General

Guideline Title


Bibliographic Source(s)


Guideline Status

This is the current release of the guideline.


Recommendations

Major Recommendations

The grades of recommendation (1A–2C) and the approach to rating the quality of evidence are defined at the end of the "Major Recommendations" field.

Proposed Indications for White Light Bronchoscopy (WLB) and Autofluorescence Bronchoscopy (AFB)

Evaluation of Patients with Sputum Atypia

In patients with severe dysplasia or carcinoma in situ (CIS) in sputum cytology who have chest imaging studies showing no localizing abnormality, standard WLB is suggested to exclude an endobronchial lesion (Grade 2C).

Remark: AFB may be used as an adjunct to WLB when available.

Follow-up of High-Grade Bronchial Intraepithelial Neoplasia (BIN)

For patients with known severe dysplasia or CIS in the central airways on biopsy, follow-up WLB is suggested (Grade 2C).

Remark: AFB may be used when available.

Remark: The timing and duration of follow-up are unknown. Physicians and patients should discuss potential risk and benefits of follow-up
bronchoscopy.

Evaluation of Patients Prior to Lung Cancer Surgery

Surgical Margins

For patients with early lung cancer undergoing resection, WLB is suggested for the delineation of tumor margins and the assessment of synchronous lesions (Grade 2C).

Remark: AFB or narrow band imaging (NBI) may be used when available.

Evaluation of Patients with Early Central Lung Cancer Prior to Curative Endobronchial Therapy

For patients being considered for curative endobronchial therapy to treat CIS or early central lung cancer, WLB is suggested over routine use of AFB (Grade 2C).

Techniques of Endobronchial Therapy

Neodymium-yttrium aluminum garnet (Nd:YAG) Laser Therapy

For patients with superficial limited mucosal lung cancer in the central airway who are not candidates for surgical resection, endobronchial treatment with photodynamic therapy (PDT), brachytherapy, cryotherapy, or electrocautery is recommended (Grade 1C).

Definitions:

Strength of the Recommendations Grading System

<table>
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<th>Grade of Recommendation*</th>
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Clinical Algorithm(s)
None provided

Scope

Disease/Condition(s)
Lung cancer
- Bronchial intraepithelial neoplasia (BIN)
- Early lung cancer of the central airways

Guideline Category
Diagnosis
Management
Treatment

Clinical Specialty
Family Practice
Oncology
Pulmonary Medicine
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 inform the clinical decisions that must be jointly made by physicians and patients in developing diagnostic, treatment, and management plans so that they can enhance the benefits and reduce the harms associated with various options
- To develop evidence-based recommendations regarding the diagnosis and treatment of intraepithelial lesions
**Target Population**

Patients with suspected or diagnosed bronchial intraepithelial neoplasia (BIN) or early lung cancer of the central airways

**Interventions and Practices Considered**

1. White light bronchoscopy (WLB)
2. Autofluorescence bronchoscopy (AFB) or narrow band imaging (NBI)
3. Endobronchial therapy with photodynamic therapy (PDT), brachytherapy, cryotherapy, or electrocautery

**Major Outcomes Considered**

- Response to treatment (complete, partial, or no response) and progression rate
- Recurrence rate

**Methodology**

**Methods Used to Collect/Select the Evidence**

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

**Description of Methods Used to Collect/Select the Evidence**

A systematic review of the literature was conducted to identify relevant studies from MEDLINE in the English language published between January 1966 and March 2012. Literature searches used the following key words: "carcinoma in situ," "preinvasive lesions," "non-small cell lung cancer," "squamous cell carcinoma," "photodynamic therapy," "electrocautery," "cryotherapy," "white light bronchoscopy," and "autofluorescence bronchoscopy." The panel also manually reviewed the reference lists of relevant studies.

The following population, intervention, comparator, outcome (PICO) questions were evaluated in this review:

1. Among patients with severe dysplasia or carcinoma in situ (CIS) in sputum cytology but with chest imaging studies showing no localizing abnormality, does bronchoscopy lead to diagnosis of preinvasive lesions or early, localized lung cancers?
2. Among patients with early lung cancer undergoing resection, does bronchoscopy assist in the delineation of tumor margins and the assessment of synchronous lesions?
3. For patients being considered for curative endobronchial therapy to treat CIS or early central lung cancer, does bronchoscopy lead to changes in the clinical management?
4. For patients with known severe dysplasia or CIS in the central airways on biopsy, does bronchoscopy improve identification of progressive lesions?
5. For patients with superficial limited mucosal lung cancer in the central airway who are not candidates for surgical resection, does endobronchial treatment with photodynamic therapy (PDT), brachytherapy, cryotherapy, and electrocautery improve outcomes such as response or progression rates?

Potentially eligible studies were reviewed by chapter authors based on pre-established criteria, such as patient population, study design, type of bronchoscopy technique used, length of follow-up, and outcomes evaluated. Studies focusing on diagnosis or bronchoscopy management of advanced lung cancer were excluded.

**Number of Source Documents**

Not stated
Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Not Given)

Rating Scheme for the Strength of the Evidence

Not stated

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

Data Abstraction

Data were abstracted from each study according to criteria specific to the different types of studies evaluated in the review (i.e., natural history, diagnosis, or treatment). Data collected included sociodemographic characteristics of the study population, inclusion and exclusion criteria, intervention(s), and length of follow-up. Relevant outcomes included rates of progression, relative sensitivity, and treatment response for questions evaluating the natural history of preinvasive lesions, the additional accuracy of autofluorescence bronchoscopy (AFB) over white light bronchoscopy (WLB), and the effectiveness of different endobronchial therapies, respectively.

Study Quality

The quality of the studies included in the review was assessed based on criteria developed by the American College of Chest Physicians (ACCP). These included type of study design, subject selection, explicit descriptions of inclusion and exclusion criteria, length of follow-up, ascertainment of the outcome, statistical analysis, funding, and conflicts of interest. Based on these factors, studies were judged as good, fair, or poor.

Statistical Analysis

Point estimates with 95% confidence interval (CI) (when available) were reported for the different outcomes of interest. No attempt was made to obtain summary estimates given the high degree of heterogeneity across studies and differences in study design, length of follow-up, and definition of outcomes measures.

Assessment of Study Quality

Systematic reviews and meta-analyses were assessed using Documentation and Appraisal Review Tool (DART) (R. L. Diekemper; B. K. Ireland, MD; and L. R. Merz, PhD, MPH, DART, unpublished data, 2012), which was developed as an improved alternative to the existing tools for use in a clinical setting. However, this tool has been adopted for use in ACCP guidelines and consensus statements since 2011.

Quality was assessed for each study as well as for the body of relevant evidence. Based on the population, intervention, comparator, and outcome (PICO) questions and volume of available literature, multiple study designs were included in the systematic reviews of the literature. Randomized controlled trials (RCTs) primarily indicate benefits, but whenever observational studies met inclusion criteria they were often helpful in identifying harms. Observational studies were also examined when RCTs were not available to answer a particular PICO question. Allowing for multiple study designs resulted in the need for multiple quality assessment tools. Tools were chosen for assessing RCTs, observational studies, and diagnostic studies. The quality assessment tool for RCTs (R. L. Diekemper, B. K. Ireland, and L. R. Merz, unpublished data, 2012) was used for assessing the quality of RCTs, and a tool developed by the committee of the ninth edition of the Antithrombotics Guidelines was used for assessing the quality of observational studies. Diagnostic studies were assessed using the Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS).

Meta-analyses

If a recently published good-quality meta-analysis was available, then it was used to inform the recommendations. When a good-quality meta-analysis was not available, guideline authors were encouraged to perform their own meta-analyses. Meta-analyses were performed when the data were fairly homogeneous. If a study was deemed poor quality, then it was not included in the pooled analysis. Heterogeneity of the pooled results
was assessed using a $\chi^2$ test and Higgins $I^2$, and a forest plot was examined for consistency of the results. The random effects model was chosen a priori as the appropriate model for pooling the data because it accounts for heterogeneity among the included studies. Results from the meta-analyses are available in the supplementary materials that can be downloaded from the Journal website under the corresponding article in the table of contents.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Panel Composition and Responsibilities

A call for applications to serve on the 3rd edition of the American College of Chest Physicians (ACCP) Lung Cancer Guidelines (LC III) panel was put forth to the ACCP membership, to past panelists, and to other organizations that have previously endorsed earlier editions of these guidelines or appointed representatives to serve on those panels. Guiding the team was the LC III Executive Committee, composed of a Panel Chair, Vice Chair, Liaison to the Guidelines Oversight Committee (GOC), and two staff members, one serving as an adviser and the other as the lead methodologist. The GOC appointed the Liaison and the Chair, who was required to be free of conflicts of interest (COI). This Executive Committee provided general oversight and guidance; multiple reviews of research questions, article outlines, manuscripts, evidence tables, and other supporting documents; and facilitation of the final conference discussions and voting. As the scope was defined, content experts in each major area were identified to serve as topic editors and nominated by the Panel Chair to be advanced to the GOC for the requisite qualifications and COI review and approval process. These topic editors organized their research and writing teams, oversaw the work of the individual members, edited separate contributions into synthesized manuscripts, presented evidence at the final conference, and managed any of their committee members who were approved with management stipulations relevant to their COIs.

Each topic editor was initially charged with proposing individuals to support their topic committees with expertise in the content area and/or methodology. With the Chair's approval, these individuals were nominated for GOC reviews for COI and expertise. In some cases, GOC staff helped to locate additional methodologic support when it was determined to be necessary for various article committees. This resulted in an international panel of >100 multidisciplinary experts across 24 articles representing the fields of pulmonary medicine, critical care medicine, thoracic surgery, medical and radiation oncology, pathology, integrative medicine, primary care, health-care research, guidelines methodology, and epidemiology. Nineteen international organizations that are also dedicated to advancing research and practice in the area of lung cancer were invited to appoint representatives to this guideline project as adjunct participants. These individuals, unless already approved panelists, were not considered full voting members of the panel, since they had not been through the same ACCP COI review, but were included at the final conference, participated fully in the discussions, and provided external review and feedback on the manuscripts and supporting documentation.

Formulating the Recommendations

In most cases the topic editors, along with the other completely non-conflicted members of the article committee, formulated the recommendations. The summarized evidence tables and profiles (where profiles existed) provided the foundation for the recommendations. In formulating the recommendations, panelists considered not only the body of evidence but also the balance between the benefits and harms and considerations of other factors, such as cost or resource availability considerations and patient values and preferences, which might vary widely for some recommendations. These additional considerations are described in a Remarks section, which appears just below the relevant recommendation in the publication, each time the recommendation appears.

Grading the Recommendations

Recommendations that are strong must be differentiated from those that are weak or weaker. Thus, the ACCP Grading System was used (see the "Rating Scheme for the Strength of the Recommendations" field), and the wording of the recommendations is explicit. This grading system has been used since 2005 and is based on two dimensions: the balance of benefits to harms and the quality of the evidence base. If the benefits clearly outweigh the harms or the harms clearly outweigh the benefits, the strength of the recommendation is considered strong and graded as a 1. In most cases, when there is strong confidence that the benefits outweigh the harms, most patients would choose the intervention endorsed in that recommendation. However, when the tradeoffs between desirable and undesirable consequences are not as clear, variability in patient preferences and values often becomes germane to the decision-making conversation.

Weak recommendations are those for which the benefits and harms are more equally balanced, and thus a clear choice is not as obvious; these are
graded with a 2. Strong recommendations are phrased, "the panel recommends," whereas weak recommendations are phrased "the panel suggests." Accompanying these indications of the strength of a recommendation is a letter score (A, B, or C) representing the grading of the body of relevant literature.

In grading the quality of the evidence, RCTs start with a high score but might be downgraded to moderate or even low based on the following criteria: limitations in the study design or conduct of the trial, imprecision, indirectness relative to the specifics of the PICO question, inconsistency in the results, and risk of reporting bias. Observational studies, on the other hand, start off as low-level evidence but can be upgraded to moderate or even high if exceptionally large and consistent treatment effects increase confidence in the findings, especially if there is a strong dose-response gradient.

The final grades are combinations reflecting the strength of the recommendation and the quality of the evidence. Strong recommendations with high quality evidence, grade of 1A, are less common than in past editions of these guidelines, since the evidence is assessed with greater rigor for most topics, and few studies without important limitations are available.

However, recommendations that do attain this score are those for which the panel could state with confidence that new studies would be unlikely to change the direction of the effect. These recommendations apply to most patients in most circumstances. But as the grades decline, patient values and preferences likely would play an increasingly greater role in determining the best treatments or interventions for each patient.

The Final Conference

As the evidence reviews were completed and the tables and profiles prepared, the manuscripts and recommendations were drafted. Members of the article committees convened by phone or e-mail to discuss the evidence and work on drafting and grading the recommendations. These discussions generally resulted in agreement on both the quality of the evidence and strength of the recommendations.

The manuscripts and supporting tables were then reviewed by members of the Executive Committee and, after several iterations, the revised versions were shared among all panelists and the representatives of invited organizations in advance of the conference. The other panelists and representatives were asked not only to provide feedback but also to review the recommendations to identify any controversies. A recommendation was deemed to be controversial if at least one person disagreed with the wording or the grading, if there was controversy in practice, if there were wide variations in practice, or if at least one person asked that it be discussed among the broader panel and association representatives. These identified controversies composed the main agenda for the conference.

The "Methodology for Development of Guidelines for Lung Cancer" (see the "Availability of Companion Document" field) for more information.

Rating Scheme for the Strength of the Recommendations

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Cost Analysis

American College of Chest Physicians (ACCP) guidelines include consideration of resources in recommendations under selected circumstances. If it is likely that resource considerations would impact the direction or strength of a recommendation, a search for cost-effectiveness studies may have been conducted. Most recommendations in these guidelines do not include a full assessment of resource considerations. However, they can be adapted to middle- and low-income countries using the ADAPTE strategies.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Internal and External Peer Review

Once Executive Committee approval was received, the articles were submitted to American College of Chest Physicians (ACCP) staff for several layers of review. All reviewers were required to undergo a full conflict of interest (COI) appraisal before being approved. In the first round of reviews, the Thoracic Oncology NetWork reviewed the content of the manuscripts and the members of the Guidelines Oversight Committee (GOC) assessed the manuscripts for adherence to the methodology and conformance with the evidence. The ACCP President also appointed members of the Board of Regents to evaluate the guidelines in depth. All comments were collated into spreadsheets to ensure that they were appropriately answered. GOC and board reviewers discussed each comment and determined which should be mandatory for the authors to amend and which were provided as suggestions for improvement. All reviews and comments were anonymous, and authors were required to respond to all mandatory issues either by revising the manuscripts or providing written justification explaining why they did not agree with the reviewers’ comments.

The revised manuscripts were submitted for round II review, simultaneously with the Journal peer review. Once the GOC and board reviewers approved the manuscripts, the ACCP President, President Elect, President Elect Designee, and Immediate Past President reviewed the guidelines. Approval was granted pending confirmation from the Board of Regents, before submission to the journal for final review by the Journal Editor. In addition to this extensive review process, which included nearly 30 individual reviewers from the ACCP leadership, external organizations were provided with opportunities to provide feedback before, during, and just after the conference. This final version was submitted for consideration for endorsement to all of the invited organizations, whether or not they sent representatives to the conference. However, once the guidelines were approved by the ACCP Board of Regents, no further changes were accepted. Organizations that provided endorsements are listed in each article.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations
The type of supporting evidence is identified and graded for each recommendation (see the “Major Recommendations” field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits
Appropriate diagnosis and treatment of bronchial intraepithelial neoplasia (BIN) and early lung cancer of the central airways

Potential Harms
- False positive findings with autofluorescence bronchoscopy (AFB)
- Given the limited data regarding the natural history of early squamous cell carcinoma (SqCC), the potential complications of many techniques, and the limited life expectancy of some patients with contraindications for surgery, additional information is necessary to determine the impact of endobronchial treatments on patient outcomes.

Qualifying Statements

Qualifying Statements
- American College of Chest Physicians (ACCP) guidelines are intended for general information only, are not medical advice, and do not replace professional medical care and physician advice, which always should be sought for any medical condition. The complete disclaimer for this guideline can be accessed at the CHEST Web site.
- Although the ACCP is moving toward the production of evidence profiles for all guideline recommendations, there were many recommendations for which profiles were not developed, mostly because of resource constraints. When possible, methodologists created evidence profiles, and all panelists were educated on how to read and interpret them. The population, intervention, comparator, and outcome (PICO)-based systematic literature review process was followed for most recommendations, but there were some that could have benefited from meta-analyses.
- One limitation of all guidelines today is that they are not able to adequately address complex patients with multiple morbidities. This is largely because these patients are generally excluded from clinical trials and are often not included in observational studies. Since guidelines are reliant on evidence published in the peer-reviewed literature, the scientific foundation impedes the process of providing good guidance for these patients and is a limitation in these guidelines. Therefore, the ACCP encourages funding agencies to ensure that topics with limited evidence are addressed in future research.

Implementation of the Guideline

Description of Implementation Strategy

Dissemination and Implementation

These guidelines are widely disseminated through the CHEST journal publication, National Guideline Clearinghouse, and Guidelines International Network library. Additional clinical resources will soon be available to users of CHEST Evidence, an upcoming tool for searching the content of America College of Chest Physicians (ACCP) guidelines.

As the expanding research into diagnostic techniques and treatment options continues to evolve, the guidelines must be updated and kept current. This edition of the ACCP Lung Cancer Guidelines will be the last to be published as a complete collection, as the ACCP is now embarking on a new living guidelines model (LGM) for revising existing recommendations and developing new recommendations as the literature evolves. This will include a continual assessment of the currency of these recommendations relevant to new research studies as they are published. The review cycle for the ACCP Lung Cancer Guidelines will begin 1 year after publication unless the content experts who monitor the literature bring a recommendation or set of related recommendations to the attention of the Guideline oversight Committee (GOC), suggesting that those
recommendations are in need of updating sooner. The new LGM will permit a more nimble approach to guideline development but also requires a point-of-care accessible vehicle, CHEST Evidence, for the users to readily search for the most current version. These features will be described in greater detail in upcoming publications. As a step in this direction, these guidelines will be published primarily online with a printed version of the Executive Summary, containing all of the recommendations, the introduction, and this article on methodology. All narratives for each article with their supporting tables, figures, and algorithms will be available online at journal.publications.chestnet.org.

Implementation Tools

Mobile Device Resources
Patient Resources
Quick Reference Guides/Physician Guides
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
Getting Better
Living with Illness

IOM Domain
Effectiveness
Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)


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

Date Released
2003 Jan (revised 2013 May)
Guideline Developer(s)

American College of Chest Physicians - Medical Specialty Society

Source(s) of Funding

- The development of this guideline was supported primarily by the American College of Chest Physicians (ACCP). The lung cancer guidelines conference was supported in part by a grant from the Lung Cancer Research Foundation. The publication and dissemination of the guidelines was supported in part by a 2009 independent educational grant from Boehringer Ingelheim Pharmaceuticals, Inc.
- Role of sponsors: The ACCP was solely responsible for the development of these guidelines. The remaining supporters played no role in the development process. External supporting organizations cannot recommend panelists or topics, nor are they allowed prepublication access to the manuscripts and recommendations. Further details on the Conflict of Interest (COI) Policy are available online at http://chestnet.org.
- See the methodology companion (see the "Availability of Companion Documents" field) for a complete discussion of the source of funding for this guideline.

Guideline Committee

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

Composition of Group That Authored the Guideline

Authors: Juan P. Wisnivesky, MD, DrPH; Rex Chin-Wei Yung, MD, FCCP; Praveen N. Mathur, MBBS, FCCP; Javier J. Zulueta, MD, FCCP

Financial Disclosures/Conflicts of Interest

- Conflicts of Interest (COI) grids reflecting the conflicts of interest that were current as of the date of the conference and voting are posted in the online supplementary materials.
- Financial/nonfinancial disclosures: The authors have reported to CHEST the following conflicts of interest: Dr Wisnivesky is a member of the research board of EHE International; has received lecture honoraria from Novartis AG; has consulted for United BioSource Corporation, IMS Health Incorporated, and Merck Pharmaceutical; and received a research grant from GlaxoSmithKline. Dr Mathur has received grant support from Spiration Inc, Boehringer Ingelheim GmbH, ERBE Elektromedizin GmbH, Bryan Corporation, Olympus, Richard Wolf Medical Instruments Corporation, Cardinal Medical Specialties, Cook, Karl Storz GmbH & Co, ALTANA, and Allegro Diagnostics Corp and received royalties from UpToDate, Inc, Thieme Medical Publishers, Inc, WB Saunders, Karger Publishers, McGraw-Hill, Informa plc, and Marcel Dekker. Dr Zulueta is a member of the Medical Advisory Board and shareholder of VisionGate, Inc. Dr Yung has reported that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.
- See the methodology companion (see the "Availability of Companion Documents" field) for a complete discussion of the conflict of interest procedures and requirements for the guideline panel.

Guideline Endorser(s)

American Association for Bronchology and Interventional Pulmonology - Medical Specialty Society
European Society of Thoracic Surgeons - Professional Association
Oncology Nursing Society - Professional Association
Society of Thoracic Surgeons - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

Guideline Availability

Available to subscribers of Chest - The Cardiopulmonary and Critical Care Journal. Also available to Chest subscribers through the Chest app for iPhone and iPad.

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:


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:


Patient Resources

The following is available:


Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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. This NGC summary was updated by ECRI Institute on November 12, 2007. The updated information was verified by the guideline developer on December 21, 2007. This NGC summary was updated by ECRI Institute on August 21, 2013.

Copyright Statement

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Disclaimer

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