



Complete Summary

GUIDELINE TITLE

Venous thromboembolism prophylaxis.

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Venous thromboembolism prophylaxis. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2008 Oct. 37 p. [35 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Venous thromboembolism prophylaxis. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2007 Jun. 52 p.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

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

- [December 3, 2008 – Innohep \(tinzaparin\)](#): The U.S. Food and Drug Administration (FDA) has requested that the labeling for Innohep be revised to better describe overall study results which suggest that, when compared to unfractionated heparin, Innohep increases the risk of death for elderly patients (i.e., 70 years of age and older) with renal insufficiency. Healthcare professionals should consider the use of alternative treatments to Innohep when treating elderly patients over 70 years of age with renal insufficiency and deep vein thrombosis (DVT), pulmonary embolism (PE), or both.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

SCOPE

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RECOMMENDATIONS

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SCOPE

DISEASE/CONDITION(S)

Venous thromboembolism

GUIDELINE CATEGORY

Prevention
Risk Assessment

CLINICAL SPECIALTY

Anesthesiology
Emergency Medicine
Family Practice
Hematology
Internal Medicine
Orthopedic Surgery
Preventive Medicine
Pulmonary Medicine
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 increase the percentage of hospitalized adult patients (18 years and older) who are appropriately assessed for venous thromboembolism risk within 24 hours of admission
- To increase the percentage of adult patients (18 years and older) who are evaluated for venous thromboembolism prophylaxis upon change in level of care, change in providers, and/or upon discharge
- To increase the percentage of hospitalized adult patients (18 years and older) who are at risk for venous thromboembolism who have received education

- within 24 hours of admission for venous thromboembolism that includes venous thromboembolism risk signs and symptoms, and treatment/prophylaxis methods available
- To improve the safety of using medications by reducing the likelihood of patient harm associated with the use of anticoagulation therapy
 - To increase the percentage of hospitalized adult patients who begin early and frequent ambulation
 - To increase the percentage of hospitalized adult patients (18 years and older) receiving appropriate pharmacological and/or mechanical prophylaxis treatment within 24 hours of admission
 - To reduce the risk of complications from pharmacologic prophylaxis
 - To increase the percentage of patients (18 years and older) who are discharged on warfarin who have an international normalized ratio within one week
 - To increase the percentage of surgical patients with recommended venous thromboembolism prophylaxis ordered
 - To increase the percentage of surgery patients who receive appropriate venous thromboembolism prophylaxis within 24 hours prior to surgery to 24 hours after surgery

TARGET POPULATION

Adult (18 years and older) hospitalized patients

INTERVENTIONS AND PRACTICES CONSIDERED

1. Assessment of venous thromboembolism risk factors
2. Patient education and early ambulation
3. Mechanical thromboprophylaxis
4. Pharmacologic prophylaxis (dalteparin, enoxaparin, fondaparinux, unfractionated heparin, warfarin)

Note: Aspirin is not recommended to be used alone for pharmacologic prophylaxis; it can be considered in combination with mechanical prophylaxis in orthopedic surgery in patients with no additional thromboembolic risk factors.

MAJOR OUTCOMES CONSIDERED

- Rate of thromboembolic events including pulmonary embolism in patients on low molecular weight heparin (LMWH) versus unfractionated heparin (UFH)
- Rate of perioperative death in patients on LMWH versus UFH
- Rate of intraoperative and postoperative bleeding (major and minor) in patients on LMWH versus UFH

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

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 – October 2008](#).

This guideline follows closely the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition) [R] and the American Society of Regional Anesthesia and Pain Medicine guidelines. Areas of divergence from the American College of Chest Physicians guideline recommendations are the use of aspirin following orthopedic procedures.

The recommendations for venous thromboembolism prophylaxis are presented in the form of a Table with 9 components, accompanied by detailed annotations.

Clinical highlights, the Table, "Thromboembolic Prophylaxis for Adult Patients", and selected annotations (numbered to correspond with the Table) follow.

Class of evidence (A-D, M, R, X) and conclusion grade (I-III, Not Assignable) definitions are provided at the end of the "Major Recommendations" field.

Clinical Highlights

1. All patients should be evaluated for venous thromboembolism risk upon hospital admission, change in level or care, change in providers, and prior to discharge. *(Aim #1)*
2. All patients should receive proper education regarding venous thromboembolism risk, signs and symptoms of venous thromboembolism, and prophylaxis methods available. *(Aim #3)*
3. Early and frequent ambulation should be encouraged when possible in all patient groups. *(Aim #5)*
4. All medical and surgical/trauma patients who have a high or very high risks for venous thromboembolism should receive anticoagulation prophylaxis unless contraindicated. *(Aim #9)*
5. Aspirin alone is not recommended for routine venous thromboembolism prophylaxis following hip/knee arthroplasty but may be considered in combination with mechanical prophylaxis methods in patients without additional risk factors. Further study is needed. *(Aim #10)*
6. Aspirin and antiplatelet drugs are not recommended for venous thromboembolism prophylaxis in other surgical patients or medically ill patients. *(Aim #6)*
7. For all patients receiving spinal or epidural anesthesia, precautions should be taken when using anticoagulant prophylaxis to reduce the risk of epidural hematoma. *(Aim #4)*
8. Risk of venous thromboembolism development continues beyond hospitalization, and the need for post-discharge anticoagulation should be assessed. *(Aim #8)*

Thromboembolic Prophylaxis for Adult Patients

1. General Recommendations
1-1 All patients should have venous thromboembolism risk assessed and addressed upon hospital admission and discharge.
1-2 All patients should have proper education regarding venous thromboembolism risk, signs and symptoms, and mechanical prophylaxis methods available.
1-3 All patients should be encouraged to ambulate as early as possible, and as frequently as possible.
1-4 All non-ambulatory patients should have, at a minimum, mechanical prophylaxis – unless contraindicated.
1-5 All patients with moderate to high risk of venous thromboembolism should have pharmacologic prophylaxis recommendations in this table – unless contraindicated.
2. Patient-Related Thromboembolic Risk Factors

- Prior history of deep vein thrombosis/pulmonary embolism (probably the most important predictor of thromboembolism)
- Active cancer or myeloproliferative disorder admission to the intensive care unit
- Extended immobility or estimated length of stay of four or more days
- Age greater than 60
- Thrombophilia – congenital or acquired
- Uncompensated congestive heart failure
- Acute respiratory failure
- Acute infection
- Inflammatory bowel disease
- Nephrotic syndrome
- Rheumatoid/collagen vascular disorder
- Obesity (body mass index ≥ 30)

3. Special Situations – General

High Risk of Bleeding

- Active significant bleeding
- Craniotomy within two weeks
- History of intracerebral hemorrhage within two weeks
- Active intracranial lesions/neoplasms/monitoring devices
- Vascular access/biopsy sites inaccessible to hemostatic control within 24 hours
- Bacterial endocarditis
- Proliferative retinopathy

(See the NGC summary of the Institute for Clinical Systems Improvement [ICSI] [Antithrombotic Supplement](#) for a more detailed discussion of risk factors for bleeding)

Thromboembolic prophylaxis

- History of heparin induced thrombocytopenia
- Platelet count $< 50,000$
- History of coagulopathy (e.g. hemophilia, von Willebrand's)

Thromboembolic prophylaxis
consult an anticoagulation
pharmacologic prophylaxis

4. Special Situations – Dose Adjustment

	Dalteparin	Enoxaparin	Fondaparinux	Unfractionated Heparin	Warfarin
Morbidly obese (body mass index ≥ 35)	No dosing recommendation available	40 mg sq every 12 hr or 50 mg sq daily	No dosing recommendation available	5,000 units sq every 8 hr or continuous IV infusion	--
Small body mass	--	30 mg sq daily if < 45 kg	Contraindicated if < 50 kg	--	--
Geriatric	2,500 units sq	Based on CrCl	Empiric dose	--	--

	daily		adjustment based on CrCl		
Renal Insufficiency (creatinine clearance [CrCl]<30)	No dosing recommendation available	30 mg sq daily	Contraindicated	--	--

5. Special Situations – Neuraxial Blockade

	Dalteparin	Enoxaparin	Fondaparinux	Unfractionated Heparin	Warfarin
	<p>Insertion: at least 12 hr after the last dose, epidural catheter not recommended with twice daily regimens.</p> <p>Removal: at least 12 hr after the last dose</p> <p>At least 2 hr before the next dose</p>	<p>Insertion: at least 12 hr after the last dose, epidural catheter not recommended with twice daily regimens.</p> <p>Removal: at least 12 hr after the last dose</p> <p>At least 2 hr before the next dose</p>	<p>Insertion: not recommended prior to insertion</p> <p>Removal: at least 36 hr after the last dose</p> <p>At least 12 hr before the next dose</p>	<p>Insertion: at least 4 hr after the last dose</p> <p>Removal: at least 4 hr after the last dose</p> <p>At least 1 hr before the next dose</p>	<p>Insertion: consent regarding highest acceptable international normalized ratio (INR) <2</p> <p>Removal: within 4 hr of initial warfarin INR <2</p>

Pharmacologic Prophylaxis

6. Hospitalized Non-Surgical Patients Including Burns

	Dalteparin	Enoxaparin	Fondaparinux	Unfractionated Heparin	Warfarin
No additional risk factors	Not recommended	Not recommended	Not recommended	Not recommended	--
Additional risk factors	5,000 units sq every 24 hr	40 mg sq every 24 hr	2.5 mg sq every 24 hr	5,000 units sq every 8-12 hr	If on warfarin for other indication, probably sufficient for venous thromboembolism (VTE) prophylaxis

7. General Gynecologic and Urologic Surgery

	Dalteparin	Enoxaparin	Fondaparinux	Unfractionated Heparin	Warfarin
Outpatient or laparoscopic procedure or C-section + no additional risk factors	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
Outpatient or laparoscopic procedure or C-section + additional risk factors or major procedure	2,500 units sq 1-2 hr preop, then every 24 hr	40 mg sq 2 hr preop, then every 24 hr	--	5,000 units sq every 12 hr postop	--
Previous venous thromboembolism, malignancy or other significant risk factors	5,000 units sq 1-2 hr preop, then every 24 hr	40 mg sq 2 hr preop, then every 24 hr	--	5,000 units sq every 8 hr postop	--

8. Bariatric Surgery

	Dalteparin	Enoxaparin	Fondaparinux	Unfractionated Heparin	Warfarin
All bariatric procedures	No dosing recommendation available	40 mg sq every 12 hours (± mechanical prophylaxis)	No dosing recommendation available	5,000 units sq every 8 hours or continuous infusion (target antiXa level 0.15-2.0) (± mechanical prophylaxis)	--

9. Orthopedic Surgery

	Dalteparin	Enoxaparin	Fondaparinux	Unfractionated Heparin	Warfarin
Hip Fracture	5,000 units sq every 24 hr beginning 12-24 hr postop + mechanical prophylaxis If surgery is	30 mg sq every 12 hr beginning 12 hr postop + mechanical prophylaxis Epidural	2.5 mg sq every 24 hr beginning 6-8 hr postop + mechanical prophylaxis Epidural catheter not	Not recommended	INR 2.5-3.0) beginning postop surgery mechanical prophylaxis (spinal

	<p>delayed, initiate between admission and surgery</p> <p>Must stop at least 12 hours prior to neuraxial anesthesia (see table section #5, "Special Situations – Neuraxial Blockade" above)</p>	<p>catheter not recommended with twice daily regimens</p> <p>If surgery is delayed, initiate between admission and surgery</p> <p>Must stop at least 12 hours prior to neuraxial anesthesia (see table section #5 above)</p>	<p>recommended with twice daily regimens</p> <p>Note: not recommended preoperative</p> <p>If surgery is delayed, initiate LMWH between admission and surgery</p>		<p>anesthe OK, bu used w epidura cathete cathete should remove within 4 hours a INR < 3 (see ta section "Specia Situatio Neurax Blockad above)</p> <p>Note: n recom prope</p> <p>If surge delayed initiate between admiss and sur</p>
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Hip replacement	5,000 units sq every 24 hr beginning 12-24 hr postop + mechanical prophylaxis	30 mg sq every 12 hr beginning 12 hr postop + mechanical prophylaxis Epidural catheter not recommended with twice daily regimens	2.5 mg sq every 24 hr beginning 6-8 hr postop + mechanical prophylaxis Epidural catheter not recommended	Not recommended	INR 2.5-3.0) beginning of surg mech prophylaxis (spinal anesthetic OK, but used w/ epidural catheter should be removed within 4 hours and INR <2

Knee replacement	5,000 units sq every 24 hr beginning 12-24 hr postop + mechanical prophylaxis	30 mg sq every 12 hr beginning 12 hr postop + mechanical prophylaxis Epidural catheter not recommended with twice daily regimens	2.5 mg sq every 24 hr beginning 6-8 hr postop + mechanical prophylaxis Epidural catheter not recommended	Not recommended	INR 2.5-3.0) beginning of surg mechan prophyl (spinal anesthes OK, but used w epidural cathete cathete should remove within 4 hours a INR <2

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Knee arthroscopy + no risk factors	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
Knee arthroscopy + risk factors	5,000 units sq every 24 hr beginning 12-24 hr postop	40 mg sq every 24 hr beginning 12-24 hr postop	Not recommended	Not recommended	Not recommended
Out of the Scope of This Guideline					
CABG, Thoracic Surgery, Neurosurgery, Spine Surgery, Multiple Trauma					

[R]

Abbreviations: CABG, coronary artery bypass graft; CrCl, creatinine clearance; hr, hours; INR, International Normalized Ratio; IV, intravenous; LMWH, low-molecular-weight heparin; preop, preoperative; postop, postoperative; sq, subcutaneous; VTE, venous thromboembolism

1. General Recommendations

1-3. All Patients Should Be Encouraged to Ambulate as Early as Possible, and as Frequently as Possible

Although no specific studies exist to document the value of patient education and early ambulation to reduce venous thromboembolism risk, the work group believes these measures are important for all venous thromboembolism risk patients, including those in the very-high-risk group.

1-4. All Non-Ambulatory Patients Should Have, at a Minimum, Mechanical Prophylaxis – Unless Contraindicated

Although mechanical prophylaxis devices have been evaluated extensively in clinical studies, their efficacy in venous thromboembolism prophylaxis remains unclear. These studies have often failed to define exactly what device was used, and frequently the devices were used in combination with other prophylaxis methods, making it difficult to prove their efficacy. Mechanical prophylaxis devices available for use include graded compression stockings, intermittent pneumatic compression devices and venous foot pumps. Graded compression stockings are frequently used in combination with either intermittent pneumatic compression or venous foot pump devices. The 2008 American College of Chest Physician guidelines identify both the advantages and the limitations of mechanical thromboprophylaxis modalities (see Table A, in the original guideline document). Mechanical prophylaxis devices, particularly graded compression stockings, can have harmful consequences, most commonly related to skin irritation and breakdown. The use of graded compression stockings is contraindicated in some patients (see

Contraindications field). If mechanical prophylaxis is utilized, careful nursing assessment and care are essential to minimizing complications.

4. **Special Situations – Dose Adjustment**

Fixed-dose prophylaxis in the morbidly obese (body mass index greater than or equal to 35) will likely result in underdosing. Current expert opinion suggests enoxaparin be increased by 25%. There are no dosing recommendations available for dalteparin or fondaparinux.

5. **Special Situations -- Neuraxial Blockade**

Neuraxial blockade is not a contraindication for pharmacologic prophylaxis. It is important to consider the use and timing of medications with neuraxial blockade. When an epidural is used for anesthesia, it is most appropriate to wait until the catheter is removed before starting pharmacologic prophylaxis. Neuraxial blockade should generally be avoided in patients with a clinical bleeding disorder.

General Guidelines:

1. All patients who receive neuraxial blockade should be monitored closely for developing back pain or signs and symptoms of spinal cord compression (weakness, saddle numbness, numbness, incontinence) after injections, during infusions, and after discontinuation of infusions.
2. Both insertion and removal of neuraxial catheters are significant events. The timing of those events and the timing of any anticoagulation drugs should be taken into consideration as well as the pharmacokinetics and pharmacodynamics of the specific anticoagulant drugs.
3. The emergence of new drugs and unexpected clinical scenarios can render any guideline obsolete. Consultation with an anesthesiologist experienced in regional anesthesia is essential for novel situations.
4. The American Society of Regional Anesthesia and Pain Medicine has developed extensive, peer-reviewed, guidelines for the practice of regional anesthesia in the presence of anticoagulation and can be used for detailed management. These guidelines are available at <http://www.asra.com>.

[R]

Neuraxial blockade (spinal or epidural anesthesia) is a valuable tool for both anesthesiologists and surgeons. The Cochrane Reviews and other sources have listed the usefulness of neuraxial blockade for both intraoperative anesthesia and postoperative analgesia. There are groups of patients that demonstrate improved morbidity and mortality with the use of regional rather than general anesthesia. Similarly the usefulness of venous thromboembolism prophylaxis in preventing morbidity and mortality in surgical patients has been well established. However, there is concern about an increased risk of perispinal hematoma in patients receiving antithrombotic medications for venous thromboembolism prophylaxis in the setting of neuraxial blockade.

Perispinal hematoma is a rare but serious complication of neuraxial blockade. Thus, it is important to consider both the use and the timing of antithrombotic medications in these patients [D], [R].

Thromboprophylactic Agents and Neuraxial Blockade

1. Subcutaneous unfractionated heparin (5,000 units twice daily or three times daily):

It is acceptable to place and maintain epidural catheters in patients on subcutaneous unfractionated heparin. Dosing should be such that the activity of the last dose is near its nadir. Epidural placement should be prior to starting the regimen or at least 6 to 8 hours after the last dose. When discontinuing the epidural catheter, an interval of at least 4 to 6 hours should have transpired since the last dose and the next heparin dose should be given no sooner than 1 to 2 hours after pulling the catheter.

2. Low-molecular-weight heparin:

Twice-daily thromboprophylactic regimens with enoxaparin or dalteparin preclude the use of epidural catheters. The catheter should be discontinued prior to the initiation of this regimen. It is permissible to maintain an epidural catheter on once-daily regimens as long as there is a protocol to closely monitor the patient. The initial dose should not be given for at least 12 hours after catheter placement. Catheter removal should also be 12 to 24 hours after the last low-molecular-weight heparin dose, and an interval of at least 2 hours should pass prior to giving the next dose.

3. Warfarin

Low levels of anticoagulation with warfarin permit retention of an epidural catheter, especially during the early stages of initiating warfarin therapy. It appears to be safe to discontinue the epidural catheter at international normalized ratio values up to 2.0, as long as it is within 48 hours of initiating warfarin therapy. Once beyond 72 hours of drug initiation, multiple coagulation factors beyond factor VII and protein C are affected, which necessitate a more conservative international normalized ratio value less than 1.5 in order to safely discontinue the epidural catheter.

4. Fondaparinux:

Inadequate data exist at this time regarding the maintenance of epidural catheters while employing this agent. Early data suggest that holding fondaparinux for 36 hours may allow safe epidural catheter removal. However, additional study is necessary before this can be endorsed. Currently, it is recommended that the epidural catheter be removed prior to initiating thromboprophylaxis with this drug.

More detailed discussion of each of these points can be reviewed at <http://www.asra.com>.

6. **Pharmacologic Prophylaxis: Hospitalized Non-Surgical Patients Including Burns**

Two recent meta-analyses of hospitalized medical patients showed a significant reduction in pulmonary embolism, a non-significant reduction in symptomatic deep vein thrombosis, and a non-significant increase in major bleeding. Anticoagulation prophylaxis had no effect in all-cause mortality [M].

The ARTEMIS trial showed fondaparinux effective for non-surgical prophylaxis without increasing the risk of clinically relevant bleeding [A].

7. **Pharmacologic Prophylaxis: General, Gynecologic and Urologic Surgery**

Studies, primarily in patients over 40 years of age, have shown that unfractionated heparin is as effective as low-molecular-weight heparin as an anticoagulant prophylactic agent for moderate- and high-risk surgical patients. [Conclusion Grade I: See Conclusion Grading Worksheet A – Annotation #7 (Selecting Heparin) in the original guideline document]

Several studies have compared low-molecular-weight heparin with unfractionated heparin. A meta-analysis concluded that low-molecular-weight heparin doses of less than 3,400 anti-Xa units every day was as effective as unfractionated heparin. At higher doses, low-molecular-weight heparin was slightly superior in preventing venous thromboembolism but had an increased risk of hemorrhage (including major hemorrhage) [A]. The European Multicenter Trial concluded that 1,750 anti-Xa units of low-molecular-weight heparin (reviparin) was equivalent to 10,000 units unfractionated heparin, with a slightly decreased rate of bleeding (8.3% vs. 11.8%) [A].

General surgical regimens have traditionally been begun preoperatively to increase efficacy. A recent study of low-molecular-weight heparin did not show an increased risk of bleeding complications when compared to postoperative administration [C].

Traditionally, heparin regimens in general surgery have been continued while the patient is hospitalized.

Refer to the original guideline document for more information.

9. **Orthopedic Surgery**

Use of Aspirin Following Hip/Knee Arthroplasty

Although it remains controversial, interest persists in the orthopedic community regarding the use of aspirin for venous thromboembolism prophylaxis following elective hip and knee arthroplasty. The debate over the use of aspirin for venous thromboembolism prophylaxis is occurring in

Minnesota and across the U.S. The work group has provided a pro/con forum to illustrate this debate (see the original guideline document). The American College of Chest Physicians recommends against the use of aspirin alone. Aspirin alone is not recommended for routine venous thromboembolism prophylaxis following hip/knee arthroplasty but may be considered in combination with mechanical prophylaxis in patients without additional venous thromboembolism risk factors. Further study is needed.

As the debate surrounding the use of aspirin continues, The American Academy of Orthopedic Surgeons has published recommendations on the prevention of symptomatic pulmonary embolism in patients undergoing total hip or knee arthroplasty [R]. These recommendations are based on a systematic review of the literature conducted by the Center for Clinical Evidence Synthesis at Tufts New England Medical Center. The recommendations risk stratify patients based on venous thromboembolism risk (standard or elevated) and risk of major bleeding (standard or elevated). This risk stratification results in four patient groups:

1. Standard venous thromboembolism risk, standard bleeding risk
2. Elevated venous thromboembolism risk, standard bleeding risk
3. Standard venous thromboembolism risk, elevated bleeding risk
4. Elevated venous thromboembolism risk, elevated bleeding risk

Recommended chemoprophylactic agents include (in alphabetical order) aspirin; low-molecular-weight heparin; synthetic pentasaccharides; and warfarin in all groups except the elevated venous thromboembolism risk, standard bleeding risk group. In this particular group, recommended agents include (in alphabetical order) low-molecular-weight heparin; synthetic pentasaccharides; and warfarin.

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)

None provided

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

Appropriate use of venous thromboembolism prophylaxis to reduce all-cause mortality and/or morbidity associated with surgical procedures and/or hospitalization

POTENTIAL HARMS

Side Effects of Anticoagulant Medications (Unfractionated Heparin and Low Molecular Weight Heparin)

- Bleeding (major and minor)
- There is concern about an increased risk of perispinal hematoma in patients receiving antithrombotic medications for venous thromboembolism prophylaxis in the setting of neuraxial blockade. Perispinal hematoma is a rare but serious complication of neuraxial blockade. Thus, it is important to consider both the use and the timing of antithrombotic medications in these patients.

Side Effects of Mechanical Methods of Venous Thromboembolic Prophylaxis

Mechanical prophylaxis devices, particularly graded compression stockings, can have harmful consequences, most commonly related to skin irritation and breakdown.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Contraindications to fondaparinux include small body mass (<50 kg) and renal insufficiency (creatinine clearance <30)
- Contraindications to the use of graded compression stockings
 - Arterial insufficiency (peripheral arterial disease, including symptoms of claudication, lower extremity pain with elevation)
 - Absent peripheral pulses
 - Dermatitis, including stasis dermatitis
 - Anatomic deformity associated with rheumatoid arthritis or Charcot joint
 - Loss of skin integrity
 - Massive edema of legs or pulmonary edema from congestive heart failure
 - Suspected or actual acute deep vein thrombosis
 - Lower extremity ischemia or gangrene
 - Vein ligation or saphenous vein harvest within six months
 - Skin graft within six months

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.
- Because surgical and hospital procedures are constantly changing, the impact of venous thromboembolism prophylaxis on mortality and morbidity may also be constantly changing. Therefore, all methods of thromboembolism prophylaxis require periodic reassessment by randomized controlled trials. That said, there are two areas that are in urgent need of randomized controlled trials:
 - Patients who require orthopedic procedures – a comparison of aspirin with each of the other pharmacologic thromboprophylactic agents (low-molecular-weight heparins, fondaparinux, warfarin)
 - Patients who require aspirin and clopidogrel due to vascular stents – a comparison of aspirin + clopidogrel (alone) with aspirin + clopidogrel + each additional pharmacologic thromboprophylactic agent (unfractionated heparin, low-molecular-weight heparins, fondaparinux, warfarin)

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for release, a member 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).

Key Implementation Recommendations

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

1. Implement a defined anticoagulation management program to individualize the care provided to each patient receiving anticoagulation therapy. *(2009 Joint Commission/National Safety Goal)*
2. (Clinics and Hospitals): Develop systems for monitoring the effects of anticoagulation therapy (heparin, low-molecular-weight heparin, warfarin and other anticoagulants) to include monitoring of outpatient therapy:
 - Use of standardized practices/protocols that include patient involvement.

(2009 Joint Commission/National Safety Goal)

3. When heparin is administered intravenously and continuously, the organization should use programmable infusion pumps.

(2009 Joint Commission/National Safety Goal)

4. Develop systems for providing patient/family education that includes the importance of follow-up monitoring, compliance issues, dietary restrictions, and potential adverse drug reactions and interactions.
 - Patient education to include documentation of the patient's own awareness of his/her risk for venous thromboembolism, signs and

symptoms of venous thromboembolism and when/how to seek treatment, and demonstrated understanding of the prescribed anticoagulation regimen.

(2009 Joint Commission/National Safety Goal)

5. Develop a policy for providing organizational education regarding anticoagulation therapy to prescriber(s), staff, patients and families.

(2009 Joint Commission/National Safety Goal)

6. Develop protocols for the initiation and maintenance of anticoagulation therapy appropriate to the medication used, to the condition being treated, and to the potential for drug interactions.

(2009 Joint Commission/National Safety Goal)

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
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 prophylaxis: percentage of adult hospitalized patients who are assessed for venous thromboembolism risk within 24 hours of admission.](#)
- [Venous thromboembolism prophylaxis: percentage of hospitalized adult patients who require hospital readmission within 30 days of discharge for conditions related to venous thromboembolism.](#)

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Venous thromboembolism prophylaxis. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2008 Oct. 37 p. [35 references]

ADAPTATION

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

DATE RELEASED

2003 Oct (revised 2008 Oct)

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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SOURCE(S) OF FUNDING

The following Minnesota health plans provide direct financial support: Blue Cross and Blue Shield of Minnesota, HealthPartners, Medica, Metropolitan Health Plan,

PreferredOne and UCare Minnesota. In-kind support is provided by the Institute for Clinical Systems Improvement's (ICSI) members.

GUIDELINE COMMITTEE

Cardiovascular Steering Committee

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ICSI has adopted a policy of transparency, disclosing potential conflict and competing interests of all individuals who participate in the development, revision and approval of ICSI documents (guidelines, order sets and protocols). This applies to all work groups (guidelines, order sets and protocols) and committees (Committee on Evidence-Based Practice, Cardiovascular Steering Committee, Women's Health Steering Committee, Preventive & Health Maintenance Steering Committee and Respiratory Steering Committee).

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

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GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Venous thromboembolism prophylaxis. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2007 Jun. 52 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 prophylaxis. Executive summary. Bloomington (MN): Institute for Clinical Systems Improvement, 2008 Oct. 1 p. Electronic copies: Available from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](#).
- ICSI pocket guidelines. May 2007 edition. Bloomington (MN): Institute for Clinical Systems Improvement, 2007.

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.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 29, 2004. It was updated by ECRI on September 16, 2005, and September 18, 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 11, 2007. This NGC summary was updated by ECRI Institute on March 14, 2008 following the updated FDA advisory on heparin sodium injection. This NGC summary was updated by ECRI Institute on April 16, 2009.

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Date Modified: 5/11/2009

