

The Vexing Problem of Guidelines and Conflict of Interest: A Potential Solution

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Issues of financial and intellectual conflict of interest in clinical practice guidelines have raised increasing concern. Professional organizations have responded by more rigorous regulation of conflict of interest. Nevertheless, tension remains between the competing goals of optimizing guideline quality by using the experience and insight of experts and ensuring that financial and intellectual conflicts of interest do not influence recommendations. The executive committee of the American College of Chest Physicians' Antithrombotic Guidelines has developed a strategy comprising 3 innovative aspects to address this tension: First, place equal emphasis on intellectual and financial conflicts and provide explicit criteria for

both; second, a methodologist without important conflicts of interest should have primary responsibility for each chapter; and third, experts with important financial or intellectual conflicts of interest can collect and interpret evidence, but only panel members without important conflicts can be involved in developing the recommendation for a specific question. These strategies may help to achieve the benefits of expert input without conflicts of interest influencing recommendations.

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Clinical guidelines play an important role in directing clinical practice and informing quality improvement initiatives (1). Nearly all guidelines are now advertised as being “evidence-based” (2).

Evidence, however, is open to interpretation (3). The composition of the panel may influence guidelines, and recommendations may be vulnerable to panelists' conflicts of interest (4). The high degree of financial conflicts of interest in many guideline panels has generated concern (5–8). Although intellectual conflicts of interest have also raised concern (9) and some organizations provide guidance regarding such conflicts (10–12), most do not address this issue.

Reporting of guideline panel members' financial conflicts has become standard practice; however, critics are skeptical that reporting financial ties minimizes the effect of conflicts (4, 13–15). Consequently, some organizations have introduced additional safeguards (10), including achieving “a reasonable balance of relationships with industry” (11) and excluding individuals with conflicts from guideline panels' leadership roles (16, 17).

Some critics view these provisions as insufficient and suggest abandoning guideline development (4) or completely excluding individuals with any industry interest (14). However, these proposals have limitations. Abandoning guideline development would require clinicians to undertake their own thorough evidence reviews, which is unrealistic. Excluding academic leaders with conflicts of interest from guideline development removes individuals who are both most likely to undertake the unreimbursed efforts associated with conducting evidence reviews for guidelines and most capable of performing a quality job efficiently. Experts with conflicts of interest may also offer unique insights into clinical context and evidence. These considerations suggest that the input of such experts into practice guidelines is desirable.

THE AMERICAN COLLEGE OF CHEST PHYSICIANS' ANTITHROMBOTIC GUIDELINES

During a span of more than 20 years, the American College of Chest Physicians (ACCP) has produced 8 iterations of guidelines for use of antithrombotic agents to prevent and treat venous and arterial thrombosis. Despite the ACCP's efforts to minimize and manage financial conflicts of interest, most experts who contributed to the first 8 iterations had both financial and intellectual conflicts.

In conjunction with a committee charged with guideline oversight for the ACCP (the Health Science and Policy Committee [HSP]), the executive committee of the ninth iteration of the antithrombotic guidelines (AT9) concluded that the previous degree of reliance on experts with conflicts of interest was problematic (15). The executive committee has therefore instituted changes in the structure of the AT9 guideline panel designed to involve experts with conflicts of interest without developing recommendations affected by those conflicts.

Overview of the Executive Committee of the AT9's Strategy for Managing Conflict of Interest

For AT9, the HSP is responsible for deciding the conditions under which individuals can and cannot participate in guideline development. Nominated candidates must disclose all remunerated industry professional activities, including research support, consultancies, stock holdings, and participation in speakers' bureaus. Acceptable candidates must, for the duration of guideline development, divest themselves of direct financial interests in relevant companies and refrain from participating in activities sponsored by the marketing departments of commercial entities or serving on industry advisory boards. The HSP reviewed 133 candidates for participation in AT9 and rejected 10 persons because of unacceptable financial conflicts.

The AT9 executive committee is responsible for ensuring that conflicts of interest among individuals who pass

the HSP's screening will not affect the recommendations. The executive committee's approach reflects a consensus of the committee itself, thrombosis experts who have collaborated on previous iterations of the ACCP guidelines, and the HSP. In contrast to the HSP's review, which is limited to financial conflicts, the executive committee addresses both intellectual and financial conflicts.

In a major departure from previous iterations, methodologists free of financial or intellectual conflicts of interest (designated "chapter editors") bear primary responsibility for each chapter of the AT9. Each chapter is also assigned a content area expert who typically has both financial and intellectual conflicts (designated a "deputy editor"). These editors have input into preparing, summarizing, and interpreting the evidence. However, deputy editors—like other panelists—are excluded from the deliberations that ultimately determine the direction and strength of recommendations on which they have conflicts. Like other organizations (11), we ensure that each AT9 panel includes sufficient persons without conflicts of interest for each individual recommendation; our threshold is to include at least 3 such persons.

Details of the Strategy

Definition of Financial and Intellectual Conflict of Interest. Important conflicts of interest prohibit panelists from active participation in the final decision-making process for the recommendations on which they have conflicts. Important financial conflicts include consultancies and advisory board memberships from industry. Recommendations for which important conflicts involving industry funding exist preclude participation not only in developing recommendations related to the specific product and indications for which industry funding was received but also from developing recommendations related to other indications for that product.

We define "intellectual conflict of interest" as academic activities that create the potential for an attachment to a specific point of view that could unduly affect an individual's judgment about a specific recommendation. Such activities include receipt of a grant or participation in research or commentary directly related to that recommendation. For AT9, our operational definition of "important intellectual conflict of interest" includes authorship of original studies and peer-reviewed grant funding by such institutions as the government or nonprofit organizations that directly relate to a recommendation. For example, an author of a randomized trial comparing 2 anticoagulant regimens for acute treatment of venous thromboembolism would have a conflict for any recommendation related to acute anticoagulant therapy for venous thromboembolism. Less important intellectual conflicts, such as participation in previous guideline panels, must be acknowledged but do not preclude participation in developing recommendations.

Documentation of Conflict. Panel members must identify all recommendations for which they have conflicts of interest and declare these conflicts to the chapter editor. The chapter editor constructs a conflict-of-interest grid that will be posted in the online supplement to AT9.

Handling Conflict Within Chapter Panels. Chapter editors ensure that their panel takes full advantage of the expertise of panel members with conflicts of interest while avoiding any influence of members with conflicts on the final recommendations. The panel's review of the conflict-of-interest grid establishes the ground rules for discussion before recommendations are drafted and alerts chapter editors and other panel members to the possibility of biased presentation of evidence, thus prompting alternative interpretations of the same data.

We believe that the key to developing conflict-free recommendations is that panel members without conflicts and, in particular, the methodologist chapter editor bear responsibility for the final presentation of evidence summaries and rating of the quality of evidence. The chapter editor is also responsible for ensuring that, during discussion of evidence, panel members with conflicts do not take an aggressive advocacy role.

We anticipate that presentation and interpretation of evidence by panel members with conflicts of interest may be biased, and this belief is the basis of the safeguards that we have instituted. The chapter editor therefore should ensure that panel members are exposed to presentations and interpretations free of that bias, in the initial discussions of the evidence by the full panel and in the final deliberation restricted to unconflicted panelists.

Panel members with an important conflict should not participate in or even be present for discussion or voting on the final rating of evidence quality or a recommendation for which they have a conflict. The chapter editor should ensure that, during these final discussions, the manner in which conflicts may have influenced earlier panel discussions is highlighted and that final ratings of evidence quality and recommendations are free of that influence.

Resolution of Disagreement Within the Panels. Disagreements (that is, lack of consensus) are resolved by a discussion that includes both conflict-free AT9 panel members from the chapter in question and conflict-free AT9 panel members from other chapters who have thoroughly reviewed the related evidence. Panel members with a conflict of interest may state their views in writing and provide supporting evidence. Participating panel members will receive these documents before the discussion. A binding vote of all conflict-free members participating in the review process ultimately decides on recommendations for which there was no initial consensus within a chapter panel.

Strengths and Limitations of This Approach

An important component of the proposed approach is an emphasis on intellectual conflicts far exceeding that of

most other organizations. The operational definition of intellectual conflict is specific, focusing on authorship of an article that bears on a recommendation. Evidence supporting a particular approach to intellectual conflict is meager; however, our review of previous antithrombotic guidelines suggests that when intellectual conflict may have influenced recommendations, the responsible individuals were usually authors of primary publications.

This new approach represents an experiment that may succeed or fail. Of the 2 primary goals we have identified—to ensure that evidence summaries and recommendations benefit fully from the insight and wisdom of experts with conflicts and to keep recommendations free from the influence of that conflict—we are confident that we will achieve the former. However, reasons for concern that intellectual or financial conflicts of interest could still taint recommendations remain.

First, restrictions on the input of experts with conflicts of interest into preparation of evidence summaries and formulation of recommendations are not absolute. Panel members without conflicts will be aware of expert opinions with conflicts of interest regarding recommendations, and a provision allows the written input of experts with conflicts into the final deliberations. This approach represents a compromise arising from discussion with experts who have made outstanding contributions to previous iterations of the guidelines. Most experts were concerned that, without these opportunities for input, less informed panel members may make misguided decisions. Furthermore, experts were reluctant to be identified as coauthors of recommendations from which they were totally excluded and believed that such exclusion would mislead the guidelines' audience.

Second, recruiting senior methodologists as chapter editors is usually not possible because of competing priorities. Therefore, most chapter editors are relatively junior. Given the status and seniority of many participating experts, chapter editors may find it difficult to exercise the requisite authority.

Despite these concerns, there are reasons to be optimistic about achieving our goals. First, the process has made all participants vividly aware of the importance of managing conflicts of interest. Second, the mechanisms in place ensure that all panel members are fully aware of who has conflicts and the nature of the conflicts for each recommendation. Third, the AT9 executive committee, 2 members of whom are senior methodologists without conflicts of interest, will support chapter editors and will themselves be alert to undue influence of experts with conflicts. Fourth, the final guideline will undergo extensive independent review.

CONCLUSION

The AT9's process for managing conflicts of interest in clinical practice guidelines offers an innovative strategy de-

signed to reconcile the competing goals of incorporating expert insights and avoiding inappropriate influence of experts with financial or intellectual conflicts. Other professional groups may find this approach, or variations of this approach, helpful in the development of their own clinical practice guidelines.

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