

KEEPING CANCER GUIDELINES CURRENT: RESULTS OF A COMPREHENSIVE PROSPECTIVE LITERATURE MONITORING STRATEGY FOR TWENTY CLINICAL PRACTICE GUIDELINES

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Abstract

Objectives: To describe a methodology used to keep practice guidelines up to date and to summarize data collected during the first year of implementing this plan with a cancer practice guidelines program.

Methods: The updating strategy includes regular searches of peer-reviewed literature and meeting proceedings, review and interpretation of new evidence, review and revision of clinical recommendations, and notification to practitioners and policy makers about new evidence and its impact on recommendations.

Results: Eighty pieces of new evidence were found relating to seventeen of the twenty guidelines included in this study. On average, four pieces of new evidence were found per guideline, but there was considerable variation across the guidelines. Of the eighty pieces, nineteen contributed to modifications of clinical recommendations in six practice guidelines, whereas the remaining evidence served to support the original recommendations. None of the modifications led to changes that advised against original recommendations. MEDLINE, the Cochrane Library, and meeting proceedings yielded many pieces of evidence, whereas CancerLit and HealthStar did not contribute significantly to the overall yield. Furthermore, key pieces of evidence that led to modifications to the recommendations were often identified by members of the disease site groups before appearing in electronic databases.

Conclusions: The updating process is resource intensive but yields important findings. In response to this evaluation, the updating protocol has been revised such that literature searches are conducted quarterly and the scope of sources searched routinely is restricted to MEDLINE, the Cochrane Library, and meeting proceedings.

Keywords: Clinical practice guidelines, Updating, Cancer

A good clinical practice guideline consists of three fundamental elements: the systematic review of the evidence, the consensus process that incorporates the opinions of stakeholders about the interpretation of the evidence and its applicability to specific situations, and the

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clinical recommendations that are informed by the first two elements (3). The systematic review at the heart of an evidence-based clinical practice guideline describes and summarizes the best available research evidence at a particular point in time. As new evidence emerges, the systematic review becomes out-of-date. More importantly, the recommendations may become obsolete because of discordance between the old and new evidence. Over the past six years, the Cancer Care Ontario Practice Guidelines Initiative (CCOPGI) has been responsible for the development of evidence-based clinical practice guidelines for Ontario's cancer system (3). In the early years of the CCOPGI, the disease site groups (DSGs) who had developed the guidelines assumed responsibility for keeping them up-to-date. However, the methods used for identifying and reporting relevant new evidence were informal. With the inauguration of the Cancer Care Ontario Program in Evidence-Based Care in 1997 (the Program), resources became available to design, implement, and evaluate an ongoing systematic guideline updating process. Formal procedures were developed by the Program's research staff (which included three health information specialists) and adopted for use across the Initiative. This study describes the Initiative's strategy for keeping these practice guidelines up-to-date and summarizes data collected during the first year of implementation.

METHODS

The updating strategy included four steps: (i) regular searches of the peer-reviewed literature and meeting proceedings by the research staff working with the DSGs, (ii) review and interpretation of the new evidence by the DSGs, (iii) review and, where applicable, revision of the clinical recommendations in response to this new evidence, and (iv) notification to practitioners and policy makers about the new evidence and recommendations.

Searches

Monthly update searching was chosen as the unit of analysis for the pilot study because the main electronic databases (e.g., MEDLINE) available to the DSG members are updated once a month by the National Library of Medicine. The primary sources of literature searched during each update were electronic sources, print sources, and "other" sources.

Electronic sources. Between June 1998 and May 1999, the research staff conducted monthly searches of the MEDLINE, CancerLit, and HealthStar electronic databases using search software from Ovid Technologies, Inc. The search strategies were designed to find practice guidelines, systematic reviews, and randomized controlled trials (RCT) directly relevant to the original guideline question (9). By using the eligibility criteria described in the original guideline report, the research staff (all trained and experienced in research methodology) reviewed the resulting list of citations and abstracts to identify potentially relevant new trials, meta-analyses and evidence-based guidelines, or updated results from trials included in the original guideline report. In addition, the Cochrane Library on CD-ROM was searched quarterly to coincide with each new issue released. The search strategies used here were based on those used for MEDLINE but included text words to maximize the potential for finding articles that were not indexed with Medical Subject Heading (in MEDLARS) headings.

Print sources. The chair of each DSG was asked to identify key journals and proceedings of meetings where new evidence was likely to emerge. Table of contents were hand-searched or viewed on Web sites of journals in circumstances where the source was not indexed by the National Library of Medicine in a timely manner.

Other sources. As investigators in clinical trials and practising clinicians, DSG members become aware of new evidence. They notified the group when new evidence in the public domain came to their attention.

Review and Interpretation of the New Evidence

The lead author of the original guideline, the chair of the DSG, and the research assistant sitting on the DSG independently reviewed the abstracts and articles found by the update searches. They considered the relevance of each item to the original guideline question and interpreted the new evidence in the context of the original guideline report. Phase III studies and full reports were given considerably more consideration than phase II studies or abstracts (see below). However, we did not set out criteria for evaluation of evidence to which each DSG had to conform. Given the variability in the evidence as a function of disease site (e.g., breast cancer versus head and neck cancer) and modality of treatment (e.g., surgery, chemotherapy, radiotherapy, combined), the one-size-fits all approach would not have been appropriate for the developers or the target audience.

Review and Revision of the Recommendations

The relevant DSGs were presented with descriptive and interpretive summaries of the new evidence as prepared by the research staff, and they were asked to choose one of the following options that best reflected the implications of the new evidence on the clinical recommendations:

1. The new evidence is consistent with the data used to inform the original practice guideline report. The recommendations in the original report remain unchanged.
2. The new evidence is consistent with the data used to inform the original practice guideline report. The strength of the recommendations in the original report has been modified to reflect this additional evidence.
3. The new evidence is inconsistent with the data used to inform the original practice guideline report. However, the strength of the new evidence does not alter the conclusions of the original document. Recommendations in the original report remain unchanged.
4. The new evidence is inconsistent with the data used to inform the original practice guideline report. The strength of the new evidence will alter the conclusions of the original document. Recommendations in the original report will change. This change is a priority issue for the DSG. Modifications to the practice guideline are now in progress.

Clinical and scientific judgment informed the choices made by the DSG members; there was no mandatory threshold of new evidence (e.g., number of studies, types of studies, magnitude of statistical findings) that had to be met before classification to categories occurred.

Communicating Updated Evidence to Practitioners

A notice, called an evidence update, was linked to each guideline on the Program's Web site (http://www.cancercare.on.ca/access_PEBC.htm) to keep practitioners aware that regular update searches were being conducted. Where new evidence emerged, this was summarized in a short evidence update bulletin. In cases for which the DSG was aware of new evidence that could change the recommendations, a notice was placed at the top of the guideline on the Web page to alert practitioners that the guideline was under review. Where new evidence rendered a guideline obsolete, the entire practice guideline report was removed from the Web site and replaced with a notice that the guideline was being rewritten and a new version was to appear shortly. More recently, we have integrated evidence updates into the original report, creating a dynamic "living" practice guideline.

Although the Web site is the main vehicle for disseminating the CCO guidelines to practitioners, all abstracts of new and updated guidelines were also distributed once a year in print. These documents from the Initiative advised the user that our guidelines are updated regularly and that new information can be found on the Web site. New in 2000, guidelines

were distributed by an interactive CD-ROM, to over 1000 target users in the province. The CD-ROM has a built-in capacity that will allow users to receive updates automatically on a periodic basis. Finally, all guidelines continue to be posted on the Web sites of the Canadian Medical Association's CPGInfobase (<http://mdm.ca/cpgsnew/cpgs>) and the U.S. National Guidelines Clearinghouse (<http://www.guideline.gov/>).

Pilot Study

The pilot study was carried out over the first year of adoption of the updating strategy described above, and data were collected prospectively for each completed practice guideline. Data collected between the beginning of June 1998 and the end of May 1999 were used to address four questions:

1. What proportion of sources of evidence initially identified in the updating strategy (e.g., MEDLINE, CancerLit, etc.) yield relevant information?
2. What type of new evidence is found?
3. What is the impact of update searching on the guideline recommendations?
4. Is monthly searching justified in terms of the effort expended and the amount of new evidence found by each search?

The first question addresses both the impact of systematic update searching on the discovery of important new evidence and on the process of updating. The second and third questions address the impact of searching as it relates to the discovery of new evidence and the implications of the evidence on the clinical recommendations of the guidelines. The last question focuses on the process of conducting update searches and was included to identify areas where our activities could be streamlined.

RESULTS

Data were available from update searches related to twenty practice guidelines over the full twelve-month period of the pilot study (4;7;10–14;16–19;24;26;28;30;34;39;41;46;48). These guidelines included seventeen guidelines on the treatment of cancer: four for breast cancer (14;28;46;48), five for gastrointestinal cancer (11–13;16;17), one for genitourinary cancer (7), one for head and neck cancer (4), and six for lung cancer (10;18;19;24;26;30). Three additional guidelines addressed the management of adverse effects from chemotherapy (34;39;41).

Yield from Updating

The first analysis addressed the yield from the sources that we searched. A total of eighty relevant pieces of new evidence were found during the pilot study. MEDLINE was always searched first as the primary source for new evidence, and, as expected, it was a useful tool. The largest proportion of the new evidence found (52.5%) came from MEDLINE. In contrast, CancerLit and HealthStar failed to add additional relevant information. The Cochrane Library yielded a significant number of studies not found in MEDLINE ($n = 5$) and represented 6.25% of all evidence found. Nonelectronic sources, such as abstracts from annual meetings and current issues of journals not yet indexed in electronic databases have proven to be an essential component of our search strategy; these yielded a total of thirty-two new pieces of evidence (40%) over the twelve-month period. Of the twenty-six abstracts discovered in the proceedings of annual meetings, twenty-five were from the 1999 meeting of the American Society of Clinical Oncology and one was from the 1998 San Antonio Breast Cancer Symposium. Six additional studies were identified by DSG members before they could be found by searches of electronic databases.

Table 1. Type of Citations Resulting from Monthly Update Searching for Twenty Completed Guidelines as a Function of Information Source

| Information source | Number per citation type | | | | Total |
|--------------------|--------------------------|--------------------------|----------------------------|-------|-------|
| | New RCT | RCT Updates ^a | Meta-analysis ^b | Other | |
| MEDLINE | 26 | 3 | 0 | 13 | 42 |
| CancerLit | 0 | 0 | 0 | 1 | 1 |
| HealthStar | 0 | 0 | 0 | 0 | 0 |
| Cochrane Library | 4 | 0 | 1 | 0 | 5 |
| Meeting abstracts | 25 | 0 | 0 | 1 | 26 |
| Other sources | 1 | 3 | 2 | 0 | 6 |
| Total | 56 | 6 | 3 | 15 | 80 |

^a Full reports of studies for which only abstract reports were available for inclusion in the original guideline.

^b Practice guidelines from other groups, quality of life studies, reports on adverse effects, economic analyses, phase II studies.

On average, four new pieces of evidence emerged per guideline over the twelve months but there was considerable variation. No new evidence emerged over twelve months for three guidelines, one new piece of evidence was found for four guidelines and two pieces for six guidelines. A greater number of reports, ranging from four to sixteen, were discovered for the remaining seven guidelines.

Type of Evidence

The second analysis addressed the type of evidence found. Of the eighty pieces of new evidence, twenty-six abstracts and fifty-four full reports were found. Examining this yield as a function of citation type (see Table 1), the bulk of the findings consisted of reports of recently published RCTs ($n = 56$). Full reports became available for six RCTs for which results were available only in abstract form at the time of completing the original practice guideline. High-quality meta-analyses are also an important source of data for guideline development, and three of these were found by update searches. One practice guideline from another guideline-development group, on the same topic as the CCO guideline, was uncovered. Two papers reported quality of life data from RCTs, and another two reported important data on adverse effects. Other studies that DSGs chose to describe in evidence update bulletins included one randomized trial not directly related to the guideline question, one phase II study, and nine economic analyses.

Impact of Update Searching on the Guidelines

The outcome of update searching, expressed in terms of the effect of new evidence on the clinical recommendations, is summarized in Table 2. Of the twenty guidelines included in the pilot study, new evidence was found and summarized in update bulletins for seventeen (4;11–14;16–19;24;26;28;30;34;35;46;48), whereas no new evidence was found for the other three guidelines (7;10;41).

Nineteen of the eighty (23.7%) pieces of new evidence found during the pilot study had an impact on the recommendations made by the guideline developers. This pivotal new evidence included results from ten new RCTs (1;2;4;8;20;22;36;38;42;45) and one long-term quality-of-life report from an RCT (43) all found by MEDLINE searches, six new RCTs reported in meeting abstracts (15;21;23;31;37;47), one new meta-analysis identified by DSG members (33), and one full report of a randomized trial found by a MEDLINE search for which only an abstract was available in the original guideline (29). Thus, of the new information that led to changes in recommendations, 63.1% were studies found in MEDLINE, 31.6% were meeting abstracts (identified by either the research

Table 2. Impact on Clinical Recommendations for the Seventeen Completed Practice Guidelines for which New Evidence Emerged

 No changes to clinical recommendations ($n = 11$)

 Changes to clinical recommendations ($n = 6$)

 Original recommendations strengthened ($n = 2$)

Chemotherapy for Stage IV Non-Small Cell Lung Cancer (26)

- 2 new RCTs (full-report) (20,44)

Adjuvant Radiotherapy and Chemotherapy for Stage II and IIIA Non-Small Cell Lung Cancer (24)

- 1 meta-analysis (33)
- 1 new RCT meeting abstract (21)

 Patient population to which the original recommendations apply modified ($n = 2$)

Erythropoietin (34)

- 1 updated RCT (29)
- 2 new RCTs (full-report) (8,45)
- 1 new RCT meeting abstract (23)

Granulocyte Colony-Stimulating Factor (39)

- 6 new RCTs (full-report) (1,2,22,36,38,42)
- 3 new RCT meeting abstracts (15,31,37)

 New evidence noted where none existed, original recommendations remain ($n = 2$)

Management of Ductal Carcinoma In Situ of the Breast (48)

- 1 new RCT meeting abstract (47)

Neoadjuvant Chemotherapy for Locally Advanced Squamous Cell Head and Neck Cancer (4)

- 1 quality of life report (43)

RCT, randomized controlled trial.

assistants or DSG members), and 5.3% were studies identified by members of the DSG.

Modifications were made to recommendations in six guidelines of the seventeen guidelines for which new evidence emerged during the pilot study (4;24;26;34;39;48). New evidence allowed the guideline developers to strengthen the recommendations for two practice guidelines (original 24, update 25; original 26, update 27). Two pieces of evidence were found for each of these guidelines and contributed to the modifications. New evidence led to an expansion of the patient populations for two other guidelines (original 34, update 35; original 39, update 40). Four new pieces of evidence contributed to changes in the recommendations for one of these guidelines (35) and nine to the other (40). In the remaining two guidelines (4;48), practitioners were made aware of important new evidence that, if confirmed by other studies, could lead to changes in the recommendations (original 6, update 13). For the first guideline (48), an abstract of an RCT from proceedings of a meeting, and for the second guideline (4), a quality of life study, contributed to these modifications. There were no instances for which a guideline was modified to advise against a treatment that had been recommended in the original practice guideline.

DISCUSSION

A total of eighty new pieces of evidence were found relating to seventeen of the twenty guidelines included in this study. Nineteen of the eighty pieces of new evidence contributed to modifications of clinical recommendations. The main contribution of these reports of eighteen RCTs and one meta-analysis was to fill in gaps in the evidence that had been identified during the development of the original practice guideline. The other new evidence found during update searching ($n = 61$) served to support existing recommendations and was summarized and posted on our Web site to keep practitioners up-to-date.

Although the bulk of the new evidence was found during scheduled update searches, our pilot project found that key pieces of new evidence (i.e., data that led to changes in individual practice guidelines) are often identified by members of the DSG before they appear in electronic databases. This finding reinforces the importance of communication among members of the guideline development groups, as well as the regular review of key journals and meeting abstracts.

DSG members have discussed, at length, the relative contributions of evidence reported in peer-reviewed publications and that from other sources. In an effort to minimize publication bias, the literature searches conducted at the beginning of the guideline-development process include peer-reviewed journals, meeting abstracts, and unpublished information from pharmaceutical manufacturers and clinical investigators. Data reported only in abstracts are included in guideline reports, but their limitations are acknowledged. They are interpreted in the context of the data available from peer-reviewed, full-report publications, and it is uncommon to base recommendations solely on evidence reported in abstract form, because it is usually of a preliminary nature.

A similar approach is taken when using evidence to modify existing guidelines. For example, only one piece of new evidence was found for the guideline on the management of ductal carcinoma in situ of the breast during the pilot study. Because this evidence was presented only in a meeting abstract, the Breast Cancer DSG opted to wait for a full report of the mature data before modifying the recommendation related to treatment with tamoxifen. The DSG, however, did believe that it was important to make practitioners aware of this new evidence and added a note to the guideline on the Program Web site. Should evidence that is inconsistent with existing recommendations be published only in abstract form, we anticipate that the DSG would postpone revision of the recommendations until the full report of the study is available.

Although the updating process led to modifications to six of the twenty guidelines included in the pilot study, none of these modifications included changes to recommendations that advised against the treatment options proposed in the original document. Given that this process is labor-intensive and will be a challenge to apply to a continually growing set of practice guidelines, the data collected as part of this pilot study have been examined to identify areas of efficiency. Although frequent searches (e.g., monthly) can minimize the delay between new evidence being published and being found, the pilot study demonstrated a small monthly yield relative to the amount of effort invested in searching. As a result, the protocol has been revised to specify update searching four times a year rather than monthly for the next year. HealthStar and CancerLit have been dropped from the list of required databases. The Initiative will continue to collect data and to use this information to modify its updating strategy to balance effectiveness and efficiency.

Policy Implications and Impact of Practice

As part of the external review of the practice guidelines (5;6), we gather data on clinicians' perceptions of and intentions to use the practice guidelines. External review is repeated for updated guidelines for which there are changes or modifications to the recommendations. Thus, we are now gathering data that will allow us track changes in perceptions and intentions over time as the practice guidelines mature and evidence is integrated into updated documents. In addition, practice guidelines relevant to new and expensive systematic therapy agents are submitted to the Policy Advisory Committee of Cancer Care Ontario in their funding policy deliberations (32); updated guidelines are streamlined into this process where appropriate. To date, updated guidelines have not led to substantive changes in policy funding decisions for these agents.

Finally, one of the primary challenges we face is to find valid, reliable, and affordable strategies to systematically evaluate the correspondence between practice guidelines and behavior, the impact of updating on the patterns that emerge, and the implications for health outcomes. Currently, a new Knowledge Management Initiative is under way in the Ontario system that will facilitate this process and will address these issues.

CONCLUSIONS

The Practice Guidelines Initiative has expanded a systematic approach to guideline development to include a successful updating strategy. By conducting a scheduled program of literature searching and review, the Initiative has been able to keep a set of twenty guidelines up-to-date and to make new evidence and revised recommendations available to practitioners and other guideline users. The key factors in this success have been the development and application of a protocol for update searching, a centralized resource group for conducting the searches and summarizing the evidence, and active participation by members of the DSGs who developed the original practice guidelines.

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