

Antithrombotic and Thrombolytic Therapy*

American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition)

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Since publication of the seventh American College of Chest Physicians (ACCP) supplement on antithrombotic and thrombolytic therapy, the results of clinical trials have provided important new information on the management of thromboembolic disorders, and the science of developing recommendations has advanced. In the accompanying supplement, we provide the new and updated recommendations and review several important changes that we have made in our guideline development process.

We again made a conscious effort to increase the participation of female authors and contributors from outside North America, the latter reflecting the widespread use and dissemination of these guidelines internationally. The grading system for the recommendations was adopted in 2006 by the ACCP for all its guidelines, is similar to the increasingly widely used Grades of Recommendation, Assessment, Development, and Evaluation approach, and is described in detail in one of the introductory chapters.

While most of the evidence on which recommendations are made remains low quality in fields of pediatric thrombosis, thrombosis in pregnancy, and thrombosis in valvular heart disease, rigorous studies in other fields have resulted in new and strong evidence-based recommendations for many indications.

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Abbreviation: ACCP = American College of Chest Physicians

Since the last publication of the conference guidelines in 2004, new important publications have addressed the management of thromboembolic disorders. In this eighth edition of the American College of Chest Physicians (ACCP) guidelines on anti-

thrombotic therapy, we update evidence-based recommendations for the use of antithrombotic and thrombolytic therapy for the management of thromboembolic conditions. We have added a chapter addressing the management of patients treated with anticoagulants and who require bridging therapy because of an intercurrent invasive procedure.

We continue to increase the number of contributors from outside North America and to address the issue of potential conflicts of interest by asking that participants declare honoraria or research funding obtained in the previous 2 years, or stocks held, from companies that may benefit from the recommendations. As in the previous (2004) ACCP guidelines, authors defined clinical questions including the patients, interventions, comparators, and outcomes of interest for each recommendation or set of recommendations. In collaboration with guideline authors, a team of librarians and research staff conducted

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comprehensive literature searches for evidence relevant to these specific questions or recommendations.¹ Authors reviewed citations and applied the predefined criteria to ascertain whether studies contributed to the evidence that underlies the recommendations.

Once again to ensure transparency and explicitness among questions, evidence, and recommendations, we use a numbering scheme to ensure that the number associated with the explicitly defined questions presented in the summary table of each chapter corresponds to the number of the section laying out the evidence, as well as any corresponding recommendations. This scheme allows readers to quickly identify the underlying question associated with each recommendation, and the relevant evidence.

The grading system in the eighth edition of the ACCP guidelines now reflects the system adopted for all ACCP guidelines,² and is similar to the Grades of Recommendation, Assessment, Development, and Evaluation system, which is being widely adopted by many guideline groups.³ As in the 2004 guidelines, if experts are very certain that benefits do or do not outweigh risks, burden, and costs, they will make a strong recommendation, in our formulation, Grade 1. If they are less certain of the magnitude of the benefits and risks, burden, and costs, and thus their relative impact, they make a weaker, Grade 2, recommendation.

The system also provides a rating of the quality of evidence (high quality, moderate quality, and low quality: "A," "B," and "C," respectively). The important changes in quality rating from 2004 are more explicitness in the criteria for downgrading or upgrading evidence, and designating high-quality evidence from observational studies with large effects as "A" rather than "C+." Randomized trials provide high-quality evidence unless they suffer from limitations in design and execution, imprecision, indirectness, inconsistency, or reporting bias. Observational studies provide weak evidence unless there are no obvious biases and the effects are very large and consistent.

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. Thus, we have omitted resource allocation considerations from all but a few recommendations in which these issues are particularly important, and in which informative evidence from economic analyses are available. For these recom-

mendations, we obtained guidance from health economists whose observations are included in the relevant discussions.

As in the 2004 recommendations, we endeavored to stay alert to the patient and community values and preferences underlying our recommendations. Once again, when values and preferences were particularly salient, we identified the underlying values associated with particular recommendations. For the first time, three individuals with a special interest, knowledge, and perspective in how values and preferences influence recommendations provided input into the guidelines.

Although the rigor with which trials for many indications are evaluated has improved dramatically, the evidence remains weak in fields of pediatric thrombosis, thrombosis in pregnancy, and thrombosis in valvular heart disease. This deficiency needs to be addressed.

CONFLICT OF INTEREST DISCLOSURES

Dr. Hirsh discloses that he has received partial support for writing two books, one on Fondaparinux and one on low-molecular-weight heparin.

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

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

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