



## Complete Summary

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### GUIDELINE TITLE

The noninvasive staging of non-small cell lung cancer: the guidelines.

### BIBLIOGRAPHIC SOURCE(S)

Silvestri GA, Tanoue LT, Margolis ML, Barker J, Detterbeck F. The noninvasive staging of non-small cell lung cancer: the guidelines. Chest 2003 Jan;123(1 Suppl):147S-56S. [70 references] [PubMed](#)

## COMPLETE SUMMARY CONTENT

SCOPE  
METHODOLOGY - including Rating Scheme and Cost Analysis  
RECOMMENDATIONS  
EVIDENCE SUPPORTING THE RECOMMENDATIONS  
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS  
IMPLEMENTATION OF THE GUIDELINE  
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT  
CATEGORIES  
IDENTIFYING INFORMATION AND AVAILABILITY

## SCOPE

### DISEASE/CONDITION(S)

Non-small cell lung cancer

### GUIDELINE CATEGORY

Diagnosis  
Risk Assessment

### CLINICAL SPECIALTY

Oncology  
Pulmonary Medicine  
Radiology

### INTENDED USERS

Physicians

### GUIDELINE OBJECTIVE(S)

To determine the test performance characteristics of noninvasive imaging procedures for staging the mediastinum and to assess the negative predictive value (NPV) of the clinical evaluation for predicting extrathoracic metastases

#### TARGET POPULATION

Patients with known or suspected lung cancer

#### INTERVENTIONS AND PRACTICES CONSIDERED

1. Mediastinal staging by computed tomography (CT) scan, positron emission tomography (PET) scan, magnetic resonance imaging (MRI) scan, and endoscopic ultrasound (EUS)
2. Detection of brain, abdominal, and bone metastasis by clinical evaluation

#### MAJOR OUTCOMES CONSIDERED

- Accuracy and utility of imaging studies and clinical evaluations for cancer staging and detecting metastasis as evaluated by:
- Sensitivity and specificity
- Negative predictive value (NPV)
- Positive predictive value (PPV)

## METHODOLOGY

#### METHODS USED TO COLLECT/SELECT EVIDENCE

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

#### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

##### Overview

As a first step in identifying the evidence for each topic, the guideline developers sought existing evidence syntheses including guidelines, systematic reviews, and meta-analyses. They searched computerized bibliographic databases including MEDLINE, Cancerlit, CINAHL and HealthStar, the Cochrane Collaboration Database of Abstracts of Reviews of Effectiveness, the National Guideline Clearinghouse, and the National Cancer Institute Physician Data Query database. Computerized searches through July 2001 used the MeSH terms lung neoplasms (exploded) and bronchial neoplasms or text searches for lung cancer combined with review articles, practice guidelines, guidelines, and meta-analyses. They also searched and included studies from the reference lists of review articles, and queried experts in the field. An international search was conducted of Web sites of provider organizations that were likely to have developed guidelines. Abstracts of candidate English language articles were reviewed by two physicians (one with methodological expertise and one with content area expertise) and a subset was selected for review in full text. Full-text articles were reviewed again by two physicians to determine whether they were original publications of a synthesis and were pertinent to at least one of the topics of the guideline. Articles described as

practice guidelines, systematic reviews, or meta-analyses were included, as were review articles that included a "Methods" section. Included articles were classified according to topic.

### Strategy specific for noninvasive staging of non-small cell lung cancer

For the topic on the noninvasive staging of non-small cell lung cancer (NSCLC), the guideline developers formulated two key questions that were to be answered by a comprehensive critical review of the published evidence:

1. What are the sensitivities and specificities of computed tomography (CT) scanning, magnetic resonance imaging (MRI), endoscopic ultrasound (EUS), and positron emission tomography (PET) scanning for detecting malignant mediastinal lymph node involvement in lung cancer patients?
2. How accurate is the clinical evaluation (i.e., symptoms, physical findings, or routine blood tests) for predicting metastatic disease among patients in whom lung cancer (i.e., NSCLC or small cell lung cancer [SCLC]) has been diagnosed?

To address these questions, Duke University, supported by a contract from the American College of Chest Physicians, conducted a computerized search of the MEDLINE bibliographic database from January 1991 to July 2001, HealthStar, and the Cochrane Library. The decision to limit the search to the past 10 years was based on the evolution of technology after consultation with diagnostic radiologists at Duke University Medical Center. Key words included lung neoplasm, bronchial neoplasm, neoplasm staging, neoplasm metastasis, lymphatic metastasis, CT, mediastinum radiography, emission-CT, adrenal gland neoplasms, and sensitivity and specificity. In addition, they searched the reference lists of included studies, selected textbooks, practice guidelines, systematic reviews, and meta-analyses in order to ensure that all relevant studies were identified. Only articles that had been published in English were considered. To address question 2, all articles described in a previously published meta-analysis evaluating tests for extrathoracic metastases also were included.

### Selection Criteria

Titles and abstracts, and the full text of all articles passing the title-and-abstract screen, were evaluated independently by at least two of the authors for inclusion or exclusion based on the following five criteria: (1) publication in a peer-reviewed journal; (2) study size of > 20 patients (except for studies involving CT scan evaluation of the mediastinum, for which > 50 patients were required); (3) patient group not included in a subsequent update of the study; (4) histologic or cytologic confirmation of mediastinal nodes or extrathoracic sites in addition to the primary tumor; and (5) availability of the raw data needed to calculate independently the sensitivity, specificity, negative predictive value, and positive predictive value (PPV) of CT scanning, positron emission tomography (PET) scanning, magnetic resonance imaging (MRI), or endoscopic ultrasound (EUS) (question 1), or, for question 2, the raw data needed to calculate the negative predictive value of the clinical evaluation. This last criterion was most important when analyzing studies that did not originally differentiate between hilar nodal involvement and mediastinal nodal involvement. Only articles meeting all five of these criteria were included.

## NUMBER OF SOURCE DOCUMENTS

Not stated

## METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus  
Weighting According to a Rating Scheme (Scheme Given)

## RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The United States Preventive Services Task Force (USPSTF) scheme offers general guidelines to assign one of the following grades of evidence: good, fair, or poor. In general, good evidence included prospective, controlled, randomized clinical trials, and poor evidence included case series and clinical experience. Trials with fair quality of evidence, for instance, historically controlled trials or retrospective analyses, were somewhere in between. In addition to the strength of the study design, however, study quality also was considered. The United States Preventive Services Task Force approach considers well-recognized criteria in rating the quality of individual studies for a variety of different types of study design (e.g., diagnostic accuracy studies and case-control studies). The thresholds for distinguishing good versus fair and fair versus poor evidence are not explicit but are left to the judgment of panelists, reviewers, and members of the executive committee.

### Assessment of the Scope and Quality of Clinical Practice Guidelines

Clinical practice guidelines identified from the systematic search were evaluated by at least four reviewers using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument.

## METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis  
Review of Published Meta-Analyses  
Systematic Review with Evidence Tables

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

### Data Abstraction

Data were abstracted from included studies and tabulated separately by type of noninvasive test (i.e., computed tomography [CT] scan, positron emission tomography [PET] scan, magnetic resonance imaging [MRI], and endoscopic ultrasound [EUS]). Studies that evaluated the mediastinum by CT or PET scan were tabulated both by correlation to nodal station and by correlation to patient. The guideline developers considered only mediastinal nodal involvement (stages N2 and N3) as being disease-positive in analyzing the studies, consistent with the 1997 revision of the lung cancer staging system. Patients with clinical or

histopathologic stage IV disease were excluded from calculations of operating characteristics if the nodal stage was not described.

Either tissue histologic confirmation or, if that was unavailable, long-term (i.e.,  $\geq$  than 1 year) clinical outcome was utilized as the reference or "gold standard" by which imaging data were compared. If neither tissue pathologic confirmation nor clinical outcome was available, then the patient was excluded from further statistical analysis.

Data from studies that described the presence or absence of symptoms or signs of metastatic disease on clinical evaluation were abstracted, with the presence or absence of extrathoracic metastases tabulated separately by the site of metastatic disease (i.e., brain, abdomen, and bone). Positive findings on neuroimaging studies (i.e., CT scan, MRI, or PET scan), abdominal CT scans, and radionuclide bone scans were used as references by which clinical evaluations for brain, abdominal, and bone metastases, respectively, were compared.

### Statistical Analysis

Summary sensitivity and specificity, and their respective confidence intervals (CIs), were calculated using statistical software for the meta-analysis of diagnosis tests (Meta-Test; New England Cochrane Center; Boston, MA). For studies that included patients with a positive and negative clinical evaluation, the sensitivity, specificity, and positive predictive value (PPV) of the evaluation for metastatic disease were calculated. As most studies of clinical evaluation included only asymptomatic patients, the primary outcome in these studies was the negative predictive value (NPV). Negative predictive values were calculated using statistical software (FAST\*PRO). Summary receiver operating characteristic (ROC) curves were generated for studies that provided information about patients with both positive and negative clinical evaluation results and for studies with tissue confirmation of disease. As with conventional ROC curves, a summary ROC curve closer to the upper left-hand corner of the graph indicates better overall diagnostic test performance. To compare the summary ROC curves, a t test comparing the intercepts was performed using a Student t test.

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

### Informal Consensus

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Each writing committee received a comprehensive list of existing systematic reviews and meta-analyses as well as guidelines published by other groups. In addition, for five of the key topics (prevention, screening, diagnosis, and staging [invasive and noninvasive], new systematic reviews were undertaken (see "Description of Methods Used to Collect the Evidence" and "Description of Methods Used to Analyze the Evidence" fields). For all other topics, writing committees were responsible for identifying and interpreting studies that were not otherwise covered in existing syntheses or guidelines.

The guidelines developed by the writing committee were distributed to the entire expert panel, and comments were solicited in advance of a meeting. During the meeting, proposed recommendations were reviewed, discussed, and voted on by the entire panel. Approval required consensus, which was defined as an overwhelming majority approval. Differences of opinion were accommodated by revising the proposed recommendation, the rationale, or the grade until consensus could be reached. The evidence supporting each recommendation was summarized, and recommendations were graded as described. The assessments of level of evidence, net benefit, and grade of recommendation were reviewed by the executive committee.

## Values

The panel considered data on functional status, quality and length of life, tolerability of treatment, and relief of symptoms in formulating guideline recommendations. Cost was not explicitly considered in the guideline development process. Data on these outcomes were informally weighted, without the use of explicit decision analysis or other modeling. The values placed on types of outcomes varied with clinical scenarios. For example, in some situations they considered life expectancy, such as the effects of early detection. In other situations they weighed quality of life more heavily, such as in palliative care and in interpreting small increases in life expectancy with chemotherapy for stage IV disease.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The guideline developer's grading scheme is a modification of the United States Preventive Services Task Force (USPSTF) grades to allow recommendations for a service when (1) evidence is poor, (2) the assessment of the net benefit is moderate to high, and (3) there is consensus among the expert panel to recommend it. This change was necessary because, unlike preventive services (i.e., the routine offering of tests or treatments to well people) in which the burden of proof is high, clinical decisions about the treatment of patients with lung cancer often must be based on an interpretation of the available evidence, even if it is of poor quality. This adaptation distinguished between interventions with poor evidence for which there is consensus (grade C) and interventions with poor evidence for which there is not consensus (grade I).

### Grades of Recommendations and Estimates of Net Benefit

The grade of the strength of recommendations is based on both the quality of the evidence and the net benefit of the service (i.e., test, procedure, etc).

**Grade A** The panel strongly recommends that clinicians routinely provide [the service] to eligible patients. An "A" recommendation indicates good evidence that [the service] improves important health outcomes and that benefits substantially outweigh harms.

**Grade B** The panel recommends that clinicians routinely provide [the service] to eligible patients. A "B" recommendation indicates at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.

Grade C The panel recommends that clinicians routinely provide [the service] to eligible patients. A "C" recommendation indicates that there was consensus among the panel to recommend [the service] but that the evidence that [the service] is effective is lacking, of poor quality, or conflicting, or the balance of benefits and harms cannot be reliably determined from available evidence.

Grade D The panel recommends against clinicians routinely providing [the service]. A "D" recommendation indicates at least fair evidence that [the service] is ineffective or that harm outweighs benefit.

Grade I The panel concludes that the evidence is insufficient to recommend for or against [the service]. An "I" recommendation indicates that evidence that [the service] is effective is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined, and that the panel lacked a consensus to recommend it.

#### Net Benefit

The levels of net benefit are based on clinical assessment. Estimated net benefit may be downgraded based on uncertainty in estimates of benefits and harms.

Substantial Benefit: Benefit greatly outweighs harm

Moderate Benefit: Benefit outweighs harm

Small/weak Benefit: Benefit outweighs harm to a minimally clinically important degree

None/negative Benefit: Harms equal or outweigh benefit, less than clinically important

#### COST ANALYSIS

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

#### METHOD OF GUIDELINE VALIDATION

Peer Review

#### DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

After extensive review within the expert panel and executive committee, the guidelines were reviewed and approved by the American College of Chest Physicians (ACCP) Health and Science Policy Committee and then by the American College of Chest Physicians Board of Regents.

## RECOMMENDATIONS

#### MAJOR RECOMMENDATIONS

Each recommendation is rated based on the levels of evidence (good, fair, poor), net benefit (substantial, moderate, small/weak, none/negative), and the grades of the recommendations (A, B, C, D, I). Definitions are presented at the end of the "Major Recommendations" field.

1. For patients with either a known or suspected lung cancer who are eligible for treatment, a computed tomography (CT) scan of the chest should be performed. Level of evidence, fair; benefit, substantial; grade of evidence, B
2. In patients with enlarged mediastinal lymph nodes on CT scans (i.e., >1 cm on the short axis), further evaluation of the mediastinum should be performed prior to surgical resection of the primary tumor. Level of evidence, fair; benefit, substantial; grade of evidence, B
3. For patients who are operative candidates, where available, a whole-body <sup>18</sup>F-fluoro-deoxy-D-glucose positron emission tomography (FDG-PET) scan is recommended to evaluate the mediastinum. Level of evidence, fair; benefit, substantial; grade of evidence, B
4. In patients with abnormal results of body F-fluoro-deoxy-D-glucose positron emission tomography scanning, further evaluation of the mediastinum with sampling of the abnormal lymph node should be performed prior to surgical resection of the primary tumor. Level of evidence, fair; benefit, substantial; grade of evidence, B
5. For patients with either a known or suspected lung cancer who are eligible for treatment, a magnetic resonance imaging (MRI) of the chest should not be performed for staging the mediastinum but should be performed in patients with non-small cell lung cancer (NSCLC) involving the superior sulcus for evaluation of the brachial plexus or for evaluation of vertebral body invasion. Level of evidence, fair; benefit, substantial; grade of evidence, B
6. For patients with either a known or suspected lung cancer, a thorough clinical evaluation (similar to that listed in Table 2 of the guidelines) should be performed. Level of evidence, good; benefit, substantial; grade of evidence, A
7. Patients with abnormal clinical evaluations should undergo imaging for extrathoracic metastases. Site-specific symptoms warrant directed evaluation of that site with the most appropriate study (e.g., head CT scan, bone scan, and abdominal CT scan). Level of evidence, good; benefit, substantial; grade of evidence, A
8. Patients with clinical stage I or II lung cancer and a normal clinical evaluation require no further imaging for extrathoracic disease. Level of evidence, good; benefit, substantial; grade of evidence, A
9. Patients with stage IIIA and IIIB disease should have routine imaging for the detection of extrathoracic metastases (e.g., head CT scan, bone scan, and abdominal CT scan). Level of evidence, poor; benefit, substantial; grade of evidence, C
10. Patients with abnormal imaging study results should not be excluded from potentially curative surgery without tissue confirmation or overwhelming clinical and radiographic evidence of metastases. Level of evidence, good; benefit, substantial; grade of evidence, A

#### Levels of Evidence

In general, good evidence included prospective, controlled, randomized clinical trials, and poor evidence included case series and clinical experience. Trials with fair quality of evidence, for instance, historically controlled trials or retrospective analyses, were somewhere in between.

### Grades of Recommendations and Estimates of Net Benefit

The grade of the strength of recommendations is based on both the quality of the evidence and the net benefit of the service (i.e., test, procedure, etc).

**Grade A** The panel strongly recommends that clinicians routinely provide [the service] to eligible patients. An "A" recommendation indicates good evidence that [the service] improves important health outcomes and that benefits substantially outweigh harms.

**Grade B** The panel recommends that clinicians routinely provide [the service] to eligible patients. A "B" recommendation indicates at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.

**Grade C** The panel recommends that clinicians routinely provide [the service] to eligible patients. A "C" recommendation indicates that there was consensus among the panel to recommend [the service] but that the evidence that [the service] is effective is lacking, of poor quality, or conflicting, or the balance of benefits and harms cannot be reliably determined from available evidence.

**Grade D** The panel recommends against clinicians routinely providing [the service]. A "D" recommendation indicates at least fair evidence that [the service] is ineffective or that harm outweighs benefit.

**Grade I** The panel concludes that the evidence is insufficient to recommend for or against [the service]. An "I" recommendation indicates that evidence that [the service] is effective is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined, and that the panel lacked a consensus to recommend it.

### Net Benefit

The levels of net benefit are based on clinical assessment. Estimated net benefit may be downgraded based on uncertainty in estimates of benefits and harms.

**Substantial Benefit:** Benefit greatly outweighs harm

**Moderate Benefit:** Benefit outweighs harm

**Small/weak Benefit:** Benefit outweighs harm to a minimally clinically important degree

**None/negative Benefit:** Harms equal or outweigh benefit, less than clinically important.

## CLINICAL ALGORITHM(S)

None provided

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

The correct staging and identification of non-small cell lung cancer disease provides the clinician with important prognostic information regarding patient survival, and also guides the decision-making process with regard to choosing the optimal treatment modality.

### POTENTIAL HARMS

Risk of false-positive and false-negative test results

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

1. The American College of Chest Physicians (ACCP) is developing a set of PowerPoint slide presentations for physicians to download and use for physician and allied health practitioners education programs.
2. The ACCP is developing a Quick Reference Guide (QRG) in print and PDA formats for easy reference.

## 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)

Silvestri GA, Tanoue LT, Margolis ML, Barker J, Detterbeck F. The noninvasive staging of non-small cell lung cancer: the guidelines. Chest 2003 Jan; 123(1 Suppl): 147S-56S. [70 references] [PubMed](#)

#### DATE RELEASED

2003 Jan

#### GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

#### GUIDELINE DEVELOPER COMMENT

The guideline development panel was composed of members and nonmembers of the American College of Chest Physicians (ACCP) who were known to have expertise in various areas of lung cancer management and care, representing multiple specialties from the following 13 national and international medical associations:

- Alliance for Lung Cancer Advocacy, Support, and Education (a patient support group)
- American Association for Bronchology
- American Cancer Society
- American College of Physicians
- American College of Surgeons Oncology Group
- American Society of Clinical Oncology
- American Society for Therapeutic Radiology and Oncology
- American Thoracic Society
- Association of Community Cancer Centers
- Canadian Thoracic Society
- National Comprehensive Cancer Network
- Oncology Nurses Society
- Society of Thoracic Surgeons

The specialties included pulmonary/respiratory medicine, critical care, medical oncology, thoracic surgery, radiation oncology, epidemiology, law, and medical ethics.

#### SOURCE(S) OF FUNDING

Funding for both the evidence reviews and guideline development was provided through an unrestricted educational grant from Bristol-Myers Squibb, which had no other role in the evidence review or guideline development process or content.

#### GUIDELINE COMMITTEE

American College of Chest Physicians (ACCP) Expert Panel on Lung Cancer Guidelines

#### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: Gerard A. Silvestri, MD, FCCP; Lynn T. Tanoue, MD; Mitchell L. Margolis, MD, FCCP; John Barker, MD; Frank Detterbeck, MD, FCCP

#### FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Information about potential conflicts of interest were collected from each member of the expert panel or writing committee at the time of their nomination in accordance with the policy of the American College of Chest Physicians (ACCP). Information on conflicts of interest for each panelist is listed in the guideline.

#### GUIDELINE STATUS

This is the current release of the guideline.

#### GUIDELINE AVAILABILITY

Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#).

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

#### AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

##### Evidence Summary

- Toloza EM, Harpole L, McCrory DC. Noninvasive staging of non-small cell lung cancer: a review of the current evidence. Chest 2003 Jan; 123(1 Suppl): 137S-146S.

##### Background Articles

- Alberts WM. Lung cancer guidelines. Introduction. Chest 2003 Jan; 123(1 Suppl): 1S-2S.
- McCrory DC, Colice GL, Lewis SZ, Alberts WM, Parker S. Overview of methodology for lung cancer evidence review and guideline development. Chest. 2003 Jan; 123(1 Suppl): 3S-6S.
- Harpole LH, Kelley MJ, Schreiber G, Toloza EM, Kolimaga J, McCrory DC. Assessment of the scope and quality of clinical practice guidelines in lung cancer. Chest 2003 Jan; 123(1 Suppl): 7S-20S.
- Alberg AJ, Samet JM. Epidemiology of lung cancer. Chest 2003 Jan; 123(1 Suppl): 21S-49S.

Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#).

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

## PATIENT RESOURCES

None available

## NGC STATUS

This NGC summary was completed by ECRI on July 22, 2003. The information was verified by the guideline developer on August 18, 2003.

## COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

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