Venous Thromboembolism Prophylaxis– Adult– Inpatient/Ambulatory– Clinical Practice Guideline

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Executive Summary

Guideline Overview

This guideline is intended to provide recommendations for identifying individual venous thromboembolism (VTE) risk and bleeding risks for adult hospitalized patients and to provide recommendations for preventative therapies based on VTE and bleeding risk.

Target Population

The recommendations within this guideline for the prevention of VTE would apply to any adult patient with the intent to remain hospitalized for greater than 24 hours. The recommendations for pharmacologic strategies used to prevent VTE would apply to adult patients receiving either unfractionated heparin (UFH), low molecular weight heparin (LMWH) or fondaparinux.

Key Practice Recommendations

1. Prevention of VTE in Hospitalized Patients[2,5]
   1.1. All hospitalized patients should be evaluated for both bleeding and VTE risk within 24 hours of admission, upon transferring level of care, and periodically during the hospital stay ***(Class I, Level B)***

2. Evaluating VTE risk in medical patients
   2.1 The Modified Padua Risk Assessment Model should be used to assess VTE risk in medical patients.[2,4] ***(Class I, Level B)***

Table 1: Modified Padua Risk Assessment Model[2,4,6,7]

Risk Factor	Points
Critically Ill	4
Inflammatory Bowel Disease	4
Active Cancer*	3
Previous VTE	3
Reduced Mobility**	3
Thrombophilic Condition***	3
Recent (< 1month) Trauma/Surgery	2
Age ≥ 70 years	1
Heart or Respiratory Failure	1
Acute Myocardial Infarction or Ischemic Stroke	1
Acute Infection or Rheumatologic Disorder	1
BMI ≥ 30	1
Ongoing Hormonal Treatment	1

   2.2 Active cancer is defined as local or distant metastases and with chemotherapy or radiation in the previous 6 months
   2.3 Reduced mobility is defined as anticipated bed rest with bathroom privileges for at least 3 days
   2.4 Thrombophilic condition is defined as defects of antithrombin, protein C or S, factor V Leiden, G20210A prothrombin mutation, or antiphospholipid syndrome

Table 2: Modified Padua Risk Assessment Score[2,4] *(Class I, Level B)*

Points	Risk	Recommendation
< 4	Low VTE Risk	VTE prophylaxis not needed
≥ 4	High VTE Risk and **Low** Bleed Risk	Pharmacologic Prophylaxis
	High VTE Risk and **High** Bleed Risk	Mechanical Prophylaxis

Table 3: VTE Prophylaxis Regimens for High VTE Risk Medical Patients[2,8-14]

Patient Population	VTE Prophylaxis Regimens
Medical patients	Enoxaparin 40 mg SQ every 24 hours ***(Class I, Level B)*** OR Heparin 5000 units SQ every 8 to 12 hours ***(Class I, Level B)***
Renal impairment (CrCl < 30 mL/min)* *Not on renal replacement therapy	Enoxaparin 30 mg SQ every 24 hours ***(Class IIa, Level B)*** OR Heparin 5000 units SQ every 8 to 12 hours ***(Class I, Level B)***
Extreme obesity patients (BMI > 40 kg/M^2)	Enoxaparin 40 mg SQ every 12 hours ***(Class IIa, Level B)***
Low body weight patients (weight < 50 kg)	Enoxaparin 30 mg SQ every 24 hours ***(Class IIb, Level C)*** OR Heparin 5000 units SQ every 8 to 12 hours ***(Class I, Level B)***

3. Evaluating VTE risk in surgical patients
   - 3.1 The Caprini Risk Assessment Model should be used to assess VTE risk in general and abdominal-pelvic surgery patients.[3,15] ***(Class I, Level B)***
   - 3.2 Each risk factor is associated with a point value and the total risk score is cumulative.

Table 4: Caprini Risk Assessment

1 Point	2 Points	3 Points	5 Points
Age 41-60	Age 61-74	Age ≥ 75	Acute spinal cord injury (< 1 mo)
Acute MI (<1 mo)	Central venous access	Established thrombophilia	Elective lower extremity arthroplasty
BMI > 25	Immobile ≥ 72 hrs	HIT	Hip, pelvis, or leg fracture (< 1 mo)
CHF exacerbation (<1 mo)	Leg plaster cast or brace	Hx of VTE	Stroke (< 1 mo)
Hx of inflammatory bowel disease	Malignancy	Family hx VTE *(1 degree relative)*	
Procedure with local anesthesia	Surgery- arthroscopic		
Swollen legs or Varicose veins	Surgery > 45 mins		
Sepsis (< 1 mo)			
Serious lung dx *ex. Pneumonia* (<1 mo)			
1 point **(For Women Only)**			
Oral contraceptives or HRT			
Pregnancy or postpartum (< 1 month)			
Hx of unexplained stillborn infant, spontaneous abortion (≥3), premature birth with toxemia or growth restricted infant			

3.3 Established thrombophilia is defined as factor V Leiden, G20210A prothrombin mutation, antiphospholipid syndrome, lupus anticoagulant, elevated serum homocysteine, and heparin induced thrombocytopenia[3,17] ***(Class I, Level B)***

Table 5: Caprini Risk Assessment Score[3,15] ***(Class I, Level B)***

Points	Risk	Recommendation
0	Very Low VTE Risk	Early and frequent ambulation
1-2	Low VTE Risk	Mechanical Prophylaxis
3-4	Moderate VTE Risk and Low Bleed Risk	Pharmacologic Prophylaxis
≥ 5	High VTE Risk and Low Bleed Risk	Mechanical AND Pharmacologic Prophylaxis
> 2	High **Bleed** Risk	Mechanical Prophylaxis

Table 6: VTE Prophylaxis Regimens for High VTE Risk General Surgical Patients[3,8-10,13,14,16,17]

Surgical Patients	Enoxaparin 40 mg SQ every 24 hours ***(Class I, Level B)*** OR Heparin 5000 units SQ every 8 to 12 hours ***(Class I, Level B)***
Renal impairment (CrCl < 30 mL/min)* *Not on renal replacement therapy	Enoxaparin 30 mg SQ every 24 hours ***(Class IIa, Level B)*** OR Heparin 5000 units SQ every 8 to 12 hours ***(Class I, Level B)***
Bariatric Surgery	Enoxaparin 40 mg SQ every 12 hours ***(Class IIa, Level B)***
Major Trauma	Enoxaparin 30 mg SQ every 12 hours ***(Class IIa, Level B)***
Abdominal/Pelvic Surgery for Cancer	Enoxaparin 40 mg SQ every 24 hours ***(Class I, Level B)***

Companion Documents

AppendixB – Padua VTE Risk Assessment Model
AppendixC – Caprini VTE Risk Assessment Model
Appendix D – Orthopedic VTE Risk Assessment

Patient Resources:

HFFY 6915 – Heparin (Unfractionated and Low Molecular Weight)
HFFY 7522 – Deep Vein Thrombosis and Pulmonary Embolism Prevention and Treatment

Scope

Adult inpatients receiving unfractionated heparin (UFH), low molecular weight heparin (LMWH),or fondaparinux therapy for the prevention of venous thromboembolism (VTE).

Intended Users:

- Physicians
- Advanced Practice Providers
- Pharmacists
- Registered Nurses

CPG objective(s):

This clinical practice guideline is intended to provide recommendations for identifying patients who are at risk for developing VTE, to provide recommended therapy options to reduce the risk of VTE during hospitalization and to provide recommended therapy options for extended VTE prophylaxis after hospital discharge.

Target Population:

The recommendations within this guideline would apply to any adult inpatient with the intent to remain hospitalized for greater than 24 hours or who are discharged on extended VTE prophylaxis.

Interventions and Practices Considered:

The clinical interventions and practices recommended in this guideline are for the use of VTE risk assessment scoring, bleeding risk considerations, and therapy options for prevention of VTE. Practices may include utilizing the Caprini risk assessment score for surgical patients and the Modified Padua risk assessment score for medical patients. Therapy options to prevent VTE may include mechanical (e.g. sequential compression devices) or pharmacologic (e.g. UFH, LMWH or fondaparinux).

Major Outcomes Considered:

The major outcome considered for this guideline is the prevention of VTE with the therapy that is most appropriate based on individual patient VTE and bleeding risk.

Guideline Metrics:

There are many metrics related to the prevention of VTE that are monitored on a regular basis. The Surgical Care Improvement Project VTE prophylaxis metric, Meaningful Use VTE Metrics, Centers for Medicare and Medicaid Services VTE Metrics, Agency for Health Research Quality Patient Safety Indicators, and Hospital Acquired VTE cases. Each case is reviewed for appropriateness of preventative therapy based on VTE risk, bleeding risk and timing of prophylaxis.

Methodology

A modified Grading of Recommendations Assessment, Development, and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology Foundation has been used to assess the Quality and Strength of the Evidence in this Clinical Practice Guideline (Appendix A).[1]

A literature search conducted in Pubmed was completed to include the following search terms: ‘venous thromboembolism prophylaxis,’ ‘VTE prophylaxis in obesity,’ ‘VTE prophylaxis in renal dysfunction,’ ‘Caprini VTE prophylaxis,’ and ‘Padua VTE prophylaxis.’

Cost Analysis:

Table. 1 Cost Analysis

Medication	Q24H	Q12H	Q8H
Heparin 5000 units	---	$4.10	$6.15
Heparin 7500 units	---	$6.15	$9.20
Enoxaparin 40 mg	$5.60	$11.2	---
Enoxaparin 30 mg	$4.20	$8.40	---
Fondaparinux 2.5 mg	$10.81	---	---

Definitions: For the purposes of this guideline the following have been defined:

1. Extreme obesity – patients with a BMI > 40 kg/M^2

2. Renal dysfunction – patients with a CrCl< 30 mL/min or evidence of stage 4 [eGFR 15-29 mL/min/1.73M2] or 5 [eGFR < 15 mL/min/M2] renal dysfunction

3. Mechanical prophylaxis – methods may include graduated compression stockings (GCS), intermittent pneumatic compression devices (IPC), and venous foot pumps (VFP).[2]

Introduction

Hospital acquired VTE has been considered the most common cause of preventable death. Due to the multitude of both patient specific risk factors and procedural risk factors it can be difficult to determine what populations are considered high risk for VTE.[2,3]
Additionally, the prevalence of hospital acquired VTE has also been difficult to determine. Studies have reported hospital acquired VTE prevalence rates anywhere between 0.8% - 11% depending on the patient population evaluated.[2-4]

There have been many risk factors identified in both the medical and surgical patient populations that can increase the risk of developing VTE. These guidelines provide recommendations on the use of risk assessment models, validated in their respective patient populations, with the intent to identify patients who are at high risk for VTE and to provide recommendations for appropriate VTE prophylaxis modalities.

Recommendations

1. Prevention of VTE in Hospitalized Patients[2,5]
   - 1.1. All hospitalized patients should be evaluated for both bleeding and VTE risk within 24 hours of admission, upon transferring level of care, and periodically during the hospital stay ***(Class I, Level B)***
   - 1.2 Documentation of initial bleeding and VTE risk should occur in the medical record within 24 hours of hospital admission or postsurgical procedure ***(Class IIb, Level C)***

2. Evaluation of Bleeding Risk
   - 2.1 There is no universally validated model to assess bleeding risk[1] ***(Class I, Level C)***
   - 2.2 Factors with a strong association with bleeding risk in medical patients:[1,2] ***(Class I, Level B)***
     - 2.2.1 Active gastroduodenal ulcer
     - 2.2.2 Bleeding in the 3 months prior to admission
     - 2.2.3 Platelet count < 50 x10^9/L

2.3 Factors with a strong association with bleeding risk in surgical patients:[3] ***(Class I, Level B)***
- 2.3.1 Active bleeding or previous major bleeding
- 2.3.2 Renal failure (CrCl < 30 mL/min)
- 2.3.3 Hepatic failure (INR > 1.5 without anticoagulants)
- 2.3.4 Thrombocytopenia
- 2.3.5 Acute stroke
- 2.3.6 Uncontrolled systemic hypertension
- 2.3.7 Concomitant use of anticoagulants, antiplatelets or thrombolytics

3. Evaluating VTE risk in medical patients

3.1 The Modified Padua Risk Assessment Model should be used to assess VTE risk in medical patients.[2,4] ***(Class I, Level B)***

Table 1: Modified Padua Risk Assessment Model[2,46,7]

Risk Factor	Points
Critically Ill	4
Inflammatory Bowel Disease	4
Active Cancer	3
Previous VTE	3
Reduced Mobility	3
Thrombophilic Condition	3
Recent (< 1month) Trauma/Surgery	2
Age ≥ 70 years	1
Heart or Respiratory Failure	1
Acute Myocardial Infarction or Ischemic Stroke	1
Acute Infection or Rheumatologic Disorder	1
BMI ≥ 30	1
Ongoing Hormonal Treatment	1

3.2 Active cancer is defined as local or distant metastases and with chemotherapy or radiation in the previous 6 months

3.3 Reduced mobility is defined as anticipated bed rest with bathroom privileges for at least 3 days

3.4 Thrombophilic condition is defined as defects of antithrombin, protein C or S, factor V Leiden, G20210A prothrombin mutation, or antiphospholipid syndrome

Table 2: Modified Padua Risk Assessment Score[2,4] *(Class I, Level B)*

Points	Risk	Recommendation
< 4	Low VTE Risk	VTE prophylaxis not needed
≥ 4	High VTE Risk and **Low** Bleed Risk	Pharmacologic Prophylaxis
	High VTE Risk and **High** Bleed Risk	Mechanical Prophylaxis

Pooled data from 3 randomized trials evaluating the efficacy of GCS for the prevention of VTE in medical patients showed no benefit in preventing DVT or PE. GCS did increase the incidence of skin breakdown and ulcers. There are no published studies for the use of IPC or VFP in medical patients. Two meta-analysis in surgical patients showed IPC reduced risk of DVT with no effect on PE.[8-10]

3.5 When utilizing mechanical prophylaxis IPC devices are preferred ***(Class IIb, Level C)***

Table 3: VTE Prophylaxis Regimens for High VTE Risk Medical Patients[2,11-17]

Patient Population	VTE Prophylaxis Regimens
Medical patients	Enoxaparin 40 mg SQ every 24 hours ***(Class I, Level B)*** OR Heparin 5000 units SQ every 8 to 12 hours ***(Class I, Level B)***
Renal impairment (CrCl < 30 mL/min)* *Not on renal replacement therapy	Enoxaparin 30 mg SQ every 24 hours ***(Class IIa, Level B)*** OR Heparin 5000 units SQ every 8 to 12 hours ***(Class I, Level B)***
Extreme obesity patients (BMI > 40 kg/M^2)	Enoxaparin 40 mg SQ every 12 hours ***(Class IIa, Level B)***
Low body weight patients (weight < 50 kg)	Enoxaparin 30 mg SQ every 24 hours ***(Class IIb, Level C)*** OR Heparin 5000 units SQ every 8 to 12 hours ***(Class I, Level B)***

A single meta-analysis evaluating 12 randomized control trials comparing heparin every 8 hour and every 12 hour dosing regimens revealed similar VTE prevention outcomes. An increase in major bleeding events was seen in the every 8 hour dosing regimen.[14]

A single meta-analysis evaluating 16 randomized control trials comparing heparin every 8 hours, every 12 hours and LMWH revealed similar VTE prevention outcomes with no differences seen in major bleeding events.[15]

3.6 Enoxaparin is the preferred pharmacologic prophylaxis agent for medical patients. ***(Class IIb, Level C)***
- 3.6.1 If UFH is heparin is used the every 12 hours dosing regimen is preferred ***(Class IIb, Level C)***

3.7 Refusal of parenteral prophylaxis[18,19]
- 3.7.1 Oral anticoagulants may be considered in high VTE risk medical patients who refuse parenteral VTE prophylaxis ***(Class IIb, Level C)***
- 3.7.2 Apixaban and rivaroxaban have both been studied in this patient population versus enoxaparin. While similar outcomes in VTE prevention were seen when compared to enoxaparin, higher major bleeding was also seen with these agents.
- 3.7.3 Apixaban 2.5 mg by mouth twice daily ***(Class IIb, Level C)***
- 3.7.4 Rivaroxaban 10 mg by mouth daily ***(Class IIb, Level C)***
- 3.7.5 Avoid use in patients with CrCl < 30 mL/min

4. Evaluating VTE risk in surgical patients
- 4.1 The Caprini Risk Assessment Model should be used to assess VTE risk in general and abdominal-pelvic surgery patients.[5,20]***(Class I, Level B)***
- 4.2 Each risk factor is associated with a point value and the total risk score is cumulative

Table 4: Caprini Risk Assessment

1 Point	2 Points	3 Points	5 Points
Age 41-60	Age 61-74	Age ≥ 75	Acute spinal cord injury (< 1 mo)
Acute MI (<1 mo)	Central venous access	Established thrombophilia	Elective lower extremity arthroplasty
BMI > 25	Immobile ≥ 72 hrs	HIT	Hip, pelvis, or leg fracture (< 1 mo)
CHF exacerbation (<1 mo)	Leg plaster cast or brace	Hx of VTE	Stroke (< 1 mo)
Hx of Inflammatory Bowel Disease	Malignancy	Family hx VTE *(1 degree relative)*	
Procedure with local anesthesia	Surgery- arthroscopic		
Swollen legs or Varicose veins	Surgery > 45 mins		
Sepsis (< 1 mo)			
Serious lung dx *ex. Pneumonia* (<1 mo)			
1 point **(For Women Only)**			
Oral contraceptives or HRT			
Pregnancy or postpartum (< 1 month)			
Hx of unexplained stillborn infant, spontaneous abortion (≥3), premature birth with toxemia or growth restricted infant			

4.3 Established thrombophilia is defined as factor V Leiden, G20210A prothrombin mutation, antiphospholipid syndrome, lupus anticoagulant, elevated serum homocysteine, and heparin induced thrombocytopenia[3,20] ***(Class I, Level B)***

Table 5: Caprini Risk Assessment Score[3,20] ***(Class I, Level B)***

Points	Risk	Recommendation
0	Very Low VTE Risk	Early and frequent ambulation
1-2	Low VTE Risk	Mechanical Prophylaxis
3-4	Moderate VTE Risk and Low Bleed Risk	Pharmacologic Prophylaxis
≥ 5	High VTE Risk and Low Bleed Risk	Mechanical AND Pharmacologic Prophylaxis
> 2	High **Bleed** Risk	Mechanical Prophylaxis

Two meta-analyses in general surgery patients showed IPC versus no prophylaxis reduced risk of DVT but did not reduce the risk of PE or mortality.[21,22]

4.4 When utilizing mechanical prophylaxis IPC devices are preferred[21,22] ***(Class IIb, Level C)***

Table 6: VTE Prophylaxis Regimens for High VTE Risk General Surgical Patients[3,11-13,16,17,23,24]

Surgical Patients	Enoxaparin 40 mg SQ every 24 hours ***(Class I, Level B)*** OR Heparin 5000 units SQ every 8 to 12 hours ***(Class I, Level B)***
Renal impairment (CrCl < 30 mL/min)* *Not on hemodialysis	Enoxaparin 30 mg SQ every 24 hours ***(Class IIa, Level B)*** OR Heparin 5000 units SQ every 8 to 12 hours ***(Class I, Level B)***
Bariatric Surgery	Enoxaparin 40 mg SQ every 12 hours ***(Class IIa, Level B)***
Major Trauma	Enoxaparin 30 mg SQ every 12 hours ***(Class IIa, Level B)***
Abdominal/Pelvic Surgery for Cancer	Enoxaparin 40 mg SQ every 24 hours ***(Class I, Level B)***

5. Special Populations
   - 5.1 Acute kidney injury (AKI) or chronic kidney disease (CKD)
     - 5.1.1 UFH is the preferred agent for patients who are on renal replacement therapy[25] ***(Class IIb, Level C)***
     - 5.1.2 Enoxaparin 30 mg every 24 hours may be considered[12,13,17,25] ***(Class I, Level B)***
       - 5.1.2.1 Consider monitoring anti-Xa level after 7-10 doses to evaluate for accumulation
       - 5.1.2.2 Goal anti-Xa 0.2-0.4 units/mL
   - 5.2 Extreme Obesity[1113,17,25]
     - 5.2.1 Optimal thromboprophylaxis has not been established ***(Class I, Level C)***
     - 5.2.2 Preferred method for VTE prophylaxis is with LMWH
       - 5.2.2.1 Enoxaparin 40 mg every 12 hours ***(Class I, Level C)***
       - 5.2.2.2 Routine anti-Xa monitoring is not recommended ***(Class IIb, Level C)***
       - 5.2.2.3 Consider monitoring anti-Xa level after 7-10 doses to evaluate for accumulation (goal 0.2 – 0.4 units/mL) ***(Class IIb, Level C)***
     - 5.2.3 Prophylactic UFH has not been adequately studied in morbidly obese patients ***(Class I, Level C)***
       - 5.2.3.1 May consider heparin 7,500 units every 8 hours[26] ***(Class IIb, Level C)***
   - 5.3 Orthopedic Surgery

Table 7: VTE Prophylaxis Regimens for Orthopedic Surgery Patients[27-35]

Total Hip Arthroplasty	CrCl ≥ 30 mL/min	CrCl < 30 mL/min
Enoxaparin	Enoxaparin 40 mg SQ every 24 hours ***(Class I, Level B)***	30 mg SQ every 24 hours (avoid use in ESRD) ***(Class IIa, Level B)***
Rivaroxaban	10 mg by mouth once daily ***(Class IIa, Level A)***	Avoid use (***Class IIb Level C)***
Apixaban	2.5 mg by mouth twice daily* ***(Class IIa, Level A)***	No adjustment recommended* Avoid use in CrCl <15 ml/min or ESRD (per Canadian labeling) (***Class IIb Level C)***
Fondaparinux	2.5 mg SQ every 24 hours ***(Class IIa, Level A)***	Avoid use (***Class IIb Level C)***
Warfarin	Target INR goal 1.8-2.2 ***(Class IIb Level C)***	Target INR goal 1.8-2.2 ***(Class IIb Level C)***
Total Knee Replacement	**CrCl ≥ 30 mL/min**	**CrCl < 30 mL/min**
Aspirin	325 mg by mouth twice daily ***(Class IIb, Level C)***	325 mg by mouth twice daily ***(Class IIb, Level C)***

Enoxaparin	Enoxaparin 30 mg SQ every 12 hours ***(Class I, Level B)***	30 mg SQ every 24 hours (avoid use in ESRD) ***(Class IIa, Level B)***
Rivaroxaban	10 mg by mouth once daily ***(Class IIa, Level A)***	Avoid Use (***Class IIb Level C)***
Apixaban	2.5 mg by mouth twice daily* ***(Class IIa, Level A)***	No adjustment recommended* Avoid use in CrCl <15 ml/min or ESRD (per Canadian labeling) (***Class IIb Level C)***
Fondaparinux	2.5 mg SQ every 24 hours ***(Class IIa, Level A)***	Avoid Use (***Class IIb Level C)***
Warfarin	Target INR goal 1.8-2.2 ***(Class IIb Level C)***	Target INR goal 1.8-2.2 ***(Class IIb Level C)***

*patients with clinically significant renal impairment or CrCl < 30 mL/min were excluded from clinical trials

5.4 History of Heparin Induced Thrombocytopenia
- 5.4.1 Unfractionated and low molecular weight heparins are not recommended.[36] ***(Class III, Level A)***
- 5.4.2 Fondaparinux 2.5 mg SQ every 24 hours[34] ***(Class IIb, Level C)***

6. Extended duration VTE prophylaxis: VTE prophylaxis prescribed on discharge.

6.1 Bariatric surgery[16,37]
- 6.1.1 Patients with high VTE risk, low bleed risk and BMI $\geq$ 55 kg/m^2 ***(Class IIb, Level B)***
- 6.1.2 Enoxaparin 40 mg SQ every 12 hours for 10 days ***(Class IIb, Level B)***

6.2 Abdominal or pelvic surgery for cancer[38,39]
- 6.2.1 Patients with a cancer diagnosis who received a traditional laparotomy or vulvectomy and is either $\geq$ 60 years or < 60 years old with a history of VTE ***(Class IIb, Level C)***
- 6.2.2 Enoxaparin 40 mg SQ every 24 hours for 28 days ***(Class IIb, Level B)***
- 6.2.3 If patient refuses 28 days of prophylactic therapy then enoxaparin or UFH may be considered for 14 days ***(Class IIb, Level C)***

6.3 Orthopedic surgery (see Table 7 for VTE prophylaxis options)[40,41]
- 6.3.1 Total hip arthroplasty: 10-14 days ***(Class I, Level B)***
- 6.3.2 Total knee arthroplasty: 10-14 days ***(Class I, Level B)***
- 6.3.3 Hip fracture surgery: 10-14 days ***(Class I, Level B)***
- 6.3.4 For major orthopedic surgery may consider extended prophylaxis to 35 days ***(Class IIb, Level B)***

6.4 If patient refuses extended duration parenteral prophylaxis then oral prophylaxis may be considered[18,19] ***(Class IIb, Level C)***
- 6.4.1 See section 3.5 for recommendations

7. Anticoagulant Monitoring[42]

7.1 Platelets (PLT)
- 7.1.1 Baseline PLT must be obtained within 48 hours before starting prophylactic therapy with heparin or enoxaparin ***(Class IIb, Level C)***
- 7.1.2 Recheck PLT 24 hours after initiating heparin or enoxaparin therapy and every other day thereafter for up to 14 days or until therapy is discontinued ***(Class IIb, Level C)***
- 7.1.3 If PLT count decreases > 50% from baseline or if PLT count falls below 100 x 10^9/L; See Heparin Induced Thrombocytopenia – Adult- CPG **(Class IIb, Level C)**

7.2 Complete Blood Count (CBC)
- 7.2.1 Obtain a baseline CBC prior to initiating anticoagulant therapy ***(Class IIb, Level C)***
- 7.2.2 Recheck CBC a minimum of every 3 days thereafter ***(Class IIb, Level C)***

7.3 After hospital discharge PLT and CBC should be monitored only as clinically indicated ***(Class IIb, Level C)***

Companion/Collateral documents (as applies to CPG content)

1. Heparin Induced Thrombocytopenia – Adult – Clinical Practice Guideline
2. UWHC Administrative Policy 8.92: Epidural and Intrathecal (Neuraxial) Anesthesia

UW Health Implementation

Potential Benefits:

The benefits of this guideline include reducing hospital acquired VTE events by providing a method for screening medical and surgical patients for VTE risk using validated risk assessment tools and providing recommendations for appropriate VTE prophylaxis therapies. Additionally, this guideline provides recommendations for patient populations where data is limited or controversial (ex. Obese patients).

Potential Harms:

While it is anticipated that hospital acquired VTE events will be reduced as high risk VTE patients receive heparin based prophylactic therapies, there is the potential risk for increased bleeding events. There is not a universally validated bleeding risk model to use system wide, but this guideline does list risk factors that are associated with higher bleeding rates for both medical and surgical patients. Additionally, prophylactic heparin based therapies have a lower risk for bleeding than compared to therapeutic doses.

Implementation Plan/Tools:

Recommendations from this guideline will be incorporated into the required VTE prophylaxis section in all admission, transfer and post-operative order sets. The risk assessment appendices will be provided as a hyperlink in the order sets.

Disclaimer

CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice 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.

References

1. Tricoci P, Allen J, Kramer J, et al. Scientific evidence underlying the ACC/AHA Clinical Practice Guidelines. *JAMA*. 2009;301(8):831-841
2. Klein RC, Le H, Schulman S, et al. and M. Hassan Murad. Prevention of VTE in Nonsurgical Patients: Antithrombotic Therapy and Prevention of Thrombosis,9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines *Chest.* 2012;141;e195S-e226S.

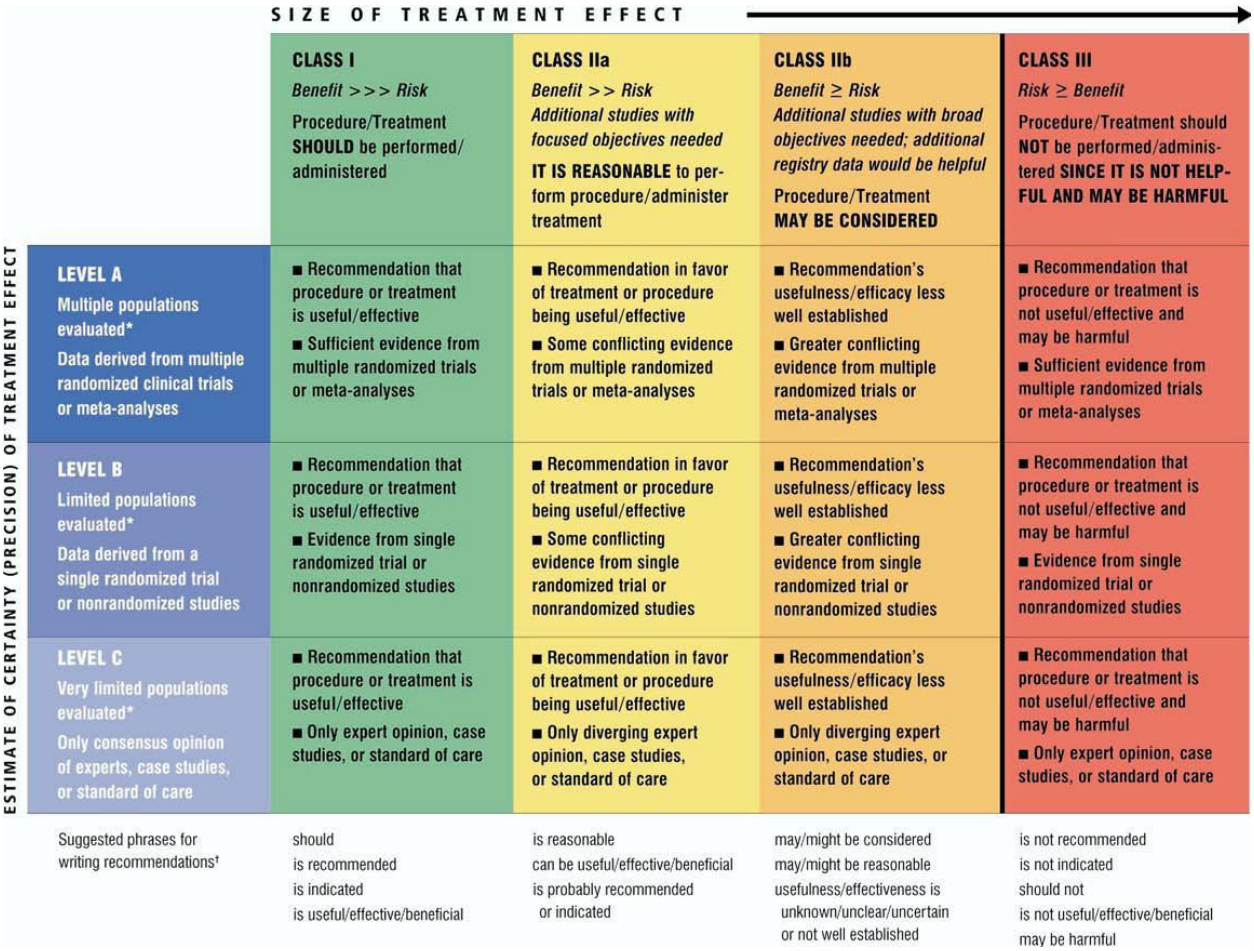
3. Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e227S-77S.
4. Barbar S, Noventa F, Rossetto V, et al. A risk assessment model for the identification of hospitalized medical patients at risk for venous thromboembolism: the Padua Prediction Score. *J Thromb Haemost.* 2010; 8(11):2450-2457.
5. Decousus H, Tupson VF, Bergman JF, et al. IMPROVE Investigators. Factors at admission associated with bleeding risk in medical patients: findings from the IMPROVE investigators. *Chest.* 2011;139(1):69-79.
6. Nguyen GC, Sam J. Rising prevalence of venous thromboembolism and its impact on mortality among hospitalized inflammatory bowel disease patients. *Am J Gastroenterol*. 2008;103:2272-80
7. Bernstein CN, Blanchard JF, Houston DS, Wajda A. The incidence of deep venous thrombosis and pulmonary embolism among patients with inflammatory bowel disease: a population-based cohort. *Thromb Haemost*. 2001;85:430-4

8. Kierkegaard A, Norgren L. Graduated compression stockings in the prevention of deep vein thrombosis in patients with acute myocardial infarction. *Eur Heart J.* 1993;14(10):1365-68
9. Dennis M, Sandercock PA, Reid J, et al. CLOTS Trials Collaboration. Effectiveness of thigh-length graduated compression stockings to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): a multicenter, randomized controlled trial. *Lancet,* 2009;373(9679):1958-65.
10. Muir KW, Watt A, Baxter G, et al. Randomized trial of graduated compression stockings for prevention of deep vein thrombosis after acute stroke. *QJM.* 2000;93(6):359-364
11. Heparin. In: *DRUGDEX® System* (internet database). Thomson Micromedex, Greenwood Village, Colorado, USA. Available at http://www.thomsonhc.com (cited October 12, 2012)

12. Enoxaparin. In: *DRUGDEX® System* (internet database). Thomson Micromedex, Greenwood Village, Colorado, USA. Available at http://www.thomsonhc.com (cited October 12, 2012)
13. Nutescu EA, Spinler SA, Wittkowsky A, and Dager W. Low-molecular-weight heparins in renal impairment and obesity: available evidence and clinical practice recommendations across medical and surgical settings. *Ann Pharmacother*. 2009; 43: 1064-83.
14. King CS, Holley AB, Jackson JL, et al. Twice daily vs three times daily heparin dosing for thromboembolism prophylaxis in the general medical population. *Chest.* 2007; 131:507-516.
15. Phung OJ, Kahn SR, Cook DJ, et al. Dosing frequency of unfractionated heparin thromboprophylaxis: a meta-analysis. *Chest.* 2011;140(2):374-381.
16. Scholten DJ, Hoedema RM, Scholten SE. A comparison of two different prophylactic dose regimens of low molecular weight heparin in bariatric surgery. *Obes Surg*. 2002; 12:19-24.
17. Duplaga BA, Rivers CW and Nutescu E. Dosing and monitoring of low-molecular-weight heparins in special populations. *Pharmacotherapy.* 2001; 21:218-34.
18. Goldhaber SZ, Leizorovicz A, Kakkar AK, et al. Apixaban versus enoxaparin for thromboprophylaxis in medically ill patients. *N Engl J Med.* 2011;365:2167-77.
19. Cohen AT, Spiro TE, Buller HR, et al. Rivaroxaban for thromboprophylaxis in acutely ill medical patients. *N Engl J Med.* 2013;368:513-23.
20. Bahl V, Hu HM, Henke PK, et al. A validation study of a retrospective venous thromboembolism risk scoring method. *Ann Surg.* 2010; 251(2):344-350.
21. Roderick P, Ferris G, Wilson K, et al. Towards evidence-based guidelines for prevention of venous thromboembolism: systemic reviews of mechanical methods, oral anticoagulation, dextran and regional anesthesia as thromboprophylaxis. *Health Technol Assess.* 2005;9(49):1-78.
22. Urbankova J, Quiroz R, Kucher N, et al. Intermittent pneumatic compression and deep vein thrombosis prevention. A meta-analysis in postoperative patients. *Thromb Haemost.* 2005;94(6):1181-5.
23. Geerts WH, Jay RM, Code KI, et al. A comparison of low-dose heparin with low-molecular-weight heparin as prophylaxis against venous thromboembolism after major trauma. *N Engl J Med*. 1996; 335: 701-7.
24. Bush S, LeClaire A, Hampp C, Lottenberg L. Review of a large clinical series: once- versus twice-daily enoxaparin for venous thromboembolism prophylaxis in high-risk trauma patients. *J Intensive Care Med*. 2011;26(2):111-5.

25. Garcia DA, Baglin TP, Weitz JI, et al. Parenteral Anticoagulants: Antithrombotic Therapy and Prevention of Thrombosis,9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e24S-43S.
26. Wang T, Milligan PE, Wong CA, et al. Efficacy and safetyof high-dose thromboprophylaxis in morbidly obese inpatients*. Thromb Haemost*. 2014; 111:88-93.
27. Turpie AG, Lassen MR, Eriksson BI, et al. Rivaroxaban for the prevention of venous thromboembolism after hip or knee arthroplasty. Pooled analysis of four studies. *Thromb Haemost*. 2011; 105(3):444-53.
28. Lassen MR, Gallus A, Raskob GE, et al. Apixaban versus enoxaparin for thromboprophylaxis after hip replacement. *N Engl J Med*. 2010; 363:2487-98.
29. Lassen MR, Raskob GE, Gallus A, et al. Apixaban versus enoxaparin for thromboprophylaxis after knee replacement (ADVANCE-2): a randomized double-blind trial. *Lancet*. 2010;375(9717):807-15.
30. Eriksson BI, Bauer, KA, Lassen MR, et al. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after hip-fracture surgery. *N Engl J Med*. 2001;345(18):1298-1304.
31. Bauer KA, Eriksson BI, Lassen MR, et al. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after elective major knee surgery. *N Engl J Med*. 2001;345(18):1305-10.
32. Rivaroxaban. In: DRUGDEX® System (internet database). Thomson Micromedex, Greenwood Village, Colorado, USA. Available at http://www.thomsonhc.com (cited August 6, 2014)
33. Apixaban. In: DRUGDEX® System (internet database). Thomson Micromedex, Greenwood Village, Colorado, USA. Available at http://www.thomsonhc.com (cited August 6, 2014)
34. Fondaparinux. In: DRUGDEX® System (internet database). Thomson Micromedex, Greenwood Village, Colorado, USA. Available at http://www.thomsonhc.com (cited August 6, 2014)
35. Falck-Ytter Y, Francis CW, Johanson NA, et al. Prevention of VET in Orthopedic Surgery Patients: Antithrombotic Therapy and Prevent of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e278S-325S.
36. Linkins L, Dans AL, Moores LK, et al. Treatment and Prevention of Heparin-Induced Thrombocytopenia: Antithrombotic Therapy and Prevent of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e419S-94S.
37. Raftopoulos I, Martindale C, Cronin A, et al. The effect of extended post-discharge chemical thromboprophylaxis on venous thromboembolism rates after bariatric surgery: a prospective comparison trial. *Surg Endosc.* 2008; 22(11): 2384-2391
38. Lyman GH, Khorana AA, Kuderer NM, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinic Oncology clinical practice guideline update. *J Clin Oncol.* 2013; 31(17):2189-2204
39. Schmeler KM, Wilson GL, Cain K. Venous thromboembolism rates following the implementation of extended duration prophylaxis for patients undergoing surgery for gynecologic malignancies. *Gynecol Oncol.* 2013; 128(2):204-208.
40. Falck-Ytter Y, Francis CW, Johanson N, et al. Prevention of venous thromboembolism in orthopedic surgery patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of CHEST Physicians evidence-based clinical practice guidelines. *CHEST.* 2012; 141: 278s-325s.
41. American Academy of Orthopedic Surgeons. Preventing venous thromboembolic disease in patients undergoing elective hip and knee arthroplasty, Evidence based guidelines and evidence report. September 24, 2011. http://www.aaos.org/research/guidelines/VTE/VTE_full_guideline.pef (accessed August 21, 2014)
42. Garcia DA, Baglin TP, Weitz JI, et al. Parenteral Anticoagulants: Antithrombotic Therapy and Prevention of Thrombosis,9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e24S-43S.

Appendix A. Modified Grading of Recommendations Assessment, Development, and Evaluation (GRADE)



ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT →			
	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	**CLASS IIa** *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	**CLASS IIb** *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	**CLASS III** *Risk ≥ Benefit* Procedure/Treatment should **NOT** be performed/administered **SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL**
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations†	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

Appendix B. Venous Thromboembolism (VTE) Prophylaxis – Adults CPG

VTE Risk in the Medical Patient – Modified Padua Risk Assessment Model – Adult – Inpatient

Risk factors for venous thromboembolism (VTE) in the medical patient

Risk Factor	Points
Critically Ill	4
Inflammatory Bowel Disease	4
Active Cancer*	3
Previous VTE	3
Reduced Mobility**	3
Thrombophilic Condition***	3
Recent (< 1month) Trauma/Surgery	2
Age ≥ 70 years	1
Heart or Respiratory Failure	1
Acute Myocardial Infarction or Ischemic Stroke	1
Acute Infection or Rheumatologic Disorder	1
BMI ≥ 30	1
Ongoing Hormonal Treatment	1

* Active cancer is defined as local or distant metastases and with chemotherapy or radiation in the previous 6 months

** Reduced mobility is defined as anticipated bed rest with bathroom privileges for at least 3 days

*** Thrombophilic condition is defined as defects of antithrombin, protein C or S, factor V Leiden, G20210A prothrombin mutation, or antiphospholipid syndrome

VTE prophylaxis recommendations based on risk score

Points	Risk	Recommendation
< 4	Low VTE Risk	VTE prophylaxis not needed
≥ 4	High VTE Risk and **Low** Bleed Risk	Pharmacologic Prophylaxis
	High VTE Risk and **High** Bleed Risk	Mechanical Prophylaxis

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Revised: 8/2014

Appendix C. Venous Thromboembolism (VTE) Prophylaxis – Adults CPG

VTE Risk in the Surgical Patient – Caprini Risk Assessment Model – Adult - Inpatient

Risk factors for venous thromboembolism (VTE) in the surgical patient

1 Point	2 Points	3 Points	5 Points
Age 41-60 years	Age 61-74 years	Age ≥ 75	Acute spinal cord injury (< 1 month)
Acute MI (<1 month)	Central venous access	Established thrombophilia*	Elective lower extremity arthroplasty
BMI > 25	Immobile ≥ 72 hours	HIT	Hip, pelvis, or leg fracture (< 1 month)
CHF exacerbation (<1 month)	Leg plaster cast or brace	Hx of VTE	Stroke (< 1 month)
Hx of inflammatory bowel disease	Malignancy	Family hx VTE *(1 degree relative)*	
Procedure with local anesthesia	Surgery- arthroscopic		
Swollen legs/ Varicose veins (current)	Surgery > 45 mins		
Sepsis (< 1 month)			
Serious lung dx *ex. Pneumonia* (<1 month)			

1 point **(For Women Only)**
Oral contraceptives or HRT
Pregnancy or postpartum (< 1 month)
Hx of unexplained stillborn infant, spontaneous abortion (≥3), premature birth with toxemia or growth restricted infant

Points are cumulative

* Established thrombophilia is defined as factor V Leiden, G20210A prothrombin mutation, antiphospholipid syndrome, lupus anticoagulant, elevated serum homocysteine, and heparin induced thrombocytopenia

VTE prophylaxis recommendations based on risk score

Points	Risk	Recommendation
0	Very Low VTE Risk	Early and frequent ambulation
1-2	Low VTE Risk	SCD
3-4	Moderate VTE Risk and Low Bleed Risk	Enoxaparin or Heparin
≥ 5	High VTE Risk and Low Bleed Risk	Enoxaparin or Heparin **AND** SCD
> 2	High **Bleed** Risk	SCD

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Appendix D. Venous Thromboembolism (VTE) Prophylaxis – Adults CPG

VTE Risk in the Surgical Orthopedic Patient – Adult - Inpatient

Orthopedic VTE Risk Assessment

Elevated VTE risk*

- Cancer (current or previous history)
- Previous DVT or PE
- Hypercoagulable state
- Multiple trauma
- Spinal cord injury

* VTE risk assessments in the orthopedic population have not been validated. Surgery specific VTE risk should outweigh a patient's contributing individual risk. Above are additional patient-specific risk factors for VTE that may be considered.

VTE prophylaxis recommendations based on risk

For moderate VTE risk one of the below should be selected (bolded preferred)

- **Enoxaparin 40 mg subcutaneous every 24 hours**
- **Warfarin**
- Aspirin
- Mechanical prophylaxis

For high VTE risk a pharmacologic agent AND mechanical agent should be selected (bolded preferred)

- **Enoxaparin 40 mg subcutaneous every 24 hours**
- **Warfarin**
- Aspirin
- **Mechanical prophylaxis**

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