Complete Summary

GUIDELINE TITLE

18-Fluorodeoxyglucose positron emission tomography in the diagnosis and staging of lung cancer: a clinical practice guideline.

BIBLIOGRAPHIC SOURCE(S)

Ung YC, Maziak DE, Vanderveen JA, Smith CA, Gulenchyn K, Evans WK, Lung Cancer Disease Site Group. 18-fluorodeoxyglucose positron emission tomography in the diagnosis and staging of lung cancer: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2007 Apr 27. 54 p. (Evidence-based series; no. 7-20). [135 references]

GUIDELINE STATUS

This is the current release of the guideline.

The EVIDENCE-BASED SERIES report, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

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SCOPE

DISEASE/CONDITION(S)

Lung cancer

- Solitary pulmonary nodules (SPN)
- Non-small cell lung cancer (NSCLC)
- Small cell lung cancer (SCLC)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Technology Assessment

CLINICAL SPECIALTY

Nuclear Medicine
Oncology
Pulmonary Medicine
Radiation Oncology
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the role of 18-fluorodeoxyglucose ($_{18}$FDG) positron emission tomography (PET) in:

- The diagnosis of solitary pulmonary nodules (SPN)
- The staging of primary non-small cell lung cancer (NSCLC) at initial diagnosis
- The staging of primary small cell lung cancer (SCLC)

TARGET POPULATION

Adult patients with lung cancer (solitary pulmonary nodules, non-small cell lung cancer, and small cell lung cancer)

INTERVENTIONS AND PRACTICES CONSIDERED

1. 18-fluorodeoxyglucose ($_{18}$FDG) positron emission tomography (PET)
2. Fine needle aspiration (FNA)

MAJOR OUTCOMES CONSIDERED

- Accuracy measures of imaging (e.g., sensitivity, specificity)
- Impact of positron emission tomography (PET) on patient management and patient outcomes

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The initial search for evidence-based reports involved the following databases and time periods: Cochrane Database of Systematic Reviews (2006, Issue 1), EMBASE (1996 through 2006, week 19), and MEDLINE (1996 through May 2006). The search terms are described in Table 1 in the original guideline document. These terms were combined with the search terms for the following publication types: practice guideline, systematic review, biomedical technology assessment, and meta-analysis. In addition, the following Web sites were searched on May 13, 2005: the Canadian Medical Association Infobase (http://mdm.ca/cpgsnew/cpgs/search/english/results.asp?Pg=3), the National Guideline Clearinghouse (http://www.guideline.gov/), the National Institute for Clinical Excellence (NICE) (http://www.nice.org.uk/); the Web site of the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) (now the Canadian Agency for Drugs and Technologies in Health) (http://www.cadth.ca/index.php/en/home) was searched on December 23, 2004, and the Centre for Reviews and Dissemination, (http://www.york.ac.uk/inst/crd/) was searched on February 1, 2005.

In addition to the databases described above, the conference proceedings of the American Society of Clinical Oncology (ASCO) (2004-2005) were searched for abstracts of relevant trials by searching for key words or scanning the index. The Physician Data Query (PDQ) clinical trials database on the Internet (http://www.cancer.gov/cancertopics/pdq/cancerdatabase) was searched for additional trials. Relevant articles and abstracts were selected and reviewed, and the reference lists from these sources were also searched for additional trials.

Study Selection Criteria

Inclusion Criteria

Evidence-based reports were selected for inclusion in this practice guideline if they reported outcomes of interest and were the following:

- Health technology assessments or practice guidelines based on a systematic review of evidence, systematic reviews, or meta-analyses that evaluated the use of positron emission tomography (PET) in the staging and diagnosis of lung cancer
- Reports fully published in English after 1999.

Articles published as full reports or as abstracts after the completion of the Institute for Clinical Evaluative Sciences (ICES) review or examining the use of PET in staging small cell lung cancer (SCLC) were selected if they were the following:

- Randomized or single-arm prospective studies that focused on 18-fluorodeoxyglucose positron emission tomography ($_{18}$FDG-PET) scanning in

the staging and diagnosis of lung cancer compared to an appropriate reference standard.
- Reports including at least one of the following measures of effectiveness/benefit: PET specificity and sensitivity, accuracy measures of staging, changes in patient management, or improvements in patient outcomes (survival).

Exclusion Criteria

Studies with ≤35 subjects. All sample sizes were included for small cell lung cancer trials.

1. Letters and editorials reporting clinical trials were not eligible.
2. Articles published in a language other than English.

NUMBER OF SOURCE DOCUMENTS

In addition to the Institute for Clinical Evaluative Sciences (ICES) report, 12 evidence-based reports (health technology assessments, practice guidelines, systematic reviews, and meta-analyses) were retrieved. An additional fifteen prospective studies (including randomized controlled trials [RCTs]) are included in this review.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The Lung Disease Site Group (DSG) decided not to statistically pool data from accuracy studies because of the availability of several meta-analyses that provided overall summaries of the diagnostic accuracy of positron emission tomography (PET) for the staging and diagnosis of primary lung cancer.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The accurate diagnosis and staging of lung cancer patients is vital for the selection of appropriate treatment. In recent years, 18-fluorodeoxyglucose positron emission tomography ($_{18}$FDG PET) scanning has emerged as a potential non-invasive imaging technique for the diagnosis and staging of lung cancer. Many studies have evaluated the accuracy of $_{18}$FDG-PET in the diagnosis and staging of lung cancer; however, there is limited evidence to determine the impact of PET on clinical management and on patient outcomes.

The majority of studies examining PET have been diagnostic accuracy studies; however, these studies are highly susceptible to bias, which can result in unreliable estimates of accuracy. Diagnostic studies with methodological limitations tend to overestimate the diagnostic performance of the test. In evaluating the evidence for PET in lung cancer, a number of limitations were present in the accuracy studies, including differences in patient selection, the use of different reference standards for verification of results, and biases in the evaluation of test results. These shortcomings in study design can affect the estimates of diagnostic accuracy. In addition, it is not clear how results from diagnostic accuracy studies translate into changes in patient management. The Disease Site Group (DSG) placed considerable weight on the findings of the randomized utility studies for the staging of primary non-small cell lung cancer (NSCLC). For other issues, accuracy of the evidence was used to support what are largely consensus recommendations.

The determination as to whether a solitary pulmonary nodule (SPN) is benign or malignant can be problematic as certain lesions cannot be diagnosed by conventional means other than surgical resection. To ensure that only patients with a potentially resectable lung cancer are taken to thoracotomy, histologic or cytologic evidence of malignancy is needed. For patients with an SPN, percutaneous fine needle aspiration biopsy (FNAB) is usually performed. However, FNAB may be contraindicated because there may be an underlying medical condition, the lesion may be inaccessible to FNAB, prior attempts at FNAB may have failed, or the patient may refuse the procedure.

Meta-analyses of studies evaluating the ability of PET to differentiate benign from malignant lesions have found the sensitivity of PET to range from 96% to 97% and specificity to range from 78% to 86%. Accuracy studies have confirmed that PET appears to have a high sensitivity, and a reasonable specificity for differentiating benign from malignant lesions as small as 1 cm in size. A mass of metabolically active cells is needed for PET to be positive and to suggest that a lesion may be malignant. With current PET scanners, it is difficult to detect malignancy in nodules that are less than 1 cm. Studies suggest that pulmonary nodules less than 1 cm or with faint or ground-glass opacity images on computed tomography (CT) cannot be evaluated accurately by PET and that both CT and PET findings should be considered to determine if surgical biopsy is necessary for small pulmonary nodules. False-negative results can also occur with low-grade malignant tumours such as well-differentiated adenocarcinomas, including bronchoalveolar cell carcinomas, due to their lower metabolic activity. False-positive results can occur in inflammatory conditions such as granulomatous disease due to the increased metabolic activity of inflammatory cells. Infection with histoplasmosis is common in Ontario and could increase the rate of false-positive PET scans.

Based on this evidence, PET is recommended for patients with SPN 1.0 cm or greater in size who cannot undergo FNAB or who have failed a prior attempt at FNAB. If the PET is positive, the probability is high that the lesion is malignant, and the patient should proceed to thoracotomy. A negative PET scan suggests that the lesion is benign but careful follow-up is indicated, as PET can be falsely negative in slow growing adenocarcinomas and bronchoalveolar carcinoma.

One study that did not meet the inclusion criteria for this report reviewed cases of NSCLC solitary extrapulmonary FDG accumulations in patients with NSCLC. Solitary extrapulmonary lesions were found in 72 of 350 patients (21%) with PET-CT imaging. 54% of lesions were solitary metastases and 46% were lesions unrelated to the primary lung tumour. This trial supports the conclusions that SPN require histopathologic diagnosis as up to half solitary extrapulmonary FDG accumulations may represent unrelated malignancies or benign disease.

After lung cancer has been diagnosed, accurate staging is essential for appropriate treatment decisions to be made. Conventional staging procedures are currently imperfect in their ability to spare patients from the morbidity and mortality of stage inappropriate therapies. Health technology assessment reports have concluded that it is difficult to quantify the improvement in diagnostic accuracy of PET in staging NSCLC due to the variations in study quality and the lack of direct evidence on whether PET improves patient outcomes. Meta-analyses found sensitivity to range from 81% to 90% and specificity to range from 89% to 90% for the distinction between N0-1 and N2-3 patients. Accuracy studies had similar results, with PET results found to be superior to CT imaging for mediastinal staging. Studies that interpreted PET images with CT results had higher accuracy than when PET was interpreted independently. Integrated PET-CT scanners also improved accuracy; however, additional studies on this type of imaging are needed as only a few small single-centre prospective studies have evaluated the accuracy of integrated PET-CT scanners, and there are no studies on the impact of PET-CT on patient outcomes. The results from one study suggest that PET is unable to detect metastatic foci smaller than 4 mm. False positives with respect to staging the mediastinum also occur with infection and inflammation. The trials suggest that a positive test result should be confirmed to ensure that patients are not denied potentially curative surgery. False-negative results can occur when the primary tumour obscures mediastinal lymph nodes, as the $_{18}$FDG uptake in the lymph nodes may not be distinguished from the avid uptake in the primary tumour. PET has also been used to detect distant metastases, but additional research is needed in this area. PET has been found to have high accuracy (89% to 96%) for detecting distant metastases and has also detected extrathoracic metastases in patients in whom conventional imaging showed no evidence of distant metastases. The role of PET in the evaluation of distant metastases appears to be greatest for adrenal and bone metastases. PET is not useful for detection of brain metastases due to the high glucose uptake of normal brain tissue.

Three randomized controlled trials have evaluated the value of preoperative PET assessment; however, two of these trials had conflicting results. These two trials randomized patients to conventional workup with or without PET. The PET in Lung Cancer Staging (PLUS) trial reported a 51% relative reduction in futile thoracotomies (p=0.003) when PET was added to conventional work up, whereas the Australian trial found no difference in the number of thoracotomies avoided

(p=0.2). A number of factors contribute to the apparent discrepancy between these trials. One factor is the difference in the patient populations between the trials. The PLUS trial included patients with suspected or proven NSCLC based on clinical, not surgical staging and as a result included patients with both benign and malignant lesions, whereas the Australian trial only included patients with histologically or cytologically proven NSCLC prior to randomization. However, the reduction in futile thoracotomies was still significant for PET (53% relative reduction, 95% confidence interval [CI] 32% to 88%) when patients with benign lesions were excluded from the analysis in the PLUS study. In addition, 29% of patients in the PLUS trial had clinical stage III disease at baseline, whereas the Australian trial only included patients demonstrating clinical stage I or II disease. Another explanation for the difference in results is that the approach to the management of patients with early stage lung cancer differed. Patients in the Australian trial with stage IIIA disease underwent surgery without further evaluation, while thoracotomy was considered futile in the PLUS trial if the patients had stage IIIA/N2 disease. Finally, the definition of futile thoracotomies (benign disease, exploratory thoracotomy, pathological stage IIIA [mediastinal node positive] or IIIB disease, or postoperative relapse or death within 12 months of randomization) in the PLUS study differed from the Australian trials definition of avoided thoracotomies (patients who were able to avoid thoracotomy as determined by the surgeon). Thus, the different designs of these studies might explain the contradicting results, demonstrating that the impact of PET on patient outcomes depends on the treatment decision-making process.

The recent POORT trial randomized patients with suspected NSCLC to traditional staging workup or up-front PET. PET did not decrease the number of staging tests required, and the agreement between the clinical and final stage were similar for both analyses. PET shortened the time to diagnosis by nine days, decreased the number of mediastinoscopies, and decreased the percentage of patients who needed one or more invasive tests for nodal staging. This is the first trial to compare conventional imaging to PET on clinically important aspects of clinical management.

$_{18}$FDG-PET has not been studied as extensively in staging patients with small cell lung cancer (SCLC). PET appears to have good accuracy (83% to 99%) in staging extensive versus limited stage disease, but further trials are needed to determine the role of PET in this setting.

Evaluation of new imaging techniques is important as "high costs, increasing demand for healthcare, increasing medical abilities and limited budgets have necessitated prioritization". PET scanning could improve the results of surgical therapy for early stage lung cancer by excluding patients from surgical resection who have evidence of metastatic disease beyond the scope of surgical resection and not evident by standard preoperative staging procedures. Similarly, the results for the management of locally advanced disease might also be expected to improve because of the addition of patients with minimal contralateral nodal disease that precluded surgery. Moreover, if PET imaging spares patients from the potential morbidity and risk of mortality from an unnecessary surgical procedure or chemo-radiotherapeutic intervention, it would not only have a significant impact on individual patients but would allow for more efficient and effective utilization of limited health care resources. Future research is needed to determine not only if PET should be integrated into the standard staging and diagnosis

process of lung cancer but also how PET would be incorporated into the diagnostic algorithm. The Ontario Clinical Oncology Group (OCOG) is currently conducting two prospective randomized controlled trials on the use of PET that have been approved by the Ontario Ministry of Health and Long-Term Care and a registry study of PET in patients with SPN. The randomized trials are examining the impact of PET on improving the management of patients with potentially surgically resectable NSCLC and the impact of PET on improving the management of patients with stage III NSCLC.

This systematic review only evaluated the role of $_{18}$FDG-PET in lung cancer. There are many other radioisotopes and biological markers that may in the future find utility in lung cancer imaging.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Development and Internal Review

This evidence-based series was developed and approved by the members of the Lung Disease Site Group (DSG) of Cancer Care Ontario's (CCO's) Program in Evidence-Based Care (PEBC).

Report Approval Panel

Prior to the submission of this evidence-based series report for external review, the report was reviewed and approved by the PEBC Report Approval Panel, which consists of two members, including an oncologist, with expertise in clinical and methodology issues. Key issues raised by the Panel included the use and presentation of evidence contained in health technology assessments apart from primary studies and the need for distinguishing studies of imaging diagnostic accuracy from those investigating utility.

External Review by Ontario Clinicians

Following the review and discussion of Sections 1 and 2 of the original guideline document and the review and approval of the report by the PEBC Report Approval Panel, the Lung Cancer DSG circulated the clinical practice guideline and systematic review to clinicians in Ontario for review and feedback.

Methods

Feedback was obtained through a mailed survey of 208 practitioners in Ontario (including 34 medical oncologists, 22 radiation oncologists, 25 surgeons, and 82 nuclear medicine specialists). The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a practice guideline. Written comments were invited. The survey was mailed out on January 30, 2007. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The survey was closed for responses at the end of March 2007. The Lung Cancer DSG reviewed the results of the survey.

The final published report reflects the integration of feedback obtained through the external review process with final approval given by the Lung DSG and the Report Approval Panel of the PEBC. Updates of the report will be conducted as new evidence informing the questions of interest emerge.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

There is limited randomized controlled trial evidence related to the impact of positron emission tomography (PET) on the clinical management of the lung cancer patient. In addition, PET technology has evolved significantly over time making it difficult to make recommendations based on studies using out-of-date imaging technologies. However, based on the interpretation of available evidence and expert consensus opinion, the Lung Cancer Disease Site Group (DSG) recommends the following:

Diagnosis of Solitary Pulmonary Nodules (SPN)

- Fine needle aspiration (FNA) biopsy is recommended as the first-line diagnostic approach in the workup of solitary pulmonary nodules. PET should be reserved for those situations in which a biopsy is inconclusive or contraindicated
    - PET appears to have a high sensitivity and specificity to differentiate benign from malignant lesions as small as 1 cm in size. Lesions less than 1 cm are difficult to categorize as they lack a sufficient mass of metabolically active cells. False-negative results can occur with low-grade malignant tumours due to their lower metabolic activity or with ground-glass opacities as may be seen in bronchoalveolar carcinomas.

Staging of Primary Non-Small Cell Lung Cancer (NSCLC)

- In the opinion of the Lung Disease Site Group, the evidence on whether the addition of PET to conventional staging or the up-front use of PET in mediastinal and extrathoracic staging changes clinical management in patients with non-small cell lung cancer is conflicting.

- Prospective studies have found that PET detects unexpected distant metastases in up to 15% of patients, which may lead to changes in patient management.
- For potential surgical candidates, mediastinoscopy is recommended to verify that PET positive mediastinal lesions are due to cancer in view of the potential for false positive results. Mediastinoscopy is necessary to ensure that a patient is not denied potentially curative surgery. A solitary extrathoracic site should also be confirmed to be metastatic, if possible, in order that a patient not be denied the chance of curative therapy.

Staging of Small Cell Lung Cancer (SCLC)

There is limited evidence on the use of PET in the staging of small cell lung cancer but three prospective trials showed good accuracy in differentiating limited from extensive stage disease.

CLINICAL ALGORITHM(S)

A clinical algorithm is provided in the original guideline document for the diagnosis of solitary pulmonary nodules.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by systematic reviews, meta-analyses, heath technology assessments, practice guidelines, and prospective studies (including randomized controlled trials).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Diagnosis of Solitary Pulmonary Nodules (SPN)

Meta-analyses found sensitivity of positron emission tomography (PET) to range from 96% to 97% and specificity to range from 78% to 86%, and the prospective studies confirmed these results.

Staging of Primary Non-Small Cell Lung Cancer (NSCLC)

Two trials randomized patients to conventional workup with or without positron emission tomography (PET). One trial reported a 51% relative reduction in futile thoracotomies (p=0.003) when PET was added to conventional workup, and the other trial found no difference in the number of futile thoracotomies avoided (p=0.2). Differences in the trial designs (patient populations, disease stage, definition of futile thoracotomies, and management of patients) may have contributed to the conflicting results.

- One trial randomized patients to traditional staging workup or up-front PET. A statistically significant difference was not found between the two groups for the mean number of staging tests performed. As well, the mean number of function tests, non-invasive procedures, invasive procedures, and thoracotomies did not significantly differ between the two arms. However, the percentage of patients who needed more than one invasive test to determine N staging and the number of mediastinoscopies was significantly lower for the PET group, and the median time to diagnosis was significantly shorter for the PET group (14 days versus [vs.] 23 days, $p<0.0001$).

Staging of Small Cell Lung Cancer (SCLC)

Three prospective studies demonstrated an accuracy of PET in staging extensive versus limited stage disease ranging from 83% to 99%.

POTENTIAL HARMS

Diagnosis of Solitary Pulmonary Nodules (SPN)

Positron emission tomography (PET): False-negative results occurred with low-grade malignant tumours, such as bronchoalveolar cell carcinomas or with ground-glass opacities. False positive results occurred in inflammatory conditions.

CONTRAINDICATIONS

CONTRAINDICATIONS

Fine needle aspiration biopsy (FNAB) may be contraindicated because there may be an underlying medical condition, the lesion may be inaccessible to FNAB, prior attempts at FNAB may have failed, or the patient may refuse the procedure.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult the evidence-based series is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Ung YC, Maziak DE, Vanderveen JA, Smith CA, Gulenchyn K, Evans WK, Lung Cancer Disease Site Group. 18-fluorodeoxyglucose positron emission tomography in the diagnosis and staging of lung cancer: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2007 Apr 27. 54 p. (Evidence-based series; no. 7-20). [135 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Apr

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Lung Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The members of the Lung Disease Site Group (DSG) disclosed potential conflict of interest relating to this practice guideline. Two of the guideline lead authors are primary investigators for the Ontario Clinical Oncology Group (OCOG) positron emission tomography imaging in stage III non-small cell lung cancer (PET-START) and PET imaging in potentially surgically resectable non-small cell lung cancers (ELPET) trials.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

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