



Complete Summary

GUIDELINE TITLE

Valvular and structural heart disease. American College of Chest Physicians evidence-based clinical practice guidelines (8th edition).

BIBLIOGRAPHIC SOURCE(S)

Salem DN, O'Gara PT, Madias C, Pauker SG. Valvular and structural heart disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):593S-629S. [265 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Salem DN, Stein PD, Al-Ahmad A, Bussey HI, Horstkotte D, Miller N, Pauker SG. Antithrombotic therapy in valvular heart disease--native and prosthetic: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):457S-82S. [234 references]

** 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

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY

DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Valvular and structural heart disease

GUIDELINE CATEGORY

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 valvular and structural heart disease

TARGET POPULATION

Patients with valvular and structural heart disease requiring treatment with anticoagulant therapy

INTERVENTIONS AND PRACTICES CONSIDERED

1. Vitamin K antagonists
2. Aspirin (ASA)
3. Antiplatelet agent (APA) therapy
4. Unfractionated heparin (UFH)
5. Low-molecular-weight heparins (LMWHs)
6. Fibrinolytic therapy
7. Emergency surgery
8. Monitoring of international normalized ratio (INR)
9. Percutaneous mitral balloon valvotomy (PMBV)
10. Transesophageal echocardiography (TEE) (preprocedural for patients being considered for percutaneous mitral balloon valvotomy [PMBV])

MAJOR OUTCOMES CONSIDERED

- Mortality
- Incidence of thrombosis
- Recurrent thromboembolism
- Incidence of major and minor hemorrhage
- Time to achieve therapeutic international normalized ratio (INR)

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

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 undesirable	Consistent evidence from RCTs without important limitations or exceptionally strong	Recommendation can apply to most patients in most circumstances; further research is very unlikely to change our

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
	effects, or <i>vice versa</i>	evidence from observational studies	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 we 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.

Rheumatic Mitral Valve Disease

Rheumatic Mitral Valve Disease with Atrial Fibrillation (AF) or a History of Systemic Embolism

1. For patients with rheumatic mitral valve disease complicated singly or in combination by the presence of AF, previous systemic embolism, or left atrial thrombus, the guideline developers recommend vitamin K antagonists (VKA) therapy (target international normalized ratio [INR], 2.5; range, 2.0 to 3.0) **(Grade 1A)**.
2. For patients with rheumatic mitral valve disease with AF who suffer systemic embolism or have left atrial thrombus while receiving VKAs at a therapeutic INR, the guideline developers suggest the addition of low-dose aspirin (ASA) (50 to 100 mg/d) therapy after consideration of the additional hemorrhagic risks **(Grade 2C)**. An alternative strategy might be the adjustment of VKA dosing to achieve a higher target INR (target INR, 3.0; range, 2.5 to 3.5) **(Grade 2C)**.

Patients with Mitral Valve Disease in Sinus Rhythm

1. In patients with rheumatic mitral valve disease and normal sinus rhythm with the left atrial diameter > 55 mm, the guideline developers suggest VKA therapy (target INR, 2.5; range, 2.0 to 3.0) **(Grade 2C)**.

Underlying values and preferences: This recommendation places a relatively high value on preventing systemic embolism and its consequences, and a relatively low value on avoiding the bleeding risk and inconvenience associated with VKA therapy.

2. In patients with rheumatic mitral valve disease and normal sinus rhythm with a left atrial diameter < 55 mm, the guideline developers do not suggest antithrombotic therapy, unless a separate indication exists **(Grade 2C)**.

Patients Undergoing Percutaneous Mitral Balloon Valvotomy (PMBV)

1. For patients being considered for percutaneous mitral balloon valvotomy (PMBV), the guideline developers recommend a preprocedural transesophageal echocardiography (TEE) to exclude left atrial thrombus **(Grade 1C)**.
2. For patients being considered for PMBV with preprocedural TEE showing left atrial thrombus, the guideline developers recommend postponement of PMBV and VKA therapy (target INR 3.0; range, 2.5 to 3.5) until thrombus resolution is documented by repeat TEE **(Grade 1C)**. If left atrial thrombus does not resolve with VKA therapy, the guideline developers recommend that PMBV not be performed **(Grade 1C)**.

Mitral Valve Prolapse

1. In patients with mitral valve prolapse (MVP) who have had systemic embolism, unexplained transient ischemic attacks (TIAs) or ischemic stroke, and do not have AF, the guideline developers recommend against any antithrombotic therapy **(Grade 1C)**.
2. In patients with MVP who have documented but unexplained TIAs or ischemic stroke, the guideline developers recommend ASA (50 to 100 mg/d) **(Grade 1B)**.
3. In patients with MVP who have AF, documented systemic embolism or recurrent TIAs despite ASA therapy, the guideline developers suggest long-term VKA therapy (target INR, 2.5; range 2.0 to 3.0) **(Grade 2C)**.

Mitral Annular Calcification

1. In patients with mitral annular calcification (MAC) complicated by systemic embolism, ischemic stroke, or TIA, who do not have AF, the guideline developers recommend ASA (50 to 100 mg/d) **(Grade 1B)**. For recurrent events despite ASA therapy, the guideline developers suggest treatment with VKA therapy be considered (target INR, 2.5; range, 2.0 to 3.0) **(Grade 2C)**. In patients with mitral annular calcification (MAC) who have a single embolus documented to be calcific, the data are not sufficient to allow recommendation for or against antithrombotic therapy.
2. In patients with MAC and AF, the guideline developers recommend long-term VKA therapy (target INR, 2.5; range, 2.0 to 3.0) **(Grade 1C)**.

Aortic Valve and Aortic Arch Disorders

Calcific Aortic Valve Disease

1. In patients with isolated calcific aortic valve disease who have not had ischemic stroke or TIA, the guideline developers suggest against antithrombotic therapy **(Grade 2C)**.
2. In patients with isolated calcific aortic valve disease who have experienced ischemic stroke or TIA not attributable to another source, the guideline developers suggest aspirin (50 to 100 mg/d) **(Grade 2C)**.

Atherosclerotic Plaque of the Aortic Arch

In patients with ischemic stroke associated with aortic atherosclerotic lesions, the guideline developers recommend low-dose ASA (50 to 100 mg/d) over no therapy (**Grade 1C**). For patients with ischemic stroke associated with mobile aortic arch thrombi, the guideline developers suggest therapy with either VKAs (target INR, 2.5; range, 2.0 to 3.0) or low-dose ASA (50 to 100 mg/d) (**Grade 2C**).

Patent Foramen Ovale (PFO) and Atrial Septal Aneurysm

1. In patients with ischemic stroke and a PFO, the guideline developers recommend antiplatelet agent (APA) therapy (**Grade 1A**), and suggest APA therapy over VKA therapy (**Grade 2A**).
2. In patients with cryptogenic ischemic stroke and PFO, with evidence of deep vein thrombosis (DVT) or another indication for VKA therapy, such as AF or an underlying hypercoagulable state, the guideline developers recommend VKA therapy (target INR, 2.5; range, 2.0 to 3.0) (**Grade 1C**).

Prosthetic Heart Valves—Mechanical Prosthetic Heart Valves

1. In patients with mechanical heart valves, the guideline developers recommend VKA therapy (**Grade 1A**). In patients immediately following mechanical valve replacement, and as dictated by clinical concerns regarding postoperative bleeding, the guideline developers suggest administration of intravenous (IV) unfractionated heparin (UFH) or subcutaneous (SC) low-molecular weight heparin (LMWH) until the INR is < 2.0 for 2 consecutive days (**Grade 2C**).
2. In patients with a bileaflet mechanical valve or a Medtronic Hall tilting-disk valve in the aortic position who are in sinus rhythm and without left atrial enlargement, the guideline developers recommend long-term VKA therapy (target INR, 2.5; range, 2.0 to 3.0) (**Grade 1B**).
3. In patients with a tilting-disk or bileaflet mechanical valve in the mitral position, the guideline developers recommend VKA therapy (target INR, 3.0; range, 2.5 to 3.5) (**Grade 1B**).
4. In patients with a caged ball or caged disk valve, the guideline developers recommend long-term VKA therapy (target INR, 3.0; range, 2.5 to 3.5) (**Grade 1B**).
5. In patients with mechanical heart valves in either or both the aortic or mitral positions, and additional risk factors for thromboembolism, such as AF, anterior-apical ST-segment elevation myocardial infarction, left atrial enlargement, hypercoagulable state, or low ejection fraction, the guideline developers recommend VKA therapy (target INR, 3.0; range, 2.5 to 3.5) (**Grade 1B**).
6. In patients with mechanical heart valves who have additional risk factors for thromboembolism, such as AF, hypercoagulable state, or low ejection fraction, or who have a history of atherosclerotic vascular disease, the guideline developers recommend the addition of low-dose ASA (50 to 100 mg/d) to long-term VKA therapy (**Grade 1B**). The guideline developers suggest aspirin not be added to VKA therapy in patients with mechanical heart valves who are at particularly high risk of bleeding; such as in patients with history of gastrointestinal (GI) bleed or in patients > 80 years of age (**Grade 2C**).
7. In patients with mechanical prosthetic heart valves who have systemic embolism despite a therapeutic INR, the guideline developers suggest the

addition of ASA (50 to 100 mg/d) if not previously provided and/or upward titration of VKA therapy to achieve a higher target INR. For a previous target INR of 2.5, the guideline developers suggest the VKA dose be increased to achieve a target INR of 3.0 (range, 2.5 to 3.5). For a previous target INR of 3.0, the guideline developers suggest the VKA dose be increased to achieve a target INR of 3.5 (range, 3.0 to 4.0) **(Grade 2C)**.

Prosthetic Heart Valves—Bioprosthetic Valves

1. In patients with a bioprosthetic valve in the mitral position, the guideline developers recommend VKA therapy (target INR, 2.5; range, 2.0 to 3.0) for the first 3 months after valve insertion **(Grade 1B)**. In the early postoperative period, in the absence of concerns for significant bleeding, the guideline developers suggest administration of IV UFH or SC LMWH until the INR is at therapeutic levels for 2 consecutive days **(Grade 2C)**. After the first 3 months, in patients who are in sinus rhythm and have no other indication for VKA therapy, the guideline developers recommend ASA (50 to 100 mg/d) **(Grade 1B)**.
2. In patients with aortic bioprosthetic valves, who are in sinus rhythm and have no other indication for VKA therapy, the guideline developers recommend aspirin (50 to 100 mg/d) **(Grade 1B)**.
3. In patients with bioprosthetic valves who have a history of systemic embolism, the guideline developers recommend VKA therapy (target INR 2.5; range, 2.0 to 3.0) for at least 3 months after valve insertion, followed by clinical reassessment **(Grade 1C)**.
4. In patients with bioprosthetic valves who have evidence of a left atrial thrombus at surgery, the guideline developers recommend VKA therapy (target INR, 2.5; range, 2.0 to 3.0) until documented thrombus resolution **(Grade 1C)**.
5. In patients with bioprosthetic valves who have additional risk factors for thromboembolism, including AF, hypercoagulable state, or low ejection fraction, the guideline developers recommend VKA therapy (target INR, 2.5; range, 2.0 to 3.0) **(Grade 1C)**. The guideline developers suggest the addition of low-dose aspirin (50 to 100 mg/d) be considered, particularly in patients with history of atherosclerotic vascular disease **(Grade 2C)**. The guideline developers suggest ASA not be added to long-term VKA therapy patients with bioprosthetic heart valves who are at particularly high risk of bleeding, such as in patients with history of GI bleed or in patients > 80 years of age **(Grade 2C)**.

Prosthetic Heart Valves—Valve Thrombosis

1. For patients with right-sided prosthetic valve thrombosis (PVT) with large thrombus size or New York Heart Association (NYHA) functional class III to IV, the guideline developers recommend administration of fibrinolytic therapy **(Grade 1C)**.
2. For patients with left-sided PVT, NYHA functional class I to II, and small thrombus area (< 0.8 cm²), the guideline developers suggest administration of fibrinolytic therapy. Alternatively, administration of IV UFH accompanied by serial Doppler echocardiography to document thrombus resolution or improvement can be considered for very small nonobstructive thrombus **(Grade 2C)**.

3. For patients with left-sided PVT, NYHA functional class III to IV, and small thrombus area ($< 0.8 \text{ cm}^2$), the guideline developers suggest fibrinolytic therapy (**Grade 2C**).
4. For patients with left-sided PVT and large thrombus area ($\geq 0.8 \text{ cm}^2$), the guideline developers suggest emergency surgery be considered. If surgery is not available or considered high-risk, the guideline developers suggest fibrinolytic therapy (**Grade 2C**).
5. For patients who have had successful resolution of PVT, the guideline developers suggest initiation of IV UFH and VKA therapy. The guideline developers suggest IV UFH be continued until a therapeutic INR is achieved. For a mechanical valve in the aortic position, the guideline developers suggest maintaining a higher INR (target, 3.5; range, 3.0 to 4.0) plus ASA (50 to 100 mg/d). For a mechanical valve in the mitral position, the guideline developers suggest maintaining a higher INR (target 4.0; range 3.5 to 4.5) plus ASA (50 to 100 mg/d) (**Grade 2C**).

Infective Endocarditis and Nonbacterial Thrombotic Endocarditis

Infective Endocarditis

1. In patients with infective endocarditis (IE), the guideline developers recommend against routine antithrombotic therapy, unless a separate indication exists (**Grade 1B**).
2. In the patient treated with VKA therapy who has IE, the guideline developers suggest VKA be discontinued at the time of initial presentation and UFH substituted, until it is clear that invasive procedures will not be required and the patient has stabilized without signs of central nervous system (CNS) involvement. When the patient is deemed stable without contraindications or neurologic complications, the guideline developers suggest reinstitution of long-term VKA therapy (**Grade 2C**).

Nonbacterial Thrombotic Endocarditis

1. In patients with nonbacterial thrombotic endocarditis (NBTE) and systemic or pulmonary emboli, the guideline developers recommend treatment with full-dose IV UFH or SC LMWH (**Grade 1C**).
2. In patients with disseminated cancer or debilitating disease with aseptic vegetations, the guideline developers suggest administration of full-dose IV UFH or SC LMWH (**Grade 2C**).

Definitions:

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

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Grade 1A	outweigh undesirable effects, or <i>vice versa</i>	limitations or exceptionally strong evidence from observational studies	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 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	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

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
		studies	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 valvular and structural heart disease

POTENTIAL HARMS

Adverse effects associated with anticoagulant therapy includes the potential for hemorrhagic complications

CONTRAINDICATIONS

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Left atrial thrombus is a contraindication to percutaneous mitral balloon valvotomy (PMBV), due to the risk of its dislodgement during catheter manipulation.

QUALIFYING STATEMENTS

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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
Staying Healthy

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Salem DN, O'Gara PT, Madias C, Pauker SG. Valvular and structural heart disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):593S-629S. [265 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

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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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: Salem DN, Stein PD, Al-Ahmad A, Bussey HI, Horstkotte D, Miller N, Pauker SG. Antithrombotic therapy in valvular heart disease--native and prosthetic: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):457S-82S. [234 references]

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

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