



Complete Summary

GUIDELINE TITLE

Antithrombotic and thrombolytic therapy for ischemic stroke. American College of Chest Physicians evidence-based clinical practice guidelines (8th edition).

BIBLIOGRAPHIC SOURCE(S)

Albers GW, Amarenco P, Easton JD, Sacco RL, Teal P. Antithrombotic and thrombolytic therapy for ischemic stroke: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):630S-69S. [219 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Albers GW, Amarenco P, Easton JD, Sacco RL, Teal P. Antithrombotic and thrombolytic therapy for ischemic stroke: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):483S-512S.

** 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 **

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY

DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

- Ischemic stroke
- Cerebral venous sinus thrombosis

GUIDELINE CATEGORY

Management
Prevention
Treatment

CLINICAL SPECIALTY

Cardiology
Critical Care
Emergency Medicine
Family Practice
Internal Medicine
Neurology
Pulmonary 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 for the use of antithrombotic and thrombolytic therapy in the management and treatment of ischemic stroke
- To update evidence-based recommendations for the use of antithrombotic and thrombolytic therapy for the management of thromboembolic conditions

TARGET POPULATION

Patients with or at risk of acute ischemic stroke

INTERVENTIONS AND PRACTICES CONSIDERED

Management/Treatment

Treatment of Acute Ischemic Stroke (AIS)

1. Thrombolytic therapy
 - Intravenous (IV) recombinant tissue plasminogen activator (tPA)
2. Early aspirin therapy

Antithrombotic Therapy for Prevention of Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) in Acute Ischemic Stroke

1. Low-dose subcutaneous (SC) heparin or low molecular weight heparins (LMWHs)
2. Intermittent pneumatic compression (IPC) devices
3. Elastic stockings

Prevention of Cerebral Ischemic Events

1. Aspirin therapy
2. Aspirin in combination with extended-release dipyridamole
3. Aspirin in combination with clopidogrel

Treatment of Cerebral Venous Sinus Thrombosis

1. Unfractionated heparin (UFH) or low-molecular-weight heparin
2. Vitamin K antagonists

Monitoring

1. International normalized ratio (INR)
2. Computed tomography (CT)
3. Magnetic resonance imaging (MRI)

Note: For patients with acute ischemic stroke, streptokinase was considered but not recommended.

MAJOR OUTCOMES CONSIDERED

- Rates of mortality and disability from ischemic stroke
- Functional status
- Frequency of recurrence
- Rates of deep vein thrombosis (DVT) and pulmonary embolism (PE) secondary to ischemic stroke
- Rates of adverse events from treatment, such as intracerebral hemorrhages (ICH)

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 undesirable effects, or <i>vice versa</i>	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; further research is very unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very 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

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
			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.

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.

Intravenous (IV) Tissue Plasminogen Activator for Acute Ischemic Stroke within 3 Hours of Symptom Onset

1. For eligible patients (see inclusion and exclusion criteria listed below) the guideline developers recommend administration of IV tissue plasminogen activator (tPA) in a dose of 0.9 mg/kg (maximum of 90 mg), with 10% of the total dose given as an initial bolus and the remainder infused over 60 min, provided that treatment is initiated within 3 hours of clearly defined symptom onset (**Grade 1A**).

Underlying values and preferences: This recommendation places relatively more weight on overall prospects for long-term functional improvement despite the increased risk of symptomatic intracerebral hemorrhage in the immediate peristroke period.

2. The guideline developers recommend that patients who are eligible for tPA be treated as quickly as possible within the 3-hour time limit (**Grade 1A**).

Remark: All unnecessary delays must be avoided as the benefits of tPA therapy diminish rapidly over time.

3. For patients with extensive (more than one third of the middle cerebral artery territory) and clearly identifiable hypodensity on CT, the guideline developers suggest not using of tPA (**Grade 2B**).

IV tPA for Acute Ischemic Stroke between 3 to 6 Hours of Symptom Onset

For patients with acute ischemic stroke of > 3 hours but < 4.5 hours, the guideline developers suggest clinicians do not use IV tPA (**Grade 2A**). For patients with acute stroke onset of > 4.5 hours, the guideline developers recommend against the use of IV tPA (**Grade 1A**).

Underlying values and preferences: This recommendation assumes a relatively low value on small increases in long-term functional improvement, a relatively high value on avoiding acute intra cranial hemorrhage and death, and a relatively high degree of risk aversion.

IV Streptokinase for Acute Ischemic Stroke Between 0 hours and 6 hours of Symptom Onset

For patients with acute ischemic stroke, the guideline developers recommend against streptokinase (**Grade 1A**).

Intra-arterial Thrombolysis for Acute Ischemic Stroke

1. For patients with angiographically demonstrated middle cerebral artery occlusion and without major early infarct signs on the baseline computed tomography (CT) or magnetic resonance imaging (MRI) scan, who can be treated within 6 hours of symptom onset, the guideline developers suggest intra-arterial thrombolytic therapy with tPA for selected patients in centers with the appropriate neurologic and interventional expertise (**Grade 2C**).
2. For patients with acute basilar artery thrombosis and without major CT/MRI evidence of infarction, the guideline developers suggest either intra-arterial or intravenous (IV) thrombolysis with tPA depending on available resources and capabilities (**Grade 2C**).

Anticoagulants for Altering Outcomes Among Acute Stroke in Patients Not Eligible for Thrombolysis

For patients with acute ischemic stroke, the guideline developers recommend against full-dose anticoagulation with IV, subcutaneous (SC), or low-molecular-weight heparins or heparinoids (**Grade 1B**).

Antiplatelet Agents for Altering Outcomes in Acute Stroke Patients Not Eligible for Thrombolysis

For patients with acute ischemic stroke who are not receiving thrombolysis, the guideline developers recommend early aspirin therapy (initial dose of 150 to 325 mg) **(Grade 1A)**.

Antithrombotic Therapy for Prevention of Deep Vein Thrombosis and Pulmonary Embolism in Acute Ischemic Stroke

1. For acute stroke patients with restricted mobility, the guideline developers recommend prophylactic low-dose SC heparin or low-molecular-weight heparins **(Grade 1A)**.
2. For patients who have contraindications to anticoagulants, the guideline developers recommend intermittent pneumatic compression (IPC) devices or elastic stockings **(Grade 1B)**.

IPC for Deep Vein Thrombosis/Pulmonary Embolism Prophylaxis in Patients With Intracerebral Hematoma

In patients with an acute intracerebral hematoma (ICH), the guideline developers recommend the initial use of IPC devices **(Grade 1B)**.

Heparin for Deep Vein Thrombosis/Pulmonary Embolism Prophylaxis in Patients With ICH

In stable patients, the guideline developers suggest low-dose SC heparin as soon as the second day after the onset of the hemorrhage **(Grade 2C)**.

Underlying values and preferences: Given the uncertainty about the risk of heparin in this setting, this recommendation places a relatively high value on reducing the consequences of thromboembolism and a relatively lower value on minimizing the risk of cerebral rebleeding.

Prevention of Cerebral Ischemic Events in Patients With Noncardioembolic Transient Ischemic Attack (TIA) or Stroke: Antiplatelet Drugs vs. Placebo or vs. an Alternative Antiplatelet Drug

1. In patients who have experienced a noncardioembolic stroke or TIA (i.e., atherothrombotic, lacunar, or cryptogenic), the guideline developers recommend treatment with an antiplatelet drug **(Grade 1A)**. Aspirin, the combination of aspirin (25 mg) and extended-release dipyridamole (200 mg twice a day [bid]) and clopidogrel (75 mg once a day [qd]) are all acceptable options for initial therapy. The guideline developers recommend an aspirin dose of 50-100 mg/day over higher aspirin doses **(Grade 1B)**.
2. In patients who have experienced a noncardioembolic stroke or TIA, the guideline developers recommend using the combination of aspirin and extended-release dipyridamole (25/200 mg bid) over aspirin **(Grade 1A)** and suggest clopidogrel over aspirin **(Grade 2B)**.

Underlying values and preferences: The implementation of the recommendation to use the combination of aspirin and extended-release dipyridamole over aspirin may vary based on cost, tolerability, availability, ease of use, and absolute risk.

3. In most patients with a noncardioembolic stroke or TIA, the guideline developers recommend avoiding long-term use of the combination of aspirin and clopidogrel (**Grade 1B**). In those with a recent acute myocardial infarction, other acute coronary syndrome, or a recently placed coronary stent, the guideline developers recommend clopidogrel plus aspirin (75-100 mg) (**Grade 1A**). The optimal duration of dual antiplatelet therapy depends on the specific cardiac indication (See other articles in the Chest journal supplement [see "Availability of Companion Documents" field]).
4. For patients who are allergic to aspirin, the guideline developers recommend clopidogrel (**Grade 1A**).

Prevention of Noncardioembolic Cerebral Ischemic Events: Oral Anticoagulants

For patients with noncardioembolic stroke or TIA, the guideline developers recommend antiplatelet agents over oral anticoagulation (**Grade 1A**).

Prevention of Cerebral Ischemic Events in Patients Undergoing Carotid Endarterectomy: Antiplatelet Agents

In patients undergoing carotid endarterectomy, the guideline developers recommend aspirin (50 to 100 mg/d) prior to and following the procedure (**Grade 1A**).

Prevention of Cardioembolic Cerebral Ischemic Events

1. In patients with atrial fibrillation (AF) who have suffered a recent stroke or transient ischemic attack, the guideline developers recommend long-term oral anticoagulation (target INR, 2.5; range, 2.0 to 3.0) (**Grade 1A**).
2. For patients with cardioembolic stroke who have contraindications to anticoagulant therapy, the guideline developers recommend aspirin at a dose of 75-325 mg/day (**Grade 1B**).
3. In patients with stroke associated with aortic atherosclerotic lesions, the guideline developers recommend antiplatelet therapy over no therapy (**Grade 1A**). For patients with cryptogenic stroke associated with mobile aortic arch thrombi, the guideline developers suggest either oral anticoagulation or antiplatelet agents (**Grade 2C**).
4. In patients with cryptogenic ischemic stroke and a patent foramen ovale, the guideline developers recommend antiplatelet therapy over no therapy (**Grade 1A**) and suggest antiplatelet agents over anticoagulation (**Grade 2A**).
5. In patients with mitral valve strands or prolapse, who have a history of TIA or stroke, the guideline developers recommend antiplatelet therapy (**Grade 1A**).

Anticoagulation for Cerebral Venous Sinus Thrombosis

In patients with venous sinus thrombosis, the guideline developers recommend that clinicians use UFH (**Grade 1B**) or LMWH (**Grade 1B**) over no anticoagulant therapy during the acute phase, even in the presence of hemorrhagic infarction. In these patients, the guideline developers recommend continued use of VKA therapy for up to 12 months (target INR, 2.5; range, 2.0-3.0) (**Grade 1B**).

Definitions:

Grading Recommendation			
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Strong recommendation, high-quality evidence, Grade 1A	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; further research is very unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very 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	Evidence from RCTs with important limitations (inconsistent results,	Best action may differ depending on circumstances or patient or society values; higher-quality research

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

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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 management of patients who require antithrombotic and thrombolytic therapy for ischemic stroke

POTENTIAL HARMS

Antithrombotic therapy is associated with minor and major hemorrhagic events.

CONTRAINDICATIONS

CONTRAINDICATIONS

Aspirin is contraindicated among those with aspirin allergy or those with active gastrointestinal (GI) bleeding.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Limitations of These Guideline Development Methods

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

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy includes local educational programs and tools offered through the American College of Chest Physicians (ACCP) Board of Governors and select other locations. The Veterans Administration (VA) will also participate in a pilot project.

IMPLEMENTATION TOOLS

Resources

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

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Albers GW, Amarenco P, Easton JD, Sacco RL, Teal P. Antithrombotic and thrombolytic therapy for ischemic stroke: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):630S-69S. [219 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

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American College of Clinical Pharmacy - Medical Specialty Society
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GUIDELINE STATUS

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This guideline updates a previous version: Albers GW, Amarenco P, Easton JD, Sacco RL, Teal P. Antithrombotic and thrombolytic therapy for ischemic stroke: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004 Sep;126(3 Suppl):483S-512S.

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

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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