Clinical experts or methodologists to write clinical guidelines?

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The guidelines by the American College of Chest Physicians (ACCP) on antithrombotic therapy, first published in 1986 and subsequently every 4 years, have become an institution.[1] One of us (JH) was a founding editor and retired from that position in June, 2008; the other (GG) has been an editor for the past three iterations. Although the ACCP guidelines have had an important impact on patients' care, we have become increasingly aware of their deficiencies and of deficiencies of clinical guidelines in general. In this Comment, we extend the case, suggested by the UK's National Institute for Health and Clinical Excellence[2] and others,[3] for changes in how guidelines are developed.

Much has changed since the ACCP published its first edition of antithrombotic guidelines. An increasing number of professional societies now publish clinical guidelines and in almost all cases they are written by clinical experts. The process of searching for evidence has become more rigorous, the grading systems more sophisticated, and the link between the evidence and the grade of the recommendations more transparent.[4] Perhaps the largest change has been in readership and in the way the recommendations are used. Recommendations initially intended to guide clinicians have been accepted by third-party insurers who use the guidelines to develop performance measures to influence payment.[5]

Other interested parties also use guidelines. Marketing departments of drug companies use guidelines to promote their compounds. Litigating attorneys use guidelines to hold physicians accountable in malpractice cases. Unless recommendations are free of bias, their use by the drug industry can lead to unnecessary increases in the cost of health care, and use by attorneys can cause irreparable harm to responsible physicians.

For these and other reasons, recommendations should be reliable and free of bias. But are they? Evidence suggests that they are not. For example there are marked differences between the ACCP[6] and the American Association of Orthopedic Surgeons[7] in their recommendations for prophylaxis against venous thromboembolism after orthopaedic surgery. There are also major differences between guidelines from the American College of Cardiology/American Heart Association and the European Society of Cardiology in their recommendation on the use of anticoagulants in patients with acute myocardial ischaemia.[8] There are other examples.[9,10]

In each case, two groups reviewed the same literature but developed different recommendations. Some of these disagreements are legitimate and caused by differences in interpretation of the evidence. Others, however, are not and are caused by bias resulting from conflicts of interest.

The most obvious conflicts of interest that might influence expert judgment arise from involvement with drug companies. Most authors contributing to guidelines declare some potential conflicts of interest because of their involvement with industry. A much less publicised conflict occurs when clinical investigators place disproportionate weight on results of studies that they, or members of their institution, co-authored. We believe that such intellectual conflicts of interest are important, but are under-appreciated and undisclosed. Prominent clinicians unduly influenced by results of their own studies can—and often do—sway a panel to support their views.

A potential conflict is just that: only potential. It does not mean that the author was biased, but leaves such a

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possibility open and therefore can tarnish the perception of the integrity of the recommendations. Moreover, potential conflicts often become real conflicts.

Can guidelines be developed by unconflicted authors? They can, but only with a radical change in the way we develop guidelines. We suggest the following approach: the literature search, directed by questions defined by clinical experts, is done by an evidence-based centre. Guideline authors, recognised methodologists free of potential conflicts of interest, seek help on specific matters of content from expert clinicians. These expert clinicians and unconflicted methodologists prepare an initial draft document that summarises and interprets the relevant evidence. The non-conflicted authors then integrate the material and, without input from panel members with potential conflicts, develop the recommendations. Thus, although the process of understanding the evidence and its clinical implications benefits from expert input, the decisions about recommendations are solely in the hands of an independent writing group of non-conflicted methodologists, thereby minimising the potential for bias.

We have sought feedback on this proposal from our fellow ACCP editors and other clinical experts. Their initial reaction was mixed, but all agreed with the main message: clinical experts who write guidelines are often influenced by (usually) declared financial conflicts and by equally important undeclared intellectual conflicts of interest. These conflicts of interest should be managed by placing the final responsibility for recommendations in the hands of unconflicted methodologists. The result will be improved integrity of future guidelines.

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JH declares that he has no conflicts of interest. GG chairs the executive for the upcoming 9th Antithrombotic Guidelines of the American College of Chest Physicians, and has contributed extensively to the GRADE working group.

1 Hirsh J, Guyatt G, Albers GW, Harrington R, Schünemann HJ. Antithrombotic and thrombolytic therapy: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008; **133:** 110S–112S
2 Rawlins MD. The decade of NICE. *Lancet* 2009; published online April 24. DOI:10.1016/S0140-6736(09)60616-4.
3 Sniderman AD, Furberg CD. Why guideline-making requires reform. *JAMA* 2009; **301:** 429–31.
4 Guyatt GH, Oxman AD, Vist GE, et al, for the GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008; **336:** 924–26.
5 Corrigan JM, Burstin H. Measuring quality of performance: where is it headed and who is making the decisions? *J Fam Pract* 2007; **56:** 4A–7A.
6 Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest* 2004; **126:** 338–400.
7 Eikelboom JW, Karthikeyan G, Fagel N, Hirsh J. American Association of Orthopedic Surgeons and American College of Chest Physicians guidelines for venous thromboembolism prevention in hip and knee arthroplasty differ: what are the implications for clinicians and patients? *Chest* 2009; **135:** 513–20.
8 Eikelboom JW, Guyatt G, Hirsh JW. Guidelines for anticoagulant use in acute coronary syndromes. *Lancet* 2008; **371:** 1559–61.
9 Rizzo JD, Somerfield MR, Hagerty KL, et al. Use of epoetin and darbepoetin in patients with cancer: 2007 American Society of Hematology/American Society of Clinical Oncology clinical practice guideline update. *Blood* 2008; **111:** 25–41.
10 Bennett CL, Silver SM, Djulbegovic B, et al. Venous thromboembolism and mortality associated with recombinant erythropoietin and darbepoetin administration for the treatment of cancer-associated anemia. *JAMA* 2008; **299:** 914–24.