International Journal of Technology Assessment in Health Care, **16:4** (2000), 959–968.

IMPROVING CLINICAL PRACTICE GUIDELINES FOR THE 21ST CENTURY

Attitudinal Barriers and Not Technology Are the Main Challenges

George P. Browman
Cancer Care Ontario, Hamilton Regional Cancer Centre, and McMaster University

Abstract

Through the use of three scenarios, this paper presents the challenges for clinical practice guidelines in the 21st century. Such challenges relate to technological developments to improve the efficiency and pace of the development process, to ensure that clinical practice guidelines are kept up to date, and to facilitate implementation of guidelines in the clinical setting. To improve and ensure the validity of the content of clinical practice guidelines, we need to address the important problem of publication bias, for which researchers, granting agencies, industry, and journal editors share responsibility. This means insisting on registration of trials at their inception, and incentives backed up by rules for funding and peer review publication that would promote behaviors to avoid publication bias. The more difficult challenges for clinical practice guidelines relate to what are referred to as attitudinal factors. To achieve optimal efficiencies in development and maintenance of clinical practice guidelines, we need to promote cooperation among various information resource providers internationally and to stress partnership over leadership. Finally, there needs to be reconciliation of the different stakeholder perspectives of the value and purpose of clinical practice guidelines so that they are used appropriately as aids to decision making and are not abused as tools for controlling clinical practice.

Keywords: Practice guidelines, Technology

The future for clinical practice guidelines in health care will be bright if they are understood as a work in progress or an evolving healthcare technology (4). Evolving technologies are, by their nature, objects for continuous improvement in response to technological and social change. Some of the current challenges facing guideline programs include the time required to carry out comprehensive and systematic reviews of the evidence, difficulties in keeping information resources current with changing evidence, and the problem of publication bias, which threatens the validity of systematic reviews based on published research. Technological innovations in communications and knowledge management have the potential to address such challenges and to transform clinical practice guidelines into a more useful decision support tool.

This work was supported by Cancer Care Ontario and the Ontario Ministry of Health.

Even with technological advances, the promising place of clinical practice guidelines in health care could be undermined by the proclivity of the human character for competitiveness where cooperation is more appropriate, and for authoritarianism where enablement is called for. These human tendencies represent what are hereafter referred to as the attitudinal factors that must be addressed if clinical practice guidelines are to be effective and accepted in the 21st century.

TECHNOLOGICAL ADVANCEMENTS

In this paper, various scenarios are used as examples of how both technological and attitudinal factors can influence the use of clinical practice guidelines. In this section, mainly technological issues are addressed. For guidelines to become more useful in the 21st century, technology will have to yield improvements in three areas: development, maintenance, and implementation.

Scenario 1

In a busy clinic, the physician encounters a new patient in consultation. The registration information has triggered a reminder on her touch screen about six guidelines that may pertain to the patient's initial diagnosis. The guidelines are embedded within a module that is linked to the electronic record, with software that automatically matches patient and disease characteristics to available clinical practice guidelines. The physician ignores the guideline prompt, remembering to disable it for the next new patient until more than registration information is available. After delving into the history and completing the examination, the physician reviews previous clinical encounters, prescription records, and test results. This information is made available by plugging a wallet-sized card in the patient's possession into the physician's wireless palm-top computer. The information is downloaded into the clinic's main record system, and the new information triggers another reminder that refers to three guidelines in the module's database. Again, the physician ignores the prompt and enters a treatment order. The clinical practice guideline prompt now focuses on a single guideline about treatment that the physician deems worth consulting.

Upon consulting the clinical practice guideline, the physician notes that it seems to diverge from recent information she thinks she came across. Using her palm-top computer, she accesses the Internet while walking toward the canteen for a coffee. She immediately consults the National Guidelines Clearinghouse™ website (www.guideline.gov/). It lists the clinical practice guideline and compares it with others on the same topic. Using the touch screen, she then accesses the "new evidence CPG update" module. She learns that the results of the recent study she remembered do not alter the guideline recommendation.

Using the "dialogue" function, the physician documents that she has discussed the treatment with the patient, who, after considering a variety of options, decides against following the recommendation. The patient confirms this by touching the appropriate label on the screen. Concerned about the patient's choice, the physician calls up aggregated data about how previous patients with this condition in the clinic have done in the past year. She discovers that the outcomes for those who agreed to follow the clinical practice guideline are slightly better than those who did not. She also examines how her patients have fared, compared with similar patients treated by others in her group practice, and shares the information with the patient. After weighing the information, the patient sticks to her original decision.

Two weeks later, the clinic's vice president for quality improvement in ambulatory services reviews the case as part of a random audit. He is able to track the series of actions taken by the physician, which were automatically recorded as part of the encounter. He is satisfied about the clinical processes used and decides to investigate why 60% of the clinic's patients with this condition refused the guideline recommendation in the past 6 months.

Guideline Development

To be useful, clinical practice guidelines need to be evidence-based (3); otherwise, they will never achieve the validity, reliability, and credibility required for adoption. The process of producing an evidence-based clinical practice guideline is systematic review of the literature

(26), bolstered by access to other equally valid information that may not be published. We estimate that it takes about 18 months for Cancer Care Ontario's Program in Evidence-based Care to produce a scientifically rigorous clinical practice guideline in the area of cancer (5). This is despite our explicit decision to take short-cuts in the systematic review process that could threaten their validity. These short-cuts are used to improve the timeliness of the guideline development process, and they include restrictions to published reports in the search for evidence, preference for peer-reviewed articles, and an emphasis on publications in English. Such compromises make evidence-based clinical practice guidelines vulnerable to several varieties of publication bias, where positive studies are more likely to be selected than negative ones in synthesizing a body of literature (8;11;12;30).

Studies to date have shown discordance in the estimates of the treatment effects of interventions between different methods of aggregating trials from either the published literature or individual patient data (21;28;33). If empirical evidence confirms such findings and they turn out to be clinically important, then unpublished sources would have to be routinely sought out, thus extending the time needed to produce a valid clinical practice guideline. The need to incorporate individual patient data could extend the time up to several years.

While the validity of systematic reviews may be improved by more comprehensive approaches, at the same time there are pressures to find more efficient techniques to accelerate the process. Those who pay for guideline development are becoming frustrated with the slow pace of the development process and the associated expense.

The key advances for dealing with publication bias will not be technological but attitudinal and/or legislative. Already, the most respected peer-reviewed journals are trying to address publication bias by declaring an "amnesty" on unpublished trials that authors wish to submit (29). The pharmaceutical and medical devices industries will have to agree to comply with such encouragement if this is to work.

While amnesty for publication of as yet unpublished trials may deal with the backlog of literature, other interventions are needed to prevent a build-up of new unpublished studies that contribute to publication bias. Calls for mandatory registration of trials are important (8;30), but this measure will not work unless there are appropriate incentives for compliance or disincentives for noncompliance. The threat of publication bias to the validity of the published body of literature is so serious that drastic policies need to be put in place. For example, those who fund clinical trials could make the flow of funds contingent on their proper registration, and journals could refuse to publish the results of trials that were not documented as registered at their inception. Given that publication bias has been rightly labeled as an issue of scientific ethics on the part of investigators (7), who seem to be the main source of the problem (11;12), both granting agencies and journals could apply the same standards they now use with respect to ethical research.

Guideline Maintenance

Having completed the exhaustive task of producing an evidence-based guideline, developers often have little energy or resources left over for maintaining them. Evidence-based clinical practice guidelines are living documents. To qualify as evidence-based, they must evolve as new evidence emerges; otherwise, their credibility suffers. For some topics, like cancer, high-quality evidence appears at a rapid pace and requires close vigilance. Key events such as national and international meetings need to be monitored for emerging data.

Keeping guidelines current will require the application of technology for systematic monitoring of the emerging literature. In addition, it is virtually impossible to keep print versions of guidelines up to date at an affordable cost. We will have to rely more on electronic journals and the Internet as the most reliable sources of up-to-date information. In the future, guidelines will exist as living electronic documents.

Guideline Implementation

The investments made available for guideline development have not been matched by investments for implementation. As difficult as the development process is, getting people to use clinical practice guidelines and other sources of research information is even more challenging (2).

Technological solutions seem ideal for implementing those interventions that empirical research indicates are effective in influencing clinical behavior change. Effective strategies such as audit and feedback and reminder systems close to the clinical encounter (10;27), as part of electronic medical record systems, can be embedded within computer decision support systems (17;18;34). Such systems have already been tested, for example, in the case of diabetes management using clinical practice guidelines (19). They can also provide access to evidence-based guidelines through the National Guidelines Clearinghouse website.

Finally, patient-mediated interventions have been shown to be effective in influencing clinical practice change (10;27). We ought to exploit the current trends for seeking patient information on the Internet to develop enabling strategies that point patients to reliable Internet sites, including those containing guidelines.

ATTITUDINAL CHALLENGES

In the previous section, we addressed technological developments that may contribute to improvements in the effectiveness and efficiency of guideline development, maintenance, and implementation. In this section, we examine certain attitudinal factors that lead to behaviors that may influence guideline programs. The following scenario highlights the issues.

Scenario 2

The American Society of Hematology wishes to assist its members in making decisions about the use of a new growth factor. The topic is placed on the agenda by an internationally renowned clinician-researcher in the United States who is eager to provide leadership in this area. He gathers together a group of like-minded clinicians and researchers as a panel of experts. He is careful to include many different stakeholders. The initial literature search for an evidence-based clinical practice guideline fails to reveal a current document. After 1 month of work, a panel member discovers the existence of the International Registry of Guidelines in Progress (currently a fictitious entity). The panel learns that a French group and an Australian group began work on such a topic about 6 months before and have made good progress. Their guideline development protocols, available on the Internet, are reviewed. The chairs of the Australian and French panels are contacted, and each is made aware of the other's work. After 1 week of intensive review, the American, French, and Australian groups decide to pool resources and collaborate on the systematic review, with each group taking responsibility for a different section. They agree that once the systematic review is complete, the consensus part of the development process for the whole guideline will be conducted separately in each country. The final recommendations from each country will be submitted to the National Guidelines Clearinghouse™ and posted on the Internet. A publication strategy is agreed to. This cooperation allows the Society to address a new clinical practice guideline of importance to its members. The topic is registered with the International Registry of Guidelines in Progress. Other groups are invited to participate. The Agency for Health and Research Quality is consulted to recruit one of its Evidence-based Practice Centers (http://www.ahrq.gov/clinic/epc/) for methodologic assistance, and the Cochrane Collaboration is contacted for additional help.

This scenario addresses the issues of information sharing and cooperation, in the context of technological advancements, which should replace the tendency for professional groups and individuals to appoint themselves as leaders or unique contributors to a field. It suggests how the willingness of people and organizations to engage in cooperative partnerships on a broad front can overcome some of the problems currently facing the clinical practice guideline movement.

If it takes so long to produce a clinical practice guideline and the investment is barely affordable, then one obvious strategy is to promote cooperation among guideline development groups to avoid duplication of effort. Replication of efforts in producing systematic reviews for guidelines by various groups cannot be justified. To be effective, clinical practice guidelines must rely on local input to the final recommendations to produce local "buy-in" (14). This can be accomplished at the stage of consensus development around the interpretation of the body of evidence emanating from a sound systematic review (5;6).

Those paying for clinical practice guidelines will not tolerate much longer duplications of effort to produce reviews that ought to be generalizable across healthcare settings. Currently, duplication seems to occur because of either lack of awareness of what other groups are doing or inherent tendencies for ambitious people to vie for status as innovators and leaders in their particular field. We need to develop cooperative partnerships for guideline development to replace traditional competitive approaches that are wasting resources. The establishment of a registry of clinical practice guidelines under development would help; it could be posted through the National Guidelines Clearinghouse website.

Examples of organizational cooperation for systematic review development include the Cochrane Collaboration (1) and the Evidence-based Practice Center network sponsored by the U.S. Agency for Health and Research Quality (http://www.ahrq.gov/clinic/epc/). The latter enterprise is based on a contracting mechanism between those who do systematic reviews and those who commission them because of a defined need. Technology assessment organizations are well positioned to take on this type of work. The results of these collaborations are available through electronic dissemination.

If guideline developers do not improve their performance using cooperative strategies, then healthcare delivery organizations will conclude that evidence-based clinical practice guidelines are not responsive to their needs and not affordable.

ENABLING GUIDELINE-BASED DECISIONS: USE VERSUS ABUSE

Scenario 3

The vice president for quality improvement of an HMO is doing her monthly review of reports of practice concordance with clinical practice guidelines for a team of practitioners. By examining routinely assembled aggregate care information across patients in the previous 6 months, she is able to learn that overall concordance of practice (formerly called compliance) with clinical practice guidelines is 70%. She notes that one particular clinician's concordance rate is 50%. Further analysis shows that the patient-related characteristics for this clinician's practice over the 6-month period are similar to those of his colleagues. She is able to determine with input from the practitioner and the statistical officer for quality control that concordance is 40% for clinical practice guidelines where limited options are available to patients, and 80% when multiple options are available. By having the data aggregated around the clinical practice guidelines with limited options, the vice president discovers that patients' preferences for treatment were documented in 90% of cases. Further analysis shows a relationship between concordance and distance of the patient from the treatment center. Review of referral patterns indicates a much higher proportion of referrrals to this practitioner from distant locations in the past 6 months, consistent with a speaking tour he had taken. Review of the clinical practice guidelines in question shows that most of the treatment options are inconvenient for patients living at a distance. Through the quality control officer, the vice president instructs the chairs of the clinical practice guideline development panels to review the applicability of the guidelines to the organization's referral base and location. The practitioner in question receives strong endorsement, as reflected in his "report card" for the month.

Guideline Use

Reconciling Stakeholder Perspectives. There is a tension among different stakeholders about the purpose of clinical practice guidelines. Clinical practice guidelines are

defined as systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances (13). This definition clearly positions clinical practice guidelines to be used within the clinical encounter in a discussion between the patient and the clinician. The definition implies strongly that clinical practice guidelines are intended to inform clinical judgments, not replace them.

On the other hand, managers of health services and the payers they serve are placing great hopes on evidence-based guidelines as a cost-containment strategy. Their faith is based on the common understanding that in health care there is little evidence to support much of what is done, and that wide variations in clinical practice are likely to be associated with variations in cost that can be controlled if we can narrow the clinical choices. There is an implicit assumption that procedures can be identified to replace more costly ones while maintaining the level of effectiveness. While this may be true on average, certain individual guidelines may result in higher costs.

The effect of guidelines on overall costs needs to be evaluated programmatically as a package to avoid inappropriate administrative decisions relating to an individual guideline when an effectiveness trade-off for lower costs cannot be supported by society's values system. For example, between 1995 and 1998, guidelines from the Cancer Care Ontario Clinical Practice Guidelines Initiative (5) contributed to a $16 million increase in government spending for new anticancer drugs. Despite this, clinical practice guidelines are viewed as a valuable information resource that helps payers justify such funding decisions. Clinical practice guidelines are also seen to contribute to cost savings by explicitly framing the boundaries within which the treatments ought to be used. In other words, in the absence of guidelines, drug costs might have been even higher if the treatments had been applied more broadly than the indications specified by the guideline recommendations.

Guidelines as an Enabling Strategy. Clinical practice guidelines ought to be deployed as enabling strategies to help clinicians and patients be aware of the evidence about what works and what does not work in health care, so that they can make better choices. At the level of the clinical encounter, guidelines may help practitioners deal with the varying quality of health information being brought to them by patients who use the Internet and the media as their information sources. Also, including clinicians as important participants in the guideline development process through consensus methods should enhance the acceptance of clinical recommendations and further enable implementation. Healthcare policy makers should commission and use clinical practice guidelines with these strategies in mind.

Guidelines and the Evaluation of Clinical Practice. More attention needs to be paid to the guideline evaluation process in the context of clinical practice patterns. Currently, such evaluation processes tend to be negatively framed, as discussed in more detail in the next section.

A discussion of clinical practice guidelines in the 21st century would not be complete without reference to current trends for making quality of care indicators available through another evolving technology, public "report cards" (9). This burgeoning field is likely to have a large steering effect on how clinical practice is carried out and reported. Care will have to be taken to ensure that such reporting improves the quality of care rather than simply the appearance of the quality of care (35). Further development of this technology should parallel guideline development. Clinical practice guidelines could play an important role in defining how these report cards can be interpreted in the context of otherwise complex healthcare decision environments. Further discussion of report cards is beyond the scope of this paper.

Guideline Abuse

We need to keep reminding ourselves that medical practice is a social activity, heavily influenced by regional practice norms and the opinions of local leaders (15;16;25;31).

Innovative implementation strategies need to use this information rather than to identify practice habits as barriers to change (22;23).

Several abuses of clinical practice guidelines should be avoided. First, guidelines are not intended to restrict legitimate healthcare choices outside the setting of the clinical encounter, and within the encounter they cannot be used in good conscience as a justification for withholding information from patients about available effective treatment alternatives. Second, where there are trade-offs in terms of costs and effectiveness, the guideline is not intended as the final arbiter in favor of cost savings. Third, clinical practice guidelines do not replace clinical judgment in issues related to legal liability, although they can be used to buttress decisions that are consistent with the guidelines. Fourth, if we are to sustain healthy and professional attitudes and relationships among providers and managers in the longer term, then the use of disincentives (such as withholding remuneration for physicians' services where guidelines are not followed) should be discouraged in favor of more thoughtful approaches, as presented in the last scenario.

The fundamental distinction between the proper use and abuse of clinical practice guidelines is manifested by the implicit inferences we make in situations where practice is found to be inconsistent with a guideline. The accepted definition of a clinical practice guideline would find the practitioner "innocent until proven guilty." This presumption has implications for how we evaluate guidelines.

Under an appropriate evaluation framework, we would approach an example of discordance between a clinical practice guideline and a particular practice by exhausting the hypothesis space, as follows:

- Did the guideline apply to the particular clinical circumstance?
- Were there other factors in the patient's situation that mitigated against the use of the recommended treatment?
- Did the patient's preference for a legitimate alternative therapy that was not included in the guideline influence the practitioner's approach?
- Is the guideline effective in communicating the message?

With an inappropriate evaluation strategy of guideline abuse, discordance between an observed practice and a guideline recommendation is interpreted at the outset as practitioner wrongdoing; hence, the tendency to use the term "compliance" to describe the relationship between a guideline recommendation and a clinical practice. What ought to be a thoughtful exercise in learning and improvement becomes an exercise in finger-pointing. Under such circumstances, manifested by policies of financial disincentives, for example, it is unlikely that clinical practice guidelines will last long as an effective tool in the 21st century. However, persistent discrepancies between what is recommended and what is practiced should serve as a flag for further exploration and, if necessary, education leading finally to penalties as the last resort.

The importance of this issue of evaluation was highlighted by an episode in Ontario, Canada following the publication of an outcomes study showing wide geographic variations across regions in breast-conserving surgery rates for early-stage breast cancer (20). The way the study results were released clearly targeted the surgeons as culprits. But preliminary follow-up data suggest that when decision aids are introduced into surgical practice, breast-conserving surgery rates may actually fall among surgeons who routinely use this technique, presumably due to patients' preferences (V. Goel, personal communication). These preferences may be linked to differences in geographic access to radiation facilities across regions, because of the need for postoperative radiation following lumpectomy.

An excellent example of why we need to be careful about our evaluation approaches is reflected in differences in the wording of guideline recommendations for the surgical management of early-stage breast cancer from Ontario's guideline initiative and from the national steering committee (24;32). The former recommends that "Women with stage I or II breast cancer who are candidates for breast conserving surgery *should be offered the choice of either* breast-conserving surgery or modified. . . ." By contrast, the national clinical practice guideline reads "For patients with stage I or II breast cancer, breast-conserving surgery followed by radiotherapy *is generally recommended*. . . ." (italics mine). These subtle differences in wording can have profound effects on how clinical practice and guidelines are interpreted and evaluated.

CONCLUSION

Clinical practice guidelines are an evolving healthcare technology. In this context, their current status should be viewed as promising. Technological advances and empirical research are needed to improve the efficiency and affordability of guideline development.

Current communications and knowledge management technologies, including use of the Internet, and the availability of evidence-based resources should allow for more effective implementation of guidelines into practice. Electronic technology is also the vehicle that will allow evidence-based guidelines to be updated regularly as new evidence emerges.

The more difficult challenges facing the guideline movement in the 21st century seem to be attitudinal rather than technological. Collaborative as opposed to competitive models of endeavor in evidence summarization and guideline development are needed to avoid replication of effort and waste of resources. Strategies need to be implemented to ensure that evidence-based guidelines truly reflect the state of the world's body of evidence. This means avoiding or minimizing publication bias. Funding agencies and journal editors need to rigorously apply rules for pre-registration of trials and for registration of clinical practice guidelines in progress.

If clinical practice guidelines are to become useful tools for clinical decision making, they need to be implemented in ways shown to influence provider behavior positively. Electronic medical record systems and software that can tailor the prompt for a guideline specific to a patient's situation are available and will enhance implementation results. Data showing a fairly rapid rise in the use of the Internet by practitioners suggest that this medium will become the dominant communication vehicle, if it is not already (34). This development will make clinical practice guidelines even more useful and reliable. Increased access to guidelines by patients, as a convenient source of summarized information, should increase their value. Clinical practice guidelines may also be a useful balance to the patient heavily armed with Internet sources of information of variable quality.

Finally, if guidelines are to find their right place in clinical practice, they must be seen as enablers for clinical decisions in the environment of the clinical encounter where patients have rights and powers. Similarly, inappropriate use (abuse) of guidelines as tools to control practice will threaten their effective use in health care.

Ultimately, patients as the consumers of health care will determine the place of clinical practice guidelines in healthcare delivery. If clinical practice guidelines are discovered to be valid, reliable, and helpful in creating a more meaningful clinical encounter, they will improve and thrive well into the 21st century.

REFERENCES

1. Bero L. The Cochrane Collaboration. Preparing, maintaining, and disseminating systematic reviews of the effects of health care. *JAMA*. 1995;274:1935-1938.

2. Bero L, Grilli R, Grimshaw JM, et al. Closing the gap between research and practice: An overview of systematic reviews of interventions to promote the implementation of research findings. *BMJ*. 1998;317:465-468.
3. Browman GP. The essence of evidence medicine: A case report. *J Clin Oncol*. 1999;17:1969-1973.
4. Browman, GP, Levine MN, Graham I, et al. The clinical practice guideline: An evolving health care technology. *Cancer Prevention and Control*. 1997;1:7-8.
5. Browman GP, Levine MN, Mohide EA, et al. The practice guidelines development cycle: A conceptual tool for practice guidelines development and implementation. *J Clin Oncol*. 1995;13:502-512.
6. Browman GP, Newman TE, Mohide EA, et al. Progress of clinical oncology guidelines development using the practice guidelines development cycle: The role of practitioner feedback. *J Clin Oncol*. 1998;16:1226-1231.
7. Chalmers I. Underreporting research is scientific misconduct. *JAMA*. 1990;263:1405-1408.
8. Chalmers I, Dickerson K, Chalmers T. Getting to grips with Archie Cochrane's agenda. All randomised trials should be registered and reported. *BMJ*. 1992;305:786-788.
9. Chassin M, Hannan EL, DeBuono BA. Benefits and hazards of reporting medical outcomes publicly. *N Engl J Med*. 1996;334:394-398.
10. Davis DA, Thomson MA, Oxman AD, Haynes RB. Changing physician performance: A systematic review of the effect of continuing medical education strategies. *JAMA*. 1995;274:700-705.
11. Dickerson K. How important is publication bias? A synthesis of available data. *AIDS Educ Prev*. 1997;9(suppl A):15-21.
12. Egger M, Zellweger T, Antes G. Randomized trials in German-language journals. *Lancet*. 1996;347:1047-1048.
13. Field MJ, Lohr KM (eds). *Institute of Medicine. Guidelines for medical practice: From development to use*. Washington, DC: National Academy Press; 1992.
14. Gates PE. Think globally, act locally: An approach to implementation of clinical practice guidelines. *Journal of Quality Improvement*. 1995;21:71-85.
15. Greco PJ, Eisenberg JM. Changing physicians' practices. *N Engl J Med*. 1993;329:1271-1274.
16. Greer AL. The state of the art versus the state of the science: The diffusion of new medical technologies into practice. *Int J Technol Assess Health Care*. 1988;4:5-26.
17. Hayward RS, Hogeterp KB, Langton D, et al. A computer-assisted design tool for the development and analysis of evidence-based automated questionnaires. *Medinfo*. 1995;8(pt 2):934-937.
18. Hunt DL, Haynes RB, Hanna SE, Smith K. Effects of computer-based clinical decision support systems on physician performance and patient outcomes. A systematic review. *JAMA*. 1998;280:1339-1346.
19. Hunt DL, Haynes RB, Hayward RSA, et al. Patient-specific evidence-based care recommendations for diabetes mellitus: Development and initial clinical experience with a computerized decision support system. *International Journal of Medical Informatics*. 1998;51:127-135.
20. Iscoe NA, Goel V, Wu K, et al. Variation in breast cancer surgery in Ontario. *Can Med Assoc J*. 1994;150:345-352.
21. LeLorier J, Grégoire G, Benhaddad A, et al. Discrepancies between meta-analyses and subsequent large randomized, controlled trials. *N Engl J Med*. 1997;337:536-542.
22. Lomas J. Diffusion, dissemination, and implementation: Who should do what? *Ann NY Acad Sci*. 1993;703:226-237.
23. Lomas J. Making clinical policy explicit. Legislative policy making and lessons for developing practice guidelines. *Int J Technol Assess Health Care*. 1993;9:11-25.
24. Mirsky D, O'Brien SE, McCready DR, et al. Surgical management of early stage invasive breast cancer (stage I and II). *Cancer Prevention and Control*. 1997;1:10-16.
25. Mittman BS. Implementing clinical practice guidelines: Social influence strategies and practitioner behavior change. *Qual Rev Bull*. 1992;18:413-422.
26. Mulrow CD, Cook DJ, Davidoff F. Systematic reviews: Critical links in the great chain of evidence. *Ann Intern Med*. 1997;126:389-391.
27. Oxman AD, Thomson MA, Davis DA, Haynes RB. No magic bullets: A systematic review of 102 trials of interventions to improve professional practice. *Can Med Assoc J*. 1995;153:1423-1431.

28. Pignon JP, Bourhis J, Domage C. Meta-analysis of chemotherapy in head and neck cancer: Individual patient data vs literature data. *Br J Cancer*. 1995;72:1062.
29. Roberts I. An amnesty for unpublished trials. One year on, many trials are unregistered and the amnesty remains open. *BMJ*. 1998;317:763-764.
30. Simes RJ. Publication bias: The case for an international registry of clinical trials. *J Clin Oncol*. 1986;4:1529-1541.
31. Soumerai SB, McLaughlin TJ, Gurwitz JH, et al. Effect of local medical opinion leaders on quality of care for acute myocardial infarction. A randomized controlled trial. *JAMA*. 1999;279:1358-1363.
32. Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. Mastectomy or lumpectomy? The choice of operation for clinical stage I and II breast cancer. *Can Med Assoc J*. 1998;158(suppl 3):S15-S21.
33. Stewart LA, Parmer MKB. Meta-analysis of the literature or meta-analysis of individual patient data: Is there a difference? *Lancet*. 1993;341:418-422.
34. Sullivan P, Buske L. Results from CMA's huge 1998 physician survey point to a dispirited profession. *Can Med Assoc J*. 1998;159:525-528.
35. Welch HG, Black WC, Fisher ES. Case-mix adjustment: Making bad apples look good. *JAMA*. 1995;273:772-773.