

Complete Summary

GUIDELINE TITLE

Treatment of non-small cell lung cancer-stage IIIA: ACCP evidence-based clinical practice guidelines. (2nd Edition)

BIBLIOGRAPHIC SOURCE(S)

Robinson LA, Ruckdeschel JC, Wagner H Jr, Stevens CW, American College of Chest Physicians. Treatment of non-small cell lung cancer-stage IIIA: ACCP evidence-based clinical practice guidelines (2nd edition). Chest 2007 Sep;132(3 Suppl):243S-65S. [113 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Robinson LA, Wagner H Jr, Ruckdeschel JC. Treatment of stage IIIA non-small cell lung cancer. Chest 2003 Jan;123(1 Suppl):202S-20S.

COMPLETE SUMMARY CONTENT

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 BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
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SCOPE

DISEASE/CONDITION(S)

Stage IIIA non-small cell lung cancer

GUIDELINE CATEGORY

Treatment

CLINICAL SPECIALTY

Family Practice
Oncology
Pulmonary Medicine
Radiation Oncology
Thoracic Surgery

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Nurses
Patients
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

To provide specific treatment guidelines that can serve as a useful tool for the clinician who deals directly with locally advanced non-small cell lung cancer

TARGET POPULATION

Patients with stage IIIA non-small cell lung cancer (NSCLC)

INTERVENTIONS AND PRACTICES CONSIDERED

Incidental (Occult) N2 Disease (IIIA₁₋₂)

1. Lung resection
2. Mediastinal lymphadenectomy
3. Systematic mediastinal lymph node sampling
4. Complete mediastinal lymph node dissection
5. Adjuvant platinum-based chemotherapy
6. Adjuvant postoperative radiotherapy after adjuvant chemotherapy

N2 Disease Identified Preoperatively (IIIA₃)

1. Multidisciplinary team evaluation that includes a thoracic surgeon
2. Induction therapy followed by surgery (only as part of a clinical trial)
3. Primary surgical resection followed by adjuvant therapy (only as part of a clinical trial)
4. Platinum-based combination chemoradiotherapy

Bulky N2 Disease (IIIA₄)

1. Combination platinum-based chemotherapy and radiotherapy
2. Concurrent chemoradiotherapy is preferred over sequential

MAJOR OUTCOMES CONSIDERED

- 5-year survival rate
- Recurrence rate

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

The American College of Chest Physicians (ACCP) chose the Duke University Center for Clinical Health Policy Research to perform formal systematic reviews of the current evidence in the five new non-small cell lung cancer (NSCLC) topic areas, as well as to provide a search for the existing guidelines, systematic reviews, and meta-analyses in all of the topics areas. In addition, the Agency for Healthcare Quality and Research (AHRQ) agreed to fund the BlueCross BlueShield Association Technology Evaluation Center to perform the formal systematic review of literature on small cell lung cancer (SCLC). The Health Outcomes Research Group of the Department of Epidemiology and Biostatistics at Memorial Sloan-Kettering Cancer Center conducted a full-scale review of the literature since the first set of guidelines in the area of screening for lung cancer to assist that particular writing group.

The formal systematic reviews of the five new topic areas were guided by the appropriate chapter editors and their writing committees, in concert with the Executive Committee of the panel.

The two EPC research teams conducted a variety of systematic computerized bibliographic database searches including the following: (1) a search for systematic reviews, guidelines, and meta-analyses published since the last ACCP lung cancer guideline (MEDLINE, The Cochrane Library, National Guidelines Clearinghouse); (2) targeted searches for reviews in each of five selected treatment sections (solitary pulmonary nodules, stage I and II, stage IIIA, stage IIIB, stage IV); these searches, run in OVID version of MEDLINE, were performed in July and August 2005 and were limited to publication years since 1995, English language, and human subjects; and (3) searches related to SCLC are described in the evidence chapter on SCLC. Search terms included the medical subject heading terms lung neoplasms (exploded) and bronchial neoplasms for the lung cancer concept. Each topic search utilized key words specific to the key questions of interest (complete search strategies are available on request from the authors).

Strategy Specific for the Treatment of Non-small Cell Lung Cancer-stage IIIA

To develop the following guidelines for stage IIIA disease, the authors conducted a systematic search of MEDLINE, HealthStar, and Cochrane Library databases up to May 2006, reviewing 15 other published clinical guidelines, 10 metaanalyses,

12 systematic reviews, and 91 primary articles with clinical trials on this topic, focusing on the most well-designed, largest peer-reviewed reports.

NUMBER OF SOURCE DOCUMENTS

128

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

High Randomized controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies*

Moderate RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies*

Low or very low Observational studies or case series

*Although the determination of magnitude of the effect based on observational studies is often a matter of judgment, the guideline developers offer the following suggested rule to assist this decision: a large effect would be a relative risk >2 (risk ratio < 0.5) [which would justify moving from weak to moderate], and a very large effect is a relative risk > 5 (risk ratio < 0.2) [which would justify moving from weak to strong]. There is some theoretical justification in the statistical literature for these thresholds (the magnitude of effect that is unlikely or very unlikely to be due to residual confounding after adjusted analysis). However, once the decision is made, authors should be explicit in justifying their decisions.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Quality of evidence is scored in three categories with high-quality evidence obtained from randomized controlled trials (RCTs) without important methodologic limitations based on the study design, the consistency of the results, and the directness of the evidence. In extraordinary circumstances, significant and consistent evidence from observational studies could also be ranked as high quality. RCTs with important methodologic limitations or flaws, inconsistent results, or indirect or imprecise results would be scored as medium quality, as well as exceptionally strong evidence from observational studies. Other observational studies or case-series data would fall into the low quality of evidence category. It is the interface of the quality of the evidence and the balance of benefits to harms or burdens that determines the strength of the

recommendation, with a 1A recommendation being the strongest and 2C the weakest.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus
Informal Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Writing committees studied the evidence and summary tables or reviewed the literature for their assigned topics, developing their arguments for the recommendations and suggested grading of those recommendations that were put forth for early drafts. The Executive Committee of the panel, composed of the Chair, Vice-Chair, methodologist, and both project managers, reviewed drafts of each chapter of the manuscript during the writing process. Sections that were determined to be potentially overlapping were shared among the appropriate chapter editors, and conference calls were organized to coordinate the placement of these sections and to confirm that there would be no conflicting information or recommendations.

A conference of the panel was convened in July 2006, prior to which time all panelists, including representatives from the invited organizations, were requested to review the complete manuscript and identify recommendations for which the proposal, wording, or grading were determined to be controversial or could be interpreted as controversial by others, incorrectly evolved from the evidence, disagreement existed with regard to the proposal or the grading, or required full panel discussion and further review for any reason. When the panelists who were present were not in unanimous agreement with the proposed recommendations or the grading of the recommendations, informal group consensus techniques were employed. After the meeting, a series of conference calls were convened to finish the discussions and finalize the recommendations. There were a few chapters for which there was insufficient time for full dialogue during the meeting; in the interest of ensuring that the recommendations followed the evidence, the conference calls were necessary. This process ensured the "buy-in" of the panelists and was deemed to be a worthwhile effort.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grade of Recommendations Scale

Grade	Recommendation
1A	Strong
1B	Strong
1C	Strong
2A	Weak
2B	Weak
2C	Weak

Relationship of Strength of the Supporting Evidence to the Balance of Benefits to Risks and Burdens

Balance of Benefits to Risks and Burdens				
Quality of Evidence	Benefits Outweigh Risks/Burdens	Risks/Burdens Outweigh Benefits	Evenly Balanced	Uncertain
High	1A	1A	2A	
Moderate	1B	1B	2B	
Low or very low	1C	1C	2C	2C

COST ANALYSIS

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

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Following final chapter revisions and incorporation of these ultimate recommendations and grading, a concluding review was conducted by the guideline panel Executive Committee. The guidelines were then submitted for review and approval to the American College of Chest Physicians Health and Science Policy Committee (ACCP HSP) Committee, as well as the Thoracic Oncology Network of the college.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the strength of evidence and recommendation grades (1A-2C) follow the recommendations.

The patients with non-small cell lung cancer (NSCLC) with stage IIIA (N2) tumors present substantial heterogeneity in clinical presentation, treatment, and prognosis. Therefore, for the purposes of generating rational treatment guidelines, the guideline developers have chosen to classify N2 tumors into four subsets (see Table below).

Table: Subsets of Stage IIIA(N₂)*

Subset	Description
IIIA ₁	Incidental nodal metastases found on final pathology

Subset	Description
	examination of the resection specimen
IIIA ₂	Nodal (single station) metastases recognized intraoperatively
IIIA ₃	Nodal metastases (single or multiple station) recognized by prethoracotomy staging (mediastinoscopy, other nodal biopsy, or positron emission tomography [PET] scan)
IIIA ₄	Bulky or fixed multistation N2 disease

*Adapted from Ruckdeschel JC. Combined modality therapy of non-small cell lung cancer. *Semin Oncol* 1997; 24:429-439.

1. *Surgical Considerations:* In patients with non-small cell lung cancer (NSCLC) who have incidental (occult) N2 disease (IIIA₂) found at surgical resection and in whom complete resection of the lymph nodes and primary tumor is technically possible, completion of the planned lung resection and mediastinal lymphadenectomy is recommended. **Grade of recommendation, 2C**
2. *Surgical Considerations:* In patients with NSCLC undergoing surgical resection, systematic mediastinal lymph node sampling or complete mediastinal lymph node dissection is recommended. **Grade of recommendation, 1B**
3. *Adjuvant Chemotherapy:* In patients with resected NSCLC who were found to have incidental (occult) N2 disease (IIIA₁₋₂) and who have good performance status, adjuvant platinum-based chemotherapy is recommended. **Grade of recommendation, 1A**
4. *Adjuvant Radiotherapy:* In patients with resected NSCLC who were found to have incidental (occult) N2 disease (IIIA₁₋₂), adjuvant postoperative radiotherapy should be considered after adjuvant chemotherapy to reduce local recurrence. **Grade of recommendation, 2C**
5. *Adjuvant Chemoradiotherapy:* In patients with resected NSCLC who were found to have incidental (occult) N2 disease (IIIA₁₋₂), combined postoperative concurrent chemotherapy and radiotherapy is not recommended except as part of a clinical trial. **Grade of recommendation, 1B**
6. In NSCLC patients with N2 disease identified preoperatively (IIIA₃), referral for multidisciplinary evaluation (which includes a thoracic surgeon) is recommended before embarking on definitive treatment. **Grade of recommendation, 1C**
7. In NSCLC patients with N2 disease identified preoperatively (IIIA₃), induction therapy followed by surgery is not recommended except as part of a clinical trial. **Grade of recommendation, 1C**
8. In NSCLC patients with N2 disease identified preoperatively (IIIA₃) who do receive induction chemoradiotherapy as part of a clinical trial, pneumonectomy is not recommended. The subsequent surgical resection in this setting should be limited to a lobectomy. If after induction chemoradiotherapy it appears that a pneumonectomy will be needed, it is recommended that pneumonectomy not be performed and treatment should be continued with full-dose radiotherapy. **Grade of recommendation, 1B**

9. In NSCLC patients with N2 disease identified preoperatively (IIIA₃), primary surgical resection followed by adjuvant therapy is not recommended except as part of a clinical trial. **Grade of recommendation, 1C**
10. In NSCLC patients with N2 disease identified preoperatively (IIIA₃), surgery alone is not recommended. **Grade of recommendation, 1A**
11. In NSCLC patients with N2 disease identified preoperatively (IIIA₃), platinum-based combination chemoradiotherapy is recommended as primary treatment. **Grade of recommendation, 1B**
12. *Surgical Considerations:* In NSCLC patients with N2 disease identified preoperatively (IIIA₃), surgical debulking procedures are not recommended. **Grade of recommendation, 1A**
13. *Surgical Considerations:* In NSCLC patients with N2 disease identified preoperatively (IIIA₃) who have incomplete resections, postoperative platinum-based chemoradiotherapy is recommended. **Grade of recommendation, 1C**
14. In patients with NSCLC who have bulky N2 disease (IIIA₄) and good performance status, radiotherapy alone is not recommended. **Grade of recommendation, 1A**
15. In patients with NSCLC who have bulky N2 disease (IIIA₄) and good performance status, combination platinum-based chemotherapy and radiotherapy are recommended. **Grade of recommendation, 1A**
16. In patients with NSCLC who have bulky N2 disease (IIIA₄), good performance status, and minimal weight loss, concurrent chemoradiotherapy is recommended over sequential chemo radiotherapy. **Grade of recommendation, 1A**

Definitions:

Quality of Evidence Scale

High - Randomized controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies*

Moderate - RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies*

Low or very low - Observational studies or case series

*Although the determination of magnitude of the effect based on observational studies is often a matter of judgment, the guideline developers offer the following suggested rule to assist this decision: a large effect would be a relative risk > 2 (risk ratio < 0.5) [which would justify moving from weak to moderate], and a very large effect is a relative risk > 5 (risk ratio < 0.2) [which would justify moving from weak to strong]. There is some theoretical justification in the statistical literature for these thresholds (the magnitude of effect that is unlikely or very unlikely to be due to residual confounding after adjusted analysis). However, once the decision is made, authors should be explicit in justifying their decisions.

Grade of Recommendations Scale

Grade	Recommendation
1A	Strong

Grade	Recommendation
1B	Strong
1C	Strong
2A	Weak
2B	Weak
2C	Weak

Relationship of Strength of the Supporting Evidence to the Balance of Benefits to Risks and Burdens

Balance of Benefits to Risks and Burdens				
Quality of Evidence	Benefits Outweigh Risks/Burdens	Risks/Burdens Outweigh Benefits	Evenly Balanced	Uncertain
High	1A	1A	2A	
Moderate	1B	1B	2B	
Low or very low	1C	1C	2C	2C

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

Appropriate treatment for patients with non-small cell lung cancer-stage IIIA

POTENTIAL HARMS

Not stated

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The publication of the *Diagnosis and Management of Lung Cancer: ACCP Evidence-Based Clinical Practice Guidelines; Second Edition* in CHEST is the first of

two dissemination vehicles. The circulation of the journal is 23,000 subscribers and libraries, including six translations and distribution to 107 countries. All subscribers received a copy of this full-text guideline. The American College of Chest Physicians (ACCP) Clinical Resource on Lung Cancer is composed of a printed publication and an accompanying CD-ROM, containing a quick reference guide for physicians and other health-care providers, patient-targeted educational materials, and a set of slides for use in educational or clinical contexts. In addition, the recommendations and grading are personal digital assistant downloadable from the clinical resource. This product is available for purchase from the ACCP. The patient education materials are accessible free of charge on www.chestnet.org.

The implementation and translation of evidence-based clinical practice guidelines facilitates knowledge uptake, critical for practice change, and should ultimately lead to better patient-focused care. The HSP Subcommittee on Implementation has proposed to collaborate with the Governors, Thoracic Oncology Network, and other groups within the ACCP to disseminate and implement the guidelines in their local communities. Residency and specialty training programs are encouraged to use the guidelines in journal clubs and grand rounds. Other organizations that were invited to send representatives to the final conference and review the proposed drafts were also requested to endorse the guidelines and market them to their membership through their own communication channels.

IMPLEMENTATION TOOLS

Patient Resources
Resources

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
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

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

DATE RELEASED

2003 Jan (revised 2007 Sep)

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Chest Physicians

GUIDELINE COMMITTEE

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

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: Lary A. Robinson, MD, FCCP; John C. Ruckdeschel, MD, FCCP; Henry Wagner, Jr, MD; Craig W. Stevens, MD, PhD, FCCP

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Funding for both the evidence review and guideline development was supported by educational grants from AstraZeneca LP, Bristol-Myers Squibb Company, Eli Lilly and Company, Genentech, and Sanofi-Aventis. Representatives from these companies were neither granted the right of review, nor were they allowed participation in any portion of the guideline development process. This precluded participation in either conference calls or conferences. No panel members or ACCP reviewers were paid any honoraria for their participation in the development and review of these guidelines.

The ACCP approach to the issue of potential or perceived conflicts of interest established clear firewalls to ensure that the guideline development process was not influenced by industry sources. This policy is published on the ACCP Web site at www.chestnet.org. All conflicts of interest within the preceding 5 years were required to be disclosed by all panelists, including those who did not have writing responsibilities, at all face-to-face meetings, the final conference, and prior to submission for publication. The most recent of these conflict of interests are documented in this guideline Supplement. Furthermore, the panel was instructed in this matter, verbally and in writing, prior to the deliberations of the final conference. Any disclosed memberships on speaker's bureaus, consultant fees, grants and other research monies, and any fiduciary responsibilities to industry were provided to the full panel in writing at the beginning of the conference and at submission for publication.

ENDORSER(S)

American Association for Bronchology - Disease Specific Society
American Association for Thoracic Surgery - Medical Specialty Society
American College of Surgeons - Medical Specialty Society
American Society for Therapeutic Radiology and Oncology
Asian Pacific Society of Respiriology - Disease Specific Society
Oncology Nursing Society - Professional Association
Society of Thoracic Surgeons - Medical Specialty Society
World Association of Bronchology - Disease Specific Society

GUIDELINE STATUS

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This guideline updates a previous version: Robinson LA, Wagner H Jr, Ruckdeschel JC. Treatment of stage IIIA non-small cell lung cancer. Chest 2003 Jan;123(1 Suppl):20S-20S.

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:

Executive Summary:

- Alberts MW. Diagnosis and management of lung cancer executive summary. Chest 2007 Sep;132(3 Suppl):1S-19.

Background Articles:

- Alberts WM. Introduction: diagnosis and management of lung cancer. Chest 2007 Sep;132(3 Suppl):20S-22.
- McCrory DC, Lewis SZ, Heitzer J, Colice GL, Alberts WM. Methodology for lung cancer evidence review and guideline development. Chest 2007 Sep;132(3 Suppl):23S-28.
- Alberg AJ, Ford JG, Samet JM. Epidemiology of lung cancer. Chest 2007 Sep;132(3 Suppl):29S-55.

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.

The following is also available:

- ACCP clinical resources: Diagnosis and management of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition).

Available from the [American College of Chest Physicians Web site](#).

PATIENT RESOURCES

The following are available:

- Lung cancer guides: lung cancer...am I at risk? Patient education guide. Northbrook (IL): American College of Chest Physicians, 2004. 12 p.
- Lung cancer guides: What if I have a spot on my lung? Do I have cancer? Patient education guide. Northbrook (IL): American College of Chest Physicians, 2004. 16 p.
- Lung cancer guides: living with lung cancer. Patient education guide. Northbrook (IL): American College of Chest Physicians, 2004. 12 p.
- Lung cancer guides: advanced lung cancer: issues to consider. Patient education guide. Northbrook (IL): American College of Chest Physicians, 2004. 12 p.

Electronic copies: Available in Portable Document Format (PDF) from the [American College of Chest Physicians \(ACCP\) Web site](#).

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NGC STATUS

This NGC summary was completed by ECRI on September 3, 2003. The information was verified by the guideline developer on October 1, 2003. This NGC summary was updated by ECRI Institute on November 27, 2007. The updated information was verified by the guideline developer on December 21, 2007.

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