# Venous Thromboembolism Prophylaxis - Pediatric - Inpatient
Clinical Practice Guideline

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Pediatric venous thromboembolism (VTE) is a life-threatening condition associated with increased morbidity, mortality, duration of hospital stay, and health care expenditures. It is increasingly being recognized as a complication of contemporary health care in the pediatric population. Estimated annual incidence among hospitalized pediatric patients is upwards of 60 events per 10,000 admissions. Neonates are at the greatest risk of thromboembolism, with a second peak in incidence noted during puberty and adolescence. Although far less common in children than adults, several underlying medical conditions place children at risk for developing VTE. One of the greatest risks for VTE in children is the insertion of central venous catheters. Additionally, other acquired conditions frequently associated with VTEs in children include infection, trauma, surgery, and immobility.

There is no standardized and validated thromboprophylaxis risk tool established in the pediatric population. These guidelines provide recommendations on the evaluation of patients at risk for VTE based on identified risk factors as well as appropriate VTE prophylaxis modalities.

Scope

Intended Users: Physicians, advanced practice providers, pharmacists, and nurses who provide care to hospitalized pediatric patients

Objective: To provide recommendations and guidance for the preventative treatment of venous thromboembolism (VTE) in hospitalized pediatric patients.

Target Population: Any pediatric inpatient who is 6 months of age or older with the intent to remain hospitalized for greater than 24 hours. The recommendations for pharmacologic strategies used to prevent VTE would apply to pediatric patients receiving either unfractionated heparin (UFH) or low molecular weight heparin (LMWH).

Patients younger than 6 months of age are excluded from this guideline due to insufficient data to sufficiently describe use in this population.

This guideline is not intended to provide recommendations for the treatment of VTE.

Recommendations

1. Prevention of VTE in hospitalized pediatric patients
   1.1 All hospitalized patients older than 6 months should be evaluated for both bleeding and VTE risk within 24 hours of admission, upon transferring level of care, and periodically during hospital stay (every 48-72 hours). (UW Health GRADE Low quality evidence, strong recommendation)
   1.2 Documentation of initial bleeding and VTE risk should occur in the medical record within 24 hours of hospital admission or postsurgical procedure. (UW Health GRADE Very low quality evidence, strong recommendation)
   1.3 Reassessment of bleeding and VTE risk should occur in the medical record when there is a change in level of care. (UW Health GRADE Very low quality evidence, strong recommendation)

2. Evaluation of Bleeding Risk
   2.1 There is no universally validated model to assess bleeding risk with the use of chemical DVT prophylaxis.
   2.2 Recommendations for specific factors associated with increased bleeding risk are included in Table 1. (UW Health GRADE Very low quality evidence, strong recommendation)
   2.2.1 If patient meets at least one of the following criteria of the “Chemical Prophylaxis NOT Recommended” list in Table 1, avoid chemical prophylaxis as risk outweighs benefit. (UW Health GRADE Very low quality evidence, strong recommendation)
2.2.2 If patient meets at least one of the following criteria in the “Consider Avoiding Chemical Prophylaxis” list in Table 1, consider avoiding chemical prophylaxis. (UW Health GRADE Very low quality evidence, conditional recommendation)

2.2.2.1 Consider consulting hematology for recommendations if patient considered at high risk for VTE, but also with high bleeding risk.  

2.2.2.2 Uncontrolled hypertension is defined as systolic or diastolic blood pressure greater than 95th percentile for age, height, and gender.

2.2.2.3 Coagulopathy is defined as INR >1.5, APTT >44 seconds, fibrinogen <100 g/dL, or platelet <50,000/microliter.

Table 1: Bleeding Risk Factors

<table>
<thead>
<tr>
<th>Chemical Prophylaxis NOT Recommended</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Intracranial hemorrhage</td>
<td>Intracranial mass</td>
</tr>
<tr>
<td>Brain ischemia/acute stroke</td>
<td>Recent lumbar puncture (&lt;24 hours ago)</td>
</tr>
<tr>
<td>Active bleeding</td>
<td>Coagulopathy</td>
</tr>
<tr>
<td>Recent thrombolytic therapy (&lt;24 hours)</td>
<td>Neurosurgical procedure</td>
</tr>
</tbody>
</table>

3. Evaluating VTE risk in medical, surgical, and trauma patients

3.1 There is no universally validated model to assess VTE risk in medical, surgical, or trauma patients.

3.2 Table 2 and Table 3 should be used to assess VTE risk. (UW Health GRADE Very low quality evidence, strong recommendation)

3.2.1 Reduced mobility is considered as decrease in movement from baseline or those unable to participate in physical therapy.

3.2.2 Central venous access device is defined as a non-tunneled catheter, tunneled catheter, or peripherally inserted central catheter (PICC).

3.2.3 Major burn is defined as more than 50% of body surface area.

3.2.4 Major surgery includes operations lasting longer than 45 minutes.

3.2.5 Critically ill is defined as patients in the critical care setting or ICU (inotropic support, mechanically ventilated).

3.2.6 Thrombophilic conditions include defects of antithrombin, protein C or S deficiency, factor V Leiden, or prothrombin gene mutation.

3.2.7 Active malignancy defined as receiving chemotherapy/radiation in previous 6 months.

3.2.8 Active inflammatory disease includes Kawasaki’s disease, inflammatory bowel disease, systemic lupus erythematosus, or nephrotic syndrome.

3.2.9 Estrogen therapy includes oral contraceptives or estrogen replacement currently taking or within past 2 weeks.

3.2.10 Obesity is defined as BMI greater than 95th percentile for age.

3.3 Risk Factor Stratification definitions

3.3.1 Low VTE risk:
• No altered mobility and 0-1 risk factors

3.3.2 Moderate VTE risk:
• No altered mobility and 2-3 risk factors
• Altered mobility and 0-1 other risk factors

3.3.3 High VTE risk:
• No altered mobility and ≥4 risk factors
• Altered mobility and ≥2 other risk factors
3.4 See Appendix B Flow Chart for recommended interventions.

Table 2: VTE Risk Factors

<table>
<thead>
<tr>
<th>Acute Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced mobility longer than 72 hours</td>
</tr>
<tr>
<td>Central venous access device</td>
</tr>
<tr>
<td>Active infection</td>
</tr>
<tr>
<td>Major trauma or burn</td>
</tr>
<tr>
<td>Major surgery</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>Critically ill</td>
</tr>
<tr>
<td>Chronic Medical Conditions</td>
</tr>
<tr>
<td>Autoimmune disorders associated with thrombosis</td>
</tr>
<tr>
<td>Thrombophilic condition</td>
</tr>
<tr>
<td>Active malignancy</td>
</tr>
<tr>
<td>Active inflammatory condition</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>Estrogen therapy</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Historical Factors</td>
</tr>
<tr>
<td>Asparaginase within previous 30 days</td>
</tr>
<tr>
<td>Recent surgery within past 30 days</td>
</tr>
<tr>
<td>History of thrombosis</td>
</tr>
<tr>
<td>Family history of VTE in a 1st degree relative &lt; 40 years old at time of clot</td>
</tr>
</tbody>
</table>

Table 3: VTE Risk Assessment

<table>
<thead>
<tr>
<th>Risk Factor Stratification</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low VTE Risk</td>
<td>• Early Ambulation</td>
</tr>
<tr>
<td></td>
<td>• No prophylaxis necessary</td>
</tr>
<tr>
<td>Moderate VTE Risk</td>
<td>• Early Ambulation</td>
</tr>
<tr>
<td>High VTE Risk and High Bleed Risk</td>
<td>• Mechanical Prophylaxis</td>
</tr>
<tr>
<td>High VTE Risk and Low Bleed Risk</td>
<td>• Early Ambulation</td>
</tr>
<tr>
<td></td>
<td>• Mechanical Prophylaxis and Pharmacologic Prophylaxis</td>
</tr>
</tbody>
</table>

4. VTE prophylaxis options

4.1 Mechanical prophylaxis: methods may include sequential compression device (SCD) or graduated compression stockings (GCS).4–7,9,11,15

4.1.1 Contraindications to mechanical prophylaxis6,15 (UW Health GRADE Low quality evidence, strong recommendation)

- Extremity has acute fracture
- Extremity has peripheral IV access
- Skin condition affecting extremity (i.e. dermatitis, burn)
- Unable to achieve correct fit due to patient size
- Lower extremity peripheral arterial insufficiency

4.2 Patients identified as high VTE risk should receive the corresponding prophylaxis based on individual considerations. (See Table 4) (UW Health GRADE Low quality evidence, strong recommendation)
4.2.1 Enoxaparin is the preferred pharmacologic prophylaxis agent for pediatric patients.\(^{16,17}\)

(UW Health GRADE Low quality evidence, strong recommendation)

4.2.1.1 Use of subcutaneous (SQ) injections is preferred due to lack of evidence of intravenous administration in the prophylactic setting.

4.2.1.2 Avoid enoxaparin or heparin if patient has hypersensitivity to enoxaparin, heparin, pork products, or any component of the formulation.\(^{6}\) (UW Health GRADE Low quality evidence, strong recommendation)

### Table 4: VTE Prophylaxis Regimens in High VTE Risk Patients\(^{1,6,8,16,18-20}\)

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Weight</th>
<th>VTE Prophylaxis Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Renal Function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60 kg</td>
<td>• Enoxaparin 0.5 mg/kg SQ every 12 hours (max 60 mg/day)(^a)</td>
<td></td>
</tr>
<tr>
<td>≥60 kg</td>
<td>• Enoxaparin 40 mg SQ every 24 hours(^b) (consider 30 mg SQ every 12 hours for total knee arthroplasty)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Heparin 5000 units SQ every 12 hours(^a)</td>
<td></td>
</tr>
<tr>
<td>Renal Impairment (CrCl &lt;30 mL/min/1.73m(^2))</td>
<td>&lt;60 kg</td>
<td>• Enoxaparin 0.5 mg/kg SQ every 24 hours(^a)</td>
</tr>
<tr>
<td></td>
<td>≥60 kg</td>
<td>• Enoxaparin 30 mg SQ every 24 hours(^a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Heparin 5000 units SQ every 12 hours(^a)</td>
</tr>
</tbody>
</table>

\(^a\)UW Health GRADE Low quality evidence, strong recommendation

\(^b\)UW Health GRADE Low quality evidence, conditional recommendation

5. Oral anticoagulants should not be used in high VTE risk patients who refuse parenteral VTE prophylaxis due to insufficient evidence in the pediatric population and lack of FDA approval.\(^{17}\) (UW Health GRADE Low quality evidence, strong recommendation)

6. Anticoagulation monitoring\(^3,18\)

6.1 Complete Blood Count (CBC)

6.1.1 Obtain baseline CBC within 48 hours of initiation of enoxaparin or heparin. (UW Health GRADE Very low quality evidence, strong recommendation)

6.2 Anti-Xa\(^5,21\)

6.2.1 Routine anti-Xa levels are not recommended.\(^1\)

6.2.2 May consider re-checking anti-Xa if the patient experiences active bleeding or has evidence of renal dysfunction while on enoxaparin therapy.\(^20\) (UW Health GRADE Very low quality evidence, conditional recommendation)

6.2.3 If an anti-Xa level is deemed necessary, it should be drawn 4-6 hours after enoxaparin administration with an anti-Xa goal of 0.1-0.3 units/mL.\(^16\)

Disclaimer

Clinical practice guidelines assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician’s judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.
**Methodology**

**Development Process**

Each guideline is reviewed and updated a minimum of every 3 years. All guidelines are developed using the guiding principles, standard processes, and styling outlined in the UW Health Clinical Practice Guideline Resource Guide. This includes expectations for workgroup composition and recruitment strategies, disclosure and management of conflict of interest for participating workgroup members, literature review techniques, evidence grading resources, required approval bodies, and suggestions for communication and implementation.

**Methods Used to Collect the Evidence:**

The following criteria were used by the guideline author and workgroup members to conduct electronic database searches in the collection of evidence for review.

**Literature Sources:**
- Electronic database search (e.g., PubMed)
- Hand-searching journals, external guidelines, and conference publications

**Time Period:** All studies to date

**Search Terms:**
- VTE prophylaxis AND pediatrics
- VTE risk factors AND pediatrics
- Enoxaparin use in pediatrics for VTE prophylaxis
- Heparin use in pediatrics for VTE prophylaxis

**Methods to Select the Evidence:**

All observational studies, randomized clinical trials, and systematic reviews/meta analyses in English were considered for the guideline development.

**Methods Used to Formulate the Recommendations:**

The workgroup members created recommendations internally via a consensus process using discussion of the literature and expert experience/opinion. If issues or controversies arose where consensus could not be reached, the topic was escalated appropriately per the guiding principles outlined in the UW Health Clinical Practice Guideline Resource Guide.

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

Internally developed recommendations, or those adopted from external sources without an assigned evidence grade, were evaluated by the guideline workgroup using an algorithm adapted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (see Figure 1).
Figure 1. GRADE Methodology adapted by UW Health

Rating Scheme for the Strength of the Evidence/Recommendations:

**GRADE Ranking of Evidence**

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>We are confident that the effect in the study reflects the actual effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.</td>
</tr>
<tr>
<td>Low</td>
<td>The true effect may differ significantly from the estimate.</td>
</tr>
<tr>
<td>Very Low</td>
<td>The true effect is likely to be substantially different from the estimated effect.</td>
</tr>
</tbody>
</table>

**GRADE Ratings for Recommendations For or Against Practice**

<table>
<thead>
<tr>
<th>Level</th>
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<tbody>
<tr>
<td>Strong</td>
<td>Generally should be performed (i.e., the net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.)</td>
</tr>
<tr>
<td>Conditional</td>
<td>May be reasonable to perform (i.e., may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.)</td>
</tr>
</tbody>
</table>

**Recognition of Potential Health Care Disparities:** None identified
Collateral Tools & Resources
The following collateral tools and resources support staff execution and performance of the evidence-based guideline recommendations in everyday clinical practice.

Metrics
- Prevention of VTE with the therapy that is most appropriate based on individual patient VTE and bleeding risk
- Rate of central venous catheter (CVC) related VTEs
- Rate of non-CVC VTE events
**Appendix A. Pediatric VTE Prophylaxis Risk Factors and Assessment**

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*a UW Health GRADE Low quality evidence, strong recommendation
b UW Health GRADE Low quality evidence, conditional recommendation
Appendix B. Pediatric Venous Thromboembolism Prophylaxis Decision Flow Chart

- Patient ≥ 6 months
  - Does not meet criteria for prophylaxis guideline
    - Yes: Alter Mobility?
      - No: Low Risk
      - Yes: Reassess risk at 48-72 hours of hospitalization
    - Yes: 0-1 Risk Factors?
      - No: Early Ambulation
      - Yes: Moderate Risk
        - Early Ambulation Mechanical Prophylaxis
  - Yes: ≥ 2 Risk Factors?
    - No: Early Ambulation Mechanical Prophylaxis
    - Yes: High Risk
      - Bleed Risk?
        - No: Mechanical Prophylaxis
        - Yes: Sequential Compression Device Graduated Compression Stockings

VTE Risk Factors
- Acute Conditions
  - Central venous access device
  - Active infection
  - Major trauma or burn
  - Major surgery
  - Pregnancy
  - Critically ill
- Chronic Medical Conditions
  - Autoimmune disorder associated with thrombosis
  - Thrombophilic conditions
- Active malignancy/cancer
- Active inflammatory condition
- Smoking
- Estrogen therapy
- Obesity

Altered Mobility
- Refers to decrease in movement from baseline or inability to participate in physical therapy

Bleeding Risk Factors
- Chemical Prophylaxis NOT recommended
  - Intracranial hemorrhage
  - Brain ischemia/acute stroke
  - Active bleeding
  - Recent thrombolytic therapy (< 24 hours)
- Consider Avoiding Chemical Prophylaxis
  - Intracranial mass
  - Lumbar puncture (< 24 hours ago)
  - Coagulopathy
  - Neurosurgical procedure
  - Pelvic fracture within past 48 hours
  - Uncontrolled hypertension
  - Recent aspirin/antiplatelet use (< 5-7 days ago)

Mechanical Prophylaxis
- Sequential Compression Device Graduated Compression Stockings

Pharmacologic Prophylaxis
- Enoxaparin (Subcutaneous)
  - Patients < 50 kg: 0.5 mg/kg Q12H
    - Renal impairment: 0.5 mg/kg Q24H
    - Patients ≥ 50 kg: 40 mg Q24H
      - (consider 30 mg Q12H in total knee arthroplasty)
    - Renal impairment: 30 mg Q24H
  - Patients ≥ 50 kg: 5000 units Q12H
    - Renal impairment: 5000 units Q24H
References