 years of age^{1,2}
 - 6.5.2 Diagnosis of DVT
 - 6.5.3 Able and willing to comply with home care
 - 6.5.4 Able to obtain necessary medications
- 6.6 Exclusion criteria (*UW Health moderate quality evidence, weak/conditional recommendation*)
- 6.6.1 Requires admission for reasons other than acute DVT
 - 6.6.2 Diagnosis of PE (see #1)
 - 6.6.3 Impending gangrene due to venous thrombosis
 - 6.6.4 Not appropriate for long term anticoagulation (unreliable, or unable to comply with follow up)
 - 6.6.5 Any stroke in the last 6 weeks
 - 6.6.6 Brain, spinal, or ophthy surgery (excludes cataract) in the last 6 weeks
 - 6.6.7 Non-cutaneous surgery in the last 2 weeks
 - 6.6.8 GI bleed in the last 2 weeks
 - 6.6.9 Active major bleeding
 - 6.6.10 Therapeutic anticoagulation at the time of diagnosis (e.g. INR ≥ 2)
 - 6.6.11 Thrombocytopenia ($< 75,000$ Plt K/uL)
 - 6.6.12 Bleeding disorder (e.g. Von Willebrand Disease)
 - 6.6.13 Creatinine clearance ≤ 30 mL/min
 - 6.6.14 Treated with thrombolytics in the ED
 - 6.6.15 Pregnant (verified by positive pregnancy test in woman of childbearing age)
 - 6.6.16 > 150 kg
- 6.7 If no to all exclusion criteria, then the patient may be managed with anticoagulant therapy in the outpatient setting with proper home instructions. See section 7 for treatment options. (*UW Health moderate quality evidence, weak/conditional recommendation*)

7. Anticoagulation Treatment Options:

Therapeutic anticoagulation should be initiated as soon as possible.^{1,2} Patient specific factors should be considered when selecting an anticoagulant, as well as the treatment setting (inpatient versus outpatient). Benefits and risks of therapy options should be discussed with the patient, being sure to incorporate their priorities in the decision making process.¹

The direct oral anticoagulants (apixaban, dabigatran, edoxaban and rivaroxaban) are now considered the preferred agents for treatment of uncomplicated VTE not caused by cancer.^{1,2} Dose adjusted vitamin K antagonist (i.e. warfarin), low molecular weight heparin (LMWH) and unfractionated heparin (UFH) remain therapeutic options and may be preferred in specific clinical scenarios.^{1,2} Therapeutic options and special considerations for use are provided below. An algorithm for selecting therapy is provided in Figure 5.

7.1 Direct Oral Anticoagulants (DOACs)

Each DOAC has data to support the use in VTE compared to traditional treatment (i.e. warfarin and LMWH). There is no published data comparing DOACs to one another.¹⁷⁻²⁰ Each provides standardized dosing, quick onset of action (2-4 hrs), no monitoring of anticoagulation status, minimal lab monitoring, and minimal food and drug interactions. DOACs may interact with P-gp inducers and inhibitors and/or CYP 3A4 inducers or inhibitors. Refer to the drug interaction profile for the specific DOAC when prescribing.²¹⁻²⁴ When selecting a DOAC consider patient specific risk factors (highlighted in Table 7) as well as cost to the patient²⁵.

- 7.1.1 DOACs are the preferred treatment option for uncomplicated VTE not caused by cancer². (*CHEST Grade 1B*)
- 7.1.2 There is no indication for overlap of parenteral anticoagulation with LMWH or UFH²⁵ (*UW Health low quality of evidence, strong recommendation*)
- 7.1.3 If using dabigatran or edoxaban for VTE treatment, use of UFH or LMWH for 5-10 days before switching to oral agent is recommended.^{21,24} (*UW Health low quality of evidence, weak/conditional recommendation*)

Table 7 Direct Oral Anticoagulant for VTE Treatment – *Listed Alphabetically*²¹⁻²⁴

DOAC	Parenteral Lead-In	Dose	Dose Adjustments	Avoid Use When:
Apixaban	No	10 mg BID x 7 days then 5 mg BID After 6 months consider 2.5 mg BID for extended therapy	None	CrCl < 25 mL/min Aspirin doses > 162 mg/day Severe liver disease (Child-Pugh C)
Dabigatran	Yes LMWH 5-10 days prior	150 mg BID	None	CrCl < 30 mL/min ALT 2x upper limit of normal Used with any P-gp inducer CrCl < 50 mL/min and any P-gp inhibitor
Edoxaban (<i>non-formulary inpatient</i>)	Yes LWMH 5-10 days prior	60 mg daily	≤ 60 kg: 30 mg daily Use with any P-gp inhibitor: 30 mg daily	CrCl < 15 mL/min Moderate to severe liver disease (Child-Pugh B or C)
Rivaroxaban	No	15 mg BID x 21 days then 20 mg daily		CrCl < 30 mL/min ALT 3X upper limit of normal or Child-Pugh B or C

- 7.1.4 Use caution with all DOACs in the setting of dual or triple antithrombotic therapy as bleeding risks may be increased.²¹⁻²⁵ (*UW Health low quality of evidence, weak/conditional recommendation*)

7.1.5 DOACs should not be used in the following conditions as they either are contraindicated or have not been adequately studied. An alternative anticoagulant should be utilized for:¹⁷⁻²⁵ (*UW Health low quality of evidence, weak/conditional recommendation*)

- Prosthetic heart valves or significant valvular disease
- Pediatric patients (age < 18 years)
- Pregnant or lactating

7.2 Warfarin

7.2.1 Preferred oral anticoagulant option for patients who are not candidates for DOAC therapy (*CHEST Grade 2C*).

7.2.2 Due to delayed onset of action, overlap of parenteral anticoagulation with either LMWH or UFH should occur for at least 5 days AND until the INR \geq 2 of two consecutive INRs.^{1,2,26-29} (*UW Health High quality evidence, strong recommendation*)

7.2.3 Warfarin should be started on the same day as parenteral anticoagulation.²⁶⁻²⁸ (*CHEST Grade 1B*)

7.2.4 A baseline INR should be resulted prior to initiating warfarin therapy (*UW Health Very Low quality evidence, strong recommendation*)

7.2.5 Table 8 provides initial dosing recommendations for warfarin, however, more information can be found:

- [Warfarin Management - CPG - Adult - Ambulatory](#)
- [Warfarin Management - CPG - Adult - Inpatient](#)

Table 8. Warfarin dosing recommendations for VTE treatment²⁶⁻²⁸

Scenario	Dosing
Healthy individuals with no other reason for hospitalization or expected rapid INR response	Warfarin 10 mg x 2 doses then 5 mg daily for 1-2 days then based on INR
All other newly diagnosed VTE patients	Warfarin 2.5 - 5 mg PO daily for 3-4 days then based on INR
Start at lower dose (2.5 mg) if multiple risk factors for warfarin sensitivity exists:	
<ul style="list-style-type: none"> • Baseline INR > 1.5 • Actual body weight (ABW) < 45 kg • Significant drug interactions • Current antiplatelet therapy 	<ul style="list-style-type: none"> • Chronic diarrhea • Alcohol abuse history • Decompensated heart failure • Malnourished or NPO > 3 days

7.2.6 Prior to discharge from the emergency department, urgent care or hospital setting a follow up care plan that includes contact with the provider or clinic who will manage warfarin, plan for a follow up INR within 3-4 days of discharge, and education on compliance, dietary advice, follow up monitoring and drug interactions and adverse drug reactions must be provided to the patient and/or caregiver prior to ED discharge.²⁶⁻²⁸ (*UW Health Low quality evidence, strong recommendation*)

7.2.7 If outpatient INR monitoring cannot be established at the time of discharge then consider an alternative oral anticoagulant or parenteral anticoagulant. (*UW Health Very Low quality evidence, weak/conditional recommendation*)

7.3 Low Molecular Weight Heparin

7.3.1 Agent of choice for treatment of VTE in patients with cancer associated VTE, during pregnancy or for transitioning to warfarin.^{1,2,29} (*CHEST Grade 2C*)

- 7.3.2 Parenteral agent of choice for rapid therapeutic anticoagulation with an onset of action within 2 hours.^{1,2,29} (*UW Health Low quality evidence, strong recommendation*)
- 7.3.3 Dosing and special considerations are listed in Table 9.

Table 9 Enoxaparin dosing and special considerations for VTE treatment^{29,30}

Drug	Dosing
Enoxaparin (CrCl > 30 mL/min)	1 mg/kg subcutaneous every 12 hours
Enoxaparin (CrCl < 30 mL/min) <i>without renal replacement therapy</i>	1 mg/kg subcutaneous every 24 hours
Special considerations:	
<ul style="list-style-type: none"> • Dose based on actual body weight (no dose capping) • Twice daily dosing is preferred • Round to the nearest pre-filled syringe size 	

- 7.3.4 Routine anti-Xa monitoring is unnecessary for most patients as there is no evidence in the adult population to support this practice. (*UW Health Very Low quality evidence, weak/conditional recommendation*)
- 7.3.5 Anti-Xa monitoring may be considered in the following circumstances:^{29,31} (*UW Health Very Low quality evidence, weak/conditional recommendation*)
- Obesity (BMI ≥ 40 kg/M²) within 48-96 hours of initiation
 - CrCl < 30 mL/min after administration of 7-10 doses
 - Pregnancy after every 1-3 months of therapy
- 7.3.6 If anti-Xa monitoring is appropriate the level should be checked 4 hours after administration of the dose.³⁰ (*UW Health Low quality evidence, weak/conditional recommendation*).
- Table 10 provides dose adjustment recommendations for twice daily LMWH based on data from pediatric patients
 - Dose should be rounded to nearest syringe size.

Table 10 LMWH dose adjustments for twice daily therapeutic dosing³¹

Anti-Xa Level (units/ml)	Hold Next Dose	Dosage Change	Next Anti-Xa Level
< 0.35	No	Increase by 25%	4 h after next dose
0.35 - 0.49	No	Increase by 10%	4 h after next dose
0.50 - 1.10	No	No	If indicated
1.11 - 1.50	No	Decrease by 20%	4 h after next dose
1.51 - 2.00	anti-Xa before next dose if \leq 0.5 unit/mL then give dose	Decrease by 30%	4 h after next dose
> 2.01	Until anti-Xa < 0.5 units/ml	Decrease by 40%	Every 12 h until anti-Xa < 0.5 units/ml

- 7.3.6 Patients at risk for rectus sheath hematoma should discuss the risks versus benefit of using LMWH. Risk factors include:³² (*UW Health Low quality evidence, weak/conditional recommendation*)
- Chronic kidney disease
 - Concomitant antiplatelet therapy
 - Concomitant immunosuppression therapies

- Concomitant steroids
- Cough
- Female
- Injection technique: too close to the belly button
- Pregnancy
- Recent abdominal surgery
- Recent trauma

7.4 Unfractionated Heparin²⁹

7.4.1 Parenteral agent of choice for patients with renal dysfunction, on renal replacement therapy or when an anticoagulant with a shorter duration of action is needed (i.e. prior to surgical procedure). (*UW Health Very Low quality evidence, weak/conditional recommendation*)

7.4.2 Dosing and special considerations are listed in Table 11, however more information can be found:

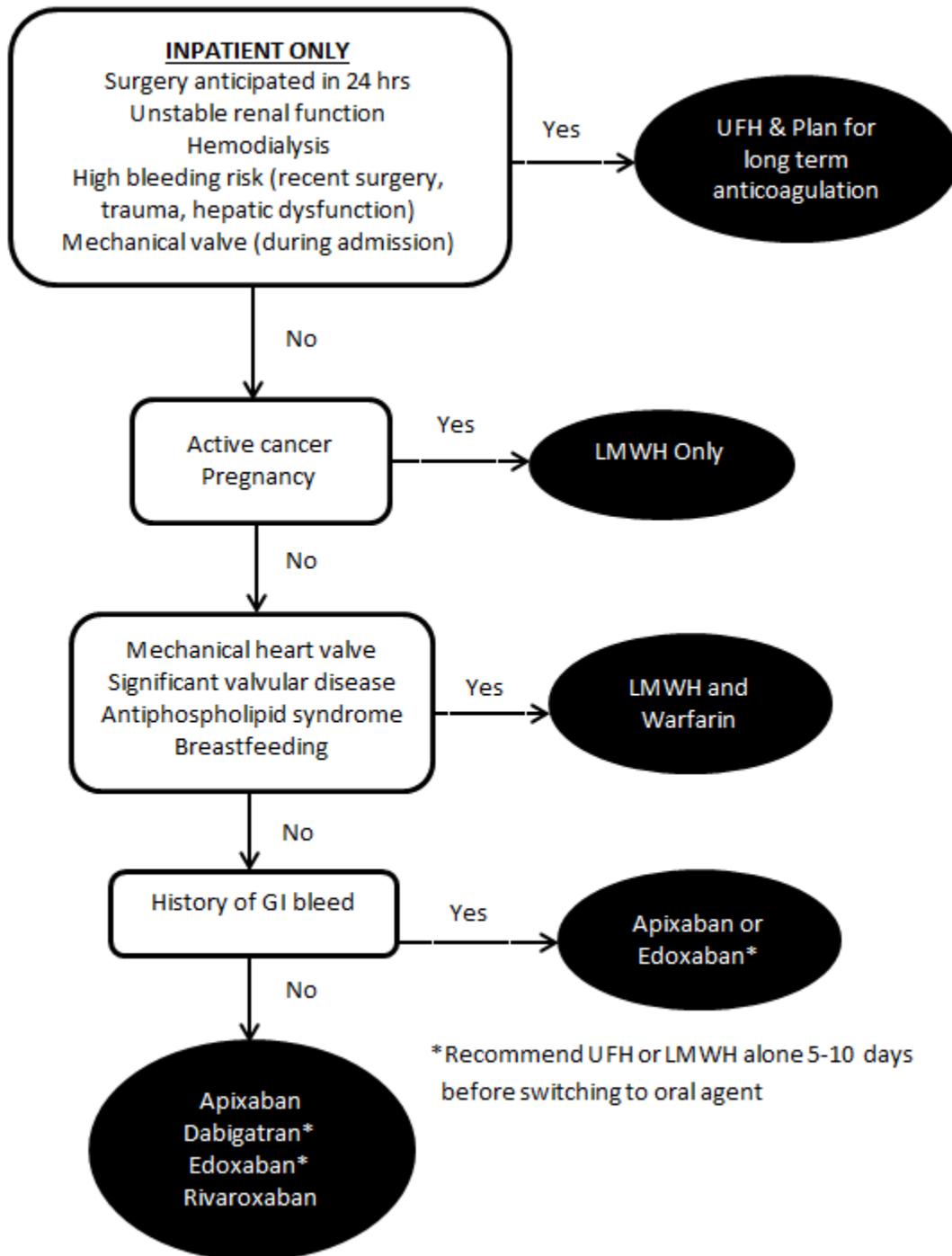
[Therapeutic Dosing of Unfractionated Heparin - CPG - Adult](#)

Table 11 UFH dosing and special considerations for selecting therapy^{29,33-34}

Drug	Dosing
Unfractionated Heparin (Intravenous)	Bolus: 80 units/kg Infusion rate: 18 units/kg/hr
Unfractionated Heparin (Subcutaneous)	Bolus: 333 units/kg Maintenance dose: 250 units/kg every 12 hours
<p>Special considerations:</p> <ul style="list-style-type: none"> • Dose based on actual body weight • Anticoagulation occurs within 18-24 hours (IV administration) • Requires frequent monitoring to ensure therapeutic levels • Subcutaneous administration requires patient education for both preparation and administration of dose 	

7.4.3 Routine monitoring is not needed for subcutaneous administration.²⁹ (*UW Health Very Low quality evidence, weak/conditional recommendation*)

Figure 5. Anticoagulation Therapy Algorithm for Inpatient and Ambulatory Settings



8. Thrombolytic Therapy Options

In a hemodynamically unstable patient with PE and significant right ventricular dysfunction, removal of the PE can improve respiratory and cardiovascular function, reduce symptoms of PE and improve survival³⁵. These, along with reducing the incidence of recurrent PE, preventing chronic thromboembolism pulmonary hypertension and improving quality of life are the main goals of thrombolytic therapy.⁹

An acute DVT in the iliac and common femoral veins have a higher risk for developing post-thrombotic syndrome (PTS). Removal of the DVT may reduce the risk of PTS and symptoms of DVT.² Additionally, in patients with limb-threatening circulatory compromise, thrombolytics can save a limb or organ and improve quality of life.⁹

However, thrombolytic strategies for removal of PE or DVT carry additional risks that must be considered (i.e. bleeding). Table 12 list both absolute and relative contraindications to thrombolytic therapy.³⁶ Strategies for thromboembolism removal may include systemic thrombolysis or catheter-directed thrombolysis.

Table 12 Contraindications to thrombolytic therapy³⁶

Absolute Contraindication	Relative Contraindication
Prior hemorrhagic CVA	Blood pressure > 180/110 mmHg
Any cerebrovascular event < 1 year	Use of anticoagulants
Active bleeding	Prolonged CPR > 10 minutes
Suspected aortic dissection	Prior gastrointestinal hemorrhage
Known intracranial neoplasm, arteriovenous malformation or aneurysm	Pregnancy
	Recent trauma (within 3 months)
	Recent surgery
	Non-compressible vascular punctures

8.1 Systemic thrombolysis

- 8.1.1 Systemic thrombolysis is indicated in massive PE with hypotension and right ventricular dysfunction.^{2,9,37} (*CHEST Grade 2B*)
- 8.1.2 It is not recommended for DVT as only partial efficacy was seen with increased bleeding when compared to anticoagulation alone.⁹ (*UW Health High quality evidence, strong recommendation*)
- 8.1.3 Systemic thrombolysis should be avoided in code situations where PE has not been confirmed. (*UW Health Weak quality evidence, weak/conditional recommendation*)
- 8.1.4 Dosing: Alteplase 100 mg intravenously infused over 2 hours.³⁶
- 8.1.5 Systemic thrombolysis is associated with an increased risk for bleeding and intracranial hemorrhage.^{2,9,36,37} (*UW Health High quality evidence, strong recommendation*)
- 8.1.6 Initiate UFH infusion at the gradual intensity after the alteplase infusion is complete. (*UW Health Weak quality evidence, weak/conditional recommendation*)

8.2 Catheter-Directed Thrombolysis (CDT)

CDT utilizes targeted therapy at the site of the thrombus. CDT has a benefit of utilizing lower doses of thrombolytics and lower incidence of intracranial hemorrhage than systemic thrombolysis.^{9,38-42} However, there are no randomized trials comparing outcomes with CDT versus systemic thrombolysis.

- 8.2.1 CDT may be considered for massive PE with hypotension and right ventricular dysfunction or in sub-massive PE with right ventricular dysfunction.^{2,9} (*UW Health Moderate quality evidence, weak/conditional recommendation*)
- 8.2.2 CDT may be considered for acute proximal DVT involving the iliac or common femoral vein at high risk for post thrombotic complications, or for limb threatening thrombosis if at low risk for bleeding.⁹ (*UW Health Moderate quality evidence, weak/conditional recommendation*)
- 8.2.3 Initiate UFH infusion prior to or during CDT procedure at the gradual intensity with no initial bolus.⁴¹ (*UW Health Moderate quality evidence, weak/conditional recommendation*)
- 8.2.4 After the alteplase infusion is complete and when the bleeding risk normalizes, transition the patient to a long term anticoagulation plan.^{9,38-42} (see section 7). (*UW Health Moderate quality evidence, weak/conditional recommendation*)

9 Surgical Intervention

- 9.1 Cardiac surgical consultation for emergent pulmonary embolectomy can be considered in the setting of significant hemodynamic instability with main or branch pulmonary arterial embolus.⁹ (*UW Health Very Low quality evidence, weak/conditional recommendation*)
- 9.2 May also consider surgical intervention with evidence of arterial embolism suggesting a patent foramen ovale (PFO) or with evidence of right heart dysfunction or strain on echocardiogram.⁹ (*UW Health Very Low quality evidence, weak/conditional recommendation*)
- 9.3 Therapeutic anticoagulation should be initiated as soon as adequate hemostasis is achieved. (*UW Health Very Low quality evidence, weak/conditional recommendation*)

10 Percutaneous Mechanical Intervention

- 10.1 Percutaneous mechanical intervention (i.e. AngioVac) may be considered if patient is not a surgical candidate and contraindications to thrombolytics exist.⁴³ (*UW Health Very Low quality evidence, weak/conditional recommendation*)
- 10.2 Initiate UFH infusion prior to or during procedure at the gradual intensity with no initial bolus. (*UW Health Moderate quality evidence, weak/conditional recommendation*)

11 Inferior Vena Cava (IVC) Filter

- 11.1 IVC filters may be considered in patients with acute VTE (within 4 weeks) who have contraindications to therapeutic anticoagulation^{1,9} (*UW Health Low quality evidence, weak/conditional recommendation*)
- 11.2 Indications for IVC filters are provided in Table 13

Table 13 Indications for IVC filter use^{1,9,42}

Approved Indications	Considerations
Contraindication to anticoagulation	Active bleeding Acute stroke Thrombocytopenia (platelet < 50)
Failure or complication from anticoagulation	Recurrent VTE while anticoagulated Bleeding while anticoagulated
Unable to achieve or maintain anticoagulation	
Relative Indications	
Massive PE with high fatality risk	Poor cardiopulmonary reserve Underlying cardiopulmonary disease Hemodynamically unstable
Massive PE treated with thrombolysis or thrombectomy	
VTE prophylaxis	Trauma with contraindication to anticoagulation Hip and knee replacement Bariatric surgery Neurosurgery Thrombolysis

11.3 IVC filters do not treat VTE. Therapeutic anticoagulation should be initiated as soon as adequate hemostasis is achieved. (*UW Health Low quality evidence, weak/conditional recommendation*)

11.4 IVC filters should be considered for removal when the risk for thrombosis or bleeding risk resolves and preferably within 6 months of placement.^{1,9} (*UW Health Low quality evidence, weak/conditional recommendation*)

Length of Anticoagulation Therapy

12 For most VTE events treatment should continue for at least 3-6 months^{1,2} (*CHEST Grade 1B*)

12.1 After 3-6 months of therapy a re-evaluation of VTE recurrence, bleeding risk, and patient preference should occur to determine if anticoagulation should continue or stop. (*UW Health Low quality evidence, weak/conditional recommendation*)

12.2 Table 14 lists recurrence rates for both provoked and unprovoked VTE.

Table 14 VTE recurrence rates^{44,45}

Type of VTE	Recurrence rates per year
Provoked (surgical)	0.7%
Provoked (non-surgical)	4%
Unprovoked	7%

12.3 For unprovoked VTE prediction tools have been used to identify lower risk women who may consider discontinuing anticoagulation. The HER DOO2 prediction tool was validated in a prospective multicenter study with a first provoked VTE.⁴⁶ The HER DOO2 prediction tool is listed in Table 15. (*UW Health High quality evidence, strong recommendation*)

12.4 Men have been shown to be associated with higher recurrent VTE rates per year for unprovoked VTE than compared to women (13.7% versus 5.5%) and should consider indefinite anticoagulation.⁴⁶ (*UW Health High quality evidence, strong recommendation*)

Table 15 HER DOO2 prediction tool⁴⁶

Risk Variables		Points
Age \geq 65 years		1
BMI \geq 30 kg/M ²		1
D Dimer \geq 250 mcg/L (while on anticoagulation therapy)		1
Signs of post-thrombotic syndrome (hyperpigmentation, swelling or redness of the leg)		1
Score		
0-1: Low Risk	May consider discontinuing anticoagulation	
\geq 2: High Risk	Continue anticoagulation indefinitely	

12.5 Additional risk factors for recurrent VTE are listed in Table 14

Table 14 Risk Factors for Recurrent VTE

Non-Reversible Risk Factors	Reversible Risk Factors
Inflammatory Bowel Disease	Hormone therapy
Antiphospholipid syndrome	Pregnancy
Male Gender	Post – partum (6-12 weeks)
Cancer	Obesity (BMI > 30 kg/M ²)
Abnormal D-Dimer (<i>after 3 months of anticoagulant therapy</i>)	

13 Discharge considerations

- 13.1 If a patient is discharged on warfarin a follow-up care plan for monitoring the INR must be in place prior to discharge from inpatient, emergency department or urgent care setting. (*UW Health Low quality evidence, weak/conditional recommendation*)
- 13.1.1 Contact must be made with the patient's primary care provider
- 13.1.2 If patient is discharged from the ED when the PCP clinic is closed, the ED case manager will contact the PCP on the following clinic day.
- 13.1.3 If outpatient INR monitoring cannot be established than an anticoagulant that does not require monitoring should be selected.
- 13.2 If an outpatient medication that can either increase bleeding or thrombotic risk is stopped, the prescribing provider will be notified of the change through either electronic medical record notification or through patient notification. (*UW Health Very Low quality evidence, weak/conditional recommendation*)
- 13.3 Follow up with a PCP should occur within 3-4 days of discharge. (*UW Health Low quality evidence, weak/conditional recommendation*)

UW Health Implementation

Potential Benefits:

Anticipated benefits associated with implementation and adherence to guidelines:

- Standardized approach to VTE management
- Avoid unnecessary admissions
- Increased patient satisfaction
- Cost avoidance (admissions, drug costs, lab costs)

Potential Harms:

Potential risks or adverse consequences associated with implementation and adherence to guidelines:

- Recurrent venous thromboembolism
- Patient non-adherence
- Possible higher readmission rate

Pertinent UW Health Policies & Procedures

1. None identified

Patient Resources

1. Health Facts For You #7522 – Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) Treatment and Prevention
2. Health Facts For You #6915 – Heparin (Unfractionated and Low Molecular Weight Heparin)
3. Health Facts For You #6900 – Warfarin (Coumadin[®], Jantoven[®])

Guideline Metrics

Using a numbered list, describe metrics to assess compliance with the stated recommendations or to gauge improvement resulting from implementation of the guideline.

NOTE: All metrics required or reported externally should be included (consider guidance from QSI).

1. Guideline adherence
2. VTE Performance Measure – VTE 3 – VTE patients with anticoagulation overlap therapy
3. VTE Performance Measure – VTE 5 – VTE discharge instructions
4. Hospital Acquired Condition – VTE events
5. Patient Safety Indicator (PSI) 12 – Post Operative VTE
6. PERT Consortium Registry – Benchmarking
7. IVC Filter Registry

Implementation Plan/Clinical Tools

1. Guideline will be posted on uConnect in a dedicated location for Clinical Practice Guidelines and externally on the uwhealth.anticoagulation.org/anticoagulation webpage.
2. Release of the guideline will be advertised in the Physician/APP Briefing newsletter.
3. Content and hyperlinks within clinical tools, documents, or Health Link related to the guideline recommendations (such as the following) will be reviewed for consistency and modified as appropriate.

Delegation Protocols

Initiation and Management of Warfarin – Adult – Ambulatory [7]

Pharmacist Management of Warfarin Delegation Protocol – Adult – Inpatient [12]

Heparin Infusion Titration Practice Protocol – Adult – Inpatient [4]

Order Sets & Smart Sets

ED – VTE Outpatient Care Discharge Order Set [4781]

IP/ED – Heparin Anticoagulation – Adult – Supplemental Order Set [4373]

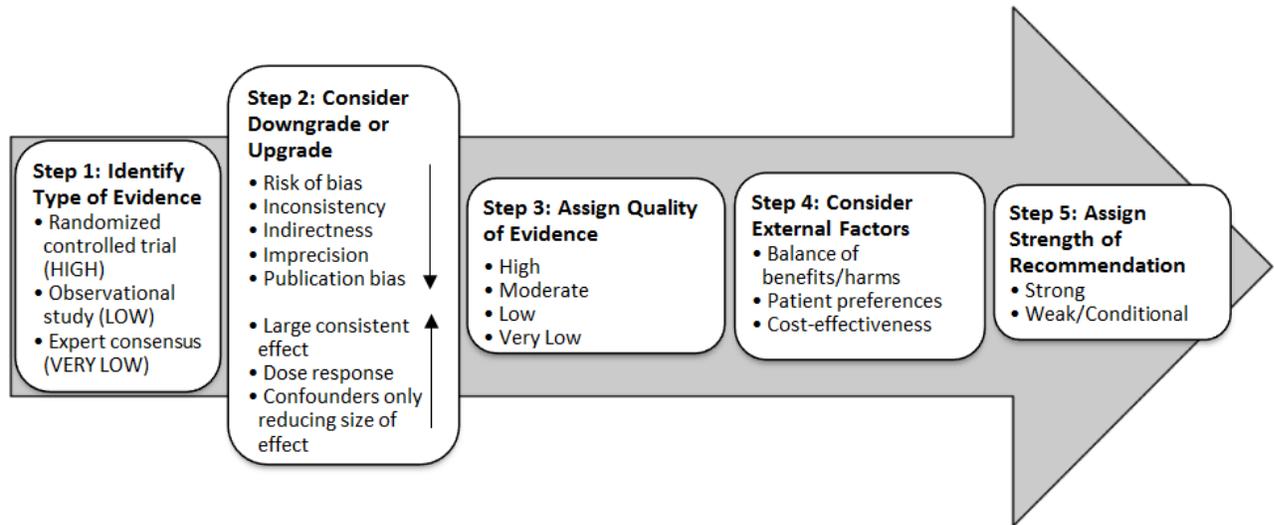
Disclaimer

Clinical practice guidelines assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is

understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

Appendix A. Evidence Grading Scheme(s)

Figure 1. GRADE Methodology adapted by UW Health



GRADE Ranking of Evidence

High	We are confident that the effect in the study reflects the actual effect.
Moderate	We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.
Low	The true effect may differ significantly from the estimate.
Very Low	The true effect is likely to be substantially different from the estimated effect.

GRADE Ratings for Recommendations For or Against Practice

Strong	The net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.
Weak/conditional	Recommendation may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.

Appendix B. Summary of Interim Revisions (As Appropriate)

Last Full Review	Summary of Revisions	Section (Page #)
MM/YY	List all revisions which were made between full periodic reviews.	

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