Controversy

Guideline controversy

DOI:10.1503/cmaj.051662

Are clinical practice guidelines unduly influenced by the financial associations and competing interests of the experts who write them? The lead editorial of our Nov. 22 issue was stimulated by a news release we had received from the Canadian Diabetes Association (CDA) that criticized the Common Drug Review (CDR) for not approving for provincial formulary listing a new long-acting insulin that the CDA had recommended in its clinical-practice guidelines. According to the CDA, the CDR's judgment was uninformed because no clinical experts were involved. In reacting to this statement, we discovered that neither the CDA's nor the CDR's expert panels revealed or even discussed potential financial conflicts of interest among the experts who were making the recommendations.

In this trio of articles, the CDA and CDR explain their guideline and recommendation processes and their rationales for not revealing authors' conflicts of interest. We also asked Dave Davis to comment more generally on the problem of producing unbiased clinical practice guidelines and solutions that are being implemented to improve guideline quality.

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The Canadian Diabetes Association guidelines: putting the evidence first

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∞ See related articles pages 335 and 337

DOI:10.1503/cmaj.051556

In a recent editorial[1] that focused on the relationship between guideline authors and industry, *CMAJ* singled out the Canadian Diabetes Association (CDA) for considerable criticism. Some of the points raised are helpful in efforts of organizations such as ours to optimize guideline development processes. However, the editorial contained a number of important misstatements and errors. Physicians and others who rely on *CMAJ* to provide a thoughtful and balanced analysis of health care issues deserve an accurate and complete picture.

The CDA published clinical practice guidelines in 2003.[2] The process for developing these guidelines, as was described in detail in the methods chapter (available: www.diabetes.ca/cpg2003/downloads/methods.pdf), was rigorous and systematic. In brief, the process involved exhaustive reviews of the literature, grading of the evidence and development of clinically directive evidence-based recommendations. In circumstances where no trial evidence had been published, consensus recommendations were required, demanding 100% agreement among the members of the steering committee.

This work was undertaken by 62 nationally recognized experts who volunteered many thousands of hours to the project and received no financial compensation. To guard against all forms of bias, several measures were in place. Each volunteer completed a full duality-of-interest disclosure, which remains on file at the CDA. Clear policies on the disclosure of potential dualities and conflicts were explicit throughout the guideline process. Furthermore, during guideline discussions and deliberations, individuals were required to state any relevant potential dualities before presenting an opinion. After presentation at the annual professional conference of the CDA and before publication, the guidelines were reviewed by over 100 external reviewers from Canada, the United States and Britain. As a final step, 3 methodologists reviewed each graded recommendation to ensure that the wording could be supported by the cited references and had been correctly graded. The CDA guidelines have been internationally acclaimed,[3] and their process of explicitly stating the evidence for each recommendation is one of the most transparent in the world.

The CDA received unrestricted educational grants from 11 pharmaceutical companies (which are acknowledged in the guidelines). These sponsors were not present during any deliberations about the guidelines and were not involved in any aspect of guideline development, literature interpretation or publication decision.

It is perhaps not surprising that the Canadian Coordinating Office for Health Technology Assessment (CCOHTA), whose mandate is "to review new drugs and provide formulary listing recommendations to participating publicly funded federal, provincial and territorial drug benefit plans in Canada," and the CDA, whose mandate is to advocate for and increase treatment options for patients, would have discordant views. In terms of transparency and broad-based review, the CDA process cannot be compared with the Common Drug Review (CDR) process. According to CCOHTA, the only information that may be publicly released is the recommendation for or against listing and the reasons for that recommendation. Compare this with the CDA process of formulating recommendations and citing and grading references in order to allow readers to arrive at their own conclusions. To hold up the government-sponsored CDR process as the standard for unbiased assessment is to ignore the completely different focus of the CDR in prioritizing deployment of the limited resources for health care. In fact, not all government-sanctioned expert formulary reviews have arrived at the same findings about glargine. In terms of formulary coverage in other jurisdictions, glargine has been listed in Quebec and also in the United Kingdom, based on the recommendation of the UK National Institute for Clinical Evidence.[4]

It is not surprising that the CDA and CCOHTA have discordant views.

The *CMAJ* editorial misrepresented the CDA as recommending that "glargine be used as an alternative for generic long-acting insulin." In fact there is no "generic" long-acting insulin available in Canada, and our recommendations for glargine are limited to specific and clearly defined clinical situations and are supported by an explicitly stated level of evidence. Based on the prespecified criteria for assigning levels of evidence, both recommendations were supported by grade B, level 2 evidence. The exact wording is as follows: "Insulin glargine should be considered for use as the basal insulin in well-controlled patients [with type 1 diabetes] who have problems controlling their fasting plasma glucose levels or to reduce overnight hypoglycemia," and "When insulin given at night is added to oral antihyperglycemic agents, insulin glargine may be preferred over NPH [neutral protamine Hagedorn] to reduce overnight hypoglycemia and weight gain."

CMAJ's rewording may mislead readers to believe that we were simply favouring glargine without qualification. We would direct readers to the relevant guideline chapters for a detailed exposition on the rationale for and references supporting these recommendations[2] (www.diabetes.ca/cpg2003/downloads/insulin.pdf and www.diabetes.ca/cpg2003/downloads/pharmacologic.pdf).

Finally, the editorial suggested that assessing evidence requires expertise in clinical trials, but not clinical practice. The case of glargine is a perfect example of how reviewers with different expertise and focus would view the literature. From a clinical perspective, only somebody who actually manages diabetes would fully appreciate the delicate balance involved in lowering hemoglobin A_{1c} levels to evidence-based targets while avoiding hypoglycemia. To discount the importance of this issue (as we believe may have occurred in the CCOHTA review) is to ignore the clinical realities of treating this complex disease.

As the CDA undertakes its next guideline revision (currently scheduled for publication in 2008), we will continue to uphold the highest standards to minimize bias while applying lessons learned from the responses of *CMAJ* and others to our 2003 guidelines. Meanwhile, we encourage physicians and health care professionals involved in the care of Canadians with diabetes to continue to apply the CDA guidelines. Canadian patients deserve no less.

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Competing interests: None declared.

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