



Complete Summary

GUIDELINE TITLE

Antithrombotic therapy for non-ST-segment elevation acute coronary syndromes. American College of Chest Physicians evidence-based clinical practice guidelines (8th edition).

BIBLIOGRAPHIC SOURCE(S)

Harrington RA, Becker RC, Cannon CP, Gutterman D, Lincoff AM, Popma JJ, Steg G, Guyatt GH, Goodman SG. Antithrombotic therapy for non-ST-segment elevation acute coronary syndromes: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):670S-707S. [163 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Harrington RA, Becker RC, Ezekowitz M, Meade TW, O'Connor CM, Vorchheimer DA, Guyatt GH. Antithrombotic therapy for coronary artery disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):513S-48S.

** 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.

- [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.
- [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.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis

RECOMMENDATIONS

EVIDENCE SUPPORTING THE RECOMMENDATIONS

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

QUALIFYING STATEMENTS

IMPLEMENTATION OF THE GUIDELINE

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY

DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Non-ST-segment elevation acute coronary syndromes

GUIDELINE CATEGORY

Management

Prevention

Treatment

CLINICAL SPECIALTY

Cardiology

Critical Care

Emergency Medicine

Family Practice

Internal Medicine

INTENDED USERS

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Patients

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Social Workers

GUIDELINE OBJECTIVE(S)

To provide evidence-based guidelines on the use of antithrombotic therapy for the treatment of patients with non-ST-segment elevation acute coronary syndromes

TARGET POPULATION

Patients with non-ST-segment elevation acute coronary syndromes

INTERVENTIONS AND PRACTICES CONSIDERED

1. Antiplatelet therapies
 - Aspirin
 - Clopidogrel
 - Glycoprotein (GP) IIb/IIIa inhibitor (abciximab, eptifibatide or tirofiban)
 - Combination use of clopidogrel and GP IIb/IIIa inhibitor
 - Ticlopidine
2. Anticoagulant therapies
 - Unfractionated heparin (UFH)
 - Low-molecular-weight heparins (LMWHs)
 - Fondaparinux
 - Bivalirudin
 - Thienopyridines
3. Monitoring of international normalized ratio (INR)
4. Maintenance of the activated partial thromboplastin time (APTT)

MAJOR OUTCOMES CONSIDERED

- Mortality
- Myocardial infarction
- Stroke
- Incidence of major and minor hemorrhage

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Process of Searching for Evidence

Defining the clinical question provided the framework for formulating eligibility criteria that guided the search for relevant evidence. In specifying eligibility criteria, authors identified not only patients, interventions, and outcomes, but also methodologic criteria. For many recommendations, authors restricted eligibility to randomized controlled trials (RCTs).

For many questions, randomized trials did not provide sufficient data, and chapter authors included observational studies when randomized trials were not the most appropriate design to address the research question. In particular, randomized trials are not necessarily the best design to understand risk groups, that is, the baseline or expected risk of a given event for certain subpopulations. Because no interventions are typically examined in questions about prognosis, one replaces interventions by the duration of exposure measured in time.

Identifying the Evidence

To identify the relevant evidence, a team of librarians and research associates at the McMaster University Evidence based practice center (EPC) conducted comprehensive literature searches. Methodologic experts (including the editors) and the EPC librarians reviewed each question to ensure the development of a comprehensive search strategy. For example, for questions about antiplatelet agents, the EPC consulted chapter authors to ensure that the search included all relevant antiplatelet agents. More specifically, authors then decided whether to include dipyridamole in a search that already included aspirin, clopidogrel, and ticlopidine.

For each question the authors provided, the librarians searched the Cochrane Database of Systematic Reviews, MEDLINE, and Embase for published English-language literature and human studies between 2002 and May 2006. To filter MEDLINE and Embase search results for RCT evidence, the librarians used the search strategy developed by the Cochrane Collaboration. These searches updated the more comprehensive and sensitive searches conducted for the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence Based Guidelines.

The EPC team conducted separate searches for systematic reviews; RCTs; and, if applicable, observational studies. For observational studies, searches were not restricted in terms of methodology. Although increasing the probability of identifying all published studies, this sensitive approach resulted in large numbers of citations for many of the defined clinical questions. Therefore, trained research assistants screened the citation list developed from the search using criteria of increased specificity to reduce the number of irrelevant citations that the authors received. These irrelevant citations included press news, editorials, narrative reviews, single-case reports, studies that included fewer participants than specified by authors as an inclusion criterion, animal studies (any nonhuman studies), and letters to the editor. Authors did not include data from abstracts of meetings for the development of recommendations, and the guideline developers did not explicitly use Internet sources to search for research data. Authors were encouraged, however, to mention abstracts that reported on groundbreaking data that were particularly relevant to a specific question in the chapters in order to alert readers that new, fully published evidence might become available shortly.

Standard Consideration of Study Quality

High-quality clinical guidelines should pay careful attention to the methodologic quality of the studies that form the basis of their recommendations. Using the example of the prevention of venous thromboembolism during air travel, Table 1 in the methodology companion (see "Availability of Companion Documents" field)

shows the criteria for assessment of study quality (randomization, concealment or treatment allocation, blinding, completeness of follow-up, and whether the analysis was performed according to the intention-to-treat principle), and Table 2 in the methodology companion (see "Availability of Companion Documents" field) shows the presentation of results that were circulated to the authors. Whereas all authors attended to these criteria, the guideline developers have summarized the results of the quality assessment for only a minority of the recommendations. Readers can find these summaries in an online appendix to the recommendations (see online supplemental data).

In assessing the quality of observational studies, the guideline developers did not make a distinction between prospective and retrospective because the key issues are unbiased sampling, high-quality measurement of patient characteristics and outcomes, and complete follow-up.

Although it is more likely that these quality criteria will be achieved in prospective studies, prospective studies may fail to achieve them, and retrospective studies may succeed. The guideline developers did make a key distinction about whether internal comparisons exist and their nature. Studies without internal comparisons received the label "case series" unless they met the following criteria: (1) a protocol existed before the date of commencement of data collection; (2) a definition of inclusion and exclusion criteria was available; (3) the study reported the number of excluded patients; (4) the study conducted a standardized follow-up, including description of schedule of follow-up, investigation of suspected outcomes, and criteria used to define outcomes; and (5) the study reported all losses to follow-up.

The guideline developers labeled studies that met these criteria "cohort studies without internal controls." Studies with internal comparisons received the label "cohort studies with concurrent controls" or "cohort studies with historical controls." These cohort studies may succeed or fail to ensure settings, similar time frames, adjustment for differences in patients' characteristics, and follow-up with patients. These features were captured in descriptive tables provided to authors when requested from the EPC.

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

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) and the methodological quality of the underlying evidence (A, B, or C). See "Grades of recommendations for antithrombotic agents" in the "Availability of Companion Documents" field and the "Rating Scheme for the Strength of the Recommendations." field.

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

Summarizing Evidence

The electronic searches also included searches for systematic reviews. If authors were satisfied with a recent high-quality systematic review, evidence from that review provided a foundation for the relevant recommendation.

Pooled analyses from high-quality systematic reviews formed summary data on which panelists based their recommendations wherever possible. Pooling offers the advantage of obtaining more precise estimates of treatment effects and allows for greater generalizability of results. However, pooling also bears the risk of spurious generalization. In general, the summary estimates of interest were the different types of outcomes conveying benefits and downsides (risk, burden, and cost). When pooled estimates of effects were not available, the McMaster University Evidence based practice center (EPC) conducted meta-analysis to obtain pooled estimates for specific questions. These were questions that authors had specifically identified.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Group-Specific Recommendations

In general, the guideline developers have endeavored to make their recommendations as specific as possible for patient subgroups differing according to risk. Whenever valid prognostic data were available, the guideline developers used them to estimate absolute effects and made recommendations accordingly. Unfortunately, reliable prognostic indexes are not usually available, limiting the extent to which such group-specific recommendations are possible.

Acknowledge Values and Preferences and Resource Use Underlying Recommendations

Under ideal circumstances, knowledge of average patient values and preferences would be available for every recommendation, the panel members would summarize these values and preferences, and they would be integrated into the recommendations that guideline developers make. The guideline developers asked all chapter chairs before beginning the searches for the relevant literature to identify recommendations that they believed were particularly sensitive to patients' values and preferences. Moderate-quality evidence regarding values and preferences bearing directly on the recommendations proved available for only the

chapter that addresses antithrombotic therapy in patients with atrial fibrillation. The panelists bore in mind what average patient values and preferences may be; the process, however, is speculative.

The guideline developer's main strategy for dealing with this unsatisfactory situation is to make the values and preferences underlying the recommendations explicit whenever the panelists believed that value and preference issues were crucial for a recommendation.

In addition, the guideline developers involved three consultants with expertise in the area of values and preferences to collaborate with the chairs of two chapters and try to ensure that the guidelines adequately represented the views of patients. This collaboration led to extensive discussions among the chapter authors and the consultants and the reflection of these discussions in the associated values and preference statements.

Finalizing and Harmonizing Recommendations

After having completed the steps the guideline developers have described above, the guideline authors formulated draft recommendations before the conference, which laid the foundation for authors to work together and critique the recommendations. Figure 1 in the methodology companion (see "Availability of Companion Documents" field) shows the process of guideline development and review. Drafts of chapters that included draft recommendations were usually distributed for peer review to at least two panel members and were always reviewed by at least one panel editor before the conference. Written critiques were prepared and returned to the authors for revision of their work. At the plenary conference, a representative of each chapter presented potentially controversial issues in their recommendations. Chapter authors met to integrate feedback and consider related recommendations in other chapters and to revise their own guidelines accordingly. Authors continued this process after the conference until they reached agreement within their groups and with other author groups who provided critical feedback. The editors of this supplement harmonized the chapters and resolved remaining disagreements between chapters through facilitated discussion. All major correspondence and discussions at the meeting were recorded in written and audio protocols and are publicly available.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality evidence, Grade 1A	Desirable effects clearly outweigh	Consistent evidence from RCTs without important limitations or	Recommendation can apply to most patients in most circumstances; further research is very

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
	undesirable effects, or <i>vice versa</i>	exceptionally strong evidence from observational studies	unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; higher quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Strong recommendation, low or very low-quality evidence, Grade 1C	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient or society values; further research is very unlikely to change our confidence in the estimate of effect
Weak recommendation, moderate-quality evidence, Grade 2B	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Best action may differ depending on circumstances or patient or society values; higher-quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Weak recommendation, low or very low-quality evidence, Grade 2C	Desirable effects closely balanced with undesirable effects	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate

*The guideline developers use the wording *recommend* for strong (Grade 1) recommendations and *suggest* for weak (Grade 2) recommendations.

COST ANALYSIS

For these guidelines, the guideline developers implemented recommendations of a recent American College of Chest Physicians (ACCP) task force on integrating resource allocation in clinical practice guidelines by restricting resource expenditure consideration to a small number of recommendations for which they were particularly relevant. The guideline developers relied on two consultants with expertise in economic assessment to help with the process of considering costs in those small numbers of recommendations that the guideline developers considered very important to the decision.

Recommendations highly sensitive to resource allocation now include value and preference statements regarding how cost issues were integrated.

Refer to "Strategies for incorporating resource allocation and economic considerations" (see "Availability of Companion Documents" field) for details of the cost analyses.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The American College of Chest Physicians (ACCP) Health Science Policy (HSP) established a process for the thorough review of all ACCP evidence-based clinical practice guidelines. After final review by the editors, the guidelines underwent review by appropriate NetWorks of the ACCP (for these guidelines, the Cardiovascular and Pulmonary Vascular NetWorks), the HSP, and the Board of Regents. The latter two have the right of approval or disapproval but usually work with the guideline authors and editors to make necessary revisions before final

approval. Each group identified primary reviewers who read the full set of chapters as well as individual committee members who were responsible for reviewing one or more chapters. The reviewers considered both content and methodology as well as whether there was balanced, not biased, reporting and adherence to HSP processes. Finally, the *CHEST* editor-in-chief read and forwarded the manuscripts for nonbiased, independent, external peer review before acceptance for publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The grades of recommendation (1A, 1B, 1C, 2A, 2B, 2C) are defined at the end of the "Major Recommendations" field.

Recommendations for Antiplatelet Therapies

1. For all patients presenting with non-ST-segment elevation acute coronary syndromes (NSTEMI ACS) without a clear allergy to aspirin, the guideline developers recommend immediate aspirin (162 to 325 mg orally [po]) and then daily oral aspirin (75 to 100 mg) (**Grade 1A**).
2. For all NSTEMI ACS patients with an aspirin allergy, the guideline developers recommend immediate treatment with clopidogrel, 300 mg po bolus, followed by 75 mg/d indefinitely (**Grade 1A**).
3. For NSTEMI ACS patients who are at moderate or greater risk (e.g., ongoing chest pain, hemodynamic instability, positive troponin, or dynamic ECG changes) for an ischemic event and who will undergo an early invasive management strategy (i.e., diagnostic catheterization followed by anatomy-driven revascularization):
 - a. The guideline developers recommend "upstream" treatment either with clopidogrel (300 mg po bolus, followed by 75 mg/d) or a small-molecule intravenous (IV) glycoprotein (GP) IIb/IIIa inhibitor (eptifibatid or tirofiban) (**Grade 1A**).
 - b. The guideline developers suggest upstream use of both clopidogrel and a small-molecule IV GP IIb/IIIa inhibitor (**Grade 2A**). Scrupulous attention to weight- and renal-based dosing algorithms must be part of eptifibatid or tirofiban administration.
 - c. For patients presenting with NSTEMI ACS, the guideline developers recommend against abciximab as initial treatment except when coronary anatomy is known and percutaneous coronary intervention (PCI) is planned within 24 hours (**Grade 1A**).
4. For NSTEMI ACS patients who are at moderate or greater risk for an ischemic event and for whom an early conservative or a delayed invasive strategy of management is to be used:
 - a. The guideline developers recommend upstream treatment with clopidogrel (300 mg oral bolus, followed by 75 mg/d) (**Grade 1A**).
 - b. The guideline developers suggest upstream use of both clopidogrel and a small-molecule IV GP IIb/IIIa inhibitor (**Grade 2B**).

5. For NSTEMI ACS patients who undergo PCI, the guideline developers recommend treatment with both clopidogrel and an IV GP IIb/IIIa inhibitor **(Grade 1A)**
 - a. The guideline developers recommend a loading dose of 600 mg of clopidogrel given at least 2 hours prior to planned PCI followed by 75 mg/d **(Grade 1B)**.
 - b. If ticlopidine is given, the guideline developers suggest that a loading dose of 500 mg be given at least 6 hours before planned PCI **(Grade 2C)**.
 - c. For PCI patients who cannot tolerate aspirin, the guideline developers suggest that the loading dose of clopidogrel (600 mg) or ticlopidine (500 mg) be given at least 24 hours prior to planned PCI **(Grade 2C)**.
 - d. The guideline developers recommend use of a GP IIb/IIIa antagonist (abciximab or eptifibatide) **(Grade 1A)** for all NSTEMI ACS patients with at least moderate risk features undergoing PCI in whom a GP IIb/IIIa inhibitor has not been started "upstream." The guideline developers recommend administration of abciximab as a 0.25 mg/kg bolus followed by a 12-hour infusion at a rate of 10 micrograms/min **(Grade 1A)** and eptifibatide as a double bolus (each 180 micrograms/kg, given 10 minutes apart) followed by an 18-hour infusion of 2.0 micrograms/kg/min **(Grade 1A)**. Appropriate dose reduction of eptifibatide must be based on renal function.
 - e. In patients undergoing PCI in whom a GP IIb/IIIa inhibitor has not been started upstream, the guideline developers recommend against the use of tirofiban as an alternative to abciximab **(Grade 1B)**.
6. For NSTEMI ACS patients who have received clopidogrel and are scheduled for coronary bypass surgery, the guideline developers suggest discontinuing clopidogrel for at least 5 days prior to the scheduled surgery **(Grade 2A)**.

Anticoagulant Therapies

1. For all patients presenting with NSTEMI ACS, the guideline developers recommend anticoagulation with unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) or bivalirudin or fondaparinux over no anticoagulation **(Grade 1A)**.
 - a. The guideline developers recommend weight-based dosing of UFH and maintenance of the activated partial thromboplastin time (APTT) between 50 and 70 seconds **(Grade 1B)**.
 - b. The guideline developers recommend against routine monitoring of the anticoagulant effect of LMWH **(Grade 1C)**. Careful attention is needed to appropriately adjust LMWH dose in patients with renal insufficiency.
2. For NSTEMI ACS patients who will undergo an early invasive strategy of management (i.e., diagnostic catheterization followed by anatomy-driven revascularization)
 - a. The guideline developers recommend UFH (with a GP IIb/IIIa inhibitor) over either LMWH or fondaparinux **(Grade 1B)**.
 - b. The guideline developers suggest bivalirudin over UFH in combination with a thienopyridine as an initial antithrombotic strategy in patients with moderate-to-high risk features presenting with a NSTEMI ACS and

- scheduled for very early coronary angiography (< 6 hours) (**Grade 2B**).
3. For NSTEMI ACS patients in whom an early conservative or a delayed invasive strategy of management is to be used:
 - a. The guideline developers recommend fondaparinux over enoxaparin (**Grade 1A**). For patients treated with upstream fondaparinux and undergoing PCI, the guideline developers recommend that additional IV boluses of UFH be given at the time of the procedure (for example, 50 to 60 U/kg) as well as additional IV doses of fondaparinux (2.5 mg if also receiving a GP IIb/IIIa inhibitor and 5 mg if not) (**Grade 1B**). Additionally, PCI operators should regularly flush the catheters with UFH during the procedure as well.
 - b. The guideline developers recommend LMWH over UFH (**Grade 1B**). The guideline developers recommend continuing LMWH during PCI treatment of patients with NSTEMI ACS when LMWH has been started as the upstream anticoagulant (**Grade 1B**). If the last dose of enoxaparin was given ≤ 8 hours prior to PCI, the guideline developers recommend no additional anticoagulant therapy (**Grade 1B**). If the last dose of enoxaparin was given 8 to 12 hours before PCI, the guideline developers recommend a 0.3 mg/kg bolus of IV enoxaparin at the time of PCI (**Grade 1B**).
 4. In low-to-moderate risk patients with NSTEMI ACS undergoing PCI, the guideline developers recommend either bivalirudin with provisional ("bail-out") GP IIb/IIIa inhibitors or UFH plus a GP IIb/IIIa inhibitor over alternative antithrombotic regimens (**Grade 1B**).

Definitions:

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality evidence, Grade 1A	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; further research is very unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very	Recommendation can apply to most patients in most circumstances; higher quality research may well have an important impact on our confidence in the estimate of effect and

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
		strong evidence from observational studies	may change the estimate
Strong recommendation, low or very low-quality evidence, Grade 1C	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient or society values; further research is very unlikely to change our confidence in the estimate of effect
Weak recommendation, moderate-quality evidence, Grade 2B	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Best action may differ depending on circumstances or patient or society values; higher-quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Weak recommendation, low or very low-quality evidence, Grade 2C	Desirable effects closely balanced with undesirable effects	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate

*The guideline developers use the wording *recommend* for strong (Grade 1) recommendations and *suggest* for weak (Grade 2) recommendations.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate monitoring and management of antithrombotic therapy in patients with non-ST-segment elevation acute coronary syndromes

POTENTIAL HARMS

Antithrombotic therapy is associated with an increased risk of minor and major hemorrhagic events.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Limitations of These Guideline Development Methods

Limitations of these guidelines include the limited quantity and quality of available studies for some patient groups. Second, it is possible that some authors followed this methodology more closely than others, although the development process was centralized by an evidence-based practice center (EPC) and supervised by the editors. Third, it is possible that the guideline developers missed relevant studies in spite of the comprehensive searching process. Fourth, despite their efforts to begin centralizing the methodologic evaluation of all studies to facilitate uniformity in the validity assessments of the research incorporated into these guidelines, resources were insufficient to conduct this evaluation for all but a few of the recommendations in each chapter. Fifth, the guideline developers performed only few statistical pooling exercises of primary study results. Finally, sparse data on patient preferences and values represent additional limitations inherent to most guideline development methods.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy includes local educational programs and tools offered through the American College of Chest Physicians (ACCP) Board of Governors and

select other locations. The Veterans Administration (VA) will also participate in a pilot project.

IMPLEMENTATION TOOLS

Resources

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

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Harrington RA, Becker RC, Cannon CP, Gutterman D, Lincoff AM, Popma JJ, Steg G, Guyatt GH, Goodman SG. Antithrombotic therapy for non-ST-segment elevation acute coronary syndromes: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):670S-707S. [163 references] [PubMed](#)

ADAPTATION

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

DATE RELEASED

2001 Jan (revised 2008 Jun)

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Chest Physicians

GUIDELINE COMMITTEE

American College of Chest Physicians (ACCP) Expert Panel on Antithrombotic and Thrombolytic Therapy

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: Robert A. Harrington, MD, FCCP; Richard C. Becker, MD, FCCP; Christopher P. Cannon, MD; David Gutterman, MD, FCCP; A. Michael Lincoff, MD; Jeffrey J. Popma, MD; Gabriel Steg, MD, FCCP; Gordon H. Guyatt, MD, FCCP; and Shaun G. Goodman, MD

Committee Co-Chairs: Jack Hirsh, MD, FCCP (*Chair*); Gordon H. Guyatt, MD, FCCP; Gregory W. Albers, MD; Robert A. Harrington, MD, FCCP; Holger J. Schünemann, MD, PhD, FCCP

Participants: Giancarlo Agnelli, MD; Pierre Amarengo, MD; Jack E. Ansell, MD; Collin Baigent; Shannon M. Bates, MD; Kenneth A. Bauer, MD; Richard C. Becker, MD; Peter B. Berger, MD; David Bergqvist, MD, PhD; Rebecca J. Beyth, MD; Christopher P. Cannon, MD; Elizabeth A. Chalmers, MB, ChB, MD; Anthony K.C. Chan, MBBS; Clifford W. Colwell, Jr., MD; Anthony J. Comerota, MD; Deborah Cook, MD; Mark A. Crowther, MD; James E. Dalen, MD; Gabrielle deVeber, MD, MHSc; Maria Benedetta Donati, MD, PhD; James D. Douketis, MD; Andrew Dunn, MD; J. Donald Easton, MD; Michael Ezekowitz, MD; Margaret Fang; William H. Geerts, MD, FCCP; Alan S. Go, MD; Samuel Z. Goldhaber, MD, FCCP; Shaun D. Goodman, MD; Michael Gould, MD, FCCP; Ian A. Greer, MD; Andreas Greinacher, MD; David Gutterman, MD, FCCP, HSP; Jonathan L. Halperin, MD; John A. Heit, MD; Elaine M. Hylek, MD; Alan Jacobson, MD; Roman Jaeschke, MD, PhD; Amir K. Jaffer, MD; Susan Kahn; Clive Kearon, MBCh, PhD; Fenella Kirkham, MBBC; Andreas Koster, MD, PhD; Michael R. Lassen, MD; Mark N. Levine, MD, MSc; Sandra Zelman Lewis, PhD; A. Michael Lincoff, MD; Gregory YH Lip, MD; Christopher Madias, MD; Warren J. Manning, MD; Daniel B. Mark, MD; M. Patricia Massicotte, MD, MSc; David Matchar, MD; Thomas W. Meade, DM, FCCP; Venu Menon, MD; Tracy Minichiello, MD; Paul Monagle, MBBS, MSc, MD, FCCP; Christopher M. O'Connor, MD; Patrick O'Gara, MD; E. Magnus Ohman, MD; Ingrid Pabinger, MD; Gualtiero Palareti, MD; Carlo Patrono, MD; Stephen G. Pauker, MD; Graham F. Pineo, MD; Jeffrey J. Popma, MD; Gary Raskob, PhD; Gerald Roth, MD; Ralph L. Sacco, MD; Deeb N. Salem, MD, FCCP; Charles-Marc Samama, MD, FCCP; Meyer Michel Samama, MD; Sam Schulman, MD, PhD; Daniel Singer, MD; Michael Sobel, MD; Shoshanna Sofaer, DrPH; Alex C. Spyropoulos, MD FCCP; Ph. Gabriel Steg, MD; Philip Teal, MD; Raymond Verhaeghe, MD; David A. Vorchheimer, MD; Theodore E. Warkentin, MD; Jeffrey Weitz, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Dr. Harrington discloses that he holds a fiduciary position as Director of the Duke Clinical Research Institute (DCRI). Either he or the DCRI have received grant monies from the following: Abbott Laboratories; Abbott Vascular Business; Acorn Cardiovascular; Actelion, Ltd; Acusphere, Inc; Adolor Corporation; Advanced Cardiovascular Systems, Inc; Air Products; PLC; Ajinomoto; Alexion, Inc; Allergan, Inc; Alsius Corporation; Amgen, Inc; Amylin Pharmaceuticals; Anadys; Angel Medical Systems, Inc; AnGes MG Inc; Angiometrx, Inc; ArgiNox

Pharmaceuticals; Ark Therapeutics; Astellas Pharma US; Astra Hassle; AstraZeneca; Atritech; Aventis; BARRX Medical, Inc; Baxter; Bayer AG; Bayer Corporation US; Berlex, Inc; Bioheart; Biolex Therapeutics; Biosense Webster, Inc; Biosite, Inc (also Biosite Diagnostics); Biosynexus; Boehringer Ingelheim; Boston MedTech Advisors; Bristol Scientific Corporation; Bristol-Myers Squibb; CanAm Bioresearch; Cardio Thoracic Systems; CardioDynamics International; CardioKinetix; CardioOptics; Celgene Corporation; Celsion Corporation; Centocor; Cerexa, Inc; Chase Medical; Chugai Pharmaceutical; Cierra Inc; Coley Pharmaceutical Group; Conor Medsystems; Corautus Genetics; Cordis; Critical Therapeutics; Cubist Pharmaceuticals; CV Therapeutics; Cytokinetics; Daiichi Sankyo; deCode Genetics; Dyax; Echosens, Inc; Eclipse Surgical Technologies; Edwards Lifesciences; Eli Lilly & Company; EnteroMedics; Enzon Pharmaceutical; EOS Electro Optical Systems; EPI-Q, Inc; ev3, Inc; Evalve, Inc; Flow Cardia Inc; Fox Hollow Pharmaceuticals; Fujisawa; Genentech; General Electric Company; General Electric Healthcare; General Electric Medical Systems; Genzyme Corporation; Getz Bros & Co, Inc; GlaxoSmithKline; GlobelImmune; Gloucester Pharmaceuticals; Guidant Pharmaceuticals; HeartScape Technologies; Hoffmann-LaRoche; Human Genome Sciences, Inc; ICAGEN; iCo Therapeutics; IDB Medical; Idenix Pharmaceutical; Indigo Pharmaceutical; INFORMD, Inc; InfraReDx; Inhibitex; Innocoll Pharmaceuticals; Inspire Pharmaceuticals; Intarcia Therapeutics; Integrated Therapeutics Group; Inverness Medical Innovations; Ischemix, Inc; Johnson & Johnson; Jomed, Inc; KAI Pharmaceuticals; Kerberos Proximal Solutions, Inc; Kinetic Concepts, Inc; King Pharmaceuticals; Kuhera Chemical Co; Lilly; Lumen Biomedical, Inc; Medical Educations Solutions Group; Medicure International; MiniMed; Medi-Flex, Inc; MedImmune; Medtronic AVE; Medtronic Diabetes; Medtronic, Inc; Medtronic Vascular; Merck Group; Microphage, Inc; Millennium Pharmaceutical; Mosby; Mycosol, Inc; NABI Biopharma; Neuron Pharmaceuticals; NicOx; NitroMed; NovaCardia Inc; Novartis AG Group; Novartis Pharmaceuticals; OLG Research; Ortho Biotech; OSI Eyetech; Osiris Therapeutics; Otsuka Pharmaceutical; Pathway Medical Technologies; PDL bio Pharma; PDxRx, Inc; Peregrine Pharmaceuticals; Pfizer; Pharmacyclics; Pharamanetics; Pharmassest; Pharsight, Inc; Portola Pharmaceutical; Proctor & Gamble; Radiant; Reata Pharmaceuticals; Recom Managed Systems, Inc; Regado Biosciences; Reliant Pharmaceuticals; Roche Diagnostic Corp; Salix Pharmaceuticals; Sanofi Pasteur, Inc (formerly Aventis-Pasteur); Sanofi-Aventis; Sanofi- Synthelabo; Schering-Plough Corporation; SciClone Pharmaceuticals; Scios; Seredigm; Sichel Technologies; Siemens; Skyline Ventures; Social Scientific Solutions; Spectranetics; Summit; Suneis; TAP Pharmaceutical Products; Tengion; Terumo Corporation; The Medicines Company; Theravance; TherOx, Inc; Thoratec Corporation; Titan Pharmaceuticals; United Therapeutics; Uptake Medical Corporation; Valleylab; Valeant Pharmaceuticals International; Valentis, Inc; Vascular Solutions, Inc; Velocimen, Inc; Veridex; Vertex Pharmaceuticals; VIASYS Healthcare; Vicuron Pharmaceuticals (formerly Versicor); ViroChem Pharma, Inc; Watson Pharmaceuticals; WebMD; Wyeth; Xsira Pharmaceuticals (formerly Norak Biosciences); and/or XTL Biopharma.

Dr. Becker reveals no real or potential conflicts of interest or commitment.

Dr. Cannon discloses that he has received grant monies from Accumetrics, AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Merck, Sanofi-Aventis, and Schering Plough.

Dr. Lincoff discloses that he has received grant monies from The Medicines Company, Sanofi, Lilly, Pfizer, Schering, and AstraZeneca. He is also on advisory committees for Sanofi, The Medicines Company, and Pfizer.

Dr. Steg discloses that he has received grant monies from Sanofi-Aventis, and consultant fees from Sanofi-Aventis, Astra- Zeneca, BMS, Boehringer Ingelheim, Takeda, Amgen, Thermedicine, MSD, GSK, and Servier. He has served on the speakers bureau at Sanofi-Aventis, AstraZeneca, BMS, Boehringer Ingelheim, Takeda, Amgen, Thermedicine, MSD, GlaxoSmithKline, and Servier.

Dr. Popma discloses that he has received monies from Cordis, Boston Scientific, Medtronic, and Abbott. He is involved with the speakers bureaus of Pfizer, BMS, Lilly, and Sanofi, and has served on advisory committees of Medtronix, BSC, Abbott, and Cordis.

Dr. Goodman discloses that he has received grant monies from Biovail, Bristol-Myers Squibb, GlaxoSmithKline, Hoffman- La Roche, Lilly, Merck, Sanofi-Aventis, Schering, and The Medicines Company. He has also received consultant fees from Bristol-Myers Squibb, GlaxoSmithKline, Hoffman-La Roche, Lilly, Sanofi-Aventis, and The Medicines Company.

Dr. Guyatt reveals no real or potential conflicts of interest or commitment.

Dr. Gutterman discloses that he has received grant monies from the Veterans Administration and the National Institutes of Health. He is also a shareholder of Johnson & Johnson and has a relative who is a vice president at Glaxo-Wellcome.

ENDORSER(S)

American College of Clinical Pharmacy - Medical Specialty Society
American Society of Health-System Pharmacists - Professional Association

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Harrington RA, Becker RC, Ezekowitz M, Meade TW, O'Connor CM, Vorchheimer DA, Guyatt GH. Antithrombotic therapy for coronary artery disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):513S-48S.

GUIDELINE AVAILABILITY

Electronic copies: Available to subscribers of the [Chest - The Cardiopulmonary and Critical Care Journal](#).

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

Executive Summary:

- Antithrombotic and thrombolytic therapy executive summary. Chest 2008 Jun; 133:71S-109S.

Background Articles:

- Antithrombotic and thrombolytic therapy. Chest 2008 Jun; 133:110S-112S.
- Methodology for antithrombotic and thrombolytic therapy guideline development. Chest 2008 Jun; 133:113S-122S.
- Grades of recommendation for antithrombotic agents. Chest 2008 Jun; 133:123S-131S.
- Strategies for incorporating resource allocation and economic considerations. Chest 2008 Jun; 133:132S-140S.

Electronic copies: Available to subscribers of the [Chest - The Cardiopulmonary and Critical Care Journal](#).

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on July 30, 2001. The information was verified by the guideline developer on September 27, 2001. This NGC summary was updated by ECRI on December 9, 2004. The updated information was verified by the guideline developer on January 12, 2005. 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 summary was updated by ECRI Institute on July 12, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Troponin-1 Immunoassay. This summary was updated by ECRI Institute on September 7, 2007 following the revised U.S. Food and Drug Administration (FDA) advisory on Coumadin (warfarin). This 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 December 8, 2008. The updated information was verified by the guideline developer on January 7, 2009.

COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2009 National Guideline Clearinghouse

Date Modified: 2/16/2009

