# Provincial Clinical Knowledge Topic
## *Deep Vein Thrombosis, Adult*
## *Emergency Department*

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| Topic Title: | Deep Vein Thrombosis, Adult | Completion Date: | |
| Clinical Working Group: | Emergency Strategic Clinical Network – Deep Vein Thrombosis | Revised Date: | September 2015 |
| Status: | Approved | Version: | 1.1 |

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## Important Information Before You Begin

The recommendations contained in this knowledge topic have been provincially adjudicated and are based on best practice and available evidence. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care. This knowledge topic will be reviewed periodically and updated as best practice evidence and practice change.

The information in this topic strives to adhere to Institute for Safe Medication Practices (ISMP) safety standards and align with Quality and Safety initiatives and accreditation requirements. Some examples of these initiatives or groups are: Health Quality Council Alberta (HQCA), Choosing Wisely campaign, Safer Health Now campaign etc.

Within this knowledge topic PICO-D questions or key clinical questions that have been used to guide research using the **P**opulation/**P**roblem, **I**ntervention, **C**omparison, **O**utcome, **D**esign format. These questions are listed in **Appendix A** and **Appendix B**.

Links to PICO questions or Appendices are throughout the document (example: **(PICO 1)**). Click on the link with your mouse to follow the link. Under the PICO question or Appendix heading you will find a link to return you to your place in the document.

## Rationale

Deep Vein Thrombosis (DVT) is a common presentation to the Emergency Department. In most cases, the presentation is with a unilateral swollen limb. Challenges exist since a number of clinical entities may mimic the findings of DVT. These include: muscle strain, lymphangitis, cellulitis, lymphedema, and Baker's cyst. The purpose of this content is to unify the approach and management of DVT.

In Alberta, during the three years from 2012, 2013 and 2014, Emergency Department (ED) visits leading to a DVT diagnosis among the 15 busiest Emergency Departments numbered 9194. The proportion of these patients who were admitted was 7.1% (657). [1]

DVT has a reported annual incidence of 1-2 per 1000. The risk increases with age to being as high as 1 in 100 for those aged over 80. Men have higher rates than women. The most common sites are the popliteal and femoral veins. Patients with DVT can progress to developing a pulmonary embolism (PE), which can occur in 50% of patients with untreated DVT. PE's are notably dangerous if left untreated with a 35% mortality rate. Even with treatment, PE still has a 5% mortality rate.[2, 3]

Up to 50% of patients diagnosed with a DVT have long term sequelae including swelling, pain and discoloration of the affected limb, known as post thrombotic syndrome. One third of patients with a DVT will have a recurrence within 10 years. [2, 3]

For patients suspected of having a DVT, only a minority (between 17-32%) will be proven to have the disease and require treatment.[2, 3]

## Goals of Management

1. Based on clinical findings/judgment and applying clinical decision rules, determine the degree of risk/likelihood of DVT for each patient.

2. Consider alternate diagnoses including: muscle strain/tear, cellulitis (rarely necrotizing fasciitis), popliteal (Baker's) cyst, venous insufficiency, or leg swelling in a paralyzed limb.

3. Recognize that patients with DVT can have associated comorbidities such as pregnancy, trauma, and infection.

4. Based on diagnostic certainty determine appropriate investigation strategy as well as the risk/benefit balance between providing treatment pending investigation versus delaying until diagnostic certainty.

5. For profoundly swollen limbs be aware of the risk of compartment syndrome and assess clinically with necessary regularity, and if truly suspicious, consult surgery or consider compartment pressure measurement.

6. Determine patient risk for anticoagulant therapy including: recent bleeding (e.g. gastrointestinal (GI) tract, epistaxis, recent surgery), previous dangerous bleeds (e.g. intracranial hemorrhage (ICH), GI bleed), or past history of adverse events on anticoagulants (e.g. difficulty maintaining stable international normalized ratio [INR], Heparin induced thrombocytopenia [HIT]), medications that will interact with anticoagulants, and renal function.

7. Provide a safe and appropriate disposition strategy. This should be outpatient therapy in most cases, however, does require a primary care physician, hematologist, general internist, or community clinic willing and able to monitor the patient's therapy and DVT resolution.

## Nursing Assessment and Documentation

This section contains specific considerations related to this topic. Standard assessment and documentation practices should still be followed.

1. Triage Assessment/Documentation
    - Canadian Emergency Department Information Systems (CEDIS) complaints:
        - "Unilateral reddened hot limb" or "Lower extremity pain" or "Upper extremity pain" or possibly "Bilateral leg swelling/edema"
    - Canadian Triage and Acuity Scale (CTAS) Modifiers:
        - most likely to be pain modifier (acute / peripheral), possibly special modifiers extensive vs localized inflammation, or possible temperature modifier if temp $38^0$C plus Systemic Inflammatory Response Syndrome (SIRS) criteria[4]
2. Initial Assessment/Documentation
    - Presenting History: Time of onset, shortness of breath (SOB), pleuritic chest pain, syncope, leg swelling, long distance travel (overseas flights or flights lasting greater than 8 hours), exogenous hormone therapy used for contraception or postmenopausal indications, hemoptysis
    - Brief screening of risk factors:
        - Exogenous hormone therapy used for contraception or postmenopausal indications
        - Surgery within previous 30 days
        - History of immobilization or hospitalization greater than or equal to 72 hours or long distance travel (overseas flights or flights lasting greater than 8 hours)
        - Obesity
        - Active cancer (treatment ongoing, within 6 months, or palliative)
        - Active malignancy (defined as any metastatic cancer or cancer not in remission)
        - Lower extremity trauma
        - Pregnancy
        - Previous DVT/ pulmonary embolism (PE)
    - Past History: previous clot, family history of clots, renal failure
    - Medications and Allergies: all meds but specifically exogenous hormone therapy used for contraception or postmenopausal indications, warfarin, direct oral anticoagulants (DOACs), antiplatelet agents, and medications that could interact with warfarin
    - Systems review:
        - Respiratory: tachypnea, dyspnea
        - Cardiovascular (CV): tachycardia, signs of dehydration, diaphoresis, pleuritic chest pain
        - Neurological: mental status
        - Gastrointestinal (GI): nausea, vomiting, abdominal pain
        - Extremities: edema, tenderness, redness, pulses, capillary refill, rash
3. Ongoing Assessment/Documentation

## Physician Assessment and Documentation

This section contains specific considerations related to this topic. Standard assessment and documentation practices should still be followed.

1. History of Present Illness
    - The dominant presenting complaint (pain, swelling, redness) to the affected limb, time of onset, associated symptoms (chest pain, sob, fever), pregnancy, recent long flight (overseas flights or flights lasting greater than 8 hours ), AND the specific Well's history related risk factors listed below
        - Active cancer (treatment ongoing, within 6 months, or palliative)
        - Paralysis, paresis or recent plaster immobilization of the lower extremities
        - Recently bedridden for 3 days or more, or major surgery within 12 weeks requiring general or regional anesthesia
        - Previously documented DVT
    - To broaden the differential diagnosis ask about: recent trauma (such as running, lifting, fighting, etc. that could have injured muscle); recent breaks to the skin in the swollen limb as potential portals of entry for infection, and any history of a previous Baker's cyst.
2. Medications & Allergies
    - All meds but specifically exogenous hormone therapy used for contraception or postmenopausal indications, warfarin, DOACs, antiplatelet agents, and medications that could interact with warfarin
3. Past History
    - Previous Venous Thromboembolism (VTE), active cancer or any history of thrombophilia
4. Review of Systems
    - Symptoms that could potentially reveal a PE such as chest pain or shortness of breath.
    - Mobility (or lack of) will play a part in discharge planning. Also look for any evidence of recent bleeds (GIB, ICH, epistaxis, etc.)
5. Family History
    - VTE (in 1st degree relative less than 50 years of age), or thrombophilia
    - Social History
    - Financial (health insurance/drug plan) and social supports available, assuming the need for initiation of antithrombotic agents (warfarin requires frequent testing and the ability to regularly access a lab and get their INR and dosing monitored; whereas DOACs are expensive without insurance such as Blue Cross as a first line choice), also need to assure adequate home support if immobile.
6. Physical Examination
    - Focus is on the affected limb. Looking for difference in calf diameter, warmth, swelling, and rash. Feeling for palpable cord or tenderness along deep vein system.
    - Documenting pulses and capillary refill AND the specific Well's physical exam criteria listed below:
        - Localized tenderness along the distribution of the deep venous system
        - Entire leg swollen
        - Calf swelling 3 cm larger than asymptomatic side

    - Pitting edema confined to the symptomatic leg
    - Collateral superficial veins (non-varicose)
- Assessing for signs of heart failure. This would include documenting lung and heart sounds.
- Assessing for signs of liver failure which could be associated with hepatic vein thrombosis e.g. Budd-Chiari Syndrome. This would include ascites and hepatomegaly.

7. Scoring Tools / Risk Scores **(Appendix D)**
    - Final Wells' Criteria for DVT listed below.[5]
        - An alternative diagnosis is at least as likely as DVT.
    - Based on 1point awarded for each of the history-driven and physical exam-driven Well's criteria and minus 2 points if an alternate diagnosis is at least as likely, we recommend using the 2-level DVT score to assist in decision making.
        - DVT **unlikely** equals a Well's score of 1 point or less.
        - DVT **likely** equals a Well's score of 2 points or more.

## Initial Decision Making

1. Is the patient unstable with a potential DVT?
    - Considerations:
        - Consider potential PE and initiate standard ACLS (Advanced Cardiac Life Support) resuscitation.

2. Is the affected limb vascularly intact?
    - Considerations:
        - If no then consider immediate vascular surgery consultation e.g. arterial compromise with phlegmasia cerulea/alba dolens (PCD).

3. Is the patient hemodynamically stable and their presentation consistent with a possible deep vein thrombosis? **(PICO 1)**
    - If yes and based on the risk score/clinical assessment is considered **likely** for DVT:
        - Option 1: order an US Venous Doppler if available within 4 hours designed to rule in the diagnosis before beginning treatment **(PICO 2)**
        - Option 2: if US Venous Doppler not available for more than 4 hours and patient is considered 'likely' or has a positive D-dimer, initiate heparin while waiting for US Venous Doppler availability (should be available within 24 hours) **(PICO 3)**
        - If D-dimer positive and DI is negative, then patient needs reassessment and if symptoms continue in 5-8 days and repeat US Venous Doppler considered **(PICO 4)**
    - If yes and based on the risk score/clinical assessment is considered **unlikely** for DVT:
        - Recommend ordering D-dimer and if positive then order US Venous Doppler
        - If D-dimer is negative then DVT is ruled out **(PICO 5)**
        - If D-dimer is positive and there is a delay in obtaining US Venous Doppler (e.g. overnight) then consider initiating heparin

4. Does this patient have a new DVT and is already on anticoagulant therapy?
    - Consider options such as inferior vena cava filter (IVC) placement, thrombolysis, and/or mechanical thrombectomy in consultation with hematology.

5. Does the patient have absolute contraindications to anticoagulation? e.g. active bleeding, surgery within the previous 30 days, recent intracerebral hemorrhage ( less than 14 days), uncontrolled severe hypertension, platelet count less than 50 x $10^9$.
   Options to be discussed with hematology.

6. Does the patient have a confirmed diagnosis of superficial thrombophlebitis?
    - Treat with NSAID's **(PICO 6)**
    - Monitor for further propagation of clot through repeat US Venous Doppler
    - Consider heparin for extensive superficial phlebitis

7. Does the patient have a suspected diagnosis of upper extremity DVT?
    - Apply D-dimer testing and US of affected limb and look for the cause **(PICO 7)**

## Order Set Components

Orders or their components have been added in **bold** text if recommended as default (e.g. **Bedrest**). All other orders and components would be selected based on the presentation needs of the patient. Orders that have more than one option for treatment have been entered in square brackets (e.g. Warfarin 5 mg [2, 2.5, 3, 4, 6, 7.5, 10 mg] PO x 1).

### Order Set Components - General Care

- Goals of Care Designation:
    - Will be important for unstable patients and admitted patients
    - Use the Resuscitation (R), Medical Management (M), Comfort Measures (C) designations and form
- Precautions and Safety:
    - Consider aids to mobility if needed
- Activity:
    - Suggest starting with 'activity as tolerated' as the default with options to include:
        - Bedrest
        - Bedrest - With Bathroom Privileges
        - Ambulate - With Assist
        - Activity as Tolerated
- Diet / Nutrition:
    - Suggest starting with 'DAT' as the default with options to include:
        - NPO
        - NPO: oral medications with sips
        - NPO: may have ice chips

- Clear Fluids Diet
- Full Fluids Diet
- Regular Diet
- Other Diet: as required

## Order Set Components - Patient Care Orders

- Vital Signs: These orders need to be re-evaluated when the patient stabilizes or by 2 hours, whichever occurs first. Vital signs to include: Respirations (RR), Pulse (P), Blood Pressure (BP), Temperature (T), and Oxygen Saturation Monitoring (O2 Sats) with options to include:
  - as per local standards
  - manual or automatic
  - q ____ hourly
  - q ____ mins
- Extremity Exam
  - document pulses and color, sensation, movement, temperature (CSMT)
  - as per local standards (suggest q2h – q4h)
  - measure limb circumference

## Order Set Components - Intravenous Orders

- Intravenous Cannula - Insert
- Options then include:
  - Saline lock
  - IV 'bolus' or 'rapid infusion' including the following:
    - Amount (e.g. 250 mL, 500 mL, 1000 mL, 2000 mL)
    - Fluid (e.g. 0.9% NaCl infusion, lactated ringers infusion, D5W - 0.9% NaCl infusion)
    - Run time (e.g.15 min, 30 min, 45, min, 60 min)
  - IV 'maintenance'
    - Rate in mL / hour (e.g. 75, 100,125, 150, 200, 250)
    - Fluid (e.g. 0.9% NaCl infusion, lactated ringers infusion)

## Order Set Components - Lab Investigations

Laboratory orders appear in **bold** text if recommended as usual default orders. Laboratory orders are <u>underlined</u> when needed to assess severity or establish a baseline. All other lab orders (e.g. investigations for possible comorbidities) are to be selected based on the presentation needs of the patient and are in regular font.

- Hematology
  - **Complete Blood Count (CBC)**
  - <u>D-dimer (quantitative) - only if Wells' score unlikely [less than or equal to 1)</u>
  - <u>PT INR</u>

  - Type and Screen
- Chemistry
  - **Electrolytes (Na, K, Cl, CO2)**
  - **Creatinine LEVEL**
  - Glucose Random LEVEL
  - Urea
  - HCG Beta
  - ALT
  - GGT
  - Alkaline Phosphatase (ALP)
  - Bilirubin Total
  - Lipase
  - Albumin LEVEL
  - Protein Total
  - Magnesium (Mg) LEVEL
  - Phosphate LEVEL
  - Calcium (Ca) LEVEL
- Blood Gases
  - Blood Gas Venous Mixed
  - Blood Gas Arterial
- Urine Tests
  - Pregnancy Test
    - Pregnancy – Point of Care Test
    - Urine Pregnancy Beta HCG
  - Urinalysis Random

## Order Set Components - Diagnostic Investigations

Proceed to Doppler ultrasound if D-dimer is positive or patient deemed “Likely” for a DVT based on Wells Score

- Standard x-rays
  - GR Chest, 2 Projections: Chest X-ray PA and Lateral
  - GR Chest, 1 Projection portable: Chest X-ray Portable

- US Venous Doppler Lower Extremity Uni, US Venous Doppler Upper Extremity Uni **(PICO 8)**
  - Right or Left arm or leg

- Outpatient Venous Doppler ultrasound (within 24 hours)
  - Right or Left arm or leg venous Doppler ultrasound
  - (ensure that anticoagulation is given prior to discharge)

- Advanced Imaging:
  - CT Extremity
  - Contrast Venography - SP Venogram Uni Lower Ext with Prep, SP Venogram Uni Upper Ext with Prep

  - MR Venogram – unilateral lower extremity
  - MR Venogram – unilateral upper extremity
- Other:
  - Electrocardiogram – 12 Lead

## Order Set Components - Medications

* * Absolute contraindications to anticoagulation include: active bleeding, recent intracerebral hemorrhage (less than 14 days), uncontrolled severe hypertension, or platelet count less than 50 x $10^9$. In these circumstances consult Hematology for advice.
* * Also important to note that for DVT likely or D-dimer positive patient needing to wait greater than 4 hours low molecular weight heparin should be initiated. Discharge anticoagulant options are described in this document under **Disposition Planning.**

1. Low molecular weight heparin (all 3 options can be used for cancer or extensive clot burden patients, but for enoxaparin dosing change suggested)
   - enoxaparin 1.5 mg/kg SUBCUTANEOUSLY daily (consider dosage reduction for GFR less than 30 mL/min)

   **OR**
   - enoxaparin 1 mg/kg SUBCUTANEOUSLY q12h (preferred for cancer patients or extensive clot burden and consider dosage reduction for GFR less than 30 mL/min)

   **OR**
   - dalteparin 200 international units/kg SUBCUTANEOUSLY daily

   **OR**
   - tinzaparin 175 units/kg SUBCUTANEOUSLY daily

2. Vitamin K Antagonist
   - warfarin tab 5 mg [1, 2, 2.5, 3, 4, 6,7.5, 10 mg] PO x 1 (requires follow up instructions with a target of INR 2 to 3)
     - if initiated in the ED needs INR initially then q2days until achieves therapeutic goal – Internal Medicine, Family Physician, Cardiologist, or anticoagulation management clinic to monitor

3. Direct oral anticoagulants **(PICO 9)** **(Appendix E)** (DOACs have been less well studied in active cancer and thrombophilia patients so suggest review with oncology or hematology prior to initiation)[12]
   - rivaroxaban 15 mg PO x 1 (a preferred agent for patients over the age of 80)

   **OR**
   - apixaban 10 mg PO x 1 (a preferred agent for patients with GFR less than 30 mL/min and for patients over the age of 80)

4. Pain Control
    - ibuprofen tab 400 mg PO q6h PRN (not to be used for patients receiving anticoagulation)

    **AND/OR**
    - acetaminophen tab - 325 mg to 650 mg PO q4h PRN (maximum 4g/day)

    **OR**
    - acetaminophen tab - 500 mg to 1000 mg PO q4h PRN (maximum 4g/day)

    **OR**
    - acetaminophen/caffeine/codeine 30 mg tab - 1 to 2 tabs PO q4h PRN

    **OR**
    - oxyCODONE/acetaminophen 5 mg/325 mg - 1 to 2 tabs PO q4h PRN

    **OR**
    - HYDROmorphone 1 to 2 mg PO q4h PRN

5. Based on the Numeric Rating Scale for Pain (where 0 is no pain and 10 is worst possible pain) consider the following medications for pain control:

    **Morphine**
    - To achieve a pain score of LESS than 4/10 in accord with patient request give:
        - morphine 2.5 to 5 mg IV q10mins (contact physician or nurse practitioner if pain not controlled after administration of 15 mg total)

        **OR**
        - morphine 2.5 to 5 mg SUBCUTANEOUSLY q1h x 1 to 2 times (contact physician or nurse practitioner if pain not controlled after administration of 2 doses)

    - And then to maintain a pain score of LESS than 4/10 in accord with patient request give:
        - morphine 2.5 to 5 mg IV q30mins PRN

        **OR**
        - morphine 2.5 to 5 mg SUBCUTANEOUSLY q2h PRN

    **OR**
    **HYDROmorphone**
    - To achieve a pain score of LESS than 4/10 in accord with patient request give:
        - HYDROmorphone 0.5 to 1 mg IV q10mins (contact physician or nurse practitioner if pain not controlled after administration of 3 mg total)

        **OR**
        - HYDROmorphone 0.5-1 mg SUBCUTANEOUSLY q1h x 1 to 2 times (contact physician or nurse practitioner if pain not controlled after administration of 2 doses)
    - And then to maintain a pain score of LESS than 4/10 in accord with patient request give:
        - HYDROmorphone 0.5 to 1 mg IV q30mins PRN

        **OR**

- HYDROmorphone 0.5 to 1 mg SUBCUTANEOUSLY q2h PRN

**OR**

**fentaNYL**

- fentaNYL 25 to 50 micrograms IV q5mins to achieve a pain score of LESS than 4/10 in accord with patient request (contact physician or nurse practitioner if pain not controlled after administration of 200 micrograms total)

6. Nausea control:
   - dimenhyDRINATE 25 to 50 mg IV/IM/PO q6h PRN

   **OR**

   - metoclopramide 5 to 10 mg IV/PO now **and then** metoclopramide 10 mg [5 mg] IV/PO q4h PRN

   **OR**

   - ondansetron 4 to 8 mg IV/PO now **and then** ondansetron 4 to 8 mg IV/PO q8h PRN

## Disposition Planning

1. Considerations for admission **(PICO 10)**
   - Massive DVT (swelling of entire limb, acrocyanosis, venous limb ischemia, or extension into iliofemoral veins or inferior vena cava).
   - Associated symptomatic pulmonary embolism (requiring supplemental O2 or at risk for cardiorespiratory deterioration).
   - High risk for anticoagulant-related bleeding (active bleeding or recent bleeding episode within 4 weeks, recent surgery or trauma [within 1 week], thrombocytopenia [platelet count less than 100 x $10^6$/L], coagulopathy, or advanced cancer with intracranial or intrahepatic metastases or apply REITE risk tool[6] http://www.mdcalc.com/riete-score-risk-hemorrhage-pulmonary-embolism-treatment/).
   - Major comorbidities or other factors that warrant inpatient care (including impaired cognitive, self-care or adequate supports to ensure compliance with outpatient care requirements).

2. Considerations for discharge
   - The majority of patients with DVT can be safely discharged home.
   - The following considerations must be addressed prior to discharge:
     - Anticoagulation method
     - Patients with DVT who were started on low molecular weight heparin (LMWH) in the emergency department may be sent home on the LMWH with a bridge to warfarin or dabigatran or can be switched to rivaroxaban or apixaban. **(Appendix E)**
     - For patients with active cancer, pregnancy, iliofemoral DVT, or submissive PE LMWH should be used alone without transition to warfarin or DOACs
     - Dosing regimens:
       - LMWH x 5-10 days + warfarin
         - enoxaparin 1.5 mg/kg SUBCUTANEOUSLY daily (consider dosage reduction for GFR less than 30 mL/min)

**OR**

- enoxaparin 1 mg/kg SUBCUTANEOUSLY q12h (preferred for cancer patients or extensive clot burden and consider dosage reduction for GFR less than 30 mL/min)

**OR**

- dalteparin 200 units/kg SUBCUTANEOUSLY daily (dose unchanged for cancer patients)

**OR**

- tinzaparin 175 units/kg SUBCUTANEOUSLY daily (dose unchanged for cancer patients)

**AND**

- warfarin 5, 2.5, 7.5, or 10 mg PO daily with INR 2nd day post discharge from the ED, to be monitored by Internal Medicine, Hematology, Family Medicine or anticoagulation management clinic where available to adjust warfarin to achieve an INR of 2-3 for 2 days before stopping LMWH

**OR**

- rivaroxaban 15 mg PO bid x 3 weeks, then 20 mg PO daily (a preferred agent for patients over the age of 80) ***Note: Alberta Health publicly funded plans, including Blue Cross, will cover 6 months of therapy with completion of a Special Authorization Form*** **(Appendix F)**

**OR**

- apixaban 10 mg PO bid x 7 days, then 5mg PO bid (recommended DOAC for patients with a GFR of less than 30 mL/min and for patients over the age of 80) ***Note: this medication is not currently covered by Alberta Health publicly funded plans***

**OR**

- LMWH x 7 days, **then start** dabigatran
  - enoxaparin 1.5 mg/kg SUBCUTANEOUSLY q daily (consider dosage reduction for GFR less than 30 mL/min)

  **OR**

  - enoxaparin 1 mg/kg SUBCUTANEOUSLY bid (preferred for cancer patients or extensive clot burden and consider dosage reduction for GFR less than 30 mL/min)

  **OR**

  - dalteparin 200 units/kg SUBCUTANEOUSLY q daily (no dosing change for cancer patients)

  **OR**

  - tinzaparin 175 units/kg SUBCUTANEOUSLY q daily (agent of choice for eGFR 20-30 mL/min; no dosing change for cancer patients)

  **THEN**

  - dabigatran 150 mg PO bid **(*Note: dabigatran is not covered by Alberta Health publicly funded plans)*** **(AppendixF)**

- *To be started only after treatment with a parenteral anticoagulant for 5-10 days and the length of therapy may vary based on individual patient assessments and bleeding risk.*
- *For treatment or prevention of DVT/PE, recommended dose adjustments are as follows[7]:*
    - *General patient population: 150 mg twice daily*
    - *For moderate renal impairment (eCrCl 30 to 50 mL/min): 110 mg twice daily*
    - *For elderly patients older than 80 years or patients at higher risk of bleeding (age older than 75 years with more than 1 risk factor for bleeding): 110 mg twice daily*
    - *For more information please access the drug monograph (Page 29 and Table 16):* http://www.boehringer-ingelheim.ca/content/dam/internet/opu/ca_EN/documents/humanhealth/product_monograph/PradaxaPMEN.pdf

❖ Please note that NSAID's have been shown to increase the risk of bleeding in patients on Rivaroxaban (Einstein trial), so NSAIDs are not recommended for any patients discharged on oral anticoagulants

- Risk and benefit of different anticoagulants. **(PICO 9)**
    - DOACs: Do not require blood tests but antidotes/reversible agents are not as established as warfarin reversal.
    - Warfarin: Requires frequent blood tests and we have ways to reverse it if necessary.

- Reasons to return to the ED
    - New onset CNS symptoms: seizures, headache, syncope, speech problems, focal weakness.
    - New onset pleuritic CP, SOB, hemoptysis.
    - New onset unprovoked bleeding (e.g. nose, oropharynx, bowels, etc.).
    - Worsening leg swelling, and increasing pain.
- Reversal of bleeding on DOACs **(Appendix E)**

3. Outpatient follow-up
    - Follow up with your family doctor / internal medicine / hematology / anticoagulation management clinic **(PICO 11)**
        - within 48 hours regarding INR follow up (F/U) and warfarin dosing if not started on DOAC.
        - within 1 week, any patient ruled out for DVT in ED but has ongoing symptoms, or was noted to have a below knee DVT on ultrasound, or patients with an extensive or persistently symptomatic superficial phlebitis should be re-evaluated and repeat Venous Doppler ultrasound strongly considered.
        - those patients with a large clot burden (ileofemoral or extending into the vena cava),

or having a 1st episode of an idiopathic DVT, who are pregnant or have pregnancy related issues, or 1st degree relatives of patient with thrombophilia should be referred to a Hematologist or coagulation clinic.

4. Patient education / discharge instructions **(Appendix C)**
   - Deep Vein Thrombosis: After Your Visit
   - How to Give a Heparin Shot: After Your Visit
   - Taking Blood Thinners Other Than Warfarin: After Your Visit
   - Taking Warfarin Safely: After Your Visit

## Rural Considerations

The major challenges and considerations from a rural perspective are:

- Capability of treating unstable patients with a possible PE.
- Timely access to appropriate lab and DI tests.
- Inpatient facilities and/or ability to transfer patients suitable for admission.
- Timely outpatient follow-up for patients in whom anti-coagulation has been initiated.

## Patient Experience and Expectations

Based on a meeting with 8 patient advisors in Calgary January 25, 2015, we received the following feedback and general recommendations regarding approaches to communication, care and patient expectations in the emergency department (ED):

1. They hoped we would be able to improve care consistency among ED providers.

   *Patient quote: "Every time I presented to the emergency department with the same condition (atrial fibrillation), each doctor provided a different treatment approach."*

2. They were supporters of care pathways, checklists, protocols, etc. wherever appropriate.

   *Patient quote: "I am a strong supporter of care pathways as whenever I/my family member receive treatment using a pathway the care seems clearer and more consistent"*

3. While none of the patients liked long waits, they could accept them better if there was clearer communication and reassessments as required.

   *Patient quote: "Nobody likes to wait and I understand that sicker patients take priority, however, there needs to be improved communication and reassessments for those patients who are waiting"*

4. They pointed out the importance of having a patient advocate accompany a sick person, but also allowing the advocate to be with the patient at decision critical points (e.g. initial assessment, treatment decision making, receiving bad news, etc.) was considered paramount.

   *Patient quote: "When I accompany my family member to the ED I am often not permitted to join them when they are moved into a treatment space. I am often told this is 'policy'."*

5. They believe that improving follow up, especially for patients being discharged from the ED and being referred to a specialist is important. This was recognized as a key safety risk for patients; having to rely on faxed referrals and a call back from the consultant's office can lead to dangerous delays or failed connections to the detriment of the patient's health and well-being.

   *Patient quote: "The current health care system is poorly coordinated with lots of gaps and delays, especially with referrals from one physician to another.*

## Preparation for Analytics

1. Key Outcomes
   - Clinical Outcomes
     - Appropriate risk stratification of suspected DVT patients.
     - Few missed or delayed DVT or PE diagnoses.

   - Process Outcomes
     - Broad use of standardized risk scoring.

- Improved access to anticoagulation clinics for long term planning.

- Patient Experience
  - Patient and family kept informed of clinical suspicions and management plan.
  - Effectively engaged in their own 'informed' decision making.
  - Disposition plan clear and met the patient's needs and expectations.

2. Data Elements for Capture
   - Patient demographics
   - CEDIS presenting complaint and CTAS score
   - ED time markers (triage to physician, physician to consult and then to admission or physician to discharge) and outcome markers (identified as CDU patient, consulted for admission, admitted to ICU or ward, died)
   - ED diagnoses ICD 10 for DVT I809, cellulitis, muscle tear/hematoma, Baker's cyst, lymphedema, venous stasis/insufficiency
   - Site and zone identifiers
   - Date and time of use of DVT order set use
   - Date and time of ED LMWH injection
   - Date and time of D-dimer ordering
   - Date and time of Doppler ordering
   - D-dimer and Doppler results
   - Discharge instructions provided
   - Time and location of next physician/clinic follow up
   - Discharge medications (using PIN [Pharmaceutical Information Network])

## References

1. Data provided by Data Integration and Management Resources (DIMR) March 2015.
2. Yusuf HR, Reyes N, Zhang QC, Okoroh EM, Siddiqi AE, Tsai J. Hospitalizations of Adults ≥60 Years of Age With Venous Thromboembolism. *Clin Appl Thromb Hemost.* 2014;20(2):136-142. doi:10.1177/1076029613493659.
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## Appendix A - PICO-D Questions (Key Clinical Questions)

For Information regarding PICO-D methodology and Grade Terminology please see **(Appendix B)**

*PICO 1:* ***In undifferentiated emergency department patients with a suspected deep vein thrombosis (DVT) [? Lower limb specified] are decision rules more effective than clinical impression in risk stratifying patients?***

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***Population, Patient or Problem*:** Undifferentiated emergency department patients with suspected DVT
***Intervention, Prognostic Factor, Exposure*:** Clinical decision rules
***Comparison***: Clinical impression
***Outcome***: Risk stratification
***Design***: Systematic reviews of randomized controlled trials (RCT) or observational studies

**Search Strategy:** Cochrane library, Medline, and PubMed for systematic reviews and clinical trials. Guidelines were searched

**Clinical Recommendation:** We suggest applying clinical decision rules to help risk stratify patients allows for a more standardized approach to patient investigation, however, there is insufficient evidence to show more favorable patient outcomes that by relying on clinical impression alone. The ability to capture standardized clinical information does allow for system performance and cost analysis along with patient outcomes. The NICE recommend using 2 level Well's to stratify patients prior to testing.[1] SIGN recommend a clinical decision rule be used in the initial assessment and do not favor Wells over Geneva scoring systems or 3 level over 2-level.[2]

Two non-randomized studies located, neither of which examined emergency department patients. One cross-sectional study compared a clinical decision rule (Oudega rule) to clinical impression of 300 general practitioners.[3] The study found that the clinical decision rule and clinical impression were both equally effective in diagnosing DVT. Fewer patients were sent for clinical testing when using the decision rule. Another study found that while the Wells Score was similarly effective in diagnosing DVT as an empirical assessment by physicians, fewer diagnostic tests were ordered using the decision rule.[4]

**Quality of Evidence**: Moderate, GRADE B. We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Strength of Recommendation:** Weak, GRADE 2

**References:**

1. Diagnosing venous thromboembolism in primary, secondary and tertiary care. National Institute for Health and Care Excellence Web site. http://pathways.nice.org.uk/pathways/venous-thromboembolism Published 2015. Updated June 8, 2015. Accessed July 7, 2015.
2. Scottish Intercollegiate Guidelines Network. Prevention and management of venous thromboembolism. http://www.sign.ac.uk/pdf/sign122.pdf Published December 2010. Accessed July 7, 2015.
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***PICO 2:* *In undifferentiated ED patients determined to be likely risk with a positive D-dimer and a negative U/S is a contrast (Computerized Tomography) CT or venogram indicated to rule out DVT?***

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***Population, Patient or Problem***: ED patients determined to be likely risk for DVT based on Well's Score for DVT & a negative ultrasound
***Intervention, Prognostic Factor, Exposure*:** contrast CT or venogram (gold standard)
***Comparison***: Repeat ultrasound in 1 week
***Outcome***: Sensitivity, specificity, appropriate treatment including follow up.
***Design***: Systematic reviews, RCTs, or Observational studies.

**Search Strategy:** Cochrane library, Medline, and PubMed for systematic reviews and clinical trials. Guidelines were searched

**Clinical Recommendation:** We suggest that in patients with a positive D-dimer, but negative U/S, a whole leg ultrasound or a repeat compression ultrasonography in 1 week are preferred over a venogram to rule out DVT. Contrast CT or venogram are not currently recommended in the case of a normal ultrasound in high risk patients unless suspicion of clots limited to the iliac or IVC.

The American College of Chest Physicians 2012 guidelines Bates 2012 recommends that patients with negative proximal compression ultrasonography but a positive D-dimer should receive either a whole-leg ultrasound, or a repeat compression ultrasonography in 1 week, over venography.[1] Both the Scottish Intercollegiate Guidelines Network (SIGN) and National Institute for Health and Care Excellence (NICE) also recommend repeat ultrasound scanning between 5-8 days later for patients at risk for DVT and a positive D-dimer and an initial negative ultrasound.[2,3]

**Quality of Evidence**: Low, GRADE C. We have little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

**Strength of Recommendation**: Weak, GRADE 2

**References:**

1. Bates SM, Jaeschke R, Stevens SM, et al. Diagnosis of DVT: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012; 141(suppl 2):e351S-e418S.
2. Scottish Intercollegiate Guidelines Network. Prevention and management of venous thromboembolism. http://www.sign.ac.uk/pdf/sign122.pdf Published December 2010. Accessed July 7, 2015.
3. Diagnosing venous thromboembolism in primary, secondary and tertiary care. National Institute for Health and Care Excellence Web site. http://pathways.nice.org.uk/pathways/venous-thromboembolism Published 2015. Updated June 8, 2015. Accessed July 7, 2015.

***PICO 3:* *In undifferentiated emergency department patients determined to be unlikely risk for deep vein thrombosis (DVT) but with a positive D-dimer should LMWH be given when doppler ultrasound is delayed?***

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***Population, Patient or Problem***: Emergency department patients determined to have a 'likely' risk for DVT OR 'unlikely' risk with a positive D-dimer waiting >12 hours for ultrasound
***Intervention, Prognostic Factor, Exposure*:** LMWH in the ED
***Comparison***: Ultrasound and initiate LMWH if study is positive for DVT
***Outcome***: PE risk, bleeding risk, time to resolution of DVT symptoms, morbidity, mortality
***Design***: Systematic reviews of RCT's or observational studies

**Search Strategy:** Cochrane library, Medline, and PubMed for systematic reviews and clinical trials. Guidelines were searched

**Clinical Recommendation:** There is insufficient evidence and lack of consensus to make a recommendation regarding which patients should receive LMWH if the Doppler ultrasound is to be delayed.

NICE guidelines recommend initiating LMWH even for unlikely DVT patients if their ultrasound testing will be delayed more than four hours and recommends that ultrasound testing always be completed within 24 hours.[1]

**Quality of Evidence**: Very Low, GRADE D. We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

**Strength of Recommendation**: Insufficient evidence

**References:**

1. Diagnosing venous thromboembolism in primary, secondary and tertiary care. National Institute for Health and Care Excellence Web site. http://pathways.nice.org.uk/pathways/venous- thromboembolism Published 2015. Updated June 8, 2015. Accessed July 7, 2015.

***PICO 4:* In undifferentiated emergency department patients determined to be likely risk for deep vein thrombophlebitis (DVT) [? Lower limb specified] with a negative ultrasound but positive D-dimer is a venogram or repeat ultrasound in 3-7 days indicated to rule out DVT?**

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***Population, Patient or Problem:*** Emergency department patients determined to be intermediate risk for deep vein thrombophlebitis (DVT) and a negative ultrasound but positive D-dimer
***Intervention, Prognostic Factor, Exposure*:** Contrast venogram
***Comparison:*** Repeat ultrasound (within 1 week)
***Outcome:*** Sensitivity, specificity, improved clinical outcome through earlier diagnosis, versus increased morbidity due to the venogram
***Design:*** Systematic reviews of RCT's or observational studies

**Search Strategy:** Cochrane library, Medline, and PubMed for systematic reviews and clinical trials. Guidelines were searched

**Clinical Recommendation:** We recommend that patients who have a 'likely' risk for DVT OR 'unlikely' risk and a positive D-dimer and an initial negative ultrasound should undergo a repeat compression US in the next week.

The 2012 guidelines of the American College of Chest Physicians (Bates 2012) recommends repeat proximal compression US or testing with a moderate or highly sensitive D-dimer over no further testing or venogram.[1] Both the Scottish Intercollegiate Guidelines Network (SIGN) and National Institute for Health and Care Excellence (NICE) also recommend repeat ultrasound scanning between 5-8 days later for patients have a 'likely' risk for DVT OR 'unlikely' risk and a positive D-dimer and an initial negative ultrasound, and do not recommend the use of venogram.[2,3]

**Quality of Evidence:** Moderate, GRADE B. We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Strength of Recommendation:** Strong, GRADE 1

**References:**

1. Bates SM, Jaeschke R, Stevens SM, et al. Diagnosis of DVT: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012; 141(suppl 2):e351S-e418S.

2. Scottish Intercollegiate Guidelines Network. Prevention and management of venousthromboembolism. http://www.sign.ac.uk/pdf/sign122.pdf Published December 2010. Accessed July 7, 2015.
3. Diagnosing venous thromboembolism in primary, secondary and tertiary care. National Institute for Health and Care Excellence Web site. http://pathways.nice.org.uk/pathways/venous-thromboembolism Published 2015. Updated June 8, 2015. Accessed July 7, 2015.

***PICO 5:*** ***In undifferentiated emergency department patients determined to be unlikely risk for deep vein thrombophlebitis (DVT) [? Lower limb specified] is a negative quantitative D-dimer sufficient to rule out DVT OR eliminate the need for further testing?***

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***Population, Patient or Problem:*** Emergency department patients determined to be 'unlikely' risk for deep vein thrombophlebitis (DVT)
***Intervention, Prognostic Factor, Exposure*****:** A negative quantitative D-dimer
***Comparison:*** Clinical impression
***Outcome:*** Rule out DVT / eliminate the need for further testing
***Design:*** Systematic reviews of RCTs or observational studies

**Search Strategy:** Cochrane library, Medline, and PubMed for systematic reviews and clinical trials. Guidelines were searched

**Clinical Recommendation:** We recommend that no further testing is required for patients 'unlikely' risk for DVT with a negative D-dimer. For 'unlikely' patients this is the recommendation whether using a qualitative of quantitative D-dimer test. Given that the high sensitivity D-dimer assays are currently in use province wide, the risk of a missed DVT with a negative D-dimer is even more unlikely.[1]

The 2012 guidelines of the American College of Chest Physicians (Bates 2012) recommends no further testing over further investigation with proximal compression US, whole-leg US, or venography if the D-dimer is negative.[2] The same recommendation is made by the Scottish Intercollegiate Guidelines Network (SIGN) and National Institute for Health and Care Excellence (NICE) guidelines and their diagnostic strategy recommendations.[3,4]

**Quality of Evidence**: Moderate, GRADE B. We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Strength of Recommendation:** Strong, GRADE 1

**References:**

1. Fancher T L, White R H, Kravitz R L. Combined use of rapid D-dimer testing and estimation of clinical probability in the diagnosis of deep vein thrombosis: systematic review. *BMJ.* 2004; 329(7470): 821.
2. Bates SM, Jaeschke R, Stevens SM, et al. Diagnosis of DVT: antithrombotic therapy and

prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012; 141(suppl 2):e351S-e418S.
3. Scottish Intercollegiate Guidelines Network. Prevention and management of venous thromboembolism. http://www.sign.ac.uk/pdf/sign122.pdf Published December 2010. Accessed July 7, 2015.
4. Diagnosing venous thromboembolism in primary, secondary and tertiary care. National Institute for Health and Care Excellence Web site. http://pathways.nice.org.uk/pathways/venous-thromboembolism Published 2015. Updated June 8, 2015. Accessed July 7, 2015.

***PICO 6:* *In emergency department patients with a diagnosis of superficial thrombophlebitis [? Upper or lower limb] do oral anticoagulants provide greater symptomatic relief and lower risk of deep venous thromboembolism (DVT) when compared to NSAIDs?***

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***Population, Patient or Problem:*** Emergency department patients with superficial thrombophlebitis
***Intervention, Prognostic Factor, Exposure*:** Oral anticoagulation
***Comparison:*** NSAID's
***Outcome:*** Lower risk of VTE and, superior pain relief
***Design:*** Systematic reviews of RCT's or observational studies

**Search Strategy:** Cochrane library, Medline, and PubMed for systematic reviews and clinical trials. Guidelines were searched

**Clinical Recommendation:** There is insufficient evidence and lack of consensus to make a recommendation regarding whether anticoagulants provide greater symptomatic relief compared to NSAIDS in patients presenting to the emergency department with a diagnosis of superficial thrombophlebitis. There are a limited number of available trials, none of which occurred within the emergency department. Three randomized controlled trials were identified. None of the identified studies were set in the emergency department. Titon 1994 compared Nadroparin vs. Naproxen in 117 patients.[1] Treatment duration was 6 days. The study found that Nadroparin treatment resulted in a significant decrease in regards to feeling of heat and redness. Another study compared Enoxaparin vs. tenoxicam which found both treatments to be equally effective in reducing the incidence of DVT.[2] Finally, the third study compared Dalteparin vs. Ibuprofen for 14 days.[3] The study found Dalteparin was superior to Ibuprofen in reducing extension of superficial thrombophlebitis, but both were equally effective in reducing pain.

A systematic review conducted a systematic review on various treatments for superficial thrombophlebitis.[4] They reviewed only the three studies comparing anticoagulants vs. NSAIDS which were detailed above (Decousus 2003, Rathbun 2012, Titon 1994). Meta-analysis found no differences in the extension or recurrence of superficial thrombophlebitis between anticoagulants vs. NSAIDS.

**Quality of Evidence**: Low, GRADE C. Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

**Strength of Recommendation**: Insufficient evidence

**References:**

1. Titon JP, Auger D, Grange P, et al. Therapeutic management of superficial venous thrombosis with calcium nadroparin.. Dosage testing and comparison with a non-steroidal anti-inflammatory agent. *Ann Cardiol Angeiol (Paris).* 1994; 43(3):160-166.
2. Decousus, H, Leizorovicz, A, Epinatm, M, et al. A Pilot Randomized Double-blind Comparison of a Low-Molecular-Weight Heparin, a Nonsteroidal Anti-inflammatory Agent, and Placebo in the Treatment of Superficial Vein Thrombosis. *Arch Intern Med.*2003; 163(14):1657-1663.
3. Rathbun SW, Aston CE, Whitsett TL. A randomized trial of dalteparin compared with ibuprofen for the treatment of superficial thrombophlebitis. *J Thromb Haemost.* 2012; 10(5): 833-839.
4. Di Nisio M, Wichers IM, Middeldorp S. Treatment for superficial thrombophlebitis of the leg.*CochraneDatabaseSystRev.*2013;(4):CD004982.DOI:10.1002/14651858.CD004982.pub5.

***PICO 7:*** ***In undifferentiated emergency department patients with suspected upper arm deep vein thrombophlebitis (DVT) does a negative quantitative D-dimer test in a low risk patient eliminate the need for further testing?***

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***Population, Patient or Problem:*** Emergency department patients with suspected upper arm DVT
***Intervention, Prognostic Factor, Exposure*:** Negative quantitative D-dimer
***Comparison:*** Upper arm venous Doppler ultrasound
***Outcome:*** Rule out DVT/ eliminate need for further testing
***Design:*** Systematic reviews of RCT's or observational studies

**Search Strategy:** Cochrane library, Medline, and PubMed for systematic reviews and clinical trials. Guidelines were searched

**Clinical Recommendation:** There is insufficient evidence and lack of consensus to make a recommendation regarding whether a negative D-Dimer test in low risk patients for DVT eliminates the need for further testing.

SIGN guidelines related to information gleaned from 2 articles evaluating upper limb venous thromboembolism pointed out that most were secondary to central lines or venous obstruction and diagnosis still relied on D-dimer and compression ultrasound.[1,2,3] Where they differ from lower limb DVTs is that they are much less likely to recur and as such rarely need to be kept on a prolonged anticoagulation regimen.

**Quality of Evidence**: Very Low, GRADE D. We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

**Strength of Recommendation:** Insufficient evidence

**References:**

1. Scottish Intercollegiate Guidelines Network. Prevention and management of venous thromboembolism. http://www.sign.ac.uk/pdf/sign122.pdf Published December 2010. Accessed July 7, 2015.
2. Flinterman LE, Van Der Meer FJ, Rosendaal FR, et al. Current perspective of venous thrombosis in the upper extremity. *J Thromb Haemost.* 2008; 6(8):1262-1266.
3. Lechner D, Wiener C, Weltermann A, et al. Comparison between idiopathic deep vein thrombosis of the upper and lower extremity regarding risk factors and recurrence. *J Thromb Haemost.* 2008; 6(8): 1269-1274.

***PICO 8: Do emergency department patients with a confirmed below knee deep vein thrombosis (DVT) on ultrasound benefit from having serial ultrasounds to monitor extension of the clot?***

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***Population, Patient or Problem:*** Emergency department patients with a below knee DVT on ultrasound
***Intervention, Prognostic Factor, Exposure*:** Serial lower limb venous Doppler ultrasounds
***Comparison:*** Clinical follow up and impression
***Outcome:*** Sensitivity, specificity, safety, mortality
***Design:*** Systematic reviews of RCT's or observational studies

**Search Strategy:** Cochrane library, Medline, and PubMed for systematic reviews and clinical trials. Guidelines were searched

**Clinical Recommendation:** We suggest serial testing if an isolated distal DVT is identified on a whole-leg ultrasound, to rule out proximal extension, over anticoagulation.

The risk of pulmonary embolism from a distal DVT is felt to be zero, however, the risk of propagation to become a proximal DVT is reportedly 21.4% supporting the recommendation for serial testing, a repeat ultrasound in 5-7 days.[1,2,3,4,5] A strategy to treat all distal DVTs would lead to overtreatment in up to 80% of patients along with a much greater patient population at risk for bleeding complications.[6,7]

**Quality of Evidence:** Low, GRADE C. Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

**Strength of Recommendation:** Weak, GRADE 2

**References:**

1. Bates SM, Jaeschke R, Stevens SM, et al. Diagnosis of DVT: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical

Practice Guidelines. *Chest*. 2012; 141(suppl 2):e351S-e418S.
2. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2012;141(suppl 2): e419S-e494S.
3. Kraaijenhagen RA , Piovella F , Bernardi E , et al. Simplification of the diagnostic management of suspected deep vein thrombosis. *Arch Intern Med.* 2002;162(8):907- 911.
4. Cogo A, Lensing AW, Koopman MM, et al. Compression ultrasonography for diagnostic management of patients with clinically suspected deep vein thrombosis: prospective cohort study.*BMJ.*1998;316(7124):17-20.
5. Birdwell BG, Raskob G , Whitsett TL, et al. The clinical validity of normal compression ultrasonography in outpatients suspected of having deep venous thrombosis. *Ann Intern Med*.1998;128(1):1-7.
6. Kakkar VV, Howe CT, Flanc C, et al. Natural history of postoperative deep-vein thrombosis. *Lancet.*1969;2(7614):230-232.
7. Philbrick JT, Becker DM. Calf deep venous thrombosis. A wolf in sheep's clothing? *Arch Intern Med*. 1988;148(10):2131-2138.

***PICO 9:* *In emergency department patients with confirmed deep vein thrombosis (DVT) [? Lower limb specified] are the newer anticoagulants as effective as or better than previous anticoagulation standards?***

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***Population, Patient or Problem:*** Emergency department patients with confirmed deep vein thrombosis (DVT)
***Intervention, Prognostic Factor, Exposure*:** Newer anticoagulants (e.g. dabigatran, rivaroxaban etc.)
***Comparison:*** Standard therapy of low molecular weight heparin and warfarin
***Outcome:*** Mortality, bleeding, propagation of venous thromboembolism
***Design:*** Systematic reviews of RCT's or observational studies

**Search Strategy:** Cochrane library, Medline, and PubMed for systematic reviews and clinical trials. Guidelines were searched

**Clinical Recommendation:** We suggest that the 3 Direct anticoagulants (DOACs) rivaroxaban, apixaban, and dabigatran have all been approved by Health Canada for the treatment of DVT and PE based on non inferiority studies comparing to the vitamin K antagonists (VKAs) such as warfarin showing no increase in VTE recurrence or bleeding risk.[1,2,3,4,]

Rivaroxaban and apixaban have initial higher twice daily dosing while dabigatran adds LMWH for the 8-11 days with a median of 9 days as a bridging strategy. Because few thrombophilia or active cancer patients were included in existing clinical trials, DOAC use in these patients should be reviewed first with Hematology or Oncology. Patients with massive VTEs will require

admission and treatment with LMWH or UFH therefore not be part of an emergency department decision making.

**Quality of Evidence**: Low, GRADE C. We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

**Strength of Recommendation**: Weak, GRADE 2

**References:**

1. Alberta Health Services. Practice Support Document HCS-115-01: Direct Oral Anticoagulant Agents.https://extranet.ahsnet.ca/teams/policydocuments/1/clp-prov-direct-oral-anticoagulant-agents-guideline-hcs-115-01.pdf. Effective April 23, 2015. Accessed July 9, 2015.
2. Healey JS, Eikelboom J, Douketis J, et al. Periprocedural bleeding and thromboembolic events with dabigatran compared with warfarin: results from the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) randomized trial.Circulation.2012;126(3):343-348.
3. Crowther MA, Schulman S. How I treat with anticoagulants in 2012: new and old anticoagulants, and when and how to switch. Blood. 2012;119(13):3016-3023.
4. Van Ryn J, Stangier J, Haertter S, et al. Dabigatran etexilate – a novel, reversible, oral direct thrombin inhibitor: interpretation of coagulation assays and reversal of anticoagulant activity. Thromb Haemost. 2010;103(6):1116-1127.
5. Crowther MA, Warkentin TE. Managing bleeding in anticoagulated patients with a focus on novel therapeutic agents. J Thromb Haemost.2009;7(suppl 1):107-110.

### *PICO 10:* ***In emergency department patients with confirmed deep vein thrombosis (DVT), are there factors that determine which patients would benefit from admission to hospital?***

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***Population, Patient or Problem:*** Emergency department patients with DVT
***Intervention, Prognostic Factor, Exposure*:** Admission to hospital
***Comparison:*** Outpatient therapy
***Outcome:*** Decreased long term morbidity (persistent leg swelling and pain), lower incidence of PE, less bleeding
***Design:*** Systematic reviews of RCT's or observational studies

**Search Strategy:** Cochrane library, Medline, and PubMed for systematic reviews and clinical trials. Guidelines were searched

**Clinical Recommendation:** We suggest that the 2007 Cochrane review by Othieno et al[1], as well as current practice support the outpatient treatment of most patients receiving a diagnosis of DVT. The findings of six randomized controlled trials involving 1708 patients with DVTs comparing home LMWH to in hospital heparin followed by oral anticoagulants, showed a lower recurrence rate of VTE for those treated at home (RR 0.6, range 0.4 to 0.9) and also having lower rates of major bleeding and fewer deaths. The major problems with many of the trials were the large number of

excluded patients without clarity for said exclusions. In addition there have not been any new studies since the broad use of the DOACs in clinical practice to see if they affect disposition decision making

A 2004 metaanalysis by Douketis[2] identified four criteria to identify those DVT patients for whom in-hospital treatment should be considered. These were: 1) massive DVT (swelling of entire limb, acrocyanosis, venous limb ischemia, or extension into iliofemoral veins or inferior vena cava); 2) associated symptomatic pulmonary embolism (requiring supplemental O2 or at risk for cardiorespiratory deterioration); 3) high risk for anticoagulant-related bleeding (active bleeding or recent bleeding episode within 4 weeks [eg peptic ulcer bleed], recent surgery or trauma [within 1 week], thrombocytopenia [platelet count less than 100 x $10^6$/L], coagulopathy, or advanced cancer with intracranial or intrahepatic metastases); or 4) major comorbidities or other factors that warrant inpatient care (including impaired cognitive, self care or adequate supports to ensure compliance with outpatient care requirements).

Cei et al[3] in a 2013 critical review of which DVT cases still need to be admitted generally agreed with the Douketis criteria but did also note that some of the Hestia criteria[4] for PE admission were also relevant to the DVT population.

The ICSI guidelines states that some patients may require hospitalization during the first 24 hours because of the need for an organized support system, and time of day considerations for home care agencies.[5] Criteria for patients be sent to outpatient therapy instead of hospitalization include good cardiorespiratory reserve, no excessive bleeding risks, and creatinine clearance greater than 30 mL/min.

**Quality of Evidence**: Very Low, GRADE D. We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

**Strength of Recommendation**: Weak, GRADE 2

**References:**

1. Othieno R, Abu Affan M, Okpo E. Home versus in-patient treatment for deep vein thrombosis. *Cochrane Database Syst Rev*.2007;18(3): CD003076. DOI:10.1002/14651858.CD003076.pub2.
2. Douketis JD. Treatment of deep vein thrombosis: what factors determine appropriate treatment?*Can Fam Physician*. 2005;51:217-223.
3. Cei M, Cei F, Mumoli N. Deep vein thrombosis: who still needs to be admitted? OA Case Reports. 2013;2(2):15.
4. Zondag W, Vingerhoets LM, Durian MF, et al. Hestia criteria can safely select patients with pulmonary embolism for outpatient treatment irrespective of right ventricular function. *J Thromb Haemost.* 2013;11(4):686-692.
5. Dupras D, Bluhm J, Felty C, et al. Institute for Clinical Systems Improvement. Venous Thromboembolism Diagnosis and Treatment Web Site https://www.icsi.org/_asset/5ldx9k/VTE0113.pdf Updated January 2013. Accessed July 9, 2015.

***PICO 11:*** ***Are there clinical indicators in patients with a new diagnosis of venous thromboembolism (VTE) which should prompt investigation or consultation to look for genetic hypercoaguable risk factors to determine length of anticoagulation?***

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***Population, Patient or Problem:*** Emergency department patients with newly diagnosed Venous Thromboembolism (VTE)
***Intervention, Prognostic Factor, Exposure*****:** Selective screening for hypercoagulability
***Comparison:*** Random screening for hypercoagulability
***Outcome:*** Sensitivity, specificity, cost effectiveness, safety
***Design:*** Systematic reviews of RCT's or observational studies

**Search Strategy:** Cochrane library, Medline, and PubMed for systematic reviews and clinical trials. Guidelines were searched

**Clinical Recommendation:** There is insufficient evidence to make a firm recommendation regarding which patients should be considered for thrombophilia testing in the emergency department prior to initiating anticoagulation.[1,2,3] We have included the criteria and link to the "Thrombophilia testing"" policy and procedure guideline for the Calgary Zone published January 2010 which stated thrombophilia testing should be considered in the following situations.[4]

1. All patients with first episode of idiopathic VTE.
2. Patients with recurrent VTE irrespective of the presence of risk factors.
3. Patients with VTE at unusual sites such as cerebral venous sinus, retinal vein thrombosis, upper extremity thrombosis, mesenteric or hepatic vein thrombosis. Screening is not routinely recommended in portal or splenic vein thrombosis or arterial thrombosis.
4. Women of child bearing age with prior idiopathic VTE or transient provocative factor such as oral contraceptives therapy, estrogen replacement therapy or pregnancy.
5. Women with two or more consecutive miscarriages during the first trimester, or one miscarriage after first trimester, or three non-consecutive miscarriages at any gestational age.
6. Women with prior severe or recurrent pre-eclampsia or unexplained fetal death after 20th week gestational age.
7. Asymptomatic first-degree relatives of individuals with proven symptomatic thrombophilia including protein C or S deficiency, antithrombin III deficiency, Factor V Leiden, Prothrombin G202210A. APLA should be tested in female relatives of child bearing age.
8. Testing should only be offered after counselling on potential implications.
9. Testing for antithrombin III should not be done in the setting of acute thrombosis or while on heparin products.
10. Testing for Protein C and Protein S should not be done in the setting of acute thrombosis or while on warfarin.
11. Testing for Protein S should not be done during pregnancy or on hormone therapy.

**Quality of Evidence:** Low, GRADE C. Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

**Strength of Recommendation:** Insufficient evidence

**References:**

1. Bates SM, Ginsberg JS. Clinical practice. Treatment of deep-vein thrombosis. *N Engl J Med.* 2004;351(3):268-277.
2. De Stefano V, Rossi E, Paciaroni K, Leone G. Screening for inherited thrombophilia: indications and therapeutic implications. *Haematologica*. 2002;87(10):1095-1108.
3. Van Cott E, Laposata M, Prins MH. Laboratory evaluation of hypercoagulability with venous or arterial thrombosis. *Arch Pathol Lab Med.* 2002;126(11):1281-1295.
4. Anticoagulation Management Services Clinical Steering Committee. *Guidelines for thrombophilia screening.* Reviewed 2007. Accessed July 9, 2015.

# Appendix B - PICO-D Methodology and GRADE Terminology

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Key components of high quality and trustworthy clinical guidance include: i) recommendations that are clearly stated and based on scientific evidence of benefits, harms and where possible, costs, and ii) a guideline rating system that is used to communicate quality and reliability of both the evidence and the strength of its recommendations. In the development of these guidelines, clinical questions were formulated based on the PICO-D format as supported by Sackett[1] and Guyatt[2] in their User's Guide to the Medical Literature to define the clinical question. The GRADE terminology, where possible, is used to address the questions regarding Quality of Evidence and Strength of Recommendations. The components of PICO-D format and the GRADE methodology are described below.

**PICO-D**

**P - Population, Patient, or Problem:** This element defines the group of patients or characteristics of the patients.
**I - Intervention, Prognostic Factor, Exposure:** This element defines the main intervention being considered.
**C - Comparison:** This element defines the main alternative to compare with the intervention, such as comparison of two drugs or tests, or a medication to no medication or placebo.
**O - Outcome:** This defines what you are trying to accomplish, measure, improve or affect.
**D - Design:** The type of question (related to diagnosis, harm/etiology, prognosis, or therapy) will define which study design is best suited to provide evidence to answer the clinical question.

Definitions of Study Types[2,3]

1. **Meta-analysis:** a statistical technique that summarizes the results of several studies in a single weighted estimate, in which more weight is given to results of studies with more events and sometimes to studies of higher quality.
2. **Systematic Review:** attempts to collate all empirical evidence that fits pre-specified eligibility criteria to answer a specific research question using explicit, systematic methods selected with a view to minimizing bias. This provides more reliable findings from which to
draw conclusions. (Antman 1992, Oxman 1993). The key characteristics of a systematic review are: i) clearly stated objectives with pre-defined eligibility criteria for studies; ii) an explicit and reproducible methodology; iii) a systematic search that attempts to identify all
studies meeting the eligibility criteria; iv) an assessment of validity for the included studies, (e.g. through the assessment of risk of bias; and v) a systematic synthesis and presentation, of the characteristics and findings of the included studies.[4]
3. **Randomized Controlled Trial (RCTs):** a trial in which participants are randomly assigned to two or more groups: at least one (the experimental group) receiving an intervention that is being tested and another (the comparison or control group) receiving an alternative treatment or placebo. This design allows assessment of the relative effects of interventions.
4. **Controlled Clinical Trial (CCTs):** a trial in which participants are assigned to two or more

different treatment groups in a non-randomized or quasi-randomized method. Examples of quasi-randomized allocation are birthdate and medical record numbers. Studies in which the randomization process is not explicitly stated as randomized are considered CCTs. CCTs are more likely to suffer from bias than RCTs.

5. **Observational Studies:**
    a. **Cohort Study**[2]**:** an observational study in which a defined group of people (the cohort) is followed over time. The outcomes of people in subsets of this cohort are compared, to examine people who were exposed or not exposed (or exposed at different levels) to a particular intervention or other factor of interest. A prospective cohort study assembles participants and follows them into the future. A retrospective (or historical) cohort study identifies subjects from past records and follows them from the time of those records to the present.
    b. **Case control study:** a study design that examines a group of people who have experienced an event (usually an adverse event) and a group of people who have not experienced the same event, and looks at how exposure to suspect (usually noxious) agents differed between the two groups. This type of study design is most useful for trying to ascertain the cause of rare events, such as rare cancers.
    c. **Case Series:** analysis of series of people with the disease (there is no comparison group in case series).

**GRADE Methodology**
Whenever possible answers are identified from recent high quality guidelines or high quality systematic reviews and recommendations provided are based on GRADE definitions. Where guidelines or systematic reviews are not available to answer certain questions rapid reviews are undertaken and/or a consensus approach used to try to answer clinically relevant questions. **Only where the evidence is supportive and the benefits clearly outweigh the harm is a "we recommend" strength of recommendation applied.**

**Table 1.** GRADE Quality of Evidence[2]

| | |
|---|---|
| High<br>GRADE A | We have high confidence that the true effect lies close to that of the estimate of the effect. |
| Moderate<br>GRADE B | We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. |
| Low<br>GRADE C | Our confidence in the effect estimate is low: The true effect may be substantially different from the estimate of the effect. |
| Very low<br>GRADE D | We have very low confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect. |

| **Table 2.** GRADE Strength of Recommendations[2] | |
|---|---|
| Strong GRADE 1 | Strong recommendation, with desirable effects clearly outweighing undesirable effects/burdens (or vice versa).<br>**Wording of Recommendation:** We recommend in favor of / We recommend against… |
| Weak GRADE 2 | Weak recommendation, with desirable effects closely balanced with undesirable effects.<br>**Wording of Recommendation:** We suggest in favor of / We suggest against … |
| Insufficient evidence or no consensus | **Wording of Recommendation:** There is insufficient evidence or the confidence in the effect estimates is so low that the panel is unable to make a recommendation regarding… |

**References:**

1. Sackett D, Richardson WS, Rosenburg W, Haynes RB. *How to practice and teach evidence based medicine.* 2nd ed. Churchill Livingstone; 1997.
2. Guyatt GH, Oxman AD, Vist GE, et al; for the GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008; 336(7650):924-926.
3. Clinical Questions, PICO & Study Designs: Formulating a Well Built Clinical Question. Dahlgren Memorial Library/ Georgetown University Medical Center. http://researchguides.dml.georgetown.edu/ebmclinicalquestions. Updated February 3, 2015. Accessed January 2015.
4. Antman EM, Lau J, Kupelnick B, Mosteller F, Chalmers TC. A comparison of results of meta-analyses of randomized control trials and recommendations of clinical experts. Treatments for myocardial infarction. *JAMA.* 1992;268(2):240-248.
5. Oxman AD, Guyatt GH. The science of reviewing research. *Ann N Y Acad Sci.* 1993;703:125-133.
6. Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions.* Version 5.1.0. West Sussex, England: The Cochrane Collaboration and John Wiley & Sons, Ltd; 2008.

## Appendix C - Patient Education and Discharge Material

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**DVT: After Your Visit**
https://myhealth.alberta.ca/health/AfterCareInformation/pages/conditions.aspx?HwId=uf8366

**How to Give a Heparin Shot: After Your Visit**
https://myhealth.alberta.ca/health/AfterCareInformation/pages/conditions.aspx?HwId=zp4251

**Taking Blood Thinners Other Than Warfarin: After Your Visit**
https://myhealth.alberta.ca/health/AfterCareInformation/pages/conditions.aspx?HwId=abo9742

**Taking Warfarin Safely: After Your Visit**
https://myhealth.alberta.ca/health/AfterCareInformation/pages/conditions.aspx?HwId=abk1586

## Appendix D - Scoring Tools / Risk Scores

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**Wells' Criteria for DVT[5]**
http://www.mdcalc.com/wells-criteria-for-dvt/

**Table 1. Two-level DVT Wells' Score**

| Clinical Characteristic | Score |
|---|---|
| Active cancer (patient receiving treatment for cancer within the previous 6 mo or currently receiving palliative treatment) | 1 |
| Paralysis, paresis, or recent plaster immobilization of the lower extremities | 1 |
| Recently bedridden for 3 days or more, or major surgery within the previous 12 wk requiring general or regional anesthesia | 1 |
| Localized tenderness along the distribution of the deep venous system | 1 |
| Entire leg swollen | 1 |
| Calf swelling at least 3 cm larger than that on the asymptomatic side (measured 10 cm below tibial tuberosity) | 1 |
| Collateral superficial veins (nonvaricose) | 1 |
| Previously documented deep-vein thrombosis | 1 |
| Pitting edema, confined to the symptomatic leg | 1 |
| Alternative diagnosis at least as likely as deep-vein thrombosis | -2 |
| **Clinical Probability** | **Points** |
| DVT unlikely | 1 point or less |
| DVT likely | 2 points or more |

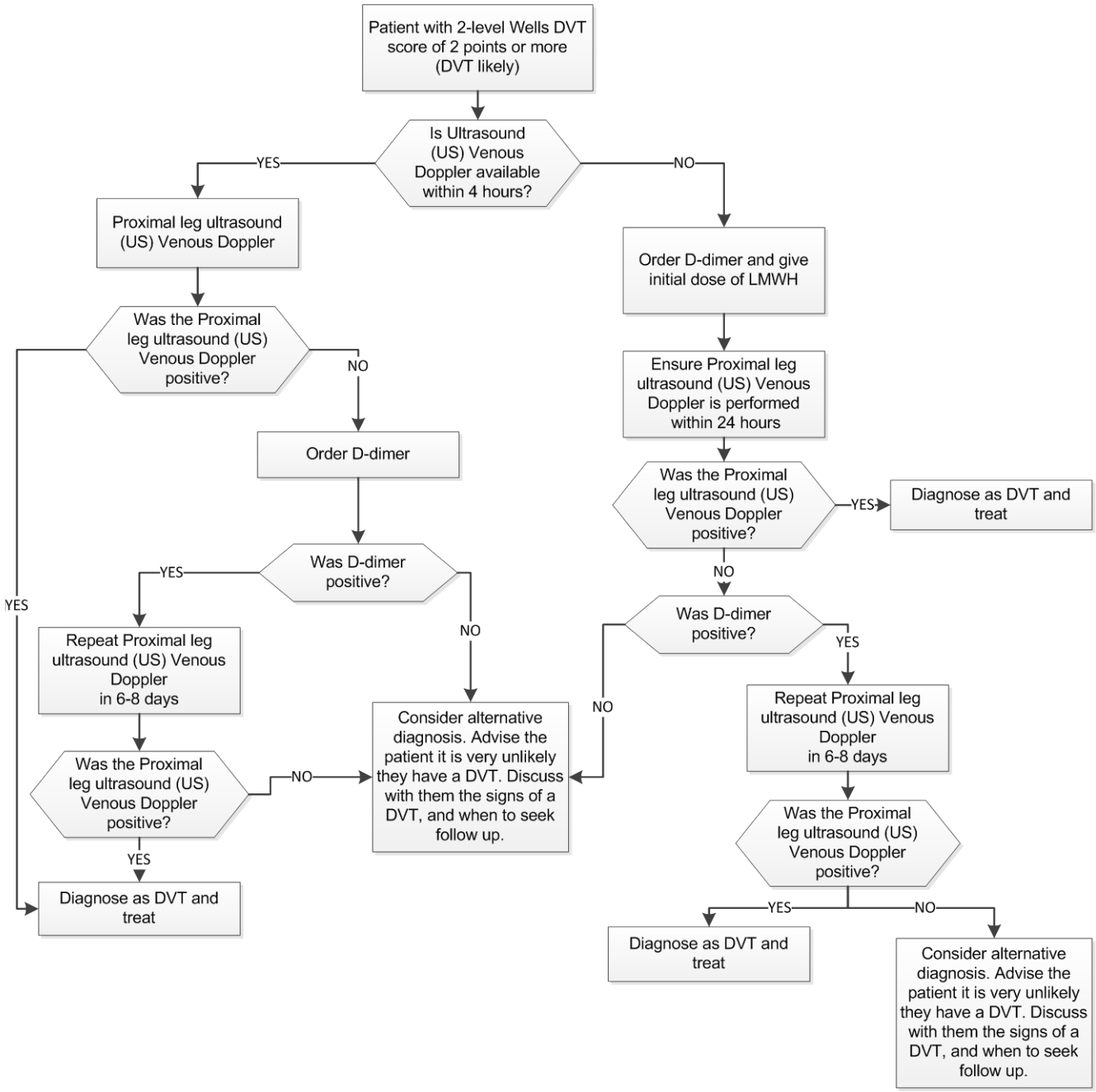
Amongst a patient population of 562 patients with suspected DVT and a final overall prevalence of 315 were categorized as unlikely and 247 as likely to have a DVT.

Of the 'unlikely' group 5.1% [16] had a DVT (95%CI 2.9-81). All except for 2 had a positive D-dimer for an initial miss rate of 0.6% with a negative predictive value for the D-dimer test of 99.1% (95% CI, 96.7 to 99.9%).

Of the 'likely' group 28.7% [71]; had a DVT (95% CI 23.1 to 34.4%), with 68 identified at the initial diagnostic ultrasound and 3 at the 1 week repeat ultrasound. Of the 181 ultrasound negative patients 100 had a positive D-dimer and a repeat ultrasound at one week identified the 3 additional DVTs. For the 81 with negative D-dimers no further testing was performed and no DVTs or PEs identified during the 3 month follow up (F/U) period. The negative predictive value of the D-dimer in the 'likely' group was 89% (955 CI 80.7 to 94.6%) however, by adding the 1 week follow up (F/U) ultrasound the negative predictive value rose to 100%.

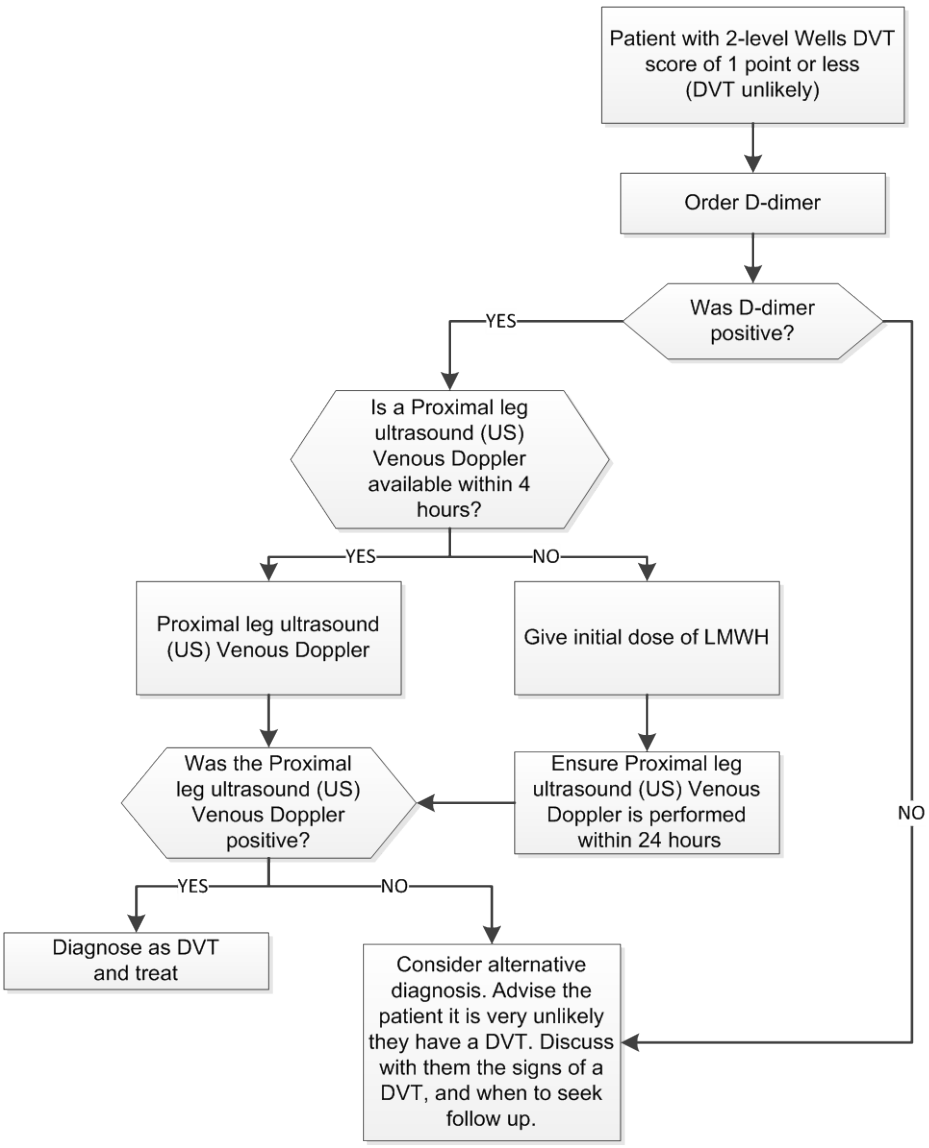
## Algorithm: Deep vein thrombosis likely based on two-level Wells score

Figure 1. Deep vein thrombosis likely based on two-level Wells score[6]



## Algorithm: Deep vein thrombosis unlikely based on two-level Wells

Figure 2. Deep vein thrombosis unlikely based on two-level Wells score[7]



**References:**

1. Wells PS, Anderson DR, Rodger M, et al. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. *N Engl J Med.* 2003;349(13):1227-1235.
2. Scarvelis D, Wells PS. Diagnosis and treatment of deep-vein thrombosis. *CMAJ*. 2006;175(9):1087-1092.
3. Wells PS, Owen C, Doucette S, Fergusson D, Tran H. Does this patient have deep vein thrombosis? *JAMA.* 2006;295(2):199-207.
4. Bates SM, Jaeschke R, Stevens SM, et al. Diagnosis of DVT: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012; 141(suppl 2):e351S-e418S. Scottish Intercollegiate Guidelines Network. Prevention and management of venous thromboembolism. http://www.sign.ac.uk/pdf/sign122.pdf Published December 2010. Accessed July 7, 2015.
5. National Institute for Health and Care Excellence (NICE) Web site. Deep vein thrombosis likely based on two-level Wells score. http://pathways.nice.org.uk/pathways/venous-thromboembolism#content=view-index&path=view%3A/pathways/venous-thromboembolism/deep- vein-thrombosis-likely-based-on-two-level-wells-score.xml. Accessed July 8, 2015.
6. National Institute for Health and Care Excellence (NICE) Web site. Deep vein thrombosis unlikely based on two-level Wells score. http://pathways.nice.org.uk/pathways/venous-thromboembolism#content=view-index&path=view%3A/pathways/venous-thromboembolism/deep- vein-thrombosis-likely-based-on-two-level-wells-score.xml. Accessed July 8, 2015.

## Appendix E - Direct Oral Anticoagulant Guideline

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**Important Note: The information contained in this appendix comes from a provincial guideline and does not show the guideline in it's entirely. The content below is not guaranteed to be up to date and it is recommended that the full guideline is accessed.**

To access the full AHS guideline go to: **https://extranet.ahsnet.ca/teams/policydocuments/1/clp-prov-direct-oral-anticoagulant-agents-guideline-hcs-115-01.pdf**

**Please see relevant VTE treatment information below from the: Direct Oral Anticoagulants Document effective April 23, 2015. Information referenced below was added in August 2015.**

---

Recommendations for the use of dabigatran, rivaroxaban, and apixaban:

- These agents do not require routine anticoagulation monitoring of PT INR or PTT.
- Specific reversal agents are not currently available to control active bleeding.
- All three drugs require some degree of renal clearance, least for apixaban and greatest for dabigatran.

***DOACS and Venous thromboembolism:***

All of the new DOAC's found to be non-inferior to VKA's based on rates of recurrence of VTE and bleeding risk. They have been studied for DVT and PE and Health Canada has approved all three agents for VTE treatment.

1. DOAC dosing: rivaroxaban and apixaban have initial higher BID dosing for VTE while dabigatran used an initial 5-10 days of LMWH or UFH.

2. Massive VTE: For patients with massive DVT or PE, not included in prior DOAC studies, it would be prudent to use standard therapies with LMWH/UFH if considering for thrombolysis or thrombectomy. LMWH is suggested for the first 3 months for proximal ileofemoral DVT or submassive PE and patients with active cancer as there is evidence for specific benefit with LMWH for these groups.

3. Thrombophilia and Cancer: Because few patients with active cancer or thrombophilia were included in clinical trials with DOACs these higher risk patients should be reviewed with Oncology or Hematology before considering DOACs for their initial management.

4. Longer term therapy/Secondary prevention: Studies looking at continuing DOACs for an additional 6-12 months, after the initial 6 month treatment period, have shown significant benefit

in preventing VTE recurrence, however, there was a significantly higher bleeding risk with dabigatran and rivaroxaban compared to placebo but equivalent to placebo when apixaban was used.

5. Medication interactions***:*** While there are not many drug interactions with the DOACs there are specific situations they should be avoided if certain drugs need to be continued including: rifampin, phenytoin, carbamazepine, clarithromycin, fluconazole and other azoles and protease inhibitors.

**Monitoring:**

- Anticoagulation monitoring is not routinely required.
- Patients who require high risk bleeding procedures, a normal INR/PTT will not exclude significant residual effect of DOAC.
- For dabigatran, a PPT value greater than 2 times normal is associated with increased risk of bleeding and a normal thrombin time can be used to exclude any significant residual anticoagulant effect.
- For Xa inhibitors (rivaroxaban and apixaban), a heparin calibrated anti-Xa level less than 0.1 will exclude any significant residual effect of rivaroxaban anticoagulant.

**Dosing:**

**Rivaroxaban is currently the only DOAC covered under Alberta Government funded insurance plans and does require a 'special request' form to be completed before the plan will agree to cover the cost.**

**Table 1. Recommended dosages:**

| Indication | Dabigatran | Rivaroxaban | Apixaban |
|---|---|---|---|
| **VTE** | LMWH x 7 days **then** dabigatran 150 mg PO BID | 15 mg PO BID x 3 weeks **then** 20 mg po daily | 10 mg PO BID x 7 days **then** 5 mg PO bid |

***Management of Bleeding on these Agents:***

[Return to Disposition Planning: Considerations for Discharge]

## A. Dabigatran

### Table 2. Patients on Dabigatran (Pradaxa) with Bleeding

| | Minor Bleeding | Moderate Bleeding | Major Bleeding |
|---|---|---|---|
| **Testing** | • CBC, INR/PTT;<br>• Creatinine | • CBC, INR/PTT;<br>• Creatinine;<br>• Fibrinogen;<br>• Type and Screen;<br>• Thrombin Time | • CBC, INR/PTT;<br>• Creatinine;<br>• Fibrinogen;<br>• Cross-match;<br>• Thrombin Time |
| **Supportive Therapy** | • Local therapy | • Local therapy/site control;<br>• Transfusion;<br>• Surgery/Intervention | • Local therapy;<br>• Transfusion;<br>• Surgery/Intervention;<br>• Consider platelet transfusion if antiplatelet agents are in use |
| **Drug Dosing** | • Hold Dabigatran;<br>• Hold antiplatelet agents | • Hold Dabigatran;<br>• Hold antiplatelet agents | • Hold Dabigatran;<br>• Hold antiplatelet agents |
| **Reversal/Removal** | • None | • Consider charcoal[a] less than 2-4 hours post-dose;<br>• Consider dialysis | • Consider charcoal[a] less than 2-4 hours post-dose;<br>• Consider dialysis |
| **Procoagulant Agents** | • None | • Tranexamic acid (10mg/kg IV or 25 mg/kg PO)[b] | • Consider FEIBA 25 - 50 unit/kg for major bleeding, 50-100 unit/kg for ICH or PCC 25 - 50 unit/kg<br>• Tranexemic acid (10 mg/kg IV)[b] |

**Note:** [a]Major upper GI bleeding is a relative contraindication for activated charcoal
[b]Upper urinary tract bleeding is a relative contraindication for Tranexamic acid, which can cause “clot colic”;

## B. Rivaroxaban/Apixaban

### Table 3. Patients on Rivaroxaban (Xarelto) or Apixaban (Eliquis) with Bleeding

| | Minor Bleeding | Moderate Bleeding | Major Bleeding |
|---|---|---|---|
| **Testing** | • CBC, INR/PTT | • CBC, INR/PTT;<br>• Fibrinogen;<br>• T &S;<br>• Anti Xa level | • CBC, INR/PTT;<br>• Fibrinogen;<br>• T &S;<br>• Anti Xa level |
| **Supportive Therapy** | • Local therapy | • Local therapy/site control;<br>• Transfusion;<br>• Surgery/Intervention | • Local Therapy;<br>• Transfusion;<br>• Surgery/intervention;<br>• Consider platelet transfusion if recent antiplatelet agents |
| **Drug Dosing** | • Hold Rivaroxaban/ Apixaban;<br>• Hold antiplatelet agents | • Hold Rivaroxaban/Apixaban;<br>• Hold antiplatelet agents | • Hold Rivaroxaban/Apixaban;<br>• Hold antiplatelet agents |
| **Reversal** | • None | • Consider charcoal[a] (no evidence for effectiveness);<br>• Not dialyzable | • Consider charcoal[a] (no evidence for effectiveness);<br>• Not dialyzable |
| **Procoagulant agents** | • None | • Tranexamic acid (10 mg/kg IV or 25 mg/kg PO)[b] | • Consider PCC 25-50 unit/kg or fixed dosage of PCC 2000 units **or** rFVIIa 40 - 90 mcg/kg;<br>• Tranexamic acid (10 mg/kg IV)[b] |

**Note:** [a]Major upper GI bleeding is a relative contraindication for activated charcoal
[b]Upper urinary tract bleeding is a relative contraindication for Tranexamic acid, which can cause “clot colic”;

***If an emergent/urgent procedure is required:***

1. For patients needing emergent surgery, reversal cannot be achieved prior to proceeding nor is there time for coagulation testing.
2. Draw blood for: CBC, INR, PTT, fibrinogen, thrombin time, anti-Xa activity, type and screen, Creatinine, then proceed and transfuse as necessary along with other products as time permits.
3. Time permitting, measure the level of effect of the oral anticoagulant agent and wait until the effect is minimal or below detection prior to proceeding.
4. Dabigatran's effect will be influenced more by renal dysfunction than that of rivaroxaban or apixaban.

**Reference:**

1. Alberta Health Services. Practice Support Document HCS-115-01:Direct Oral Anticoagulant Agents. https://extranet.ahsnet.ca/teams/policydocuments/1/clp-prov-direct-oral-anticoagulant-agents-guideline-hcs-115-01.pdf. Effective April 23, 2015. Accessed July 9, 2015.

## Appendix F - Apixaban/Dabigatran/Rivaroxaban – Alberta Blue Cross Special Authorization Request Form

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To access the request form click here: https://www.ab.bluecross.ca/dbl/pdfs/60019.pdf

## Appendix G - Glossary of Terms

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| Term | Definition |
|---|---|
| **Budd-Chiari – also known as Chiari syndrome** | http://www.medilexicon.com/medicaldictionary.php?t=87817 |
| **Phlegmasia cerulea dolens** | http://www.medilexicon.com/medicaldictionary.php? t=68163 |
| **Direct Oral Anticoagulant (DOAC)** | Previously called New/Novel Oral Anticoagulants – dabigatran, rivaroxaban, apixaban |

## Appendix H - Clinical Working Group Membership

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We would like to acknowledge the contributions of the Provincial Clinical Knowledge Working Group members as follows. Your participation and time spent is appreciated.

Emergency Department Deep Vein Thrombosis Knowledge Topic Working Group Membership

| Name | Title | Role | Zone |
|---|---|---|---|
| *Knowledge Lead* | | | |
| Michael Bullard | Physician | Knowledge Lead | Provincial |
| *Topic Lead* | | | |
| Pat San Agustin | Physician | Topic Lead | Provincial |
| *Working Group Members* | | | |
| Brian Holroyd | Physician | Working Group Member | Edmonton Zone |
| Dan Banmann | Physician | Working Group Member | South Zone |
| Eddy Lang | Physician | Working Group Member | Calgary Zone |
| Harvey Woytiuk | Physician | Working Group Member | North Zone |
| Jenn Pritchard | Physician | Working Group Member | Edmonton Zone |
| Richard Martin | Physician | Working Group Member | Central Zone |
| Sam Chow | Physician | Working Group Member | Edmonton Zone |
| Shawn Dowling | Physician | Working Group Member | Calgary Zone |
| Simon Ward | Physician | Working Group Member | Central Zone |
| Ali Kirkham | Physician | Working Group Member | Edmonton Zone |
| Katherine Smith | Physician | Working Group Member | Edmonton Zone |
| Paul Parks | Physician | Working Group Member | South Zone |
| James Andruchow | Physician | Working Group Member | Calgary Zone |
| Ni Lam | Physician | Working Group Member | Edmonton |
| Chris Hall | Physician | Working Group Member | Calgary Zone |
| Andrew McRae | Physician | Working Group Member | Calgary Zone |
| Lyle Thomas | Physician | Working Group Member | Central Zone |
| Alexis Mageau | Registered Nurse | Working Group Member | Calgary Zone |
| Jennine Desmarais | Registered Nurse | Working Group Member | North Zone |
| Bonnie Niebergall | Registered Nurse | Working Group Member | South Zone |
| Laura Fowler | Registered Nurse | Working Group Member | Central Zone |
| Margaret Dymond | Registered Nurse | Working Group Member | Edmonton Zone |
| Maria Janik | Registered Nurse | Working Group Member | Edmonton Zone |
| Monique Fernquist | Registered Nurse | Working Group Member | Provincial |
| Sara Noseworthy | Registered Nurse | Working Group Member | Calgary Zone |
| Shelly Lynn Franklin | Registered Nurse | Working Group Member | North Zone |
| Thora Skeldon | Registered Nurse | Working Group Member | Central Zone |
| *Multidisciplinary* | | | |
| Bruce Ritchie | Physician | Content Expert | Edmonton Zone |
| Elizabeth Mackay | Physician | Content Expert | Calgary Zone |
| Nicholas Myers | Physician | Primary Care Representative | Calgary Zone |

| | | | |
|---|---|---|---|
| Bill Anderson | Physician - Diagnostic Imaging Representative | Content Expert | Provincial |
| Stafford Dean | DIMR representative | Content Expert | Provincial |
| James Wesenberg | Laboratory Representative | Content Expert | Provincial |
| Steve Freriks | Pharmacy Representative | Content Expert | Provincial |
| Rod Elford | Physician | Primary Care Representatives | Calgary Zone |
| Sophia Christoforakis | SCN Representative | Surveyor | Provincial |

*Thank you to the following clinicians who participated in the colleague review process. Your time spent reviewing the knowledge topics and providing valuable feedback is appreciated. Ian Wishart, Donald Nixon, Lori Jordens, Essam Elbeshti, Scott Ross, Jennifer Lowerison, Adrienne Haponiuk, Cam MacGougan, Aref Yeung.*

**For questions or feedback related to this knowledge topic please contact Clinical Knowledge Topics by emailing ClinicalKnowledgeTopics@ahs.ca**