



Complete Summary

GUIDELINE TITLE

Venous thromboembolism.

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Venous thromboembolism. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2007 Jun. 91 p. [212 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Venous thromboembolism. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2006 Feb. 91 p.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [February 28, 2008, Heparin Sodium Injection](#): The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.
- [August 16, 2007, Coumadin \(Warfarin\)](#): Updates to the labeling for Coumadin to include pharmacogenomics information to explain that people's genetic makeup may influence how they respond to the drug.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

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SCOPE

DISEASE/CONDITION(S)

- Deep vein thrombosis (DVT)
- Pulmonary embolism (PE)
- Venous thromboembolism (VTE)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology
Family Practice
Hematology
Internal Medicine
Pulmonary Medicine
Radiology
Vascular Surgery

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Health Plans
Hospitals
Managed Care Organizations
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To prevent progression or recurrence of thromboembolic disease
- To reduce the risk of complications from anticoagulation therapy
- To improve quality of care and cost-effectiveness of the diagnosis and treatment of venous thromboembolism (VTE)

TARGET POPULATION

Adult patients age 18 and over with venous thromboembolism (VTE)

Note: The treatment guidelines are not intended for patients with familial bleeding disorders.

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation of Deep Vein Thrombosis (DVT)

1. Clinical evaluation, examination, and patient history
2. Clinical pretest probability model (protocol) of deep vein thrombosis (DVT), such as the Wells Model
3. D-dimer assays
4. Venous duplex ultrasound with compression
5. Serial compression ultrasounds
6. Computed tomography (CT) venography of the iliac and vena cava
7. Contrast venography (proximal, intra-abdominal)

Note: Magnetic resonance imaging (MRI) was considered but not recommended.

Diagnosis/Evaluation of Pulmonary Embolism (PE)/Risk Assessment

1. Assessment of patient's clinical signs and symptoms, such as dyspnea, pleuritic chest pain, and tachypnea
2. Patient history and physical examination, including risk factor assessment for venous thromboembolism (VTE)
3. Laboratory evaluation, including chest x-ray; arterial blood gasses; and electrocardiogram (EKG)
4. Clinical pretest probability model for predicting probability of pulmonary embolism
5. D-dimer (enzyme-linked immunosorbent Assay [ELISA] or automated luminescence immunoassay [LIA])
6. Echocardiography
7. Ventilation/perfusion (V/Q) lung imaging
8. Computed tomographic pulmonary angiography (CTPA)
9. Duplex ultrasound with compression

Treatment/Management/Prevention

1. Consideration of complications/comorbidities
2. Anticoagulation using:
 - Low molecular weight heparin (LMWH), such as enoxaparin, tinzaparin, and dalteparin
 - Unfractionated heparin (UFH)
 - Fondaparinux

- Warfarin
- 3. Baseline and periodic platelet counts during heparin therapy
- 4. Patient education on the use of anticoagulation
- 5. Graded compression stockings
- 6. Inferior vena cava (IVC) filters
- 7. Direct thrombin inhibitors such as lepirudin, argatroban, and bivalirudin for treatment of heparin-induced thrombocytopenia
- 8. Activated partial prothromboplastin time (aPPT) monitoring during direct thrombin inhibitor therapy
- 9. Intravenous (IV) thrombolytic therapy
- 10. Surgical thrombectomy

MAJOR OUTCOMES CONSIDERED

- Sensitivity, specificity, positive/negative predictive value, and utility of diagnostic tests
- Patient signs and symptoms
- Patient response to treatment
- Recurrence of thrombosis
- Complications of treatment (e.g., bleeding, heparin-induced thrombocytopenia)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A literature search of clinical trials, meta-analysis, and systematic reviews is performed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Key conclusions (as determined by the work group) are supported by a conclusion grading worksheet that summarizes the important studies pertaining to the conclusion. Individual studies are classed according to the system presented below, and are designated as positive, negative, or neutral to reflect the study quality.

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

Study Quality Designations

The quality of the primary research reports and systematic reviews are designated in the following ways on the conclusion grading worksheets:

Positive: indicates that the report or review has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis.

Negative: indicates that these issues (inclusion/exclusion, bias, generalizability, and data collection and analysis) have not been adequately addressed.

Neutral: indicates that the report or review is neither exceptionally strong nor exceptionally weak.

Not Applicable: indicates that the report is not a primary reference or a systematic review and therefore the quality has not been assessed.

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

- Randomized, controlled trial

Class B:

- Cohort study

Class C:

- Nonrandomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

New Guideline Development Process

A new guideline, order set, and protocol is developed by a 6- to 12-member work group that includes physicians, nurses, pharmacists, other healthcare professionals relevant to the topic, along with an Institute for Clinical Systems Improvement (ICSI) staff facilitator. Ordinarily, one of the physicians will be the leader. Most work group members are recruited from ICSI member organizations, but if there is expertise not represented by ICSI members, 1 or 2 members may be recruited from medical groups or hospitals outside of ICSI.

The work group will meet for seven to eight three-hour meetings to develop the guideline. A literature search and review is performed and the work group members, under the coordination of the ICSI staff facilitator, develop the algorithm and write the annotations and footnotes and literature citations.

Once the final draft copy of the guideline is developed, the guideline goes to the ICSI members for critical review.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The guideline developers reviewed published cost analyses.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Critical Review Process

Every newly developed guideline or a guideline with significant change is sent to ICSI members for Critical Review. The purpose of critical review is to provide an opportunity for the clinicians in the member groups to review the science behind the recommendations and focus on the content of the guideline. Critical review also provides an opportunity for clinicians in each group to come to consensus on feedback they wish to give the work group and to consider changes necessary across systems in their organization to implement the guideline.

All member organizations are expected to respond to critical review guidelines. Critical review of guidelines is a criterion for continued membership within the Institute for Clinical Systems Improvement (ICSI).

After the critical review period, the guideline work group reconvenes to review the comments and make changes, as appropriate. The work group prepares a written response to all comments.

Approval

Each guideline, order set, and protocol is approved by the appropriate steering committee. There is one steering committee each for Respiratory, Cardiovascular, OB/GYN, and Preventive Services. The Committee for Evidence-based Practice approves guidelines, order sets, and protocols not associated with a particular category. The steering committees review and approve each guideline based on the following:

- Member comments have been addressed reasonably.
- There is consensus among all ICSI member organizations on the content of the document.
- Within the knowledge of the reviewer, the scientific recommendations within the document are current.
- Either a critical review has been carried out, or to the extent of the knowledge of the reviewer, the changes proposed are sufficiently familiar and sufficiently agreed upon by the users that a new round of critical review is not needed.

Once the guideline, order set, or protocol has been approved, it is posted on the ICSI Web site and released to members for use. Guidelines, order sets, and protocols are reviewed regularly and revised, if warranted.

Revision Process of Existing Guidelines

ICSI scientific documents are revised every 12 to 36 months as indicated by changes in clinical practice and literature. Every 6 months, ICSI checks with the work group to determine if there have been changes in the literature significant enough to cause the document to be revised earlier than scheduled.

Prior to the work group convening to revise the document, ICSI members are asked to review the document and submit comments. During revision, a literature search of clinical trials, meta-analysis, and systematic reviews is performed and reviewed by the work group. The work group will meet for 1-2 three-hour meetings to review the literature, respond to member organization comments, and revise the document as appropriate.

If there are changes or additions to the document that would be unfamiliar or unacceptable to member organizations, it is sent to members to review prior to going to the appropriate steering committee for approval.

Review and Comment Process

ICSI members are asked to review and submit comments for every guideline, order set, and protocol prior to the work group convening to revise the document.

The purpose of the Review and Comment process is to provide an opportunity for the clinicians in the member groups to review the science behind the

recommendations and focus on the content of the order set and protocol. Review and Comment also provides an opportunity for clinicians in each group to come to consensus on feedback they wish to give the work group and to consider changes needed across systems in their organization to implement the guideline.

All member organizations are encouraged to provide feedback on order sets and protocol, however responding to Review and Comment is not a criterion for continued membership within ICSI.

After the Review and Comment period, the work group reconvenes to review the comments and make changes as appropriate. The work group prepares a written response to all comments.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC) and the Institute for Clinical Systems Improvement (ICSI): For a description of what has changed since the previous version of this guidance, refer to "[Summary of Changes Report -- June 2007](#)."

The recommendations for venous thromboembolism are presented in the form of three algorithms, accompanied by detailed annotations. Algorithms on [Deep Vein Thrombosis \(DVT\) Diagnosis](#); [Pulmonary Embolism \(PE\) Diagnosis](#); and [Venous Thromboembolism \(VTE\) Treatment](#) are provided. Clinical highlights and selected annotations (numbered to correspond with the algorithm) follow.

Class of evidence (A-D, M, R, X) ratings and key conclusion grades (I-III, Not Assignable) are defined at the end of the "Major Recommendations" field.

Clinical Highlights and Recommendations

- A clinical pretest probability assessment should be completed in patients with suspected venous thromboembolism. (*Annotations #2, 17*)
- D-dimer can be used as a negative predictor to eliminate need for further testing. (*Annotations #4, 10, 17*)
- Confirm diagnosis of DVT with imaging study, preferably duplex ultrasound (with compression). (*Annotation #13*)
- In patients with a high clinical pretest probability for PE, begin low-molecular-weight heparin (LMWH) without delay. (*Annotation #17*)
- Computed tomography (CT) angiography combined with clinical pretest probability scoring and D-dimer testing has the predictive value to safely diagnose or rule out pulmonary embolism in patients. Additional diagnostic testing is necessary only when clinical symptoms persist or progress. (*Annotations #17, 27*)
- Achieve rapid effective anticoagulation with LMWH. (*Annotation #35*)
- In patients with acute VTE, heparin (unfractionated heparin [UFH] or LMWH) should be given for at least four days and until the international normalized ratio (INR) is 2.0 for two consecutive times. (*Annotation #36*)
- Arrange for home therapy in appropriate patients. (*Annotation #39*)

- Graded compression stockings help prevent post-phlebotic syndrome. All patients should be assessed for the need for compression graded stockings. (*Annotation #43*)

Deep Vein Thrombosis (DVT) Diagnosis Algorithm Annotations

1. Leg Symptoms/Clinical Suspicion of DVT

Key Points:

- Clinical evaluation and examination and patient history are important to the diagnosis of DVT.
- Clinical findings alone are poor predictors of the presence or severity of thrombosis.

Among patients with pain and swelling of the leg, some will have DVT. Recent unilateral swelling and pain above or below the knee without explanatory bone or joint trauma is suspicious for DVT.

As part of the evaluation, record onset, location, and character of patient's leg pain and swelling.

Factors increasing risk include:

- Patient's history of past VTE, family history of VTE
- Pregnancy, post partum, or current estrogen use
- Recent trauma or surgery
- Immobilization
- Presence of cancer
- Varicosities
- Airline flight longer than 8 hours

Exam findings may include erythema, warmth, and superficial thrombophlebitis with a palpable tender cord over a superficial vein. In the most severe form, phlegmasia cerulea dolens, the venous drainage of the lower extremity is acutely and severely obstructed threatening limb viability. This may require other treatment (see Annotation # 44, "Other Therapies.")

It is well known that clinical findings are poor predictors of the presence or severity of thrombosis; therefore, determining pretest probability is necessary in managing the diagnostic process.

The work group feels that patients with signs and symptoms of PE should be evaluated according to the PE Diagnosis Algorithm. Please refer to Annotation #14, "Clinical Signs and Symptoms of PE."

Evidence supporting this recommendation is of classes: D, R

2. Determine Clinical Pretest Probability

Key Points:

- Use a formal protocol to determine a patient's clinical pretest probability of DVT.

The work group recommends the use of a formal protocol to determine a patient's pretest probability of DVT. This can guide the choice of test(s) needed to triage patients for this condition, which can have minimal signs and symptoms but lead to serious consequences if left untreated. Please refer to Appendix A, "Wells Model of the Clinical Pretest Probability of DVT" in the original guideline document for an example of a clinical pretest probability model protocol.

Evidence supporting this recommendation is of class: B, C, M, R

3. Low Clinical Pretest Probability

Key Points:

- Patients with low clinical pretest probability of DVT and negative D-dimer are considered to have DVT ruled out and no further testing is needed.

Patients with a low clinical pretest probability of DVT such as a score of zero on Wells scoring can be safely managed by testing for D-dimer before ordering duplex ultrasound (with compression) of the leg. If D-dimer is negative, ultrasound can be omitted, and repeat ultrasound is not needed in one week as previously recommended unless new or progressive clinical symptoms occur.

Evidence supporting this recommendation is of class: B, C, M, R

4. D-dimer Test

Key Points:

- D-dimer assays with a high sensitivity have been proven to have a strong negative predictive value for patients with a low pretest probability of DVT and PE.
- The greatest utility of the D-dimer test is in the emergency department and its "negative predictive value." Patients with recent trauma or surgery will have increased plasma D-dimer levels that will decrease the sensitivity and predictive value of the D-dimer test.

D-dimer testing is most appropriate in ambulatory care settings and for patients with recent onset of symptoms who are not currently on anticoagulation therapy. For patients with suspected DVT, D-dimer may decrease the need for initial and subsequent radiological investigation. The usefulness is dependent on the method used for D-dimer determination [Conclusion Grade II: See Conclusion Grading Worksheet A -- Annotations #4 and 10 (DVT D-dimer) in the original guideline document].

Refer to the original guideline document for more information about D-dimer.

See the ICSI Technology Assessment report, "[D-Dimer Testing for Deep vein Thrombosis and Pulmonary Embolism](#)" (#70, 2003) for a more comprehensive review of D-dimer testing and methodologies.

Evidence supporting this recommendation is of class: C

6. DVT Excluded - Out of Guideline

Patients with a low clinical pretest probability of DVT and a negative (reliable) D-dimer assay have a very low (less than 2%) risk of subsequent finding of DVT. These patients can be followed clinically with no further radiologic evaluation unless warranted by new or progressive clinical symptoms.

Evidence supporting this recommendation is of class: C

7. Moderate/High Clinical Pretest Probability

Key Points:

- Patients with moderate or high clinical pretest probability should have a venous duplex ultrasound (with compression) ordered as the first test.
- D-dimer assay can be used after a negative duplex ultrasound (with compression) result to determine further radiologic testing needs.

Patients with moderate or high clinical pretest probability have a 15 to 70% risk of DVT. Because of the high incidence of DVT in this population, venous duplex ultrasound (with compression) should be ordered as the first test, and D-dimer assay can be used after a negative ultrasound result to determine further radiologic testing needs.

8. Perform Duplex Ultrasound (with Compression)

Key Points:

- Duplex ultrasound (with compression) is considered to be the primary diagnostic device and should be the first radiologic choice for evaluation of proximal DVT.
- The combined use of clinical pretest probability and duplex ultrasound (with compression) is effective in confirming or excluding the diagnosis of DVT.
- Duplex ultrasound (with compression) can find thrombi in the calf; however, a negative test cannot always exclude DVT and further testing may be needed.

Patients with a low clinical pretest probability of DVT and a positive D-dimer assay should receive a duplex ultrasound (with compression) to confirm the diagnosis of DVT. The ability to diagnose DVT may vary depending on the proximity of the suspected DVT site. In addition, the interpretation of the duplex ultrasound can be difficult in patients with a previous history of DVT.

Consider consulting with the interpreting physician. (See Annotation #12, "Follow-Up Studies/Second Duplex Ultrasound (3-7 Days) or Venography.")

Patients with a moderate/high clinical pretest probability of DVT should receive a duplex ultrasound (with compression) as the first test to diagnose DVT. A negative result on the venous ultrasound can be followed by D-dimer to determine further radiologic testing needs. A positive result on the ultrasound confirms the diagnosis of DVT.

Proximal (popliteal vein and above)

Duplex ultrasound (with compression) is considered to be the primary diagnostic device and should be the first choice for evaluation.

Calf (below popliteal vein)

Some calf thrombi can be found by duplex ultrasound (with compression). However, a negative test cannot exclude an isolated calf DVT.

Evidence supporting this recommendation is of classes: A, C, R

10. D-dimer Test for Moderate/High Pretest

Key Points:

- It has been found safe to withhold anticoagulation in outpatients with a moderate to high clinical suspicion, a negative duplex ultrasound, and a negative D-dimer.

It is safe to withhold anticoagulation among outpatients with a negative duplex ultrasound (with compression) and a "negative" D-dimer (measured by whole blood latex agglutination or enzyme-linked immunosorbent assay [ELISA], respectively).

For patients with suspected DVT, D-dimer testing may decrease the need for initial and subsequent radiological investigation. The usefulness is dependent on the method used for the D-dimer determination. *[Conclusion Grade II: See Conclusion Grading Worksheet A -- Annotations #4 and #10 (DVT D-dimer) in the original guideline document.]*

Evidence supporting this recommendation is of classes: B, C

12. Follow-Up Studies/Second Duplex Ultrasound (Three to Seven Days) or Venography

Key Points:

- If DVT is strongly suspected and there is a positive D-dimer despite a negative initial ultrasound, consider venography or repeat ultrasound in three to seven days.

Clinical pretest probability and venous duplex ultrasound are adequate to rule in or rule out DVT in the majority of cases. If DVT is strongly suspected despite a negative initial ultrasound, consider venography or repeat ultrasound in 3 to 7 days. Please refer to Appendix A, "Wells Model of the Clinical Pretest Probability of DVT," in the original guideline document.

The combined use of clinical pretest probability and duplex ultrasound (with compression) is effective in confirming or excluding the diagnosis of DVT in the majority of cases. If clinical suspicion of DVT is high and ultrasound is negative, consider further testing, such as repeat ultrasound for suspected calf thrombosis or venography for suspected proximal thrombosis.

[Conclusion Grade I: See Conclusion Grading Worksheet B -- Annotation #12 (DVT Diagnosis Confirmation) in the original guideline document.]

- Serial ultrasonography

When calf thrombosis is suspected but the initial ultrasound is negative, serial ultrasound is an acceptable alternative to venography. Ultrasonography appears to be superior to impedance plethysmography for this purpose. If a thrombus is discovered, anticoagulation is recommended.

- Computed tomography (CT) venography of the inferior vena cava and the iliac veins

This is performed at some institutions to visualize proximal obstructions. The common, superficial, and deep femoral veins can be done as well. CT venography does not include the distal calf veins. Newer techniques include spiral contrast CT and magnetic resonance (MR) venography, which have shown excellent results in preliminary studies. This effectiveness has included ilio caval thrombi. Currently these techniques could be considered in patients with unusual diagnostic situations including suspected ilio caval clots or in patients with contraindications for venography

- Contrast venography (proximal, intra-abdominal)

This is generally considered the historical gold standard for the accurate diagnosis. However, it has numerous drawbacks including cost, discomfort to the patient, significant resource use, availability, requirement of foot vein cannulation, use of intravenous (IV) contrast, and secondary thrombi. For these reasons, venography is generally reserved for difficult diagnostic cases. It can help distinguish between old and new clots.

- Magnetic resonance imaging (MRI) – due to cost and time MRI is not recommended.

Evidence supporting this recommendation is of classes: A, C, R

13. DVT Confirmed - See [Venous Thromboembolism \(VTE\) Treatment Algorithm](#)

Key Points:

- Proximal thrombosis should be treated with anticoagulation unless contraindicated.
- Thrombosis of the calf veins is common and carries significant risk of propagation. Patients benefit from anticoagulation treatment.
- Patients with thrombosis of the calf not treated with anticoagulation should be followed by serial duplex ultrasound to rule out proximal progression.

Proximal Thrombosis (at or above the popliteal vein)

Proximal thrombosis should be treated with anticoagulation unless contraindicated. (See Annotation #34, "Complicated Venous Thromboembolism or Comorbidities?") Additional information can also be found in the National Guideline Clearinghouse (NGC) summary of the Institute for Clinical Systems Improvement (ICSI) [Antithrombotic Therapy Supplement](#).

Calf Thrombosis (below the popliteal vein)

Increasing evidence suggests that patients with **symptomatic** calf DVT benefit from treatment similar to that for proximal DVT. Thrombosis of the calf veins is common and carries significant risk of propagation, including propagation into the proximal deep veins. If not treated, these patients should be followed by serial duplex ultrasounds to rule out proximal progression of thrombus to popliteal vein.

Following patients with **suspected** thrombosis limited to the calf veins and treating with anticoagulation only for proximal extension on serial studies may be an acceptable alternative to anticoagulation. However, the safety of this approach in patients with confirmed symptomatic calf DVT has not been studied.

Evidence supporting this recommendation is of classes: A, C, D, R

Pulmonary Embolism (PE) Diagnosis Algorithm Annotations

14. Clinical Signs and Symptoms of PE

Key Points:

- PE should be considered in patients who present with the three most frequent signs and symptoms: dyspnea, pleuritic chest pain, and tachypnea.

PE should be considered in patients that present with the three most frequent signs and symptoms: dyspnea, pleuritic chest pain, and tachypnea. Less frequent signs/symptoms are cough, hemoptysis, fever, syncope, diaphoresis,

nonpleuritic chest pain, apprehension, rales, increased pulmonic component of the second heart sound ($\wedge S_2P$), wheezing, hypotension, tachycardia, cyanosis, or pleural rub. Massive pulmonary embolism can present with hemodynamic instability or cardiac arrest. Clinical findings are nonspecific and should not be used as the only criteria to diagnose PE.

Evidence supporting this recommendation is of classes: A, C, R

15. Clinically Unstable?

Massive PE should be considered in the following circumstances: any hemodynamic instability, severe hypoxemia or respiratory distress, a ventilation perfusion (V/Q) or angiogram with 50% of the perfusion absent, an echocardiogram showing right heart strain or failure, an elevated pulmonary artery pressure, or a spiral CT suggesting severe occlusion. Massive PE has up to a tenfold greater mortality, and treatment with thrombolytics appears to favorably affect the outcome. A recent study has also suggested that there may be some benefit for the use of thrombolytics in submassive PE. In this circumstance, specialty consultation and consideration of thrombolytics may be appropriate.

Patients who present with signs and symptoms of massive PE (syncope, hypotension, tachycardia, and hypoxia) may require evaluation and treatment different than that recommended in this guideline. In patients with suspected massive PE, echocardiography can be used as a diagnostic and management tool.

Evidence supporting this recommendation is of classes: A, B, D, M, R

17. Estimate Clinical Pretest Probability (CPTP – Wells Score)

Key Points:

- If the clinical pretest probability score is high (six or more), begin heparin without delay.
- If high-risk, begin heparin without delay.
- Chest x-ray (CXR), arterial blood gases (ABGs), electrocardiogram (EKG), and other tests as indicated for alternative diagnoses considered.

For the purposes of the diagnosis of pulmonary embolism, the work group has combined moderate pretest probability and high pretest probability into the PE Likely.

If the clinical pretest probability score is high, begin heparin promptly (a tool for determining pretest probability is shown in annotation Appendix B, "Model for Predicting Clinical Pretest Probability for PE" in the original guideline document).

Patients presenting with signs and symptoms of PE need:

- **Complete history and physical exam.** Risk factor assessment for venous thromboembolic disease plays a role in determining the pretest probability of PE. Risk factors include previous history of venous thromboembolism, recent surgery, immobilization, paresis, personal or family history of inheritable thrombophilic disorder or personal history of acquired thrombophilia (e.g. antiphospholipid antibody, cancer, estrogen, pregnancy or myeloproliferative disorder).
- **Estimate Pretest Probability.** The clinical evaluation can also lead to suspicion of an alternative diagnosis. Careful review and application of the pretest probability model by all providers is recommended.
- **CXR, ABGs, EKG** and other tests as indicated for alternative diagnoses considered.

A simplified clinical pretest probability scoring system may improve diagnostic accuracy by being easy to use consistently and alerting clinicians to the need for further testing.

Evidence supporting this recommendation is of classes: B, C, M, R

18. CPTP Results?

The new simplified algorithm validates the dichotomized groups proposed by Wells and includes patients categorized in an earlier study as low and some of those in the moderate probability group.

PE Less Likely (score <4)

- Less Likely Clinical Pretest Probability

The Christopher Study Investigators found that in patients with a less likely score for PE, D-dimer levels should be measured and can provide diagnostic information to rule out PE.

PE Likely (score >4)

- Likely Clinical Pretest Probability

The data from Wells and the Christopher Study Investigators found that in patients likely to have a PE, a CT scan should be the next test and can safely exclude a PE.

For the purposes of the diagnosis of pulmonary embolism, the work group has combined moderate pretest probability and high pretest probability into PE Likely probability.

Evidence supporting this recommendation is of classes: A, B, C, R

20. D-dimer Results?

In patients with PE Less Likely, the Christopher Study Investigators found that patients with negative D-dimer levels could safely be observed without

further investigation, as the incidence of nonfatal VTE was 0.5% in the subsequent three months. This data is consistent with other studies. In this group it is safe to withhold anticoagulation therapy and follow these patients clinically.

If the D-dimer is positive, further evaluation is necessary to adequately exclude a PE.

The sensitivity of the D-dimer may be reduced if the duration of symptoms or signs of venous thromboembolism exceeds two or three days prior to testing. Likewise, the sensitivity may be reduced if the patient has been receiving heparin therapy. Because a procedure or surgery increases the plasma D-dimer level, the clinical utility of the D-dimer is greatest for evaluation of outpatients (e.g., emergency department).

Usually, suspected venous thromboembolism patients with recent trauma or surgery are inappropriate for D-dimer testing and should proceed directly to a diagnostic imaging study for deep vein thrombosis or pulmonary embolism (e.g., duplex ultrasound [with compression] of the leg, high resolution chest CT angiography).

Evidence supporting this recommendation is of classes: B, C, R

21. Risk of PE Is Very Low

Key Points:

- It is important to evaluate patients for other diagnoses when PE has been excluded.

Patients with a negative D-dimer and PE Less Likely Clinical Pretest Probability have a low incidence of pulmonary embolism. It is safe to withhold anticoagulation therapy and follow these patients clinically.

Patients with a negative CT angiography and PE Less Likely Clinical Pretest Probability and positive D-dimer results can safely have pulmonary embolism excluded and followed clinically in the outpatient setting.

Patients with persistent symptoms or symptoms that progressively worsen should have further diagnostic testing. Ultrasound (with compression) should be used to improve the clinical likelihood of disease and avoid more invasive testing.

Patients who have had PE excluded need to have the evaluation for other diagnoses completed and appropriate treatment and follow-up initiated. In particular, pericarditis, myocardial infarction, and pneumonia should be excluded in appropriate circumstances. When performed, computed tomographic pulmonary angiography (CTPA) will frequently help identify alternative causes such as pericardial effusion, pneumonia and pleural effusion.

Evidence supporting this recommendation is of classes: B, C, R

23. Perform Computed Tomographic Pulmonary Angiography (CTPA)

Key Points:

- Non-invasive pulmonary vascular imaging studies are recommended as the initial radiologic evaluation.

CPTA is the first line study of choice unless a contraindication exists, then V/Q would be preferred.

Computed tomography should be performed with at least a 2.5 mm thickness by 1.25 mm incrementation.

The choice of initial imaging study depends on several factors including how readily available the tests are, the resolution of images obtained, underlying illnesses/conditions including renal status of the patient, and experience of the radiologists.

Non-invasive pulmonary vascular imaging studies are recommended as the initial diagnostic evaluation in most patients with suspected PE. Both V/Q scans and CT pulmonary angiography have a relatively high degree of specificity when they are read respectively as "high probability" scan results or "positive" for PE. A negative V/Q scan also has a high degree of specificity. However, either a **non-diagnostic** (intermediate or low radiologic probability scan results) or a negative CT pulmonary angiogram suffer from lack of sensitivity and usually require further diagnostic studies. V/Q scanning is not always readily available and other pulmonary processes such as chronic obstructive pulmonary disease (COPD) and congestive heart failure can influence its specificity.

V/Q imaging follows a different diagnostic algorithm. See Appendix C in the original guideline document for more information.

Evidence supporting these recommendations is of classes: A, C, R

24. CT Results?

Key Points:

- CT pulmonary angiography has become the most commonly used radiographic test to be used to evaluate patients for PE.

CT pulmonary angiography offers the clinician a new screening tool for detection of pulmonary embolism. It has been rapidly introduced into clinical practice and, in some institutions, is easier to obtain than a V/Q scan. CT pulmonary angiography is also more useful in patients with underlying cardiac disease and COPD/asthma. When alternative diagnoses are likely, CT pulmonary angiography is especially good as it can rule out PE and confirm other diagnoses with one test.

For patients with CT scan results that cannot clearly confirm or rule out the possibility of PE due to the patient's condition and comorbidities or due to scan technical limitation, clinicians should review the clinical pretest probability and D-dimer results to determine what further work up may be indicated.

Refer to the original guideline document for more information regarding CT pulmonary angiography.

Evidence supporting this recommendation is of classes: A, B, M, R

25. Diagnosis of PE

Patients with a positive CTPA scan and Likely PE clinical pretest probability are essentially confirmed positive for PE. They can be considered for treatment with no further diagnostic testing.

Evidence supporting this recommendation is of classes: A, C, R

28. PE Less Likely and Positive D-dimer Results

In patients with an unlikely pretest probability but positive D-dimer and normal CTPA, no treatment is necessary. Further work up only if warranted by clinical suspicion.

29. PE Likely and Negative D-dimer Results

It appears to be safe to withhold anticoagulation while pursuing a non-invasive strategy of serial ultrasonography in order to further evaluate for thromboembolism in this patient population.

Irrespective of D-dimer result, venous imaging should be performed.

The risks associated with a misdiagnosis of PE are typically more severe than those associated with a misdiagnosis of DVT. Higher negative predictive values are required to safely use D-dimer to exclude PE. The evidence, to date, suggests that current assays, with the possible exception of ELISA and rapid ELISA methods, are not acceptable for use in excluding PE in patients with clinical suspicion of PE. *[Conclusion Grade III: See Conclusion Grading Worksheet C – Annotation #29 (Perform D-dimer and Assess Clinical Pretest Probability) in the original guideline document].*

Evidence supporting this recommendation is of classes: A, B, R

30. PE Likely with Positive D-dimer Results

A significant incidence of PE is found in patients with a negative CT pulmonary angiography associated with a high clinical pretest probability. Bilateral duplex ultrasound (with compression) of the leg is recommended to improve the diagnosis of VTE without performing invasive tests. Pulmonary

angiography can be considered if clinical suspicion remains high or the patient's condition deteriorates.

Evidence supporting this recommendation is of classes: A, B, R

31. Perform Duplex Ultrasound (with Compression) of the Leg

Key Points:

- Duplex ultrasound (with compression) should be used to improve clinical likelihood of disease and avoid more invasive testing in patients with negative lung imaging results.

In patients with negative CT pulmonary angiography results and a PE Likely clinical probability, further evaluation with duplex ultrasound (with compression) should be used to improve clinical likelihood of disease and avoid more invasive testing. Please refer to Appendix C in the original guideline document for sample ultrasound orders.

The diagnosis of lower extremity deep vein thrombosis has been advocated to be an important adjunct to the diagnosis of pulmonary emboli. Venous duplex ultrasonography (DUS) is the most common method for DVT diagnosis. DUS accuracy for lower extremity DVT is as high as 98%, though studies are negative in greater than 50% of pulmonary embolism cases. Total thrombus embolism and proximal migration may account for a number of negative studies. Venous DUS reliability is also limited when evaluating iliac and pelvic veins and the inferior vena cava, which likely accounts for a significant number of negative studies.

When DUS is negative, the incorporation of clinical pretest probability can improve diagnostic accuracy and potentially avoid unnecessary pulmonary angiography. Several studies of DUS performed after *nondiagnostic* V/Q scans have shown that pulmonary angiography can be avoided in 15% to 40% of patients when DVT is identified.

Clinical pretest probability is an important adjunct to DUS at this point. In cases of suspected pulmonary embolism where non-invasive tests do not confirm its presence, pulmonary angiography should be performed.

Evidence supporting this recommendation is of classes: C, D, M, R

32. Ultrasound Results?

A positive ultrasound usually confirms the diagnosis of DVT and requires treatment regardless of the presence or absence of PE. If the ultrasound is negative, further evaluation may be warranted, dependent upon the patient's clinical pretest probability.

Venous Thromboembolism (VTE) Treatment Algorithm Annotations

34. Complicated Venous Thromboembolism or Comorbidities?

Key Points:

- Patients with complicated venous thromboembolism or certain comorbidities may require therapy that is different than patients with uncomplicated venous thromboembolism. The work group felt that these patients should be identified and treated individually rather than by a standard guideline.
- Complications or comorbidities of venous thromboembolism include massive PE, contraindications to anticoagulation, known history of heparin-induced thrombocytopenia (HIT), extensive iliofemoral thrombosis/phlegmasia, pregnancy, familial bleeding and clotting disorders, and severe renal dysfunction.

Massive PE

Patients who present with symptoms of PE associated with hemodynamic or respiratory compromise should be evaluated for massive PE. These patients may require treatment other than that discussed in the guideline.

Massive PE should be considered in the following circumstances: any hemodynamic instability, severe hypoxemia or respiratory distress, a V/Q or angiogram with 50% of the perfusion absent, an echocardiogram showing right heart strain or failure, an elevated pulmonary artery pressure, or a spiral CT suggesting severe occlusion. Massive PE has up to a tenfold greater mortality and treatment with thrombolytics appears to favorably affect the outcome. A recent study has also suggested that there may be some benefit for the use of thrombolytics in submassive PE. In this circumstance, specialty consultation and consideration of thrombolytics may be appropriate.

Patients with hemodynamic compromise may require immediate thrombolytic therapy. Normotensive PE patients with right ventricle (RV) dysfunction should be treated in-hospital (at least initially) where their vital signs can be closely monitored. Such patients should be considered for thrombectomy (either catheter-directed or open), thrombolysis, and/or inferior vena cava (IVC) filter placement if blood pressure support (i.e., pressors and augmentation of intravascular volume) is required, and possibly if hypoxemia cannot be corrected with supplemental oxygen therapy.

Evidence supporting this recommendation is of classes: A, B, D, M, R

Contraindications to Anticoagulation

Absolute contraindications would include patients who have active severe hemorrhage or recent intracranial hemorrhage. Relative contraindications include: recent or imminent surgery, trauma, anemia (hematocrit less than 30), renal disease, history of gastrointestinal hemorrhage, active peptic ulcer disease, and liver disease.

These patients require more intense monitoring for bleeding complications if given anticoagulation therapy. If not treated with anticoagulation therapy, serial ultrasounds for untreated calf DVT, or IVC filters for proximal DVT are

indicated. (See Annotation #44, "Other Therapies.") Please refer to the NGC summary of ICSI's [Antithrombotic Therapy Supplement](#) for more information on contraindications to anticoagulation.

Evidence supporting this recommendation is of classes: A, B

Known History of Heparin-Induced Thrombocytopenia (HIT)

Thrombocytopenia can complicate heparin therapy. Both a non-immune and a more serious immune mediated platelet associated immunoglobulin G (IgG) reaction, HIT, have been described. If the patient has previously received heparin, especially within the past 3 months, thrombocytopenia may occur within hours or days.

Patients with HIT should not be treated with either unfractionated heparin (UFH) or low- molecular-weight heparin (LMWH). Direct thrombin inhibitors have been used successfully in this circumstance. (See Annotation # 44, "Other Therapies.") Please refer to the NGC summary of ICSI's [Antithrombotic Therapy Supplement](#) for more information on HIT.

Evidence supporting this recommendation is of class: C

Extensive Iliofemoral Thrombosis/Phlegmasia

Patients found to have extensive iliofemoral disease or evidence of phlegmasia will likely require inpatient monitoring and longer course of heparin/LMWH therapy than patients with uncomplicated DVT. Thrombolytic therapy may be of benefit in these patients for possible reduction of post-thrombotic complications. (See Annotation #44, "Other Therapies.")

Pregnancy

In pregnancy, warfarin is contraindicated because it crosses the placenta and is associated with embryopathy, central nervous system (CNS) abnormalities, and neonatal bleeding. Subcutaneous UFH, twice daily, has been the standard therapy in pregnancy. LMWH has shown no increased fetal complication, and was shown to have fewer bleeding complications than UFH.

Renal clearance of enoxaparin may be increased during pregnancy.

Anticoagulation will need to continue 4 to 6 weeks after delivery because the postpartum period is itself a high-risk time for thrombosis.

Please refer to the NGC summary of ICSI's [Antithrombotic Therapy Supplement](#) for more information on anticoagulation therapy during pregnancy.

Evidence supporting this recommendation is of classes: A, D, M

Familial Bleeding Disorders

Because of the complexity and controversy surrounding the use of standard anticoagulation to treat DVT in patients with familial bleeding disorders, these patients are excluded from the guideline. There is little data that has addressed the use of low-molecular-weight heparin in these patients. Although treatment for these patients may be similar to that found in the algorithm, the work group felt that these patients should be treated individually and not be included in the guideline.

Severe Renal Dysfunction (creatinine clearance less than 30 mL/minute)

These patients require closer monitoring for bleeding complications and dosing adjustments if LMWH is used. Patients with significant renal impairment (creatinine clearance less than 30 mL/min) can accumulate LMWH. The recommended doses in these patients are currently:

- Enoxaparin 1 mg/kg **ONCE** daily for therapeutic (treatment) doses. *(Normal renal function dose is 1 mg/kg twice daily or 1.5 mg/kg once daily)*
- Enoxaparin 30 mg **ONCE** daily for prophylactic doses. *(Normal renal function dose is 30 mg twice daily or 40 mg once daily)*

Please refer to the NGC summary of ICSI's [Antithrombotic Therapy Supplement](#) for more information on anticoagulation therapy in patients with renal dysfunction.

Evidence supporting this recommendation is of classes: B, C

35. Low-Molecular-Weight Heparin (LMWH)/Unfractionated Heparin (UFH)/Fondaparinux

Key Points:

- Unfractionated heparin (UFH) and low-molecular-weight heparin (LMWH) should be considered for the initial treatment of PE.
- LMWH is the preferred heparin for the initial anticoagulation for most patients with DVT.
- Heparin-induced thrombocytopenia (HIT) is a recognized complication of heparin therapy.

UFH or LMWH should be considered for the initial treatment of PE. LMWH is the preferred heparin for the initial anticoagulation of patients with DVT. It is as safe and as effective as continuous UFH. Suitable patients can be safely treated with LMWH in the outpatient setting. *[Conclusion Grade I: See Conclusion Grading Worksheet D -- Annotation #35 (Low Molecular Weight Heparin) in the original guideline document]*

Heparin should be continued for at least 5 days after the initiation of warfarin therapy and until INR is above 2.0 for two consecutive days.

Low-Molecular-Weight Heparin (LMWH)

LMW heparins provide reliable anticoagulation levels when given subcutaneously on a weight-determined dosing schedule. No laboratory monitoring of the intensity of anticoagulation is required for LMWH, except for special circumstances.

Please note that LMWH may not be appropriate for patients with renal insufficiency (creatinine clearance less than 30 mL/min). (See Annotation #34, "Complicated Venous Thromboembolism or Comorbidities?")

- Enoxaparin 1.0 mg/kg subcutaneously twice daily is the recommended treatment for DVT (Food and Drug Administration [FDA] approved for inpatients and outpatients).
- Enoxaparin 1.5 mg/kg subcutaneously once daily (FDA approved for inpatient venous thromboembolism treatment). Risk factors for therapy failure with once-daily dosing include obesity (greater than 100 kg), cancer, and chronic kidney disease. Twice-daily dosing (enoxaparin 1 mg/kg subcutaneously, twice daily) is recommended for obese patients and patients with cancer.
- Tinzaparin (Innohep®) 175 anti-Xa IU/kg subcutaneously once daily (FDA approved for venous thromboembolism treatment [not available in the U.S.])
- Dalteparin 100 IU/kg subcutaneously twice daily (not FDA approved for venous thromboembolism treatment)
- Dalteparin 200 IU/kg subcutaneously once daily (The effectiveness of once-daily dosing is controversial) (not FDA approved for venous thromboembolism treatment)

Studies of LMWH have generally excluded pregnant patients. However, neither unfractionated nor LMWH cross the placenta, and pregnant patients are suitable candidates for either form of therapy.

The decision for hospital or home therapy is not mutually exclusive. A patient could be started on LMWH in the hospital and discharged to continue therapy at home at any time during the course of therapy.

Evidence supporting this recommendation is of classes: A, B, C, R

Unfractionated Heparin (UFH)

UFH is administered by continuous IV infusion following a bolus dose. Heparin-induced thrombocytopenia is a recognized complication of UFH therapy. (See Annotation #44, "Other Therapies.")

Refer to the original guideline document for more information on UFH.

Evidence supporting this recommendation is of classes: A, C, R

Fondaparinux

Fondaparinux, a sodium pentasaccharide, is administered by subcutaneous injection once daily for the treatment of deep vein thrombosis and pulmonary

embolism. The usual dose is 5 mg for patient less than 50 kg, 7.5 mg for patients 50 to 100 kg, or 10 mg for patients over 100 kg. Fondaparinux treatment should be continued for a least five days and until a therapeutic oral anticoagulant effect is established (INR 2.0 to 3.0). Warfarin sodium should be initiated as soon as possible, usually within 72 hours.

The heparin assay (anti-factor-Xa) has been used to monitor effects of fondaparinux; however, new calibrators other than heparin will need to be established. In most clinical situations, monitoring may not be necessary. A platelet count should be obtained prior to the initiation of fondaparinux and periodically to check for bleeding. There is one report of HIT with fondaparinux.

Heparin-Induced Thrombocytopenia (HIT)

Both UFH and LMWH are associated with HIT. HIT is an immune-mediated reaction to heparins. It occurs in 2% to 3% of patients treated with UFH and less than 1% of patients treated with LMWH. This syndrome can be associated with paradoxical increased risk for venous and arterial thrombosis. Patients who develop HIT without associated thrombosis will have a significant risk for thrombosis in the subsequent 100 days. Patients with a history of HIT should not be treated with UFH or LMWH.

HIT should be suspected in patients who develop a skin lesion reaction at the injection site, have a systemic reaction to a bolus administration of heparin, or develop a greater than 50% decrease in platelet count from baseline labs while on heparin.

Delayed-onset HIT is an increasingly recognized form of this disorder. The possibility of delayed-onset HIT should be considered in any patient presenting with thromboembolism after a recent hospitalization.

Patients suspected of having any form of HIT should have their heparin stopped while antibody testing for HIT is performed. Patients with a high clinical probability of having HIT should be treated with an appropriate alternative anticoagulant before antibody test results are available. Direct thrombin inhibitors (DTIs) are the alternative anticoagulant of choice for patients with HIT. Three brands are FDA approved: lepirudin, argatroban, and most recently, bivalirudin.

If a patient is receiving warfarin when there is a high clinical probability of HIT, the warfarin should be stopped. The warfarin effect should be reversed with vitamin K, and DTI therapy should be initiated. Low-maintenance doses of warfarin can be restarted during DTI therapy after the platelet count has significantly improved and there is clinical improvement in the patient's thrombosis. There should be at least a five-day overlap of the DTIs and warfarin. The DTI therapy should be continued until the platelet count stabilizes. See Annotation #44, "Other Therapies" for more information.

Although in vitro data has not demonstrated cross-reactivity of fondaparinux with HIT antibodies, additional studies are needed before its use can be considered.

Please refer to the NGC summary of ICSI's [Antithrombotic Therapy Supplement](#) for more information on low molecular weight and unfractionated heparins, synthetic pentasaccharides, and HIT.

Evidence supporting this recommendation is of class: A

36. Warfarin

Key Points:

- A high-loading dose of warfarin (greater than 10 mg) is of no clinical use and should be discouraged.
- A 10 mg initial dose of warfarin has been associated with early over-anticoagulation and, when compared to a 5 mg initial dose, was no more effective in achieving a therapeutic INR by day 4 or 5 of therapy.
- A therapeutic range of anticoagulation to keep the INR at 2.5 (range 2.0 to 3.0) is recommended for patients with VTE.
- Heparin (UFH or LMWH) should be given for at least four days and until the INR is 2.0 two consecutive days.

It has been shown that oral anticoagulation with warfarin decreases the complications and recurrence rate of thrombosis.

It is recommended that warfarin therapy be initiated with a dose of 5 mg (less in patients with risks for increased sensitivity to warfarin) with dosage adjustments based on results of INR testing.

- A high-loading dose of warfarin (greater than 10 mg) is of no clinical use and should be discouraged. A high-loading dose induces a rapid but excessive reduction in Factor VII activity, predisposing patients to hemorrhage in the first few days of therapy. It fails to achieve a significantly more rapid decline of the other vitamin K dependent coagulation factors (II, IX and X) above that achieved without a loading dose.
- A 10 mg initial dose of warfarin has been associated with early over-anticoagulation and, when compared to a 5 mg initial dose, was no more effective in achieving a therapeutic INR by day 4 or 5 of therapy.

A therapeutic range of anticoagulation to keep the INR at 2.5 (range 2.0 to 3.0) is recommended for patients with VTE.

In patients with suspected hypercoagulable state (Protein C or Protein S deficiency), the patient should be adequately anticoagulated with heparin before warfarin is started at a low dose (2 to 5 mg).

The NGC summary of the ICSI's [Antithrombotic Therapy Supplement](#) contains additional information on warfarin therapy including an appendix on interactions with warfarin.

Evidence supporting this recommendation is of classes: A, B, D, R

37. Outpatient Treatment Appropriate?

Key Points:

- Home therapy with LMWH is as safe and effective as in-hospital therapy with standard UFH for patients with uncomplicated VTE.
- Because of decreased cardiorespiratory reserve, patients presenting with **symptomatic** PE should initially be treated in-hospital.

Medical criteria for safe outpatient therapy include:

- Uncomplicated venous thromboembolism. (See Annotation #34, "Complicated Venous Thromboembolism or Comorbidities?")
- Good cardiorespiratory reserve
- No excessive bleeding risks
- Creatinine clearance greater than 30 mL/minute

Because of decreased cardiorespiratory reserve, patients presenting with **symptomatic** PE should initially be treated in-hospital.

Other considerations include:

- Patients need to be taught how to administer the drug and recognize complications.
- Daily INRs will be needed to guide the institution of warfarin therapy. The warfarin dose will need to be adjusted to the INR.
- Patients will need resources to answer questions and deal with problems.

Evidence supporting this recommendation is of classes: A, C, D

38. Inpatient Treatment

Therapy is discussed in Annotation #35, "Low-Molecular-Weight Heparin (LMWH)/Unfractionated Heparin (UFH)/Fondaparinux" and in Annotation #36, "Warfarin."

39. Outpatient Protocol

Key Points:

- Patients may need hospitalization during the first 24 hours to start therapy promptly.
- Graded compression stockings (not Teds) combined with early ambulation does not cause any increase in pulmonary embolism and gives more rapid resolution of pain and swelling.

Because of the need for an organized support system and time-of-day considerations for home care agencies, many patients may need hospitalization during the first 24 hours to start therapy promptly.

All stable VTE patients

- Daily LMWH shots self-administered, caregiver-administered, or daily clinic visits. The patient will need to be geographically accessible to have INRs drawn and receive care for problems that arise.
- Daily INR for transitioning to warfarin treatment after 2 days of adequate anticoagulation. (For details see [Antithrombotic Therapy Supplement](#))
- Duration of anticoagulation to be determined by the supervising physician.

DVT patients

- If the criteria in Annotation # 37 can be met, DVT treatment can be started in the outpatient setting; otherwise hospitalize until teaching, medication, and close follow-up can be assured.
- For DVT, use graduated compression stockings (not Teds) on the affected leg to reduce the risk of postphlebotic syndrome.
- Graded compression stockings (not Teds) combined with early ambulation does not cause any increase in pulmonary embolism and gives more rapid resolution of pain and swelling.

Please refer to the NGC summary of the ICSI's [Antithrombotic Therapy Supplement](#) for a discussion of complications during anticoagulation therapy.

Evidence supporting this recommendation is of classes: A, D, R

40. Patient Education

Patients should be instructed on the use of anticoagulation. Please refer to the NGC summary of ICSI's [Antithrombotic Therapy Supplement](#) for more information on patient education. Patient education materials are also available. (See the Support for Implementation section in the original guideline document).

41. Complications During Therapy?

Key Points:

- Patients with complicated venous thromboembolism or certain comorbidities may require therapy that is different than patients with uncomplicated venous thromboembolism. These patients should be identified and treated individually rather than by a standard guideline.

Patients with complicated venous thromboembolism or certain comorbidities may require therapy that is different than patients with uncomplicated venous thromboembolism. These patients should be identified and treated individually rather than by a standard guideline.

Patients on UFH or LMWH therapy who have bleeding, thrombocytopenia, or osteoporosis may require individual adjustments in therapy. HIT should be suspected if the platelet count drops 50% or more from baseline labs.

Patients on warfarin therapy who experience bleeding or skin necrosis, or who become pregnant may require individual adjustments in therapy.

The development of a complication attributable to anticoagulation requires action by the health care team. Sometimes, as with HIT, the drug must be discontinued. The most common complication, bleeding, may require a dosage adjustment, discontinuation of the drug, or further evaluation in the setting of gastrointestinal or genitourinary bleeding. Specific actions are best determined in a case-by-case basis by the clinician, who can appropriately weigh the risks and benefits of continued anticoagulation therapy and who can take into account the timing of the complication.

Please refer to the NGC summary of ICSI's [Antithrombotic Therapy Supplement](#) for more information on potential complications of anticoagulation therapy.

42. Anticoagulation Failure?

Key Points:

- Recurrent symptomatic DVT or PE during adequate heparin or warfarin treatment represents failure of treatment and needs objective documentation, especially as a new DVT may be difficult to distinguish from postphlebotic syndrome.
- If a patient fails on warfarin therapy, heparin or LMWH may need to be reinstituted.

Recurrent symptomatic DVT or PE during adequate heparin or warfarin treatment represents failure of treatment and needs objective documentation, especially as a new DVT may be difficult to distinguish from postphlebotic syndrome.

Active cancer is the most common cause of warfarin failure.

Antiphospholipid antibodies may be the cause of anticoagulant failure. In these patients, recurrence was most likely in the 6 months following cessation of warfarin, and higher INRs of greater than or equal to 3.0 were more effective than 2 to 3. Aspirin did not help.

In certain circumstances, alternate treatment such as an inferior vena cava filter may be indicated. If a patient fails on warfarin therapy, heparin or LMWH may need to be reinstituted. The work group felt these patients should be identified and treated individually rather than by a standard guideline. The 7th American College of Chest Physicians (ACCP) Consensus Conference on Antithrombotic Therapy provides the following recommendations regarding placement of an IVC filter:

- For most patients with DVT, the work group recommends **against** the routine use of a vena cava filter in addition to anticoagulants.
- The work group suggests placement of an inferior vena cava filter in patients with a contraindication for or a complication of anticoagulant treatment, as well as in those with recurrent thrombophlebitis despite adequate anticoagulation.
- In PE patients with a contraindication for a complication of anticoagulant treatment as well as those with recurrent thromboembolism despite adequate anticoagulation, the work group suggests placement of an inferior vena cava filter.

Evidence supporting this recommendation is of classes: A, B, C, R

43. Continued Anticoagulation With Follow-Up and Secondary Prevention

Key Points:

- The length of anticoagulation therapy should be individualized to the patient and the circumstances that caused VTE.
- Patient who have had VTE remain at risk for recurrence for up to 10 years.

Graded Compression Stockings (not Teds)

Knee-high 30 to 40 mm Hg custom fitted, graded compression stockings help alleviate symptoms of edema and pain in patients who have postphlebotic syndrome. One report showed that graded compression stockings reduced the incidence of postphlebotic syndrome by 50% in patients with acute DVT. For chronic or recurrent venous stasis ulcer, consultation with a vascular surgeon should be considered.

Evidence supporting this recommendation is of classes: A, C, D

Duration of Anticoagulation

The most appropriate duration of warfarin anticoagulation should be individualized depending on the estimated risk of VTE recurrence and the risk of a complication (e.g., bleeding) due to warfarin therapy. The 7th American College of Chest Physicians (ACCP) Consensus Conference on Antithrombotic Therapy recommends:

- Transient risk (e.g., surgery, immobilization, estrogen use, trauma): 3 months. Shorter treatment periods are associated with a higher rate of recurrence and are not recommended.
- Idiopathic or medical risk: 6 to 12 months
 - Patients with documented antiphospholipid antibodies or two or more thrombophilic conditions should be treated for 12 months and considered for indefinite anticoagulation therapy.
 - Patients with documented deficiency of antithrombin, protein C or S, factor V Leiden, prothrombin 20210 mutation, homocysteinemia, or high factor VIII conditions should be

treated for 6 to 12 months and considered for indefinite anticoagulation therapy.

- Recurrent disease or continued risk factors: indefinite
 - Patients with cancer should be initially treated for 3 to 6 months with LWMH and then with anticoagulation therapy indefinitely or until the cancer is resolved.
 - Patients with two or more episodes of documented DVT should receive anticoagulation therapy indefinitely.

Refer to the original guideline document for more information on duration of coagulation.

Evidence supporting this recommendation is of classes: A, B, R

Anticoagulation Management

A coordinated effort for follow-up of patients started on warfarin is required to minimize the risks of both hemorrhagic and thrombotic complications while on treatment. In the first several weeks of anticoagulation, INRs need to be checked at least weekly. After stabilization, the interval between INRs can be increased from weekly to biweekly, up to but not beyond 4 weeks.

A goal INR target of 2.5 is recommended for the majority of patients who are kept on long-term anticoagulation. Patients who have recurrent VTE on adequate anticoagulation with coumadin may require a higher target INR (e.g. 3.0). One study suggested protection against recurrence in patients who were initially treated for 6 to 12 months at the target INR of 2.5, then treated to an INR range of 1.5 to 2.0. However, a recent study comparing long-term anticoagulation at INR 2.5 versus INR 1.5 to 2.0 showed greater protection against recurrence with the higher target INR of 2.5.

Anticoagulation clinics and computerized dosing programs have helped assist in the management and monitoring of patients on warfarin therapy. These areas of anticoagulation are evolving at this time.

Please refer to the NGC summary of ICSI's [Antithrombotic Therapy Supplement](#) for more information on establishing and maintaining anticoagulation clinics.

Supporting evidence is of classes: A, C, R

Long-Term Complications

Long-term complications for patients treated for DVT include recurrent VTE, postphlebitic syndrome, and bleeding while on anticoagulation therapy. There is a high recurrence rate (10% to 15% per year) of thromboembolic disease in patients with idiopathic DVT. Patients should be counseled when discontinuing warfarin to watch for and report signs of recurrence immediately. Ambulatory exercise programs are unlikely to exacerbate symptoms and may result in improved leg muscle flexibility.

Postphlebotic syndrome is characterized by symptoms of heaviness of the leg, fatigue, and pain with findings of dependent edema, skin pigmentation, and venous varicosities. It can be associated with long-term sequelae of subcutaneous fibroses, chronic ulceration, and recurrent infections. It appears that most of the sequelae of postphlebotic syndrome can be attributed to the loss of valvular function. One prospective study revealed that within 2 years of a DVT there was a severe hemodynamic impairment (similar to that seen in established postphlebotic limbs) in one-fifth of patients with calf DVT, and in up to one-half of patients with more extensive proximal DVT. Symptoms were worse after major DVT involving proximal vessels.

Evidence supporting this recommendation is of classes: C, D, R

Look for Malignancy?

Some patients who present with idiopathic DVT may have occult malignancy. However extensive work-ups in asymptomatic patients beyond appropriate cancer screening have not shown benefit.

In patients with known cancer, risk of DVT is increased. In patients who have idiopathic DVT, there may be cancer present at the time of presentation in 3% to 12% of cases.

Evidence supporting this recommendation is of classes: B, C

Thrombophilia

Certain patients should be tested for thrombophilia. This testing should be done 2 weeks after discontinuation of anticoagulation. (See the original guideline document for laboratory test values prevalent in patients with DVT). The work group recommends consideration be given to a discussion with a thrombophilia expert for:

- Patients who have recurrent thromboembolic disease
- Patients with first idiopathic DVT who:
 - Are less than 50 years of age
 - Have a family history of VTE among one or more first-degree relatives
 - Have an unusual site of spontaneous thrombosis
 - Have massive venous thrombosis

Evidence supporting this recommendation is of class: B, C, D, R

Activity Level

There is no evidence that restriction of activity is of benefit nor is there evidence to determine the appropriate activity level. The physician needs to be guided by individual patient circumstance, including pain and swelling.

Ambulatory exercise programs are unlikely to exacerbate symptoms and may result in improved leg muscle flexibility.

Evidence supporting this recommendation is of classes: A, C

44. Other Therapies

Key Points:

- Direct thrombin inhibitors have been used to treat HIT successfully.
- Thrombolytic therapy results in a more rapid clot resolution but does not significantly reduce mortality or risk of recurrent PE.

Inferior Vena Cava (IVC) Filters

Treatment is required due to risk of mortality. Accepted indications for inferior vena caval interruption include:

- Patients with PE or proximal DVT and contraindications to anticoagulation
- Progressive thromboembolism, despite *adequate* anticoagulation, and
- Patients with underlying pulmonary hypertension in whom a PE would likely be fatal.

Consultation with a specialist is strongly recommended prior to placement of a filter, as long-term sequelae of filter placement include increased risks of recurrent DVT and PE.

IVC filter is the procedure of choice in patients with a contraindication or complication of anticoagulation, who are at high-risk for proximal vein thrombosis, who experience recurrent thromboembolism despite adequate anticoagulation, who have chronic recurrent PE with pulmonary hypertension, or who are undergoing pulmonary embolectomy or pulmonary endarterectomy.

Multiple filter types are available, and all are effective in preventing PE. The Greenfield filter has the longest practical usage for IVC.

Evidence supporting this recommendation is of classes: A, C, R

Serial Ultrasound in Calf DVT

Serial ultrasound (e.g., at 3 and 7 days) may be useful to evaluate for propagation of thromboses in two groups of patients:

- Patients with a positive diagnosis of a calf thrombosis, but contraindications to anticoagulation therapy
- Patients with clinical suspicion of calf thrombosis, but initial negative ultrasound. In general, patients with symptomatic calf DVT who do not have contraindications to anticoagulation will do better if treated similar to those with a proximal DVT.

It is safe to withhold anticoagulation in patients with whom serial compression ultrasound is negative over five to seven days, if the initial study includes the femoral vein, the popliteal fossa, and scan to the trifurcation of the calf veins.

Although serial compression ultrasound testing is safe, it is often inconvenient for patients and healthcare providers, and may not be cost-effective. When patient follow-up cannot be guaranteed, serial compression ultrasound protocols should not be utilized.

Evidence supporting this recommendation is of classes: A, B, C, D, R

Treatment of Heparin-Induced Thrombocytopenia (HIT)

Patients developing HIT while on heparin therapy should be taken off all UFH and LMWH. Direct thrombin inhibitors have been used to treat HIT successfully. Direct thrombin inhibitors approved for the treatment of HIT include lepirudin, argatroban, and bivalirudin. Direct thrombin inhibitors must be administered by continuous IV infusion necessitating hospitalization. Direct thrombin inhibitor therapy must be monitored by measuring the activated partial thromboplastin time (aPPT).

Please refer to the NGC summary of ICSI's [Antithrombotic Therapy Supplement](#) for more information on HIT.

Evidence supporting this recommendation is of class: R

Intravenous (IV) Thrombolytic Therapy

Lytic therapy has been used in patients with extensive iliofemoral disease who demonstrate evidence of vascular compromise (phlegmasia). Lytic therapy has been touted as potentially reducing the long-term postphlebotic consequences of proximal DVT through early thrombolysis, restoration of patency, and preservation of venous valve function. When utilized, catheter-directed lytic therapy is preferred over systemic lytic therapy. This therapy has been suggested as a means of reducing the incidence of post-thrombotic syndrome. However, long-term randomized studies comparing this therapy to standard anticoagulation have not been performed. Management should be individualized and is most appropriate for patients with massive iliofemoral thrombosis. Consultation with a specialist is strongly recommended prior to initiation of lytic therapy.

Thrombolytic therapy results in more rapid clot resolution, but it does not significantly reduce mortality or the risk of recurrent PE in hemodynamically stable patients. Pooled data shows thrombolytic therapy has an increased incidence of major hemorrhage and intracranial hemorrhage as compared to UFH therapy alone. Elevated diastolic blood pressure is a risk factor for intracranial hemorrhage.

Evidence supporting this recommendation is of classes: A, D, M, R

Surgical Thrombectomy

In a highly select group of patients, surgical venous thrombectomy has been utilized. These patients typically have extensive venous thrombosis and have contraindications for anticoagulation and lytic therapy. Surgical thrombectomy has historically been utilized to reduce acute symptomatology in patients with iliofemoral thrombosis and was touted to reduce the risk of postphlebotic syndrome development. Management should be individualized. The morbidity and mortality associated with this surgical procedure deems it be a procedure of last choice.

Evidence supporting this recommendation is of class: D

Definitions:

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

- Randomized, controlled trial

Class B:

- Cohort study

Class C:

- Nonrandomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

CLINICAL ALGORITHM(S)

Detailed and annotated clinical algorithms are provided in the original guideline document for:

- [Deep Vein Thrombosis \(DVT\) Diagnosis](#)
- [Pulmonary Embolism \(PE\) Diagnosis](#)
- [Venous Thromboembolism \(VTE\) Treatment](#)
- V/Q (Ventilation/Perfusion) Lung Imaging algorithm is provided in Appendix C of the original guideline document.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

In addition, key conclusions contained in the Work Group's algorithm are supported by a grading worksheet that summarizes the important studies pertaining to the conclusion. The type and quality of the evidence supporting these key recommendations (i.e., choice among alternative therapeutic approaches) is graded for each study.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Prevention of progression or recurrence of thromboembolic disease
- Reduced risk of complications from anticoagulation therapy
- Improved quality of care and cost-effectiveness of the diagnosis and treatment of venous thromboembolism

POTENTIAL HARMS

Diagnosis

The risks associated with a misdiagnosis of pulmonary embolism (PE) are typically more severe than those associated with a misdiagnosis of deep vein thrombosis (DVT). Higher negative predictive values are required to safely use D-dimer to exclude pulmonary embolism.

Treatment

- Patients on unfractionated heparin (UFH) or low molecular weight heparin (LMWH) therapy who have bleeding, thrombocytopenia, or osteoporosis may require individual adjustments in therapy. Heparin-induced thrombocytopenia (HIT) should be suspected if the platelet count drops 50% or more from baseline labs.
- Patients on warfarin therapy who experience bleeding, skin necrosis, or who become pregnant may require individual adjustments in therapy.
- The development of a complication attributable to anticoagulation requires action by the health care team. Sometimes, as with heparin-induced thrombocytopenia, the drug must be discontinued. The most common complication, bleeding, may require a dosage adjustment, discontinuation of the drug, or further evaluation in the setting of gastrointestinal or genitourinary bleeding. Specific actions are best determined in a case-by-case basis by the clinician, who can appropriately weigh the risks and benefits of continued anticoagulation therapy and who can take into account the timing of the complication.
- Refer to the National Guideline Clearinghouse (NGC) summary of the Institute for Clinical Systems Improvement (ICSI) [Antithrombotic Therapy Supplement](#) for more information on potential complications of anticoagulation therapy.
- Thrombolytic therapy has an increased incidence of major hemorrhage and intracranial hemorrhage as compared to UFH therapy alone.

- The morbidity and mortality associated with surgical thrombectomy deems it to be a procedure of last choice.

Long-Term Complications

Long-term complications for patients treated for deep vein thrombosis include recurrent venous thromboembolism, postphlebotic syndrome, and bleeding while on anticoagulation therapy. Postphlebotic syndrome is characterized by symptoms of heaviness of the leg, fatigue and pain with findings of dependent edema, skin pigmentation and venous varicosities. Patients should be counseled when discontinuing warfarin to watch for signs of recurrence and report them immediately.

CONTRAINDICATIONS

CONTRAINDICATIONS

Contraindications to Anticoagulation

Absolute contraindications would include patients who have active severe hemorrhage or recent intracranial hemorrhage. Relative contraindications include: recent or imminent surgery, trauma, anemia (hematocrit less than 30), renal disease, history of gastrointestinal hemorrhage, active peptic ulcer disease, and liver disease.

These patients require more intense monitoring for bleeding complications if given anticoagulation therapy. If not treated with anticoagulation therapy, serial ultrasounds for untreated calf deep vein thrombosis (DVT), or inferior vena cava (IVC) filters for proximal deep vein thrombosis are indicated. Please refer to the National Guideline Clearinghouse (NGC) summary of the Institute for Clinical Systems Improvement (ICSI) [Antithrombotic Therapy Supplement](#) for more information on contraindications to anticoagulation.

Known History of Heparin-Induced Thrombocytopenia (HIT)

Patients with heparin-induced thrombocytopenia should not be treated with either unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH). Direct thrombin inhibitors have been used successfully in this circumstance (see Annotation #44). Please refer to the NGC summary of the ICSI [Antithrombotic Therapy Supplement](#) for more information on heparin-induced thrombocytopenia.

Pregnancy

In pregnancy, warfarin is contraindicated because it crosses the placenta and is associated with embryopathy, central nervous system (CNS) abnormalities, and neonatal bleeding. Subcutaneous UFH, twice daily, has been the standard therapy in pregnancy. Low molecular weight heparin has shown no increased fetal complication, and was shown to have fewer bleeding complications than UFH. Anticoagulation will need to continue 4 to 6 weeks after delivery because the postpartum period is itself a high-risk time for thrombosis.

Please refer to the NGC summary of the ICSI's [Antithrombotic Therapy Supplement](#) for more information on anticoagulation therapy during pregnancy.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.
- This clinical guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients are urged to consult a health care professional regarding their own situation and any specific medical questions they may have.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for general implementation, a medical group can choose to concentrate on the implementation of that guideline. When four or more groups choose the same guideline to implement and they wish to collaborate with others, they may form an action group.

In the action group, each medical group sets specific goals they plan to achieve in improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment, and tobacco cessation.

Detailed measurement strategies are presented in the original guideline document to help close the gap between clinical practice and the guideline recommendations. Summaries of the measures are provided in the National Quality Measures Clearinghouse (NQMC).

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Clinical Algorithm
Pocket Guide/Reference Cards
Quality Measures

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

RELATED NQMC MEASURES

- [Venous thromboembolism \(VTE\): percentage of adult patients treated for VTE who have been assessed for the need for graded compression stockings.](#)
- [Venous thromboembolism \(VTE\): percentage of adult patients who have a high clinical pretest probability for pulmonary embolism \(PE\) who received low molecular weight heparin \(LMWH\) during evaluation.](#)
- [Venous thromboembolism \(VTE\): percentage of adult patients receiving heparin therapy for VTE who have a baseline platelet count before starting heparin, and then a platelet count every other day for at least the first 3 days of therapy.](#)
- [Venous thromboembolism \(VTE\): percentage of adult patients suspected of deep vein thrombosis \(DVT\) who have leg duplex ultrasound with compression performed despite a low clinical pretest probability and a negative D-dimer test.](#)
- [Venous thromboembolism \(VTE\): percentage of patients diagnosed with VTE who meet the criteria for low-molecular-weight heparin \(LMWH\) and for whom LMWH is used.](#)
- [Venous thromboembolism \(VTE\): percentage of low-molecular-weight heparin \(LMWH\)-eligible patients with deep vein thrombosis \(DVT\) treated in an outpatient setting.](#)

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Venous thromboembolism. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2007 Jun. 91 p. [212 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1998 Jun (revised 2007 Jun)

GUIDELINE DEVELOPER(S)

Institute for Clinical Systems Improvement - Private Nonprofit Organization

GUIDELINE DEVELOPER COMMENT

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers, Allina Medical Clinic, Altru Health System, Aspen Medical Group, Avera Health, CentraCare, Columbia Park Medical Group, Community-University Health Care Center, Dakota Clinic, ENT Specialty Care, Fairview Health Services, Family HealthServices Minnesota, Family Practice Medical Center, Gateway Family Health Clinic, Gillette Children's Specialty Healthcare, Grand Itasca Clinic and Hospital, HealthEast Care System, HealthPartners Central Minnesota Clinics, HealthPartners Medical Group and Clinics, Hutchinson Area Health Care, Hutchinson Medical Center, Lakeview Clinic, Mayo Clinic, Mercy Hospital and Health Care Center, MeritCare, Mille Lacs Health System, Minnesota Gastroenterology, Montevideo Clinic, North Clinic, North Memorial Care System, North Suburban Family Physicians, Northwest Family Physicians, Olmsted Medical Center, Park Nicollet Health Services, Pilot City Health Center, Quello Clinic, Ridgeview Medical Center, River Falls Medical Clinic, Saint Mary's/Duluth Clinic Health System, St. Paul Heart Clinic, Sioux Valley Hospitals and Health System, Southside Community Health Services, Stillwater Medical Group, SuperiorHealth Medical Group, University of Minnesota Physicians, Winona Clinic, Ltd., Winona Health

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GUIDELINE COMMITTEE

Cardiovascular Steering Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

In the interest of full disclosure, ICSI has adopted the policy of revealing relationships work group members have with companies that sell products or services that are relevant to this guideline topic. The reader should not assume that these financial interests will have an adverse impact on the content of the guideline, but they are noted here to fully inform readers. Readers of the guideline may assume that only work group members listed below have potential conflicts of interest to disclose.

No work group members have potential conflicts of interest to disclose.

ICSI's conflict of interest policy and procedures are available for review on ICSI's Web site at <http://www.icsi.org>.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Venous thromboembolism. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2006 Feb. 91 p.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](#).

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Venous thromboembolism. Executive summary. Bloomington (MN): Institute for Clinical Systems Improvement, 2007 Jun. 1 p. Electronic copies: Available from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](#).
- ICSI pocket guidelines. April 2006 edition. Bloomington (MN): Institute for Clinical Systems Improvement, 2006. 298 p.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

Additionally, the appendices to the [original guideline document](#) include models for predicting clinical pretest probability for deep vein thrombosis and pulmonary embolism, as well as sample ultrasound orders.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on February 15, 2000. The information was verified by the guideline developer on March 15, 2000. This summary was updated by ECRI on December 14, 2001 and verified by the guideline developer on January 9, 2002. The summary was updated by ECRI on January 28, 2004, July 28, 2004, July 14, 2005, and May 10, 2006. This summary was updated by ECRI on March 6, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Coumadin (warfarin sodium). This summary was updated by ECRI Institute on June 22, 2007 following the U.S. Food and Drug Administration (FDA) advisory on heparin sodium injection. This NGC summary was updated by ECRI Institute most recently on September 10, 2007. This summary was updated by ECRI Institute on March 14, 2008 following the updated FDA advisory on heparin sodium injection.

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