Complete Summary

GUIDELINE TITLE

Antithrombotic therapy in atrial fibrillation: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy.

BIBLIOGRAPHIC SOURCE(S)

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. [199 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline is updates a previous version: Albers GW, Dalen JE, Laupacis A, Manning WJ, Petersen P, Singer DE. Antithrombotic therapy in atrial fibrillation. Chest 2001 Jan;119(1 Suppl):194S-206S.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

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

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

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **
SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis
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QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Ischemic stroke associated with nonvalvular atrial fibrillation

GUIDELINE CATEGORY

Prevention

CLINICAL SPECIALTY

Cardiology
Emergency Medicine
Family Practice
Internal Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To present evidence-based recommendations for antithrombotic therapy in patients with nonvalvular atrial fibrillation (AF) for the purpose of preventing strokes

TARGET POPULATION

Patients with atrial fibrillation

These guidelines are *not* intended for use in the following patients:

- Patients with atrial fibrillation associated with rheumatic mitral valve disease
- Patients with atrial fibrillation associated with prosthetic heart valves

Note: For information regarding rheumatic mitral valve disease and prosthetic heart valves, see the National Guideline Clearinghouse Guideline summary Antithrombotic Therapy in Valvular Heart Disease - Native and Prosthetic.

INTERVENTIONS AND PRACTICES CONSIDERED

Prevention of Strokes

1. Adjusted dose warfarin therapy
2. Aspirin therapy
3. Intravenous (IV) unfractionated heparin or low-molecular-weight heparin

Note: Aspirin plus low-fixed-dose warfarin therapy is considered but not recommended.

MAJOR OUTCOMES CONSIDERED

- Effectiveness and safety of antithrombotic therapy in preventing strokes in patients with atrial fibrillation, as evidenced by rates of ischemic stroke, vascular death, and major bleeds
- Relative risk reduction for strokes

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. Prior to searching for the evidence, methodological experts and librarians reviewed each question to ensure that the librarians could derive a comprehensive search strategy.

In specifying eligibility criteria, authors not only identified patients, interventions, and outcomes, but also methodological criteria. For most therapeutic studies, authors restricted eligibility to randomized controlled trials (RCTs).

For many questions, RCTs did not provide sufficient data, and article authors also included observational studies. This was also true when randomized trials were not the most appropriate design to use for addressing the research question. In particular, randomized trials are not necessarily the best design to understand risk groups (e.g., the baseline or expected risk of a given event for certain subpopulations). Because there are no interventions examined in questions about prognosis, one replaces interventions by the exposure, which is time.

Identifying the Evidence

To identify the relevant evidence, a team of librarians at the University at Buffalo conducted comprehensive literature searches. For each question the authors

provided, the librarians developed sensitive (but not specific) search strategies, including all languages, and conducted separate searches for systematic reviews, RCTs, and, if applicable, observational studies. The librarians searched the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effectiveness and Cochrane Register of Controlled Trial, the ACP Journal Club, MEDLINE, and Embase for studies published between 1966 and June 2002 in any language. To filter MEDLINE and Embase search results for RCT evidence, the librarians used the search strategy developed by the Cochrane Collaboration (full strategy available in Appendix online at: http://www.chestjournal.org/content/vol126/3_suppl_1).

For observational studies, they restricted their searches to human studies. Searches were not further restricted in terms of methodology. While increasing the probability of identifying all published studies, this sensitive approach resulted in large number of citations for many of the defined clinical questions. Therefore, trained research assistants screened the citation list developed from the search and removed any apparently irrelevant citations. These irrelevant citations included press news, editorials, narrative reviews, single case reports, animal studies (any nonhuman studies), and letters to the editor. Authors included data from abstracts of recent meetings if reporting was transparent and all necessary data for the formulation of a recommendation were available. The guideline developers did not explicitly use Internet sources to search for research data.

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, C+, or C). See "Rating Scheme for the Strength of the Recommendations."

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 searching 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, wherever possible, the evidence base of the recommendations. Pooling offers the advantage of obtaining more precise estimates of treatment effects and allows for a 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 benefit and downsides (i.e., risk, burden, and cost).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The strength of any recommendation depends on the following two factors: the trade-off between the benefits and the risks, burdens, and costs; and the strength of the methodology that leads to the treatment effect. The guideline developers grade the trade-off between benefits and risks in the two categories: 1, in which the trade-off is clear enough that most patients, despite differences in values, would make the same choice; and 2, in which the trade-off is less clear, and individual patients´ values will likely lead to different choices.

When randomized trials provide precise estimates suggesting large treatment effects, and the risks and costs of therapy are small, treatment for average patients with compatible values and preferences can be confidently recommended.

If the balance between benefits and risks is in doubt, methodologically rigorous studies providing **Grade A** evidence and recommendations may still be weak (**Grade 2**). Uncertainty may come from less precise estimates of benefit, harm, or costs, or from small effect sizes.

There is an independent impact of validity and consistency, and the balance of positive and negative impacts of treatment on the strength of recommendations. In situations in which there is doubt about the value of the trade-off, any recommendation will be weaker, moving from **Grade 1** to **Grade 2**.

Grade 1 recommendations can only be made when there is a relatively clear picture of both the benefits and the risks, burdens, and costs, and when the balance between the two clearly favors recommending or not recommending the intervention for the typical patient with compatible values and preferences. A number of factors can reduce the strength of a recommendation, moving it from **Grade 1** to **Grade 2**. Uncertainty about a recommendation to treat may be introduced if the following conditions apply: (1) the target event that is trying to be prevented is less important (confident recommendations are more likely to be made to prevent death or stroke than asymptomatic deep vein thrombosis); (2) the magnitude of risk reduction in the overall group is small; (3) the probability of the target event is low in a particular subgroup of patients; (4) the estimate of the treatment effect is imprecise, as reflected in a wide confidence interval (CI) around the effect; (5) there is substantial potential harm associated with therapy; or (6) there is an expectation for a wide divergence in values even among

average or typical patients. Higher costs would also lead to weaker recommendations to treat.

The more balanced the trade-off between benefits and risks, the greater the influence of individual patient values in decision making. Virtually all patients, if they understand the benefits and risks, will take aspirin after experiencing a myocardial infarction (MI) or will comply with prophylaxis to reduce the risk of thromboembolism after undergoing hip replacement. Thus, one way of thinking about a **Grade 1** recommendation is that variability in patient values is unlikely to influence treatment choice in average or typical patients.

When the trade-off between benefits and risks is less clear, individual patient values may influence treatment decisions even among patients with average or typical preferences.

Grade 2 recommendations are those in which variation in patient values or individual physician values will often mandate different treatment choices, even among average or typical patients. An alternative, but similar, interpretation is that a **Grade 2** recommendation suggests that clinicians conduct detailed conversations with patients to ensure that their ultimate recommendation is consistent with the patient's values.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grade of Recommendation	Clarity of Risk/Benefit	Methodological Strength of Supporting Evidence	Implications
1A	Clear	Randomized controlled trials (RCTs) without important limitations	Strong recommendation; can apply to most patients in most circumstances without reservation
1C+	Clear	No RCTs, but strong RCT results can be unequivocally extrapolated, or overwhelming evidence from observational studies	Strong recommendation; can apply to most patients in most circumstances
1B	Clear	RCTs with important limitations (inconsistent	Strong recommendation; likely to apply to most patients

Grade of Recommendation	Clarity of Risk/Benefit	Methodological Strength of Supporting Evidence	Implications
		results, methodological flaws*)	
1C	Clear	Observational studies	Intermediate-strength recommendation; may change when stronger evidence is available
2A	Unclear	RCTs without important limitations	Intermediate-strength recommendation; best action may differ depending on circumstances or patients' or societal values
2C+	Unclear	No RCTs, but strong RCT results can be unequivocally extrapolated, or overwhelming evidence from observational studies	Weak recommendation; best action may differ depending on circumstances or patients' or societal values
2B	Unclear	RCTs with important limitations (inconsistent results, methodological flaws*)	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances
2C	Unclear	Observational studies	Very weak recommendation; other alternatives may be equally reasonable

**These situations include RCTs with both lack of blinding and subjective outcomes, where the risk of bias in measurement of outcomes is high, or RCTs with large loss to follow-up.*

COST ANALYSIS

While conference participants agreed that recommendations should reflect economic considerations, incorporating costs is fraught with difficult challenges. For most recommendations, formal economic analyses are unavailable. Even when analyses are available, they may be methodologically weak or biased. Furthermore, costs differ radically across jurisdictions, and even sometimes across hospitals within jurisdictions.

Because of these challenges, the guideline developers consider economic factors only when the costs of one therapeutic option over another are substantially different within major jurisdictions in which clinicians make use of these recommendations. As a result, in jurisdictions in which resource constraints are severe, alternative allocations may serve the health of the public far better than some of the interventions that are designated as **Grade 1A**. This will likely be true for all less industrialized countries and, with the increasing promotion of expensive drugs with marginal benefits, may be increasingly true for wealthier nations. Furthermore, recommendations change (either in direction or with respect to grade) only when the guideline developers believe that costs are high in relation to benefits. Instances in which costs have influenced recommendations are labeled in the "values and preferences" statements associated with the recommendation.

AF Following Cardiac Surgery

Patients who acquire AF following coronary artery bypass graft (CABG) surgery often demonstrate hemodynamic instability that requires inotropic support, intra-aortic balloon counterpulsation, or reoperation for bleeding. The associated risk of thromboembolism, particularly ischemic stroke, occurs at a rate of 1 to 6%, and carries a high mortality rate (13 to 41%). The risk of thromboembolism increases to almost 9% among CABG patients $\geq$75 years of age. The economic impact of stroke after coronary revascularization is estimated to exceed $2 to $4 billion annually worldwide, related to prolonged intensive care and total hospitalization days as well as long-term disability costs.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline authors formulated draft recommendations prior to the conference that served as the foundation for authors to work together and critique the recommendations. Drafts of all articles including draft recommendations were available for review during the conference. A representative of each article presented potentially controversial issues in their recommendations at plenary

meetings. Article authors met to integrate feedback, to consider related recommendations in other articles, 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 had provided critical feedback. Finally, the editors of this supplement harmonized the articles and resolved remaining disagreements through facilitated discussion.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The rating scheme is defined at the end of the "Major Recommendations" field.

Long-term Antithrombotic Therapy for Chronic Atrial Fibrillation (AF) or Atrial Flutter, Anticoagulants and Antiplatelet Agents

Atrial Fibrillation

1. In patients with persistent (also known as "sustained," and including patients categorized as "permanent" in certain classification schemes) or paroxysmal (intermittent) AF (PAF) at high risk of stroke (i.e., having any of the following features: prior ischemic stroke, transient ischemic attack (TIA), or systemic embolism, age >75 years, moderately or severely impaired left ventricular systolic function and/or congestive heart failure, history of hypertension, or diabetes mellitus), the guideline developers recommend anticoagulation with an oral vitamin K antagonist (VKA), such as warfarin (target international normalized ratio [INR], 2.5; range 2.0 to 3.0) (**Grade 1A**).
2. In patients with persistent AF or PAF, age 65 to 75 years, in the absence of other risk factors, the guideline developers recommend antithrombotic therapy (**Grade 1A**). Either an oral VKA, such as warfarin (target INR, 2.5; range 2.0 to 3.0), or aspirin, 325 mg/d, are acceptable alternatives in this group of patients who are at intermediate risk of stroke.
3. In patients with persistent AF or PAF <65 years old and with no other risk factors, the guideline developers recommend aspirin, 325 mg/d (**Grade 1B**).

   Underlying values and preferences: Anticoagulation with an oral VKA, 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 (see 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 burden of managing anticoagulation.

Atrial Flutter

1. For patients with atrial flutter, the guideline developers suggest that antithrombotic therapy decisions follow the same risk-based recommendations as for AF (**Grade 2C**).

Valvular Heart Disease and Atrial Flutter

1. For patients with AF and mitral stenosis, the guideline developers recommend anticoagulation with an oral VKA, such as warfarin (target INR, 2.5; range 2.0 to 3.0) (**Grade 1C+**).
2. For patients with AF and prosthetic heart valves, the guideline developers recommend anticoagulation with an oral VKA, such as warfarin (**Grade 1C+**).

   Remark: The target intensity of anticoagulation may be INR 3.0 (range, 2.5 to 3.5), i.e., higher than the usual target INR of 2.5 (range 2.0 to 3.0), and it may be appropriate to add aspirin, depending on type of prosthesis, its position, and other risk factors (See the National Guideline Clearinghouse summary of the ACCP guideline Antithrombotic Therapy in Valvular Heart Disease - Native and Prosthetic).

AF Following Cardiac Surgery

1. For 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 several weeks following reversion to normal sinus rhythm (NSR), particularly if patients have risk factors for thromboembolism (**Grade 2C**).

Anticoagulation for Elective Cardioversion of AF or Atrial Flutter Patients

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 (target INR, 2.5; range, 2.0 to 3.0), for 3 weeks before elective cardioversion and for at least 4 weeks after successful cardioversion (**Grade 1C+**).

   Remark: This recommendation applies regardless of a patient´s risk factor status. Continuation of anticoagulation beyond 4 weeks is based on whether the patient has experienced more than one episode of AF and on their risk factor status. Patients experiencing more than one episode of AF should be considered as having PAF (See recommendations above under "Atrial Fibrillation").

2. For patients with AF of ≥48 hours or of unknown duration undergoing pharmacologic or electrical cardioversion, an alternative to the strategy outlined above is anticoagulation (immediate unfractionated intravenous (IV) heparin with target partial thromboplastin time [PTT] of 60 s [range, 50 to 70 s], or at least 5 days of warfarin with target INR of 2.5 [range, 2.0 to 3.0] at the time of cardioversion) and a screening multiplane transesophageal echocardiography (TEE) be performed. If no thrombus is seen and cardioversion is successful, 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**).

Remark: The utility of the conventional and TEE-guided approaches is likely comparable. These recommendations apply regardless of a patient´s risk factor status. Continuation of anticoagulation beyond 4 weeks is based on whether the patient has experienced more than one episode of AF and on their risk factor status. Patients experiencing more than one episode of AF should be considered as having PAF (see recommendations above under "Atrial Fibrillation").

3. For patients with AF of known duration <48 hours, the guideline developers suggest that cardioversion be performed without 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 low-molecular-weight heparin (LMWH) (at full deep vein thrombosis [DVT] 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 under "Anticoagulation for elective cardioversion of AF or atrial flutter patients") is a reasonable alternative strategy. Postcardioversion anticoagulation is based on whether the patient has experienced more than one episode of AF and on their risk factor status. Patients experiencing more than one episode of AF should be considered as having PAF (see recommendations above under "Atrial Fibrillation").

4. For emergency cardioversion where a TEE-guided approach is not possible, the guideline developers suggest IV unfractionated heparin (target PTT, 60 s; range, 50 to 70 s) be started as soon as possible, followed by 4 weeks of anticoagulation with an oral VKA, such as warfarin (target INR, 2.5; range 2.0 to 3.0) if NSR persists after cardioversion (**Grade 2C**).

   Remark: Continuation of anticoagulation beyond 4 weeks is based on whether the patient has experienced more than one episode of AF and on their risk factor status. Patients experiencing more than one episode of AF should be considered as having PAF (see recommendations above under "Atrial Fibrillation").

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

Grade of Recommendation	Clarity of Risk/Benefit	Methodological Strength of Supporting Evidence	Implications

Grade of Recommendation	Clarity of Risk/Benefit	Methodological Strength of Supporting Evidence	Implications
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1B	Clear	RCTs with important limitations (inconsistent results, methodological flaws*)	Strong recommendation; likely to apply to most patients
1C	Clear	Observational studies	Intermediate-strength recommendation; may change when stronger evidence is available
2A	Unclear	RCTs without important limitations	Intermediate-strength recommendation; best action may differ depending on circumstances or patients' or societal values
2C+	Unclear	No RCTs, but strong RCT results can be unequivocally	Weak recommendation; best action may differ depending on

Grade of Recommendation	Clarity of Risk/Benefit	Methodological Strength of Supporting Evidence	Implications
		extrapolated, or overwhelming evidence from observational studies	circumstances or patients' or societal values
2B	Unclear	RCTs with important limitations (inconsistent results, methodological flaws*)	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances
2C	Unclear	Observational studies	Very weak recommendation; other alternatives may be equally reasonable

**These situations include RCTs with both lack of blinding and subjective outcomes, where the risk of bias in measurement of outcomes is high, or RCTs with large loss to follow-up.*

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 therapy to prevent ischemic strokes

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

Interpreting the Recommendations

Clinicians, third-party payers, institutional review committees, or the courts should not construe these guidelines in any way as absolute dictates. In general, anything other than a **Grade 1A** recommendation indicates that the article authors acknowledge that other interpretations of the evidence, and other clinical policies, may be reasonable and appropriate. Even **Grade 1A** recommendations will not apply to all circumstances and all patients. For instance, the guideline developers have been conservative in their considerations of cost and have seldom downgraded recommendations from **Grade 1** to **Grade 2** on the basis of expense. As a result, in jurisdictions in which resource constraints are severe, alternative allocations may serve the health of the public far better than some of the interventions that are designated as **Grade 1A**. This will likely be true for all less industrialized countries and, with the increasing promotion of expensive drugs with marginal benefits, may be increasingly true for wealthier nations.

Similarly, following **Grade 1A** recommendations will at times not serve the best interests of patients with atypical values or preferences or of those whose risks differ markedly from those of the usual patient. For instance, consider patients who find anticoagulant therapy extremely aversive, either because it interferes with their lifestyle (e.g., prevents participation in contact sports) or because of the need for monitoring. Clinicians may reasonably conclude that following some **Grade 1A** recommendations for anticoagulation therapy for either group of patients will be a mistake. The same may be true for patients with particular comorbidities (e.g., a recent gastrointestinal bleed or a balance disorder with repeated falls) or other special circumstances (e.g., very advanced age) that put them at unusual risk.

The guideline developers trust that these observations convey their acknowledgment that no recommendations or clinical practice guidelines can take into account the often compelling and unique features of individual clinical circumstances. No clinician, and no body charged with evaluating a clinician´s actions, should attempt to apply these recommendations in a rote or blanket fashion.

Limitations of Guideline Development Methods

The limitations of these guidelines include the possibility that some authors followed this methodology more closely than others, although the development process was centralized and supervised by the editors. Second, it is possible that

the guideline developers missed relevant studies despite the comprehensive searching process. Third, the guideline developers did not centralize the methodological evaluation of all studies to facilitate uniformity in the validity assessments of the research incorporated into these guidelines. Fourth, if high-quality meta-analyses were unavailable, the guideline developers did not statistically pool primary study results using meta-analysis. Finally, sparse data on patient preferences and values, resources, and other costs represent additional limitations that are inherent to most guideline development methods.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Guideline Implementation Strategies

A full review of implementation strategies for practice guidelines is provided in the companion document titled "Antithrombotic and Antithrombolytic Therapy: From Evidence to Application." The review suggests that there are few implementation strategies that are of unequivocal, consistent benefit, and that are clearly and consistently worth resource investment. The following is a summary of the recommendations (see "Major Recommendations" for a definition of the recommendation grades).

To encourage uptake of guidelines, the guideline developers recommend that appreciable resources be devoted to distribution of educational material (**Grade 2B**).

They also suggest that:

- Few resources be devoted to educational meetings (**Grade 2B**)
- Few resources be devoted to educational outreach visits (**Grade 2A**)
- Appreciable resources be devoted to computer reminders (**Grade 2A**)
- Appreciable resources be devoted to patient-mediated interventions to encourage uptake of the guidelines (**Grade 2B**)
- Few resources be devoted to audit and feedback (**Grade 2B**)

IMPLEMENTATION TOOLS

Patient Resources
Personal Digital Assistant (PDA) Downloads
Quick Reference Guides/Physician Guides
Resources
Slide Presentation
Tool Kits

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, 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. [199 references] PubMed

ADAPTATION

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

DATE RELEASED

2001 Jan (revised 2004 Sep)

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

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GUIDELINE COMMITTEE

American College of Chest Physicians Consensus Panel on Antithrombotic and Thrombolytic Therapy

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Dr. Singer has received research support from DuPont Pharma, now Bristol-Myers Squibb, and is a consultant for AstraZeneca.

Dr. Albers has received research support and honoraria as a consultant from AstraZeneca, Bristol- Myers Squibb, Boehringer Ingelheim, Genentech and Sanofi-Arganon.

Dr. Dalen is a consultant for DuPont Pharma, now Bristol-Myers Squibb, AstraZeneca, and Sanofi-Organon.

Dr. Go has nothing to declare.

Dr. Halperin has received research support from AstraZeneca and is a consultant for AstraZeneca. He is on the speaker's bureau for Bristol-Myers Squibb and Sanofi.

Dr. Manning is a consultant for AstraZeneca, Bristol-Myers Squibb, and Phillips Medical Systems.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline is updates a previous version: Albers GW, Dalen JE, Laupacis A, Manning WJ, Petersen P, Singer DE. Antithrombotic therapy in atrial fibrillation. Chest 2001 Jan;119(1 Suppl):194S-206S.

GUIDELINE AVAILABILITY

Electronic copies: Available from 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:

- The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Evidence-based guidelines. Northbrook, IL: ACCP, 2004 Sep.
- Methodology for guideline development for the Seventh American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.
- Applying the grades of recommendation for antithrombotic and thrombolytic therapy: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.
- Hemorrhagic complications of anticoagulant treatment: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.
- Antithrombotic and thrombolytic therapy: from evidence to application: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.
- Platelet-active drugs: the relationships among dose, effectiveness, and side effects: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.

Electronic copies: Available from the Chest - The Cardiopulmonary and Critical Care Journal Web site.

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

The following is also available:

- Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence-based guidelines; quick reference guide. Northbrook, IL: ACCP, 2004 Sep. Personal Digital Assistant (PDA) download available at ACCP Web site.

Additional implementation tools are also available:

- Clinical resource: antithrombotic and thrombolytic therapy. Northbrook, IL. ACCP, 2004. Ordering information: Available from the ACCP Web site.

PATIENT RESOURCES

The following is available:

- A patient's guide to antithrombotic and thrombolytic therapy. In: Clinical resource: antithrombotic and thrombolytic therapy. Northbrook (IL): American College of Chest Physicians (ACCP). 2004.

Ordering information is available from the ACCP Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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