



Complete Summary

GUIDELINE TITLE

Antithrombotic therapy in atrial fibrillation. American College of Chest Physicians evidence-based clinical practice guidelines (8th edition).

BIBLIOGRAPHIC SOURCE(S)

Singer DE, Albers GW, Dalen JE, Fang MC, Go AS, Halperin JL, Lip GY, Manning WJ. Antithrombotic therapy in atrial fibrillation: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):546S-92S. [281 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

This guideline is updates a previous version: Singer DE, Albers GW, Dalen JE, Go AS, Halperin JL, Manning WJ. Antithrombotic therapy in atrial fibrillation: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):429S-56S.

** 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)

Atrial fibrillation

Note: Atrial fibrillation (AF) is the most common significant cardiac rhythm disorder and is an important independent risk factor for ischemic stroke.

GUIDELINE CATEGORY

Management

Prevention

Risk Assessment

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 discuss antithrombotic therapy for patients with atrial fibrillation (AF)
- To update evidence-based recommendations for the use of antithrombotic and thrombolytic therapy for the management of thromboembolic conditions

TARGET POPULATION

Patients with atrial fibrillation (AF)

INTERVENTIONS AND PRACTICES CONSIDERED

1. Assessment of risk factors
2. Oral vitamin K antagonist (VKA), warfarin
3. Aspirin
4. Monitoring international normalized ratio (INR) and partial thromboplastin time (PTT)
5. Transesophageal echocardiography (TEE)-guided and non-TEE-guided cardioversion
6. Anticoagulation for elective cardioversion (unfractionated heparin [UFH], low-molecular-weight heparin [LMWH])
7. Antithrombotic management of atrial flutter
8. Repeat TEE before attempting additional cardioversion
9. Management of AF in specific populations

MAJOR OUTCOMES CONSIDERED

- Target international normalized ratio
- Mortality
- Recurrent episodes of atrial fibrillation
- Atrial flutter

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.

Atrial Fibrillation

1. In patients with Atrial Fibrillation (AF), including those with paroxysmal AF, who have had a prior ischemic stroke, transient ischemic attack (TIA), or systemic embolism, the guideline developers recommend long-term anticoagulation with an oral vitamin K antagonist (VKA), such as warfarin, targeted at an international normalized ratio (INR) of 2.5 (range, 2.0 to 3.0) because of the high risk of future ischemic stroke faced by this set of patients (**Grade 1A**). Timing of the initiation of VKA therapy after an acute ischemic stroke involves balancing the risk of hemorrhagic conversion with short-term risk of recurrent ischemic stroke and is addressed in the "Ischemic Stroke" chapter of the original guideline document (see the National Guideline Clearinghouse (NGC) summary of the American College of Chest Physicians (ACCP) guideline [Antithrombotic and Thrombolytic Therapy for Ischemic Stroke](#)).
2. In patients with AF, including those with paroxysmal AF, who have two or more of the following risk factors for future ischemic stroke, the guideline developers recommend long-term anticoagulation with an oral VKA, such as warfarin, targeted at an INR of 2.5 (range, 2.0 to 3.0) because of the increased risk of future ischemic stroke faced by this set of patients (**Grade 1A**). Two or more of the following risk factors apply: (1) age > 75 years, (2) history of hypertension, (3) diabetes mellitus, and (4) moderately or severely impaired left ventricular systolic function and/or heart failure.

Remark: Recommendations 1 and 2 above correspond to a recommendation of oral VKA therapy for individuals with a score ≥ 2 using the Congestive heart failure, Hypertension, Age, Diabetes, Stroke (doubled) risk scoring system (CHADS₂) classification. For these and all other recommendations of long-term therapy in this chapter, "long-term" means lifelong unless a contraindication emerges.

3. In patients with AF, including those with paroxysmal AF, with only one of the risk factors listed below, the guideline developers recommend long-term anti-thrombotic therapy (**Grade 1A**), either as anticoagulation with an oral VKA, such as warfarin, targeted at an INR of 2.5 (range, 2.0 to 3.0) (**Grade 1A**), or as aspirin, at a dose of 75 to 325 mg/d (**Grade 1B**). For these patients at

intermediate risk of ischemic stroke, the guideline developers suggest a VKA rather than aspirin (**Grade 2A**). This set of patients with AF is defined by having one of the following risk factors: (1) age > 75 years, (2) history of hypertension, (3) diabetes mellitus, or (4) moderately or severely impaired left ventricular systolic function and/or heart failure.

4. In patients with AF, including those with paroxysmal AF, aged \leq 75 years and with none of the other risk factors listed above, the guideline developers recommend long-term aspirin therapy at a dose of 75 to 325 mg/d (**Grade 1B**) because of their low risk of ischemic stroke.

Underlying values and preferences: Anticoagulation with oral VKAs, such as warfarin, has far greater efficacy than aspirin in preventing stroke, and particularly in preventing severe ischemic stroke, in AF. The guideline developers recommend the option of aspirin therapy for lower risk groups in recommendations 3 and 4, above, estimating the absolute expected benefit of anticoagulant therapy may not be worth the increased hemorrhagic risk and burden of anticoagulation. Individual lower-risk patients may rationally choose anticoagulation over aspirin therapy to gain greater protection against ischemic stroke if they value protection against stroke much more highly than reducing risk of hemorrhage and the burden of managing anticoagulation. Our recommendations assume that the patient is not at high risk for bleeding and that good control of anticoagulation will occur.

Remarks: These recommendations apply to patients with persistent or paroxysmal AF and not to patients with a single brief episode of AF due to a reversible cause, such as an acute pulmonary infection. The optimal dose of aspirin for patients with AF is unclear. The largest effect of aspirin was seen in the first Stroke Prevention in AF (SPAF I) trial, which used aspirin at 325 mg/d. However, generalizing from trials of aspirin for all antithrombotic indications and from physiologic studies, the guideline developers feel the best balance of efficacy and safety is achieved at low doses of aspirin, i.e., 75 to 100 mg/d (see the "Antiplatelet Drugs" chapter of the original guideline document [listed in "Availability of Companion Documents" field.]

Atrial Flutter

For patients with atrial flutter, the guideline developers recommend that antithrombotic therapy decisions follow the same risk-based recommendations as for AF (**Grade 1C**).

Valvular Heart Disease and AF

1. For patients with AF and mitral stenosis, the guideline developers recommend long-term anticoagulation with an oral VKA, such as warfarin (target INR 2.5; range, 2.0 to 3.0) (**Grade 1B**).
2. For patients with AF and prosthetic heart valves, the guideline developers recommend long-term anticoagulation with an oral VKA, such as warfarin, at an intensity appropriate for the specific type of prosthesis (**Grade 1B**). See the "Valvular and Structural Heart Disease" chapter in the original guideline document or the NGC summary [Valvular and Structural Heart Disease](#).

AF Following Cardiac Surgery

For patients with AF occurring shortly after open-heart surgery and lasting ≥ 48 hours, the guideline developers suggest anticoagulation with an oral VKA, such as warfarin, if bleeding risks are acceptable (**Grade 2C**). The target INR is 2.5 (range, 2.0 to 3.0). The guideline developers suggest continuing anticoagulation for 4 weeks following reversion to and maintenance of normal sinus rhythm, particularly if patients have risk factors for thromboembolism (**Grade 2C**).

Anticoagulation for Elective Cardioversion of AF

1. For patients with AF of ≥ 48 hours or of unknown duration for whom pharmacologic or electrical cardioversion is planned, the guideline developers recommend anticoagulation with an oral VKA, such as warfarin, at a target INR of 2.5 (range, 2.0 to 3.0) for 3 weeks before elective cardioversion and for at least 4 weeks after sinus rhythm has been maintained (**Grade 1C**).

Remark: This recommendation applies to all patients with AF, including those whose risk factor status would otherwise indicate a low risk for stroke. Patients with risk factors for thromboembolism should continue anticoagulation beyond 4 weeks unless there is convincing evidence that sinus rhythm is maintained. For patients with recurrent episodes of AF, recommendations 1, 2, 3, and 4 under the "Atrial Fibrillation" section above, apply.

2. For patients with AF of ≥ 48 hours or of unknown duration who are undergoing pharmacologic or electrical cardioversion, the guideline developers recommend either immediate anticoagulation with intravenous (IV) unfractionated heparin (UFH) (target partial thromboplastin Time (PTT), 60 s; range, 50 to 70 s), or low-molecular-weight heparin (LMWH) (at full deep vein thrombosis (DVT) treatment doses), or at least 5 days of warfarin (target INR of 2.5; range, 2.0 to 3.0) at the time of cardioversion and performance of a screening multiplane transesophageal echocardiography (TEE). If no thrombus is seen, cardioversion is successful, and sinus rhythm is maintained, the guideline developers recommend anticoagulation (target INR, 2.5; range, 2.0 to 3.0) for at least 4 weeks. If a thrombus is seen on TEE, then cardioversion should be postponed and anticoagulation should be continued indefinitely. The guideline developers recommend obtaining a repeat TEE before attempting later cardioversion (**all Grade 1B** addressing the equivalence of TEE-guided vs. non-TEE-guided cardioversion; see recommendation 1 above).

Remark: The utility of the conventional and TEE-guided approaches is likely comparable. This recommendation applies to all patients with AF, including those whose risk factor status would otherwise indicate a low risk for stroke. Patients with risk factors for thromboembolism should continue anticoagulation beyond 4 weeks unless there is convincing evidence that sinus rhythm is maintained. For patients with recurrent episodes of AF, recommendations 1, 2, 3, and 4 under the "Atrial Fibrillation" section above, apply.

3. For patients with AF of known duration < 48 hours, the guideline developers suggest that cardioversion be performed without prolonged anticoagulation (**Grade 2C**). However, in patients without contraindications to

anticoagulation, the guideline developers suggest beginning IV heparin (target PTT, 60 s; range, 50 to 70 s) or LMWH (at full DVT treatment doses) at presentation (**Grade 2C**).

Remark: For patients with risk factors for stroke, it is particularly important to be confident that the duration of AF is < 48 hours. In such patients with risk factors, a TEE-guided approach (see recommendation 2 above) is a reasonable alternative strategy. Postcardioversion anticoagulation is based on whether the patient has experienced more than one episode of AF and on his or her risk factor status. For patients with recurrent episodes of AF, recommendations 1, 2, 3, and 4 under the "Atrial Fibrillation" section above, apply.

4. For emergency cardioversion in the hemodynamically unstable patient, the guideline developers suggest that IV UFH (target PTT of 60 s with a target range of 50 to 70 s) or LMWH (at full DVT treatment doses) be started as soon as possible, followed by at least 4 weeks of anticoagulation with an oral VKA, such as warfarin (target INR of 2.5; range, 2.0 to 3.0) if cardioversion is successful and sinus rhythm is maintained (**Grade 2C**).

Remark: Long-term continuation of anticoagulation is based on whether the patient has experienced more than one episode of AF and on his or her risk factor status. For patients experiencing more than one episode of AF, recommendations 1, 2, 3, and 4 under the "Atrial Fibrillation" section above, apply.

5. For cardioversion of patients with atrial flutter, the guideline developers suggest use of anticoagulants in the same way as for cardioversion of patients with AF (**Grade 2C**).

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	Evidence from RCTs with important limitations (inconsistent results,	Recommendation can apply to most patients in most circumstances; higher quality research may well have an

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
	effects, or <i>vice versa</i>	methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	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
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

Effective use of antithrombotic/anticoagulant therapy to treat and prevent atrial fibrillation

POTENTIAL HARMS

- Intracranial hemorrhage (ICH) is the only hemorrhagic complication that regularly produces deficits as great as or greater than the ischemic strokes antithrombotic therapy is designed to prevent.
- Systemic embolism is the most serious complication of cardioversion and may follow external or internal direct current (DC), pharmacologic, and spontaneous cardioversion of atrial fibrillation (AF).

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

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Singer DE, Albers GW, Dalen JE, Fang MC, Go AS, Halperin JL, Lip GY, Manning WJ. Antithrombotic therapy in atrial fibrillation: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):546S-92S. [281 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: Daniel E. Singer, MD; Gregory W. Albers, MD; James E. Dalen, MD, MPH, FCCP; Margaret C. Fang, MD, MPH; Alan S. Go, MD; Jonathan L. Halperin, MD; Gregory Y. H. Lip, MD; Warren J. Manning, 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 Amarenco, 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, MBCh; 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. Singer discloses that he has received grant monies from the US Public Health Service (research grant No. AB15478), the National Institute on Aging, the National Institutes of Health, and the Eliot B. and Edith C. Shoolman Fund of the

Massachusetts General Hospital. He has served as a consultant to Medtronic, Boehringer Ingelheim, Bayer HealthCare, Johnson & Johnson, Sanofi-Aventis, and Daiichi Sankyo Inc.

Dr. Albers discloses that he has received grant monies from the National Institutes of Health, Astra, Genentech, Bristol-Myers Squibb, Sanofi, Boehringer Ingelheim, NMT Medical, and Aventis. He is also on the speakers bureau for Boehringer Ingelheim, and advisory committees for Astra, Aventis, Boehringer Ingelheim, NMT Medical, Bristol-Myers Squibb, and Sanofi.

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

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

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

Dr. Halperin discloses that he has received consulting fees from Astellas Pharma, Bayer AG Healthcare, Boehringer Ingelheim, Daiichi Sankyo Pharma, GlaxoSmithKline, Johnson & Johnson, and Sanofi-Aventis.

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

Professor Lip discloses that he has received grant monies from the British Heart Foundation, Sanofi, and AstraZeneca. He is also on the speaker bureaus for AstraZeneca and Bayer, and has served on an advisory committee for AstraZeneca, Daiichi Sankyo, Bayer, and Astellas.

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: Singer DE, Albers GW, Dalen JE, Go AS, Halperin JL, Manning WJ. Antithrombotic therapy in atrial fibrillation: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004 Sep;126(3 Suppl):429S-56S.

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 as of October 31, 2001. This NGC summary was updated by ECRI on December 8, 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 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 November 26, 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

